



A Novel Framework for Management of Oropharyngeal Cancers

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Abstract

Aim: Traditional oral cancer screening of visual examination and palpation do not effectively differentiate between premalignant mucosal lesions, benign inflammatory conditions, and normal mucosal variance. Current studies have shown that even subtle mucosal abnormalities may lead to malignancies. Although histopathologic examination from incisional biopsy is the “gold standard” in identifying malignancy, it is often difficult to identify lesion borders without supplementary technology to enhance visualization. Despite treatment advances, the disease’s overall five-year survival rate has not improved in the past three decades and the prognosis remains poor. The high lethality from oropharyngeal cancer is due to challenges in early detection. In fact, early diagnosis is critical to increase success rate of therapy.

Method: A multidisciplinary logic model and program intervention is proposed to reduce health disparity and costs associated with oral cancer treatment.

Results: The short-term impact is an improved quality of life for oropharyngeal cancer patients. The intermediate impact is that patients will have an improved prognosis. The long-term impacts are overall reduced healthcare costs, and decreased deaths caused by oropharyngeal cancers. With 100% of patients receiving HPV vaccination and are immune, it should eliminate oropharyngeal cancers associated with HPV.

Conclusions: Oral health providers need to be aware of the emerging roles that the human papillomavirus (HPV), fluorescent technology, and salivary biomarkers have in the prevalence and diagnosis of oral and/or oropharyngeal cancers. Dental and medical providers need to inform health policy makers, stakeholders and public health educators for cancer control efforts.

Keywords

Oropharyngeal cancers; HPV; Oral cancer screenings; Salivary-based molecular diagnostics; HPV vaccinations; Medicine-Dentistry integration; Health care systems

Introduction

Oropharyngeal cancer is an adverse health outcome associated with specific behaviors such as tobacco/alcohol usage, immune suppression, and specific viral exposures [1,2]. Oropharyngeal cancers involve the tongue, mucosa, floor of the mouth, soft palate, tonsils, salivary glands, and pharynx. The incidence is expected to increase due to the prevalence of HPV. It has one of the lowest five-year survival rates of all major cancers, due to delayed diagnosis since early lesions are asymptomatic, difficult to identify and palpate. Heavy tobacco (smoking/smokeless), betel quid, and alcohol usage among middle age males (>45 years) are strong synergistic risk factors for oropharyngeal cancers. Oropharyngeal cancers represent 5% of all diagnosed cancers with some variations in incidence by subsites across world regions [3]. It is one of the most common cancers among Southeast Asian males due to use of heavy tobacco and betel quid. However, there is an association in individuals with oropharyngeal cancer who are young, otherwise healthy non-smokers, acquiring HPV (Human Papilloma Virus) infection [3]. Studies have found a greater depth of tumor invasion in non-smokers and non-drinkers in squamous cell carcinoma [3]. Additionally, it is hypothesized that HPV acts as a catalytic agent in tumor progression in nasopharyngeal and palatal metastasized carcinomas [3,4]. Despite treatment advances, the disease’s overall five-year survival rate has not improved in the past three decades and the prognosis remains poor. The high lethality from oropharyngeal cancer is due to challenges in early detection. In fact, early diagnosis is critical to increase success rate of therapy.

Traditional oral cancer screening of visual examination and palpation do not effectively differentiate between premalignant mucosal lesions, benign inflammatory conditions, and normal mucosal variance. Current studies have shown that even subtle mucosal abnormalities may lead to malignancies; oral health providers need to be aware of the emerging roles that the human papillomavirus (HPV), fluorescent technology, and salivary biomarkers have in the prevalence and diagnosis of oral and/or oropharyngeal cancers

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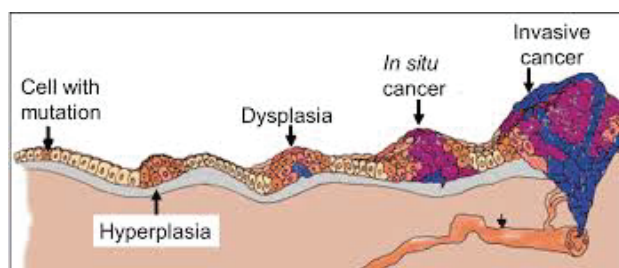


Figure 1: Oropharyngeal Cancer Progression

[1,4-7] although histopathologic examination from incisional biopsy is the “gold standard” in identifying malignancy, it is often difficult to identify lesion borders without supplementary technology to enhance visualization. Several diagnostic aids can assist in the early detection of oral neoplasia. For example, chemiluminescence and tissue autofluorescence has facilitated the earlier detection of dysplasia [7-9] (Figure 1). Salivary-based molecular diagnostic can allow screening of an entire population for a chair-side diagnosis of multiple oral and systemic diseases at the dental office. Salivary fluid is easily accessible; it contains steroid hormones, antibodies, growth factors cytokines, chemokines, nucleic acids, proteins, and potential pharmacological medications. Salivary diagnostics is reported to have the potential to detect malignancy at its earliest cellular stage [2,4,5,10-12] (Figure 1). In this program intervention, there are three health objectives for the target population in reducing their risk for oropharyngeal cancers. This includes routine annual chairside oral cancer screening with adjunctive methods (chemiluminescence, Vizilite/VEL scope, and staining, salivary-based molecular diagnostics) during periodic dental exams. Secondly, patients need to be vaccinated for HPV, since there is a proven causation of specific subtypes of squamous cell carcinoma on the pharynx and lingual and palatine tonsils and HPV infection [3]. Finally, patients should receive tobacco and alcohol cessation support and education. Tobacco and alcohol separately have been shown to be risk factors for oral and pharyngeal cancers [13,14]. Tobacco was found to cause more leukoplakic (white) type abnormalities, while alcohol caused more erythroplakic (red) lesions, which are more difficult to differentiate from benign inflammatory mucosa. Alcohol is a mucosal irritant that interferes with DNA repair that has been observed across different geographic regions and populations [14]. It is imperative to address the risks of alcohol and tobacco for the success of this intervention.

Intervention

Several interventions can be feasibly implemented in the dental clinic to improve health outcomes. These interventions are chemiluminescence, salivary diagnostics, HPV vaccinations, and tobacco/alcohol cessation initiatives. There needs to be a coordinated effort to bridge dental clinics, laboratory, and primary medical care to ensure success in implementing these health interventions. The use of chemiluminescence and other adjunctive screening methods (Vizilite/velscope/staining) will aid in identifying pre-dysplastic lesions that are not visible in incandescent light. Increasing visualization has proven success in medicine with mammograms and Pap smears for breast and cervical cancers, respectively. In dentistry, erythroleukoplakic (red-white) lesions are challenging to distinguish from normal tissue; they are severely dysplastic and will become malignant. Improved visualization of these clinical subtypes will promote earlier treatment and elevate the prognosis. This would involve the application of chemiluminescent light kit and 1% toluidine blue by a dentist or dental specialist. Oral squamous cell carcinoma is preceded by potentially premalignant mucosal lesions which necessitates the ability to detect abnormality at its most incipient stage. This can be achieved by increasing public awareness about annual oral cancer screening and by identifying asymptomatic premalignant lesions using diagnostic aids. Dentists and dental specialists will deliver the intervention during periodic exams or when they observe a possible lesion during routine and referred

treatment. If a suspicious lesion is identified, it can be biopsied by the dentist or referred to an oral surgeon specialist. The stakeholders are patients, dentists, and dental specialists. The underlying assumptions are that patients would consent to biopsy if the provider identified a suspicious lesion and those clinicians are performing thorough cancer screenings. Potentials barriers include the insurance not reimbursing for the cost of the enhanced screening and financial cost of the chemiluminescent light kit and stain.

Another valuable intervention is a screening strategy is saliva testing for molecular markers, such as HPV during dental appointments. Salivary fluid is easily accessible; it has the potential to detect malignancy at its earliest cellular stage and identify diseases beyond oropharyngeal cancers. Previously saliva biomarkers have been used to predict the prognosis and success of treatment with periodontal disease, diabetes, and Sjorgen's Syndrome [2,5,10-12]. One specific study found that saliva contained a detectable amount of long non-coding lncRNA which could be potential markers of oral squamous cell carcinoma [12]. HPV is a significant molecular marker for subtypes of oral squamous cell carcinoma; there are commercially available tests (OraRisk HPV, Oral DNA) to identify individuals that are at higher risk of developing oropharyngeal cancers. The saliva can be easily retrieved during any dental appointment and shipped to pathology laboratory for analysis. In this step of the intervention, the stakeholders are patients, dentists, and dental specialists, primary care physicians, pathologists, and laboratory technicians. The underlying assumptions are the tests have specificity and sensitivity to provide reproducible results for a population and that patient's can provide adequate salivary fluid for the test. Potentials barriers include the insurance not reimbursing for the cost of the salivary molecular markers. One component of the intervention is prevention through HPV vaccinations. Dentists should increase patient engagement for HPV vaccinations. HPV is etiologically linked to a limited subset of oral cavity cancers. 1 The American Dental Association (ADA) has urged dental clinics to educate and provide referral forms to patients for HPV vaccination and consider the feasibility in administering the vaccination. Implementation of this intervention will require improving dentists and hygienists' self-efficacy to communicate HPV prevention. Additionally, it will require partnering with physicians to reinforce the importance of vaccination for prophylaxis and therapeutic benefit. Even when patients are infected with HPV and receive the vaccine, B cell memory is improved, thereby providing a therapeutic benefit [15]. Also, the Center for Disease Control (CDC) recommends prophylaxis vaccination for individuals between the ages 15 through 26 years, and for immune compromised persons. Dentists may refer all patients to their primary care physician for administration of the HPV vaccine. The stakeholders are patients, parents, dentists, primary care physicians and nurse practitioners. The underlying assumptions are that patients/parents would be receptive to receiving the education and consent for the vaccine. Potentials barriers include the insurance not reimbursing for the cost of the vaccination for patients above the age of 25, and therapeutic benefit may not be reimbursable by insurance.

An additional component of prevention is tobacco/alcohol cessation initiatives. These initiatives would include a campaign with online ads, in-office video, displays, and mobile formats. Patients would also be educated on the effects vaping and alcohol consumption and oral cancer. Hygienists, dentists, and dental specialists can referral patients at any time for tobacco/alcohol cessation programs to their physician. This intervention can be feasibly delivered by a trained physician/psychiatrist and behavioral psychologist. It would include telephone counseling, behavioral therapy, problem-solving session, controlled medication (nicotine replacement products), over the counter (nicotine patch, gum, lozenge), and prescription non-nicotine medications (Zyban and Chantix) and alcohol withdrawal medications. Medicaid expansion and most private health insurance plans are required to cover a comprehensive tobacco cessation benefit for plan members. The stakeholders are patients, dentists, psychiatrists, behavioral psychologists, and primary care physicians. The underlying assumptions are that patients would fully participate

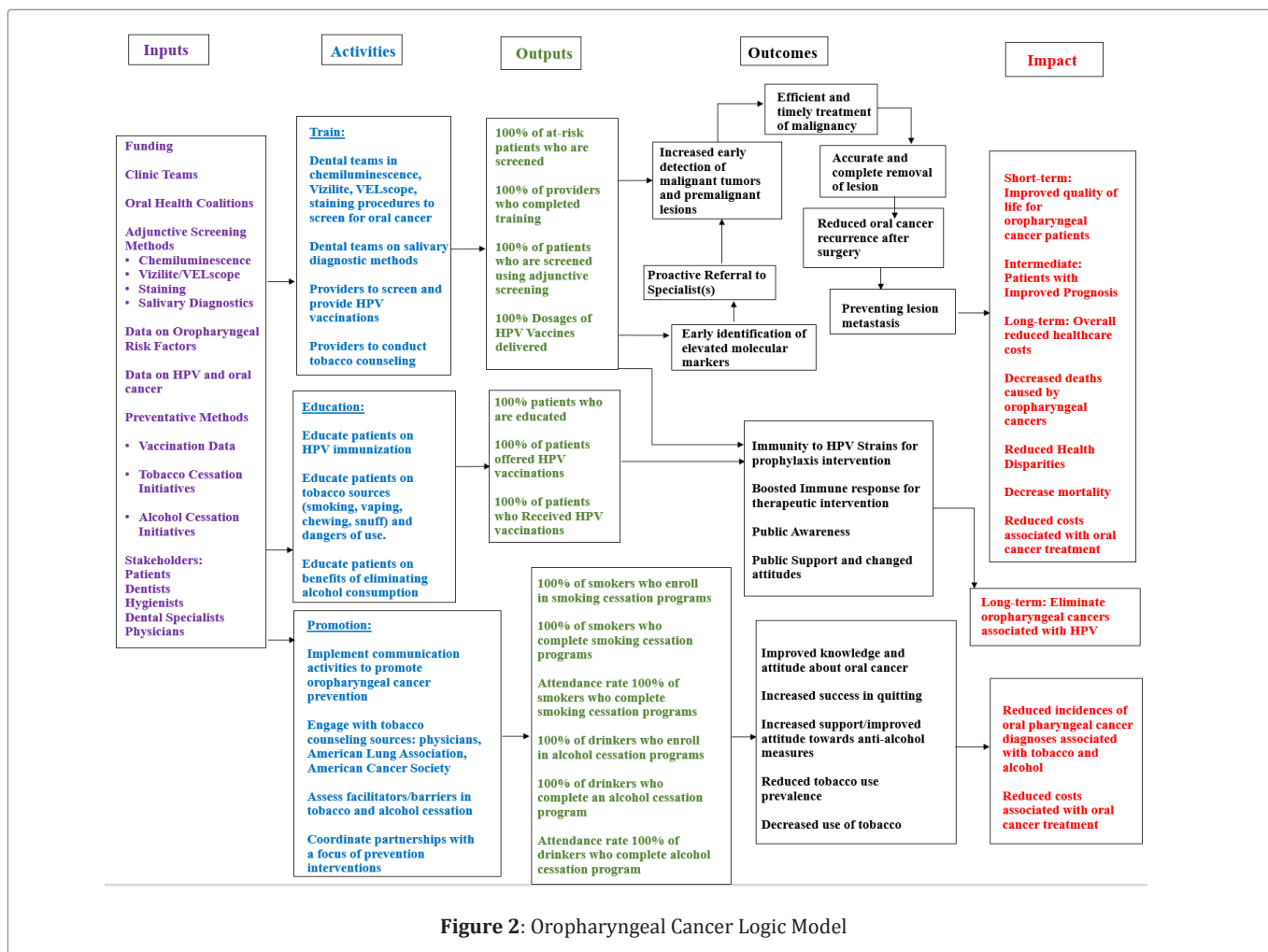


Figure 2: Oropharyngeal Cancer Logic Model

in cessation programs with realistic goals to completion and they would report alcohol/tobacco usage accurately on their health history. Potentials barriers include patient non-compliance and the insurance not reimbursing for the cost of an alcohol cessation program. Motivation interviewing can be incorporated into the early treatment of alcohol dependence. The counseling style of the physician strongly influences patient outcomes and certain aspect of physician behavior influence the probability that a patient that consumes alcohol will seek further consultation. This intervention will require physicians all other health care providers to be trained in motivation counseling. Patients should have realistic and attainable goals instead of suddenly stopping. Studies have shown that the primary care physician can be a powerful influencer for the patient to accept treatment, especially when the physician is empathic without being judgmental [14]. These interventions are aligned with the social learning and cognitive theories in that addiction is rooted in the way people observe and learn from our peers and role models. Emphasis would be on forming new behavioral patterns; human behavior is directed by personal factors, environmental influences, and self-regulation. The intervention will only be sustainable if patients learn to modify their attitudes and behaviors related to tobacco and alcohol use and increase their life skills to handle stressful circumstances that would trigger their maladaptive coping mechanisms [16-18].

Logic Model

Oropharyngeal cancers have high morbidity because most tumors are identified late through traditional oral cancer screening of clinical examination and palpation. Therefore, preventative interventions and methods to facilitate early diagnosis are important in effective treatment to increase survivability and improve quality of life after treatment. The Resources/Inputs are using adjunctive screening methods and prevention strategies (Figure 2). Adjunctive screening methods include use of chemiluminescence (Vizilite/VELscope) and

staining, as well salivary diagnostics. If clinic teams are trained in these diagnostic methods, and are educated in promoting vaccination, this logic model will be implemented, resulting in prevention and timely treatment for oropharyngeal cancer (Figure 2). Activities include training dental teams in these methods to ensure thorough cancer screening and providing tobacco counseling and referral. Education is a require component to provide information on HPV immunization, tobacco sources and risk of use, as well as discussing the benefits of eliminating alcohol consumption. Dentists should play a greater role in improving immunization rates among their patients. Promotion will be possible by reaching out to other resources such as the American Lung Association and American Cancer Society to coordinate partnerships. Outputs would include screened patients for oral cancer; tobacco, alcohol use, and elevated molecular markers in the saliva characteristic for oropharyngeal cancers [19-21]. Outputs would also include patients educated on prophylactic and therapeutic benefits of HPV vaccination. It aims for all patients to be vaccinated from HPV. Additional outputs include smokers and alcohol drinkers who enroll, attend, and complete smoking/alcohol cessation programs. Outcomes are discriminating benign from malignant mucosal lesions (and its dysplasia precursors), detecting elevated molecular markers, vaccination, and tobacco cessation. An early identification of an elevated molecular marker would initiate a proactive referral to a specialist for treatment. The output will result in increased early detection of malignant tumors and premalignant lesion outcomes. Accurate and complete removal of the lesions will promote a reduced oral cancer recurrence after surgery and prevent lesion metastasis (Figure 2). Another outcome is immunity to HPV strains from prophylactic intervention and a boosted immune response from therapeutic intervention. Public awareness and public support will be achieved through knowledge about oral cancer. It will also result in increased support and improved attitude towards anti-alcohol/anti-tobacco measures to decrease its use. This logic model

Logic Component	Indicators	Measurement
Inputs/Resources	Reports of staff and funding status.	Compare the nature and extent of influences before (baseline) and after the program.
Activities	Descriptions of all planned activities. Reports of actual activities. Descriptions of participants and attendance.	Compare actual activities provided, length of attendance and patient/participant feedback.
Outputs	Reports and percentages of services performed and attendance rate.	Compare the quality and quantity of actual against expected.
Outcomes	Participant attitudes toward tobacco, alcohol, HPV vaccination, knowledge of oral cancer, skills, intentions, and behaviors.	Compare the measures before and after the program intervention.
Impact	Quality of life, Costs of treatment	Number of Oropharyngeal cancer cases and prognosis

Table 1: Performance Indicators and Measurement for Each Logic Component

will result in reduced health disparity and reduced costs associated with oral cancer treatment. The short-term impact is an improved quality of life for oropharyngeal cancer patients. The intermediate impact is that patients will have an improved prognosis. The long-term impacts are overall reduced healthcare costs, and decreased deaths caused by oropharyngeal cancers. With 100% of patients receiving HPV vaccination and are immune, it should eliminate oropharyngeal cancers associated with HPV [22].

There should also be reduced incidences of oropharyngeal cancer diagnoses associated with tobacco and alcohol. The underlying assumptions include 100% participation, attendance, compliance and completion. The barriers of dental care access and utilization include cost, situational anxiety towards treatment, and lack of access in rural/underserved areas, and social influence. Psychological barriers to health behavior change include high levels of psychological distress, no concern with the future consequences of health decisions, lack of knowledge of health risks, and lower self-efficacy to change health behavior. Additional barriers include lack of social support, and networks of friends and family with unhealthy and sedentary lifestyles (Table 1). Quantitative data will be collected in terms of how many patients tested positive and had a detectable premalignancy/dysplastic lesion. Qualitative data will be collected to include patient health history, intraoral photo and radiographs, and interviews with dentists and hygienists. Measures will be compared before and after the program intervention. The plan for feasibility includes incorporating these interventions within the existing established system of the annual periodic exam and during routine dental appointments. The key to long-term sustainability is flexibility, strong interdisciplinary partnerships and leveraging resources across multiple levels. Success will be determined by participation and completion of all components of the intervention. The results will be shared to inform health policy makers, stakeholders and public health educators for cancer control efforts.

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