**OSHR - Oral Health, Cancer, and Cancer Risk**

**Subtopics:**

**General**

**OH and Colon Cancer and Oral Microbes (Fn), Colorectal Cancer Early Detection**

**OH and Liver Cancer**

**Poor Periodontal Health and Cancer Risk**

**Oral and Oropharyngeal Cancers**

**Esophageal Cancer**

**Poor Oral Health and Cancer Risk**

**Poor Dental Health and Pancreatic Cancer Risk**

**Oral Microbiome and Pancreatic Cancer Risk**

**OH Care to Reduce HPV Cancer Risk**

**OH and Leukemia**

**Orodental Complications in Childhood Acute Myeloid Leukemia**

**Periodontal Disease and Breast Cancer**

**General**

# Rivera M, Coleman D, Henriquez P (2023). Managing the Oral-Systemic Link to Reduce Cancer Risk: Through preventive efforts and early diagnosis and treatment, dental teams can play a vital role in managing oral and systemic diseases — including many forms of cancer. (Course Advertisement.) At: <https://decisionsindentistry.com/article/managing-oral-systemic-link-reduce-cancer-risk/>

Nath S, Ferreira J, McVicar A, Oshilaja T, Swann B (2022). Rise in oral cancer risk factors associated with the COVID-19 pandemic mandates a more diligent approach to oral cancer screening and treatment. *J Am Dent Assoc* 153(6): 495–499. The COVID-19 pandemic has brought about a public health crisis of substantial scale. As of January 2022, there had been over 281 million confirmed cases of COVID-19 worldwide and over 5.4 million deaths reported to the World Health Organization.[1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8898066/#bib1) In response to the pandemic, global lockdowns, social distancing, and quarantine procedures were imposed. Because of the high risk of transmission of COVID-19 due to aerosols and other occupational exposures, many countries suspended elective oral health care during the pandemic. According to the American Cancer Society, oral cancer is a cancer within the oral cavity including the buccal mucosa, the teeth, the gums, the front two-thirds of the tongue, the floor of the mouth below the tongue, the bony roof of the mouth and the retromolar trigone. Oral cancer is a major health concern in both high- and low-income countries. The American Cancer Society’s estimates for oral cancer in the United States in 2021 included about 54,010 new cases of oral cavity or oropharyngeal cancer, with an overall 5-year survival rate of approximately 60%.

City of Hope (2022). Rick factors lor oral cancer. At: <https://www.cancercenter.com/cancer-types/oral-cancer/risk-factors>

Zhang X, Liu B, Lynn HS, Chen K, Dai H (2022). Poor oral health and risks of total and site-specific cancers in China: A prospective cohort study of 0.5 million. At**:** <https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00060-8/fulltext> **DOI:** <https://doi.org/10.1016/j.eclinm.2022.101330> **Abstract: Background:** There is a strong connection between oral health and overall wellness. We aim to examine the association between poor oral health and the risk of developing or dying of cancer, and whether the association differs by residential area. **Methods:** Between 2004 and 2008, a total of 510,148 adults free of cancer were included from the China Kadoorie Biobank study and thereafter followed up to 2015. Poor oral health was assessed from a self-reported baseline questionnaire and defined as a combination of rarely brushing teeth and always gum bleeding. We used Cox proportional hazards models to estimate the hazard ratio (HR) of cancer risk and its associated 95% confidence interval (CI) according to oral health status. **Findings:** Overall, 14.9% of participants (19.7% in rural areas and 8.8% in urban areas) reported poor oral health at baseline. After 4,602,743 person-years of follow-up, we identified 23,805 new cancer cases and 11,973 cancer deaths, respectively. Poor oral health was associated with higher risks of total cancer incidence (HR: 1.08, 95% CI: 1.04–1.12) and death (HR: 1.10, 95% CI: 1.05–1.16). For the site-specific cancers, poor oral health was significantly associated with higher risk of stomach cancer incidence (cases: 2964, HR: 1.10, 95% CI: 1.00–1.22), esophageal cancer incidence (cases: 2119, HR: 1.19, 95% CI: 1.07–1.33), esophageal cancer death (cases: 1238, HR: 1.29, 95% CI: 1.12–1.49), liver cancer incidence (cases: 2565, HR: 1.18, 95% CI: 1.06–1.32), and liver cancer death (cases: 1826, HR: 1.20, 95% CI: 1.05–1.36). This positive association was stronger among rural residents compared to urban residents (interaction test P < 0.01). **Interpretation:** Our findings indicate that poor oral health is associated with higher risk for cancers, especially digestive system cancers. Promotion of oral health in the general population, especially for rural residents, could have valuable public health significance in preventing major systemic diseases. **Funding:** Supported by grants (2021YFC2500400, 2016YFC0900500, 2016YFC0900501, 2016YFC0900504) from the National Key Research and Development Program of China, grants from the Kadoorie Charitable Foundation in Hong Kong and grants grants (088158/Z/09/Z, 104085/Z/14/Z, 202922/Z/16/Z) from Wellcome Trust in the UK. CKB is supported by the Kadoorie Charitable Foundation (KCF) in Hong Kong. **Keywords:** [Oral health](https://www.thelancet.com/action/doSearch?AllField=%22Oral%20health%22&ISSN=2589-5370), [Oral hygiene](https://www.thelancet.com/action/doSearch?AllField=%22Oral%20hygiene%22&ISSN=2589-5370), [Gum bleeding](https://www.thelancet.com/action/doSearch?AllField=%22Gum%20bleeding%22&ISSN=2589-5370), [Tooth brushing](https://www.thelancet.com/action/doSearch?AllField=%22Tooth%20brushing%22&ISSN=2589-5370), [Gastronintestinal cancer](https://www.thelancet.com/action/doSearch?AllField=%22Gastronintestinal%20cancer%22&ISSN=2589-5370), [Cohort study](https://www.thelancet.com/action/doSearch?AllField=%22Cohort%20study%22&ISSN=2589-5370).

Harvard U (2020). At: <https://www.health.harvard.edu/cancer/gum-disease-linked-to-an-increased-risk-for-cancer> Having gum disease increases your risk for many health problems other than tooth loss, such as heart disease. To add to the list, a study from Harvard summarized in a letter published online July 20, 2020, by the journal *Gut* suggests that the microbes camping out between your teeth and gums may affect your risk for cancers of the stomach and esophagus. Harvard scientists analyzed health data from two large studies that included almost 150,000 men and women. In up to 28 years of follow-up, people with a history of periodontal (gum) disease were 43% more likely to develop esophageal cancer and 52% more likely to develop gastric (stomach) cancer compared with people whose gums were healthier. The risk was even higher in those with gum disease severe enough to cause tooth loss. The study is observational and doesn't prove that gum disease causes cancer, but it could mean that someday doctors will include a look at your gum health when assessing your overall risk. Fortunately, it's easy to prevent gum disease. The American Dental Association recommends that you brush your teeth twice per day, floss at least once per day, and get a dental exam and cleaning regularly.

Michaud DS (2019). **Chapter 11: Oral Infections and Cancer.** In Glick M (2019), *The Oral- Systemic Health Connection*, 2nd ed. (Quintessence, ISBN 9780867158083). Pp 231-241**. Book Chapter**

Chung M, York BR, Michaud DS (2019). Oral Health and Cancer. *Curr Oral Health Rep* 6(2): 130–137. DOI: 10.1007/s40496-019-0213-7 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6927401/> **Abstract: Purpose of review:** Recently published studies have provided new evidence for a role of oral health on risk of cancer. This review summarizes the latest research on this topic, including several new cohort studies that have examined associations on periodontal disease and cancer risk. **Recent findings:** The most consistent findings for associations with periodontal disease have been observed for lung cancer; five out of seven studies have reported statistically significant increases in risk of lung cancer. For pancreatic, colorectal and head and neck cancers, the associations are less consistent across studies, and the overall summary relative risk estimates are not statistically significant. However, these associations remain of interest, given the limitations of existing data (i.e., measurement error in periodontal disease assessment and small sample sizes), and growing support for biological mechanisms on how bacteria previously linked to periodontal disease may play a role in carcinogenesis. **Summary:** Future studies need improved assessment of periodontal disease in population-based studies to determine if heterogeneity of current studies resides with measurement error. Periodontal disease treatment and prevention may turn out to be important targetable cancer prevention strategies. **Keywords:**periodontal disease, lung cancer, pancreatic cancer, colorectal cancer, head and neck cancer, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*

Jordão HWT, McKenna G, McMenamin ÚC, Kunzmann AT, Murray LJ, Coleman HG (2019). The association between self-reported poor oral health and gastrointestinal cancer risk in the UK Biobank: A large prospective cohort study. *United European Gastroenterology Journal*, 2019; 205064061985804 DOI: 10.1177/2050640619858043At:[*https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6826526/*](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6826526/)**Abstract: Background:** Controversy remains as to whether poor oral health is independently associated with gastrointestinal cancers, due to potential confounding by smoking, alcohol and poor nutrition. The aim of this study was to investigate the association between oral health conditions and gastrointestinal cancer risk. **Methods:** Data from the large, prospective UK Biobank cohort, which includes n = 475,766 participants, were analysed. Cox proportional hazard models were applied to estimate the relationship between gastrointestinal cancer risk and self-reported poor oral health (defined as painful gums, bleeding gums and/or having loose teeth), adjusting for confounders. **Results:** During an average six years of follow-up, n = 4069 gastrointestinal cancer cases were detected, of which 13% self-reported poor oral health. Overall, there was no association between self-reported poor oral health and risk of gastrointestinal cancer detected (hazard ratio 0.97, 95% confidence interval 0.88–1.07). In site-specific analysis, an increased risk of hepatobiliary cancers was observed in those with self-reported poor oral health (hazard ratio 1.32, 95% confidence interval 0.95–1.80), which was stronger for hepatocellular carcinoma (hazard ratio 1.75, 95% confidence interval 1.04–2.92). **Conclusion:** Overall there was no association between self-reported poor oral health and gastrointestinal cancer risk. However, there was a suggestion of an increased risk of hepatobiliary cancer, specifically hepatocellular carcinoma. **Keywords:**Gastrointestinal cancer, liver cancer, poor oral health, epidemiology.

Michaud, DS (2019). Oral Infections and Cancer. *The Oral-Systemic Health Connection*, Michael Glick, ed., 2nd ed. (Quintessence Publishing, 2019), Chapter 11, pp. 231-241.

Michaud DS, Fu Z, Shi J, Chung M (2017). Periodontal Disease, Tooth Loss, and Cancer Risk. *Epidem Reviews* 39. DOI: 10.1093/epirev/mxx006 Abstract: Periodontal disease, which includes gingivitis and periodontitis, is highly prevalent in adults and disease severity increases with age. The relationship between periodontal disease and oral cancer has been examined for several decades, but there is increasing interest in the link between periodontal disease and overall cancer risk, with systemic inflammation serving as the main focus for biological plausibility. Numerous case-control studies have addressed the role of oral health in head and neck cancer, and several cohort studies have examined associations with other types of cancers over the past decade. For this review, we included studies that were identified from either 11 published reviews on this topic or an updated literature search on PubMed (between 2011 and July 2016). A total of 50 studies from 46 publications were included in this review. Meta-analyses were conducted on cohort and case-control studies separately when at least 4 studies could be included to determine summary estimates of the risk of cancer in relation to 1) periodontal disease or 2) tooth number (a surrogate marker of periodontal disease) with adjustment for smoking. Existing data provide support for a positive association between periodontal disease and risk of oral, lung, and pancreatic cancers; however, additional prospective studies are needed to better inform on the strength of these associations and to determine whether other cancers are associated with periodontal disease. Future studies should include sufficiently large sample sizes, improved measurements for periodontal disease, and thorough adjustment for smoking and other risk factors.

Han, YW (2015). *Fusobacterium nucleatum*: a commensal-turned pathogen. *Curr. Opin. Microbiol.* 23, 141–147. DOI: 10.1016/j.mib.2014.11.013 At: <https://pubmed.ncbi.nlm.nih.gov/25576662/> Abstract: Fusobacterium nucleatum is an anaerobic oral commensal and a periodontal pathogen associated with a wide spectrum of human diseases. This article reviews its implication in adverse pregnancy outcomes (chorioamnionitis, preterm birth, stillbirth, neonatal sepsis, preeclampsia), GI disorders (colorectal cancer, inflammatory bowel disease, appendicitis), cardiovascular disease, rheumatoid arthritis, respiratory tract infections, Lemierre's syndrome and Alzheimer's disease. The virulence mechanisms involved in the diseases are discussed, with emphasis on its colonization, systemic dissemination, and induction of host inflammatory and tumorigenic responses. The FadA adhesin/invasin conserved in F. nucleatum is a key virulence factor and a potential diagnostic marker for F. nucleatum-associated diseases. Copyright © 2014 Elsevier Ltd. All rights

**OH and Colon Cancer and Oral Microbes (Fn), Colorectal Cancer Early Detection**

# Columbia Univ. Irving Medical Center (2022). Solutions for Colorectal Cancer Early Detection Linked to Oral Health. Notes from the Lab: The Han Lab. At: <https://www.cancer.columbia.edu/news/solutions-colorectal-cancer-early-detection-linked-oral-health>

Baik JE, Li L, Shah MA, Freedburg DA, Jin Z, Wang TC, Han YW (2022). Circulating IgA antibodies against the *Fusobacterium nucleatum* adhesin FadA are a potential biomarker for colorectal neoplasia. At: *Cancer Research Communications* CRC-22-0248. At: <https://aacrjournals.org/cancerrescommun/article/doi/10.1158/2767-9764.CRC-22-0248/709679/Circulating-IgA-antibodies-against-the> DOI: <https://doi.org/10.1158/2767-9764.CRC-22-0248> Abstract: Fusobacterium nucleatum (Fn) is a gram-negative oral anaerobe and prevalent in colorectal cancer (CRC). Fn encodes a unique amyloid-like adhesin, FadAc, consisting of intact pre-FadA and cleaved mature FadA (mFadA), to promote CRC tumorigenesis. We aimed to evaluate circulating anti-FadAc antibody levels as a biomarker for CRC. Circulating anti-FadAc IgA and IgG levels were measured by ELISA in two study populations. In Study 1, plasma samples from CRC patients (n=25) and matched healthy controls (n=25) were obtained from University Hospitals Cleveland Medical Center. Plasma levels of anti-FadAc IgA were significantly increased in CRC patients (n=25; mean ± SD: 1.48±1.07 ug/ml) compared to matched healthy controls (n=25; 0.71±0.36 ug/ml) (p= 0.001). The increase was significant in both early (stages I & II) and advanced (stages III & IV) CRC. In Study 2, sera from 50 CRC patients and 50 patients with advanced colorectal adenomas were obtained from the Weill Cornell biobank. Anti-FadAc antibody titers were stratified according to the tumor stage and location. Similar as Study 1, serum levels of anti-FadAc IgA were significantly increased in CRC patients (n=50; 2.06±1.47 ug/ml) compared to patients with colorectal adenomas (n=50; 1.49±0.99 ug/ml; p= 0.025). Significant increase was limited to proximal cancers, but not distal tumors. Anti-FadAc IgG was not increased in either study population, suggesting that Fn likely translocates through the gastrointestinal tract and interact with colonic mucosa. Anti-FadAc IgA, but not IgG, is a potential biomarker for early diagnosis of colorectal neoplasia, especially for proximal tumors.

# Kim GW, Kim Y-S, Lee SH, Park SG, Kim DH, Cho JY, Hahm KB, Hong SP, Kim DH, Cho JY, Hahm KB, Hong SP, Yoo J-H (2019). *Sci Rep*.  9: 7528. Periodontitis is associated with an increased risk for proximal colorectal neoplasms. Periodontitis is associated with an increased risk for proximal colorectal neoplasms. At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6525177/> Abstract: Periodontitis is associated with an increased risk for proximal colorectal neoplasms. Abstract: Interval colorectal cancers detected after colonoscopy are known to be highly associated with proximal colorectal neoplasms (CRNs). This cross-sectional study investigated whether periodontitis could be a risk factor for proximal CRNs in healthy individuals. A total of 2504 subjects who received a colonoscopy and dental exam were enrolled in this study. We divided the subjects into the periodontitis group (n = 216) and the control group (n = 2288). The periodontitis group was defined as subjects who had one or more teeth with a probing pocket depth (PPD) ≥4 mm. The prevalence of proximal CRNs was significantly higher in the periodontitis group (25.0%) than in the control group (12.3%) (*P* < 0.001). Independent risk factors for proximal CRNs in the multivariate analysis were periodontitis, smoking, age, waist circumference, and triglycerides, and those for proximal advanced CRNs were periodontitis, age, and family history of CRC. However, periodontitis was not a risk factor for overall CRNs and advanced CRNs. Periodontitis was associated with an increased risk of proximal CRNs (odds ratio [OR], 1.525; 95% confidence intervals [95% CI], 1.071–2.172) and proximal advanced CRNs (OR, 2.671; 95% CI, 1.088–6.560). Periodontitis might be associated with proximal CRNs and proximal advanced CRNs. Subject terms: Risk factors, Colorectal cancer

Chun-Han L, Kwon S, Wang L, Polychronidis G, Knudsen MD, Zhon R, Ogino S, Giovannucci EL, Chan AT, Song M (2020). Periodontal disease, tooth loss, and risk of oesophageal and gastric adenocarcinoma: a prospective study. DOI: <http://dx.doi.org/10.1136/gutjnl-2020-321949> At: <https://gut.bmj.com/content/70/3/620> We read with great interest the study by Coker et al  that provided supportive evidence for the role of oral microbiota in gastric cancer. A few studies also highlighted the possible link with oesophageal cancer.2–4 However, there is a lack of robust epidemiologic data on whether periodontal disease and tooth loss, indicators of oral microbial dysbiosis, are associated with these two cancers.

Here, we prospectively examined the association of history of periodontal disease and tooth loss with the risk of oesophageal and gastric adenocarcinoma in 98 459 women from the Nurses’ Health Study (1992–2014) and 49 685 men from the Health Professionals Follow-up Study (1988–2016). Dental measures, demographics, lifestyle, and diet were assessed using validated follow-up questionnaires. Self-reported cancer diagnosis was confirmed by review of medical records. We used Cox proportional hazards models to calculate the hazard ratios (HRs) and 95% confidence intervals (CIs). We also examined the independent association of history of periodontal disease and tooth loss in a joint analysis.

Over 22–28 years of follow-up, we documented 199 cases of oesophageal adenocarcinoma and 238 cases of gastric adenocarcinoma. History of periodontal disease was associated with a 43% and 52% increased risk of oesophageal adenocarcinoma (multivariable-adjusted HR (aHR) 1.43, 95% CI 1.05 to 1.96) and gastric adenocarcinoma (aHR 1.52, 95% CI 1.13 to 2.0) (table …

Lo C-H, Nguyen LH, Wu K, Ogino S, Chan AT, Giovannuci EL, Song M (2020). Periodontal Disease, Tooth Loss, and Risk of Serrated Polyps and Conventional Adenomas. *Cancer Prev Res* 13(8): 699-706. DOI: 10.1158/1940-6207.CAPR-20-0090 At: <https://cancerpreventionresearch.aacrjournals.org/content/13/8/699.abstract> Abstract: Growing data indicate an association between periodontal disease and the development of cancer. However, the evidence for colorectal cancer has been inconsistent and longitudinal study examining its precursor lesions is lacking. We prospectively collected information on periodontal disease and number of tooth loss in the Nurses' Health Study (1992–2002) and the Health Professionals Follow-up Study (1992–2010). Polyp diagnosis was acquired via self-reported questionnaires and confirmed through review of medical records. We used logistic regression to calculate the multivariate-adjusted ORs and 95% confidence intervals (CI) with adjustment for smoking and other known risk factors for periodontal disease and colorectal cancer. In this study, we included 17,904 women and 24,582 men. We documented 2,336 cases of serrated polyps and 4,102 cases of conventional adenomas among 84,714 person-endoscopies throughout follow-up. The ORs of serrated polyps and conventional adenomas comparing individuals with and without periodontal disease were 1.17 (95% CI, 1.06–1.29) and 1.11 (95% CI, 1.02–1.19), respectively. Compared with participants without tooth loss, those who lost ≥4 teeth had 20% (OR, 1.20; 95% CI, 1.03–1.39) greater risk of serrated polyps (Ptrend 0.01). Among never smokers, similar associations with periodontal disease were observed for both serrated polyps (OR, 1.20; 95% CI, 1.02–1.41) and conventional adenomas (OR, 1.12; 95% CI, 1.00–1.26). History of periodontal disease and possibly higher number of tooth loss may modestly increase the risk of developing colorectal precursor lesions.

Shang F-M, Liu H-L (2018).*Fusobacterium nucleatum* and colorectal cancer: A review**.** *World J Gastrointest Oncol*10(3): 71-81. DOI: [10.4251/wjgo.v10.i3.71](https://doi.org/10.4251%2Fwjgo.v10.i3.71)At:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5852398/> **Abstract:** *Fusobacterium nucleatum* (*F. nucleatum*) is a Gram-negative obligate anaerobe bacterium in the oral cavity and plays a role in several oral diseases, including periodontitis and gingivitis. Recently, several studies have reported that the level of *F. nucleatum* is significantly elevated in human colorectal adenomas and carcinomas compared to that in adjacent normal tissue. Several researchers have also demonstrated that *F. nucleatum* is obviously associated with colorectal cancer and promotes the development of colorectal neoplasms. In this review, we have summarized the recent reports on *F. nucleatum* and its role in colorectal cancer and have highlighted the methods of detecting *F. nucleatum* in colorectal cancer, the underlying mechanisms of pathogenesis, immunity status, and colorectal cancer prevention strategies that target *F. nucleatum*. **Keywords:***Fusobacterium nucleatum*, Carcinoma, Colon and rectal carcinoma, Host immunity, Gut microbiome

# Han YW, Shi W, Huang GT, Kinder Haake S, Park NH, Kuramitsu H, Genco RJ. (2000). Interactions between periodontal bacteria and human oral epithelial cells: *Fusobacterium nucleatum* adheres to and invades epithelial cells. *Infect Immun*. 2000:68:3140–3146. At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC97547/> Abstract: Bacteria are causative agents of periodontal diseases. Interactions between oral bacteria and gingival epithelial cells are essential aspects of periodontal infections. Using an in vitro tissue culture model, a selected group of gram-negative anaerobic bacteria frequently associated with periodontal diseases, including Bacteroides forsythus, Campylobacter curvus, Eikenella corrodens, Fusobacterium nucleatum, Porphyromonas gingivalis, and Prevotella intermedia, were examined for their ability to adhere to and invade primary cultures of human gingival epithelial cells (HGEC). The effects of these bacteria on the production of interleukin-8 (IL-8), a proinflammatory chemokine, were also measured. These studies provided an initial demonstration that F. nucleatum adhered to and invaded HGEC and that this was accompanied by high levels of IL-8 secretion from the epithelial cells. The attachment and invasion characteristics of F. nucleatum were also tested using KB cells, an oral epithelial cell line. The invasion was verified by transmission electron microscopy and with metabolic inhibitors. Invasion appeared to occur via a “zipping” mechanism and required the involvement of actins, microtubules, signal transduction, protein synthesis, and energy metabolism of the epithelial cell, as well as protein synthesis by F. nucleatum. A spontaneous mutant, lam, of F. nucleatum, isolated as defective in autoagglutination, was unable to attach to or invade HGEC or KB cells, further indicating the requirement of bacterial components in these processes. Sugar inhibition assays indicated that lectin-like interactions were involved in the attachment of F. nucleatum to KB cells. Investigation of these new virulence phenotypes should improve our understanding of the role of F. nucleatum in periodontal infections.

Rubinstein MR, Wang X, Liu W, Hao Y, Cai G, and Han YW (2013). *Fusobacterium nucleatum* promotes colorectal carcinogenesis by modulating E-cadherin/β-catenin signaling via its FadA adhesin. *Cell Host Microbe* 14, 195–206. DOI: 10.1016/j.chom.2013.07.012

**OH and Liver Cancer**

Oral Health Foundation <https://www.dentalhealth.org/news/startling-new-research-finds-poor-oral-health-can-make-you-more-likely-to-develop-liver-cancer#:~:text=A%20new%20study%20from%20Queen's,develop%20cancer%20of%20the%20liver>

Abed J, Maalouf N, Manson AL, Earl AM, Parhi L, Emgård JEM, Klutstein M, Tayeb S, Almogy G, Atlan KA, Chaushu S, Israeli E, Mandelboim O, Garrett WS and Bachrach G (2020) Colon Cancer-Associated *Fusobacterium nucleatum* May Originate From the Oral Cavity and Reach Colon Tumors via the Circulatory System. *Front. Cell. Infect. Microbiol.* 10:400. DOI: 10.3389/fcimb.2020.00400

<https://www.dentalhealth.org/news/startling-new-research-finds-poor-oral-health-can-make-you-more-likely-to-develop-liver-cancer> (2019).

Paddock C (2019). Study ties unhealthy gums to liver cancer risk. <https://www.medicalnewstoday.com/articles/325528#Reason-for-link-is-unclear>

*Sage* (2019) Poor oral health linked to a 75% increase in liver cancer risk. *ScienceDaily.* Retrieved June 19, 2019 from [www.sciencedaily.com/releases/2019/06/190617125124.htm](http://www.sciencedaily.com/releases/2019/06/190617125124.htm)

**Poor Periodontal Health and Cancer Risk**

Rajesh KS, Thomas D, Hegde S, Kumar MSA (2013). Poor periodontal health: A cancer risk? *J Indian Soc Periodontol* 17(6): 706–710 DOI: [10.4103/0972-124X.124470](https://doi.org/10.4103%2F0972-124X.124470) At:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3917197/> **Abstract:** Evidence indicates that chronic infections and inflammation are associated with increased risk of cancer development. There has also been considerable evidence that proves the interrelationship between bacterial and viral infections and carcinogenesis. Periodontitis is a chronic oral infection thought to be caused by gram-negative anaerobic bacteria in the dental biofilm. Periodontal bacteria and viruses may act synergistically to cause periodontitis. Many studies have shown that periodontal pockets may act as reservoirs for human papilloma virus, cytomegalovirus, Epstein Barr virus, and suspected agents associated with oral cancer. Periodontitis, characterized by epithelial proliferation and migration, results in a chronic release of inflammatory cytokines, chemokines, growth factors, prostaglandins, and enzymes, all of which are associated with cancer development. This review article intends to shed light on the association between periodontal health and carcinogenesis. **Keywords:**Carcinoma, inflammation, microorganisms, poor oral hygiene, virus.

Jewett, A., Hume, W. R., Le, H., Huynh, T. N., Han, Y. W., Cheng, G., et al. (2000). Induction of apoptotic cell death in peripheral blood mononuclear and polymorphonuclear cells by an oral bacterium, *Fusobacterium nucleatum*. *Infect. Immun.* 68, 1893–1898. DOI: 10.1128/IAI.68.4.1893-1898.2000

### Printz C (2021). Study adds evidence to link between gum disease and cancer risk. Researchers observe connection with gastric, esophageal cancer. *Cancer* 127: 495-496. At: <https://acsjournals.onlinelibrary.wiley.com/journal/10970142> DOI: <https://doi.org/10.1002/cncr.33438>

**Oral and Oropharyngeal Cancers**

# Mathur R, Singhavi HR, Malik A, Nair S, Chaturvedi (2019). Role of Poor Oral Hygiene in Causation of Oral Cancer—a Review of Literature. [*Indian J Surg Oncol*](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6414580/) 10(1): 184–195. DOI: [10.1007/s13193-018-0836-5](https://doi.org/10.1007%2Fs13193-018-0836-5) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6414580/> Abstract: Oral squamous cell carcinomas (OSCC) are among the commonest cancers in South East Asia and more so in the Indian subcontinent. The role of tobacco and alcohol in the causation of these cancers is well-documented. Poor oral hygiene (POH) is often seen to co-exist in patients with OSCC. However, the role of poor oral hygiene in the etio-pathogenesis of these cancers is controversial. We decided to evaluate the available literature for evaluating the association of POH with OSCC. A thorough literature search of English-language articles in MEDLINE, PubMed, Cochrane Database of Systematic Reviews, and Web of Science databases was conducted, and 93 relevant articles were short-listed. We found that POH was strongly associated with oral cancers. It aids the carcinogenic potential of other known carcinogens like tobacco and alcohol. Even on adjusting for known confounding factors like tobacco, alcohol use, education, and socio-economic strata, presence of POH exhibits higher odds of developing oral cancer. ****Keywords:****Mouth neoplasm, Oral cancer, Poor oral hygiene, Tooth brushing, Dental visits, Missing teeth.

# Bouvard V et al. (2022). IARC Perspective on Oral Cancer Prevention. *New Engl J Med* 387(21) : 1999-2005. Online at: <https://www.nejm.org/doi/full/10.1056/NEJMsr2210097>

# Mayo Clinic (2022). Mouth Cancer. At. <https://www.mayoclinic.org/diseases-conditions/mouth-cancer/symptoms-causes/syc-20350997>

# CDC(2022). HPV and Oropharyngeal Cancer. At: <https://www.cdc.gov/cancer/hpv/basic_info/hpv_oropharyngeal.htm#:~:text=HPV%20can%20infect%20the%20mouth,cancers%20in%20the%20United%20States>. **Human papillomavirus (HPV) can cause serious health problems, including warts and cancer.**

# Amer Cancer Soc (2011). Risk Factors for Oral Cavity and Oropharyngeal Cancers. At: <https://www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/causes-risks-prevention/risk-factors.html> *J Maxillofac Oral Surg*. 2011 Jun; 10(2): 132–137. A risk factor is anything that increases a person’s chance of getting a disease such as cancer. Different cancers have different risk factors. Some risk factors, like smoking, can be changed. Others, like a person’s age or family history, can’t be changed. But risk factors don't tell us everything. Having a risk factor, or even many, does not mean that a person will get the disease. And many people who get the disease have few or no known risk factors.

Ram H, Sarkar J, Kumar H, Konwar R, Bhatt MLB, Mohammad S (2011). Oral Cancer: Risk Factors and Molecular Pathogenesis. Online 2011 Apr 22. DOI: [10.1007/s12663-011-0195-z](https://doi.org/10.1007%2Fs12663-011-0195-z) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177522/> Abstract: **Introduction** Oral cancer is one of the most common cancers and it constitutes a major health problem particularly in developing countries. It is one of the leading causes of death. Tobacco and alcohol consumption appears to be the major determinants of oral cancer. **Materials and methods** The literature search was carried out in NCBI Pubmed database using keywords “oral cancer”, “risk factor”, “epidemiology” and “patho\*”. Some basic information was also obtained from textbook and medical university websites. **Results** Several risk factors have been well characterized to be associated with oral cancer with substantial evidences. The development of oral cancer is a multistep process involving the accumulation of genetic and epigenetic alterations in key regulatory genes. Experimental pathological studies of oral cancer in animal models and direct molecular genetic analysis of oral cancer subjects in recent times have revealed a substantial amount of knowledge on specific gene alterations or other genetic mechanisms involved in initiation and subsequent progression. **Conclusion** Considering known risk factors, oral cancer appears to be to a certain extent, a preventable disease. Recent development of molecular picture of pathoprogression and molecular genetic tools opens the avenue for easier diagnosis, better prognostication and efficient therapeutic management. **Keywords:**Oral cancer, Epidemiology, Molecular biology, Risk factor

# Sadri I (2014). Should marijuana users be worried that smoking causes oral cancer? *Dentistry IQ* At: <https://www.dentistryiq.com/dentistry/oral-cancer/article/16360502/should-marijuana-users-be-worried-that-smoking-causes-oral-cancer> Introduction: For decades, oral cancer was strictly linked to tobacco and alcohol abuse. However in recent years, new cases of oral cancer among nontobacco users have been linked to the HPV virus, and oral cancer awareness has become more mainstream with high-profile patients. As a great number of nontobacco users use marijuana habitually, it begs the question, *Does marijuana use cause oral cancer?* Dr. Iman Sadri addresses the question here.

# Henry JA, Oldfield WLJ, Kon OM (2003). Comparing cannabis with tobacco. *Brit Med J* 326(7396): 942–943. DOI: [10.1136/bmj.326.7396.942](https://doi.org/10.1136%2Fbmj.326.7396.942) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1125867/>

# Esophageal Cancer

# Zhang J, Belloco R, Sandborg-Englund G, Jingru Y, Chen MS, Ye W (2022). Poor Oral Health and Esophageal Cancer Risk: A Nationwide Cohort Study. *Cancer Epidemiol Biomarkers Prev* 31(7):1418-1425 DOI: [10.1158/1055-9965.EPI-22-0151](https://doi.org/10.1158/1055-9965.epi-22-0151) At: <https://pubmed.ncbi.nlm.nih.gov/35477184/> Abstract: ****Background:****Previous research indicates that poor dental health increases risks for certain types of cancers, including esophageal cancer. This study aimed to investigate the association with esophageal cancer using Swedish Dental Health Register. ****Methods:****This is a prospective cohort study. The exposures were dental diagnoses classified into healthy, caries, root canal infection, mild inflammation, and periodontitis, as well as number of remaining teeth, at baseline and during multiple visits. The outcome was the incidence of esophageal cancer, which was further divided into esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC). Cox proportional hazards models were used to estimate hazard ratios (HR) and its corresponding confidence intervals (CI). ****Results:****A total of 5,042,303 individuals were included in the study and 1,259 EAC and 758 ESCC cases were identified. Root canal infection at baseline was associated with 41% higher risk for EAC (HR, 1.41; 95% CI, 1.10-1.82), whereas periodontitis at baseline was linked to 32% and 45% higher risks for respective histopathological subtypes (HR for EAC, 1.32; 95% CI, 1.13-1.53; HR for ESCC, 1.45; 95% CI, 1.20-1.75). Fewer remaining teeth at baseline also increased the risks for both histopathological types of esophageal cancer, with a dose-response effect (Ptrend < 0.01). Cox regression analyses with time-varying exposures corroborated the above-mentioned results. ****Conclusions:****Impaired dental health before cancer diagnosis is associated with excess risks for both histopathological subtypes of esophageal cancer. ****Impact:****Our study provided corroborating evidence for the association between poor oral health and esophageal cancer risk. ©2022 American Association for Cancer Research.

Muszyński D, Kudra A, Sobocki BK, Folwarski M, Vitale E, Filetti V, Dudzic W, Kazmierczak-Siedlecka, Polom K (2022). Esophageal cancer and bacterial part of gut microbiota - A multidisciplinary point of view.DOI: [10.3389/fcimb.2022.1057668](https://doi.org/10.3389/fcimb.2022.1057668) At: <https://pubmed.ncbi.nlm.nih.gov/36467733/> There is an urgent need to search for new screening methods that allow early detection of esophageal cancer and thus achieve better clinical outcomes. Nowadays, it is known that the esophagus is not a sterile part of the gastrointestinal tract. It is colonized with various microorganisms therefore a "healthy" esophageal microbiome exists. The dysbiotic changes of esophageal microbiome can lead to the development of esophageal diseases including esophageal cancer. There is a strong consensus in the literature that the intestinal microbiome may be involved in esophageal carcinogenesis. Recently, emphasis has also been placed on the relationship between the oral microbiome and the occurrence of esophageal cancer. According to recent studies, some of the bacteria present in the oral cavity, such as *Tannerella forsythia*, *Streptococcus anginosus*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Fusobacterium nucleatum* may contribute to the development of this cancer. Moreover, the oral microbiome of patients with esophageal cancer differs significantly from that of healthy individuals. This opens new insights into the search for a microbiome-associated marker for early identification of patients at high risk for developing this cancer. **Keywords:**16S rRNA gene sequencing; esophageal cancer; esophageal microbiome; gut microbiome; oral microbiome. Copyright © 2022 Muszyński, Kudra, Sobocki, Folwarski, Vitale, Filetti, Dudzic, Kaźmierczak-Siedlecka and Połom.

# Xie F-J, Zhang Y-P, Zheng O-Q, Jin H-C, Wang F-L, Chen M, Shao L, Zou D-H, Yu X-M, Mao W-M (2013). *Helicobacter pylori* infection and esophageal cancer risk: an updated meta-analysis. At: <https://pubmed.ncbi.nlm.nih.gov/24106412/> DOI: [10.3748/wjg.v19.i36.6098](https://doi.org/10.3748/wjg.v19.i36.6098) Abstract: ****Aim:****To clarify the association between Helicobacter pylori (H. pylori) infection and the risk of esophageal carcinoma through a meta-analysis of published data. ****Methods:****Studies which reported the association between H. pylori infection and esophageal cancer published up to June 2013 were included. The odds ratios (ORs) and corresponding 95%CIs of H. pylori infection on esophageal cancer with respect to health control groups were evaluated. Data were extracted independently by two investigators and discrepancies were resolved by discussion with a third investigator. The statistical software, STATA (version 12.0), was applied to investigate heterogeneity among individual studies and to summarize the studies. A meta-analysis was performed using a fixed-effect or random-effect method, depending on the absence or presence of significant heterogeneity. ****Results:****No significant association between H. pylori infection and esophageal squamous cell carcinoma (ESCC) risk was found in the pooled overall population (OR = 0.97, 95%CI: 0.76-1.24). However, significant associations between H. pylori infection and ESCC risk were found in Eastern subjects (OR = 0.66, 95%CI: 0.43-0.89). Similarly, cytotoxin-associated gene-A (CagA) positive strains of infection may decrease the risk of ESCC in Eastern subjects (OR = 0.77, 95%CI: 0.65-0.92), however, these associations were not statistically significant in Western subjects (OR = 1.26, 95%CI: 0.97-1.63). For esophageal adenocarcinoma (EAC) the summary OR for H. pylori infection and CagA positive strains of infection were 0.59 (95%CI: 0.51-0.68) and 0.56 (95%CI: 0.45-0.70), respectively. ****Conclusion:****H. pylori infection is associated with a decreased risk of ESCC in Eastern populations and a decreased risk of EAC in the overall population. ****Keywords:****Cancer risk; Esophageal carcinoma; Helicobacter pylori; Meta-analysis.

# Lindkvist B, Johansen D, Stacks T, Concin H, Bjørge T, Almquist M, Häggström C, Engeland A, Hallmans G, Nagel G, Jonsson H, Selmer R, Ulmer H, Tretli S, Stattin P, Manjer J (2014). Metabolic risk factors for esophageal squamous cell carcinoma and adenocarcinoma: a prospective study of 580,000 subjects within the Me-Can project. *BMC Cancer* 14:103 DOI: [10.1186/1471-2407-14-103](https://doi.org/10.1186/1471-2407-14-103) At: <https://pubmed.ncbi.nlm.nih.gov/24548688/> Abstract: **Background:**Obesity is associated with an increased risk of esophageal adenocarcinoma (EAC) and a decreased risk of esophageal squamous cell carcinoma (ESCC). However, little is known about the risk of EAC and ESCC related to other metabolic risk factors. We aimed to examine the risk of EAC and ESCC in relation to metabolic risk factors, separately and combined in a prospective cohort study. ****Methods:****The Metabolic Syndrome and Cancer cohort includes prospective cohorts in Austria, Norway and Sweden, with blood pressure, lipids, glucose and BMI available from 578 700 individuals. Relative risk (RR) for EAC and ESCC was calculated using Cox's proportional hazards analysis for metabolic risk factors categorized into quintiles and transformed into z-scores. The standardized sum of all z-scores was used as a composite score for the metabolic syndrome (MetS). ****Results:****In total, 324 histologically verified cases of esophageal cancer were identified (114 EAC, 184 ESCC and 26 with other histology). BMI was associated with an increased risk of EAC (RR 7.34 (95% confidence interval, 2.88-18.7) top versus bottom quintile) and negatively associated with the risk of ESCC (RR 0.38 (0.23-0.62)). The mean value of systolic and diastolic blood pressure (mid blood pressure) was associated with the risk of ESCC (RR 1.77 (1.37-2.29)). The composite MetS score was associated with the risk of EAC (RR 1.56 (1.19-2.05) per one unit increase of z-score) but not ESCC. ****Conclusions:****In accordance with previous studies, high BMI was associated with an increased risk of EAC and a decreased risk of ESCC. An association between high blood pressure and risk of ESCC was observed but alcohol consumption is a potential confounding factor that we were not able to adjust for in the analysis. The MetS was associated with EAC but not ESCC. However this association was largely driven by the strong association between BMI and EAC. We hypothesize that this association is more likely to be explained by factors directly related to obesity than the metabolic state of the MetS, considering that no other metabolic factor than BMI was associated with EAC.

# Abnet CC, Kamangar F, Islami F, Nasrollahzadeh D, Brennan P, Aghcheli K, Merat S, Pourshams A, Marjani HA, Ebadati A, Sotoudeh M, Boffetta P, Malekzadeh R, Dawsey SM (2008). Tooth loss and lack of regular oral hygiene are associated with higher risk of esophageal squamous cell carcinoma. *Cancer Epidemiol Biomarkers Prev*. 17(11): 3062-8. DOI: 10.1158/1055-9965.EPI-08-0558. PMID: 18990747; PMCID: PMC2586052. At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2586052/> Abstract: We tested the association between tooth loss and oral hygiene and the risk of esophageal squamous cell carcinoma (ESCC) in people living in a high risk area of Iran. We used a case-control study of pathologically-confirmed ESCC cases (N=283) and controls (N=560) matched on sex, age, and neighborhood. Subjects with ESCC had significantly more decayed, missing, or filled teeth with a median (interquartile range) of 31 ([23](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2586052/#R23)-[32](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2586052/#R32)) compared to controls 28 ([2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2586052/#R2)-[32](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2586052/#R32)) (P=0.0045). And subjects with ESCC were significantly more likely than controls to fail to practice regular oral hygiene, 78% versus 58%. In multivariate adjusted conditional logistic regression models having 32 decayed, missing, or filled teeth compared to ≤15 conferred an OR (95% CI) of 2.10 (1.19-3.70). Compared to daily tooth brushing, practicing no regular oral hygiene conferred an OR (95% CI) of 2.37 (1.42-3.97). Restricting the analysis to subjects that had never smoked tobacco did not materially alter these results. We found significant associations between two markers of poor oral hygiene, a larger number of decayed, missing, or filled teeth and lack of daily tooth brushing, and risk of ESCC in a population at high risk for ESCC where many cases occur in never smokers. Our results are consistent with several previous analyses in other high risk populations. Keywords: Tooth loss, tooth brushing, esophagus, squamous, cancer.

# Poor Oral Health and Cancer Risk

# Zhang X, Liu B, Lynn HS, Chen K, Dai H (2022). Poor oral health and risks of total and site-specific cancers in China: A prospective cohort study of 0.5 million adults. *The Lancet: eclinical Medicine* 101330. DOI: <https://doi.org/10.1016/j.eclinm.2022.101330> At: <https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00060-8/fulltext> Summary: Poor oral health and risks of total and site-specific cancers in China: A prospective cohort study of 0.5 million adults. Background: There is a strong connection There is a strong connection between oral health and overall wellness. We aim to examine the association between poor oral health and the risk of developing or dying of cancer, and whether the

association differs by residential area. **Methods:** Between 2004 and 2008, a total of 510,148 adults free of cancer were included from the China Kadoorie Biobank study and thereafter followed up to 2015. Poor oral health was assessed from a self-reported baseline questionnaire and defined as a combination of rarely brushing teeth and always gum bleeding. We used Cox proportional hazards models to estimate the hazard ratio (HR) of cancer risk and its associated 95% confidence interval (CI) according to oral health status. **Findings:** Overall, 14.9% of participants (19.7% in rural areas and 8.8% in urban areas) reported poor oral health at baseline. After 4,602,743 person-years of follow-up, we identified 23,805 new cancer cases and 11,973 cancer deaths, respectively. Poor oral health was associated with higher risks of total cancer incidence (HR: 1.08, 95% CI: 1.04–1.12) and death (HR: 1.10, 95% CI: 1.05–1.16). For the site-specific cancers, poor oral health was significantly associated with higher risk of stomach cancer incidence (cases: 2964, HR: 1.10, 95% CI: 1.00–1.22), esophageal cancer incidence (cases: 2119, HR: 1.19, 95% CI: 1.07–1.33), esophageal cancer death (cases: 1238, HR: 1.29, 95% CI: 1.12–1.49), liver cancer incidence (cases: 2565, HR: 1.18, 95% CI: 1.06–1.32), and liver cancer death (cases: 1826, HR: 1.20, 95% CI: 1.05–1.36). This positive association was stronger among rural residents compared to urban residents (interaction test P < 0.01). **Interpretation:** Our findings indicate that poor oral health is associated with higher risk for cancers, especially digestive system cancers. Promotion of oral health in the general population, especially for rural residents, could have valuable public health significance in preventing major systemic diseases. **Funding:** Supported by grants (2021YFC2500400, 2016YFC0900500, 2016YFC0900501, 2016YFC0900504) from the National Key Research and Development Program of China, grants from the Kadoorie Charitable Foundation in Hong Kong and grants grants (088158/Z/09/Z, 104085/Z/14/Z, 202922/Z/16/Z) from Wellcome Trust in the UK. CKB is supported by the Kadoorie Charitable Foundation (KCF) in Hong Kong.

**Poor Dental Health and Pancreatic Cancer Risk**

Yu J, Ploner A, Chen MS, Zhang J, Sandborg-Englund G, Ye W (2022). Poor dental health and risk of pancreatic cancer: a nationwide registry-based cohort study in Sweden, 2009–2016. *Brit J Cancer* 127: 2133–2140. DOI: <https://doi.org/10.1038/s41416-022-02018-8> **Abstract:** Background: Previous studies have reported inconsistent results regarding the association between poor dental health and pancreatic cancer risk. This study aimed to assess this association using a well-functioning nationwide dental health registry in Sweden. Methods: Information of exposures (dental caries, root canal infection, mild inflammation, and periodontitis; the number of teeth) was ascertained from the Swedish Dental Health Register, and occurrence of pancreatic cancer was identified from both cancer and cause of death registries. Hazard ratios (HRs) were estimated using Cox models. Results: During a median of 7.2 years of follow-up, 10,081 pancreatic cancers were identified among 5,889,441 individuals. Compared with the healthy status, a higher risk of pancreatic cancer was observed in individuals with root canal infection, mild inflammation, and periodontitis in the <50 age group (*P* for trend <0.001). In the 50–70 age group, only the subgroup with periodontitis had an excess risk (multivariable-adjusted HR = 1.20, 95% confidence interval [CI] 1.11–1.29). No positive association with statistical significance was observed in the 70+ age group. Individuals with fewer teeth tended to have a higher risk in all age groups. Conclusions: Our results confirmed the association between poor dental health

**Oral Microbiome and Pancreatic Cancer Risk**

Fan X, Alekseyenko AV, Wu J, Peters BA, Jacobs EJ, Gapstur SM, Purdue MP, Abnet CC, Stolzenberg-Solomon R, Miller G, Ravel J, Hayes RB, Ahn J (2016). Human oral microbiome and prospective risk for pancreatic cancer: a population-based nested case-control study. At: <https://gut.bmj.com/content/67/1/120.abstract> DOI: <http://dx.doi.org/10.1136/gutjnl-2016-312580> **Abstract:** **Objective** A history of periodontal disease and the presence of circulating antibodies to selected oral pathogens have been associated with increased risk of pancreatic cancer; however, direct relationships of oral microbes with pancreatic cancer have not been evaluated in prospective studies. We examine the relationship of oral microbiota with subsequent risk of pancreatic cancer in a large nested case–control study. **Design:** We selected 361 incident adenocarcinoma of pancreas and 371 matched controls from two prospective cohort studies, the American Cancer Society Cancer Prevention Study II and the National Cancer Institute Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. From pre-diagnostic oral wash samples, we characterised the composition of the oral microbiota using bacterial 16S ribosomal RNA (16S rRNA) gene sequencing. The associations between oral microbiota and risk of pancreatic cancer, controlling for the random effect of cohorts and other covariates, were examined using traditional and L1-penalised least absolute shrinkage and selection operator logistic regression. **Results:** Carriage of oral pathogens, Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans, were associated with higher risk of pancreatic cancer (adjusted OR for presence vs absence=1.60 and 95% CI 1.15 to 2.22; OR=2.20 and 95% CI 1.16 to 4.18, respectively). Phylum Fusobacteria and its genus Leptotrichia were associated with decreased pancreatic cancer risk (OR per per cent increase of relative abundance=0.94 and 95% CI 0.89 to 0.99; OR=0.87 and 95% CI 0.79 to 0.95, respectively). Risks related to these phylotypes remained after exclusion of cases that developed within 2 years of sample collection, reducing the likelihood of reverse causation in this prospective study. **Conclusions”** This study provides supportive evidence that oral microbiota may play a role in the aetiology of pancreatic cancer.

# OH Care to Reduce HPV Risk

# Casey SM, Paiva T, Perkins RB, Villa A, Murray EJ (2022). Could oral health care professionals help increase human papillomavirus vaccination rates by engaging patients in discussions? DOI: <https://doi.org/10.1016/j.adaj.2022.09.014> *J Amer Den Assoc* At: <https://jada.ada.org/article/S0002-8177(22)00608-0/fulltext> Abstract: Background: Oral health care professionals are well positioned to contribute to the prevention of human papillomavirus

care (HPV)–related oropharyngeal and other HPV-related cancers through engaging patients in conversations about HPV vaccination. This scoping review evaluates evidence regarding oral health care provider knowledge of, and discussion related to, HPV prevention, transmission, and associated risks, including oropharyngeal cancer. This review outlines relevant barriers to, and facilitators of, this knowledge and discussion. In addition, to determine the potential population that could be reached by an oral health care provider for a conversation about HPV vaccination, this review evaluates the prevalence of HPV vaccination as well as dental visits in a US population. **Types of Studies Reviewed:** Four databases were systematically searched (MEDLINE [PubMed], EMBASE, APA PsycInfo, Cumulative Index to Nursing and Allied Health Literature). Studies written in English and conducted in the United States were eligible. Eligibility criteria were not restricted to publication year or oral health care provider type. Behavioral Risk Factor Surveillance System 2018 data were analyzed to evaluate the prevalence of HPV vaccination and dental visits among patients aged 18 through 49 years. **Results:** After duplicate record removal and second-stage screening, 32 full-text articles were retrieved, and data were independently extracted by 2 reviewers. Twenty-four studies were included in this review. Knowledge regarding HPV prevalence, transmission, disease processes, and risks varied. In general, discussions related to HPV in dental settings were infrequent. Facilitators to improve knowledge and discussion included guidance from professional dental organizations, education, and communication skills. Behavioral Risk Factor Surveillance System data showed that most people who are not vaccinated have visited their oral health care providers in the past year, highlighting the potential role of oral health care providers regarding discussion of HPV and promoting awareness and acceptance of vaccination. **Conclusions and Practical Implications:** This review indicates that discussions related to HPV were infrequent in the oral health care setting, which may be related to lack of knowledge and communication skills among oral health care professionals; however, evidence exists supporting the interest of oral health care professionals in improving vaccine uptake to prevent oropharyngeal cancer.

Bui TC, Markham CM, Ross MW, Mullen PD (2013). Examining the association between oral health and oral HPV infection. DOI: [10.1158/1940-6207.CAPR-13-0081](https://doi.org/10.1158/1940-6207.capr-13-0081) Cancer Prev Res (Phila) 6(9): 917-924. At: <https://pubmed.ncbi.nlm.nih.gov/23966202/> **Abstract:** Oral human papillomavirus (HPV) infection is the cause of 40% to 80% of oropharyngeal cancers; yet, no published study has examined the role of oral health in oral HPV infection, either independently or in conjunction with other risk factors. This study examined the relation between oral health and oral HPV infection and the interactive effects of oral health, smoking, and oral sex on oral HPV infection. Our analyses comprised 3,439 participants ages 30 to 69 years for whom data on oral HPV and oral health were available from the nationally representative 2009-2010 National Health and Nutrition Examination Survey. Results showed that higher unadjusted prevalence of oral HPV infection was associated with four measures of oral health, including self-rated oral health as poor-to-fair [prevalence ratio (PR) = 1.56; 95% confidence interval (CI), 1.25-1.95], indicated the possibility of gum disease (PR = 1.51; 95% CI, 1.13-2.01), reported use of mouthwash to treat dental problems in the past week (PR = 1.28; 95% CI, 1.07-1.52), and higher number of teeth lost (Ptrend = 0.035). In multivariable logistic regression models, oral HPV infection had a statistically significant association with self-rated overall oral health (OR = 1.55; AA95% CI, 1.15-2.09), independent of smoking and oral sex. In conclusion, poor oral health was an independent risk factor of oral HPV infection, irrespective of smoking and oral sex practices. Public health interventions may aim to promote oral hygiene and oral health as an additional measure to prevent HPV-related oral cancers.

# OH and Leukemia

# Owlia F, Ansarinia A, Ardakani HV (2021). Oral neglect as a marker of broader neglect: a cross-sectional investigation of orodental consultation letter of leukemic admitted patients in Iran. *BMC Oral Health* 21, Article number 413. At: <https://bmcoralhealth.biomedcentral.com/articles/10.1186/s12903-021-01775-x> DOI: <https://doi.org/10.1186/s12903-021-01775-x> Abstract: Background: Leukemia is the main malignant hematologic disease of children with different oral manifestations and clinical features. Attention to the oral manifestations is essential for better management. This study assessed the oral and dental consultations conducted in the admitted leukemic patients of an Iranian teaching hospital. Methods: In this descriptive cross-sectional study, medical records of patients admitted in Yazd Shahid Sadoughi Hospital were evaluated. Records of 300 patients with leukemia were randomly selected. Data including demographic information on age, sex, type of oral problems, prescribed instructions and leukemia type were extracted from archived records and registered on the checklist. Finally, Data were analyzed by SPSS17 using Chi-square test. Results: The results showed the average age ± SD of patients were 24.36 ± 23.91 with a range of 4 days to 86 years. Among 300 files, 167 belonged to males (55.7%) and 133 pertained to females (44.3%). The most prevalent type of underlying disease was ALL (Acute lymphocytic leukemia) with the frequency of 180 persons (60%). Only 12 (4%) of patients were referred to a specialist due to oral problems. Of all cases of consultation requests, 75% received consultation because of dental problems and 25% for mucosal problems. There was a statistically significant difference between age and consultation request (P = 0.002). Conclusions: According to the results of this study, orodental consultation request rate for admitted leukemic patients was low. Pediatric hematologist and oncologists to some extent had more interest to consult due to oral and dental problems rather than others.

Lim H-C, Kim C-S. (2014). Oral Signs of acute leukemia for early detection. *J Periodontal Implant Sci.* 44(6): 293-299. DOI**:** <https://doi.org/10.5051/jpis.2014.44.6.293>At: <https://jpis.org/DOIx.php?id=10.5051/jpis.2014.44.6.293> **Abstract : Purpose:** Systemic disease can manifest oral signs at an early phase, which may be crucial for the diagnosis and timing of treatment. This report describes two patients who presented with gingival enlargement as an early sign of acute leukemia. **Methods:** Two patients presented with oral symptoms including severe gingival enlargement. The progress of their symptoms was associated with underlying systemic disease. **Results:** The patients were transferred to the Department of Hematology and diagnosed with acute myelomonocytic leukemia. They received appropriate treatment and survived. **Conclusions:** Gingival enlargement can be caused by underlying systemic diseases. Accurate diagnosis and timely referral are important for preventing a fatal situation. It must be emphasized that some oral signs and symptoms may be closely correlated with systemic diseases.

**Orodental complications in Childhood Acute Myeloid Leukemia**

Cammarata-Scalisi F, Girardi K**,** Strocchio L, Merli P, Garret-Bernardin A, Galeotti A, Magliarditi F, Inserra A, Callea M (2020).Oral Manifestations and Complications in Childhood Acute Myeloid Leukemia**.** DOI: [10.3390/cancers12061634](https://doi.org/10.3390/cancers12061634) At: <https://pubmed.ncbi.nlm.nih.gov/32575613/>   
*Cancers (Basel)* 2020 Jun 19;12(6):163. **Abstract:** Acute myeloid leukemia (AML) is a heterogeneous group of diseases, whose classification is based on lineage-commitment and genetics. Although rare in childhood, it is the most common type of acute leukemia in adults, accounting for 80% of all cases in this age group. The prognosis of this disease remains poor (especially in childhood, as compared to acute lymphoblastic leukemia); however, overall survival has significantly improved over the past 30 years. The health of the oral cavity is a remarkable reflection of the systemic status of an individual. Identification of the signs and symptoms of oral lesions can act as a warning sign of hidden and serious systemic involvement. Moreover, they may be the presenting feature of acute leukemia and provide important diagnostic indicators. Primary oral alterations are identified in up to 90% of cases of acute myeloid leukemia and consist of petechiae, spontaneous bleeding, mucosal ulceration, gingival enlargement with or without necrosis, infections, hemorrhagic bullae on the tongue, and cracked lips. Poor oral hygiene is a well-known risk factor for local and systemic infectious complications. Oro-dental complications due to AML treatment can affect the teeth, oral mucosa, soft and bone tissue, and contribute to opportunistic infections, dental decay, and enamel discoloration. The treatment of acute myeloid leukemia is still associated with high mortality and morbidity. The management is multimodal, involving aggressive multidrug chemotherapy and, in most cases, allogenic bone marrow transplantation. Periodontal and dental treatment for patients with leukemia should always be planned and concerted with hematologists. **Keywords:**leukemia; acute myeloid leukemia; oral manifestations; treatment.

**Periodontal Disease and Breast Cancer**

Freudenheim JL, Genco RJ, LaMonte MJ, Millen AE, Hovey KM, Mai X, Nwizu N, Andrews CA, Wactawski-Wende J. Periodontal Disease and Breast Cancer: Prospective Cohort Study of Postmenopausal Women. Cancer Epidemiol Biomarkers Prev. 2016 Jan;25(1):43-50. doi: 10.1158/1055-9965.EPI-15-0750. Epub 2015 Dec 21. DOI: [10.1158/1055-9965.EPI-15-0750](https://doi.org/10.1158/1055-9965.epi-15-0750) At: <https://pubmed.ncbi.nlm.nih.gov/26689418/> **Abstract: Background:**Periodontal disease has been consistently associated with chronic disease; there are no large studies of breast cancer, although oral-associated microbes are present in breast tumors. **Methods:**In the Women's Health Initiative Observational Study, a prospective cohort of postmenopausal women, 73,737 women without previous breast cancer were followed. Incident, primary, invasive breast tumors were verified by physician adjudication. Periodontal disease was by self-report. HRs and 95% confidence intervals (CI) were estimated by Cox proportional hazards, adjusted for breast cancer risk factors. Because the oral microbiome of those with periodontal disease differs with smoking status, we examined associations stratified by smoking. **Results:**2,124 incident, invasive breast cancer cases were identified after mean follow-up of 6.7 years. Periodontal disease, reported by 26.1% of women, was associated with increased breast cancer risk (HR 1.14; 95% CI, 1.03-1.26), particularly among former smokers who quit within 20 years (HR 1.36; 95% CI, 1.05-1.77). Among current smokers, the trend was similar (HR 1.32; 95% CI, 0.83-2.11); there were few cases (n = 74) and the CI included the null. The population attributable fraction was 12.06% (95% CI, 1.12-21.79) and 10.90% (95% CI, 10.31-28.94) for periodontal disease among former smokers quitting within 20 years and current smokers, respectively. **Conclusion:**Periodontal disease, a common chronic inflammatory disorder, was associated with increased risk of postmenopausal breast cancer, particularly among former smokers who quit in the past 20 years. **Impact:**Understanding a possible role of the oral microbiome in breast carcinogenesis could impact prevention. ©2015 American Association for Cancer Research.