



Editorial

The relative distribution of oral cancer in the United States by subsite



Cheong and colleagues recently concluded that there is “a severe lack of accurate epidemiological data on oral cancer” based on a careful review of several international data sources [1]. Nevertheless, an estimated 354,864 new cases and 177,384 deaths from oral cavity cancer will occur worldwide in 2018, with the highest incidence rates in Melanesia and South Central Asia [2]. In India, oral cancer is among the three most common malignancies, accounting for over 30% of cancers—likely due to the widespread practice of chewing betel quid [3]. Regional differences in exposure to various carcinogens affect not only the incidence rate but also the specific subsite of the oral cavity where tumors develop.

Anatomic subsites within the oral cavity include the lips, oral tongue, floor of mouth, hard palate, buccal mucosa, retromolar trigone, and gums. The gums are subdivided into the mucosa overlying the mandibular alveolar ridge (lower gum) and maxillary alveolar ridge (upper gum). Lip locations can be classified based on upper versus lower lip, labial commissures, vermilion versus mucosal surfaces, and overlapping variations. The oral tongue is subdivided into four anatomic areas: anterior tip, lateral borders, dorsal surface, and ventral surface. However, because the oral tongue is contiguous with the oropharyngeal base of tongue, much like the mucosal surface of the hard palate is contiguous with the soft palate, advanced primary tumors often overlap both the oral cavity and the oropharynx.

The relative distribution of primary malignancies among the specific oral cavity subsites varies widely based on geographic location. Most studies cite oral tongue or lip as the most common primary site of oral cancer. However, buccal mucosa is the most common site for oral cavity malignancy in parts of Southeast Asia [4], and a large retrospective analysis identified the gums as the most common oral cavity site of squamous cell carcinoma in Nigeria, accounting for 55% of cases [5]. A recently published German study identified the anterior base/floor of the mouth as the oral cavity site most frequently involved by cancer, cumulatively accounting for 43% of cases [6].

The cancer incidence among various oral cavity subsites has not been well documented for individuals living in the United States (US). Among 3300 *de novo* intraoral cancers treated at the University of Texas M.D. Anderson Cancer Center between 1970 and 1999, the most frequently involved anatomic sites in descending order were oral tongue, floor of mouth, retromolar trigone, alveolar ridge, hard palate, and lastly buccal mucosa [7]. However, there are major limitations in extrapolating epidemiological findings from the former study to the entire country. In particular, lip cancer was omitted from this analysis, and the population treated at a single institution several decades ago may not accurately reflect the current distribution in the US. A recent study utilizing the Surveillance, Epidemiology, and End Results (SEER) 9 database included 20,647 patients with oral cavity squamous cell carcinoma (omitting lip cancer) diagnosed between 1975 and 2013 [8].

Floor of mouth (34.4%) and oral tongue (34.3%) represented the most common disease subsites, followed in descending order by gums (12.4%), retromolar trigone (9.1%), buccal mucosa (7.4%), and hard palate (2.6%). This study was limited by inclusion of registry data from only nine areas in the US, including approximately 9.4% of the population.

The American Cancer Society’s annual report of cancer statistics estimates new cancer cases and deaths from oral cavity cancer in combination with pharyngeal cancers based on data from SEER, the National Program of Cancer Registries, and the North American Association of Central Cancer Registries [9]. These pooled data obscure the incidence of newly diagnosed oral cavity cancer and the relative distribution by subsite in the US.

To quantify the relative incidence of oral cavity cancer in the US by primary tumor subsite, the National Cancer Database (NCDB) was queried for adult subjects age 18 or older with oral cancer diagnosed between January 1, 2004 and December 31, 2015. In an effort to exclude oropharyngeal primaries, subjects with the International Classification of Diseases for Oncology Classification of Diseases Third Edition (ICD-O-3) code for oral cavity overlap with pharynx (C148, $n = 1996$) were excluded. Subjects with the following ICD-O-3 codes were also excluded because the specific oral cavity subsite could not be determined: other mouth overlapping (C068, $n = 699$) and mouth not otherwise specified (C069, $n = 4038$). The remaining subjects were included for further analysis, and the results are summarized in Table 1 and Fig. 1.

Importantly, NCDB data are hospital-based rather than population-based. Approximately 70% of newly diagnosed cancer cases in the US are captured at the institutional level from more than 1500 accredited cancer programs. Therefore, the overall national incidence is considerably higher than the number of cases reported in Table 1. Despite under-ascertainment, the relative distribution of oral cancer by subsite should be fairly representative based on the large sample size from a broad array of hospital environments across the US. However, smaller hospitals in non-urban locations are not as well represented in the NCDB, and epidemiological factors among those in rural population may vary [10]. Another limitation in interpreting these data is that certain overlapping and not otherwise specified codes were included. Thus, cancers of the oral tongue and hard palate may be overestimated by including an indeterminate number of oropharyngeal primaries. Nevertheless, oral tongue remains the most common subsite of oral cancer in the US even with omission of ICD-O-3 codes C028 and C029.

As depicted in Fig. 1, the floor of mouth is the second most common subsite for oral cancer in the US. The third most frequent anatomic subsite is the lower/upper gum. Over the twelve years analyzed, only 16 cases of odontogenic malignancies were identified by histologic

Table 1
Number and distribution of new oral cancer cases reported in the National Cancer Database between 2004 and 2015 by primary tumor subsite.

ICD-O-3 code	Site description	Total N [†]	Average N/year [†]	Percent
<i>Lip cancer</i>				
C000	External Lip: Upper NOS	1580		
C001	External Lip: Lower NOS	7210		
C002	External Lip: NOS	265		
C003	Lip: Upper Mucosa	362		
C004	Lip: Lower Mucosa	1701		
C005	Lip: Mucosa NOS	103		
C006	Lip: Commissure	335		
C008	Lip: Overlapping	145		
C009	Lip NOS	663		
Total		12,364	1030	11.0%
<i>Oral tongue cancer*</i>				
C020	Tongue: Dorsal NOS	2619		
C021	Tongue: Border, Tip	7389		
C022	Tongue: Ventral NOS	6244		
C023	Tongue: Anterior NOS	8768		
C028	Tongue: Overlapping	2566		
C029	Tongue NOS	18,699		
Total		42,285	3857	41.2%
<i>Alveolar ridge cancer</i>				
C030	Gum: Upper	3465		
C031	Gum: Lower	7411		
C039	Gum NOS	1611		
Total		12,487	1041	11.1%
<i>Floor of mouth cancer</i>				
C040	Mouth: Anterior Floor	5634		
C041	Mouth: Lateral Floor	1232		
C048	Mouth: Overlapping Floor	867		
C049	Floor of Mouth NOS	11,532		
Total		19,265	1605	17.2%
<i>Hard palate cancer*</i>				
C050	Hard Palate	4813		
C058	Palate: Overlapping	918		
C059	Palate NOS	1108		
Total		6839	478	6.1%
<i>Buccal mucosa cancer</i>				
C060	Cheek Mucosa	7700		
C061	Mouth: Vestibule	558		
Total		8258	688	7.4%
<i>Retromolar trigone cancer</i>				
C062	Retromolar Area	6780		
Total		6780	565	6.0%
<i>All oral cavity cancer sites*</i>				
Total		112,278	9357	100%

Abbreviations: International Classification of Diseases for Oncology Classification of Diseases Third Edition (ICD-O-3); Not otherwise specified (NOS).

[†] The National Cancer Database captures approximately 70% of new cancer diagnoses in the United States. Thus, the overall national incidence is underreported based on these data.

* Excludes base of tongue (C019, n = 53,734), lingual tonsil (C024, n = 1493), soft palate (C051, n = 6126), uvula (C052, n = 829), and oral cavity overlap with pharynx (C148, n = 1996). The inclusion of C028, C029, and C058 may overestimate the number of oral cavity cases due to potential inclusion of some oropharyngeal primary tumors.

codes. If the mandibular and maxillary alveolar ridges are considered as separate and distinct primary sites, then lip cancer represents the third most common site for oral cancer in the US. Although the retromolar trigone and hard palate account for a similar proportion of oral cavity cancers (approximately 6% each), the latter is more likely to be the least frequently involved site due to potential overestimation with inclusion of soft palate primary tumors within C058 and C059.

In conclusion, this report provides contemporary epidemiological

data regarding the incidence and subsite distribution of oral cancer for individuals living in the US.

Disclaimer

The data used in the study are derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical

Oral Cancer Incidence by Primary Tumor Subsite in the US, 2004-2015

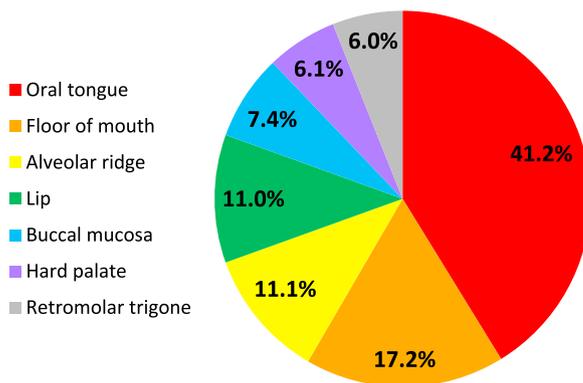


Fig. 1. Oral cancer incidence by primary tumor subsite in the United States between 2004 and 2015.

methodology employed, or the conclusions drawn from these data by the investigator.

Conflict of interest

None declared.

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