

Articles

Relevant Articles to Medical Dental Integration

Dental Practice and Prediabetes and Diabetes

Am Diabetes Assoc SoC2020 Diabetes Care Volume 43, Supplement 1, January 2020 Screening in Dental Practices Because periodontal disease is associated with diabetes, the utility of screening in a dental setting and referral to primary care as a means to improve the diagnosis of prediabetes and diabetes has been explored (69–71), with one study estimating that 30% of patients ≥ 30 years of age seen in general dental practices had dysglycemia (71). Further research is needed to demonstrate the feasibility, effectiveness, and cost-effectiveness of screening in this setting. 69. Lalla E, Kunze C, Burkett S, Lamster IB. Dental Findings and Identification of undiagnosed hyperglycemia. *J Dent Res* 2013; 92: 808- 892. 70. Lalla E, Cheng B, Kunzel C, Burkett S, Lamster IB. Dental findings and identification of undiagnosed hyperglycemia. *J Dent Res* 2013;92:888–892 71. Herman WH, Taylor GW, Jacobson JJ, Burke R, Brown MB. Screening for prediabetes and type 2 diabetes in dental offices. *J Public Health Dent* 2015;75:175–182 Table 4.4—Referrals for initial care management c Eye care professional for annual dilated eye exam c Family planning for women of reproductive age c Registered dietitian nutritionist for medical nutrition therapy c Diabetes self-management education and support c Dentist for comprehensive dental and periodontal examination c Mental health professional, if indicated Periodontal Disease Periodontal disease is more severe, and may be more prevalent, in patients with diabetes than in those without and has been associated with higher A1C levels (94–96). Longitudinal studies suggest that people with periodontal disease have higher rates of incident diabetes. Current evidence suggests that periodontal disease adversely affects diabetes outcomes, although evidence for treatment benefits remains controversial (24,97). In a randomized clinical trial, intensive periodontal treatment was associated with better glycemic control (A1C 8.3% vs. 7.8% in control subjects and the intensive-treatment group, respectively) and reduction in inflammatory markers after 12 months of follow-up (98). 24. Borgnake WS, Ylöstalo PV, Taylor GW, Genco RJ. Effect of periodontal disease on diabetes: systematic review of epidemiologic observational evidence. *J Periodontol* 2013; 84(Suppl.): S135–S152 94. Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A, Batayha WQ. Periodontal status of diabetics compared with nondiabetics: a metaanalysis. *J Diabetes Complications* 2006;20:59–68 95. Casanova L, Hughes FJ, Preshaw PM. Diabetes and periodontal disease: a two-way relationship. *Br Dent J* 2014;217:433–437 A, Batayha WQ. Periodontal status of diabetics compared with nondiabetics: a metaanalysis. *J Diabetes Complications* 2006;20:59–68 95. Casanova L, Hughes FJ, Preshaw PM. Diabetes and periodontal disease: a two-way relationship. *Br Dent J* 2014;217:433–437 96. Eke PI, Thornton-Evans GO, Wei L, Borgnacke WS, Dye BA, Genco RJ. Periodontitis in US adults: National Health and Nutrition Examination Survey 2009-2014. *J Am Dent Assoc* 2018;149:576–588.e6 97. Simpson TC, Weldon JC, Worthington HV, et al. Treatment of periodontal disease for glycaemic control in people with diabetes mellitus. *Cochrane Database Syst Rev* 2015 11: CD004714 98. D’Aiuto F, Gkranias N, Bhowruth D, et al.; TASTE Group. Systemic effects of periodontitis treatment in patients with type 2 diabetes: a 12 month, single-centre, investigator-masked, randomised trial. *Lancet Diabetes Endocrinol* 2018; 6:954–965 Index: periodontal disease, S4, S22, S45 What I have on file for topics: • Fisketjon PM, Johnson EL (2018). Periodontal Disease and Diabetes: Perceptions, Communication, and Referral Between

Rural Primary Care Physicians and Dentists. *Diabetes Spectrum*

ds170049. <https://doi.org/10.2337/ds17-0049> At:

<https://spectrum.diabetesjournals.org/content/early/2018/04/06/ds17-0049> Abstract:

Background and objective. Connections between oral health and systemic disease, specifically diabetes, are well described in the literature. Screening strategies for diabetes in dental settings and dental screenings in diabetes care settings exist. The purpose of this study was to evaluate the communication and referral patterns between dentists and physicians in a rural state with respect to recognition of dental disease and diabetes. Methods. Surveys were sent to the members of the North Dakota Academy of Family Physicians, the North Dakota Medical Association, and the North Dakota Dental Association. Results. Overall, 92 responses were collected, with 100% of responding physicians and 55% of responding dentists answering “yes” to a perceived link between oral and systemic health. Physician respondents tended to make a referral for dental evaluation in patients with prediabetes or diabetes more often than dentists referred patients with periodontal disease to physicians. Conclusion. Awareness of the link between dental disease and diabetes and of the need for referral is higher among physicians than among dentists. Opportunity exists to improve awareness and increase referrals. • Wisconsin Dept. of Health Services (2020). Wisconsin Diabetes Mellitus Essential Care Guidelines. At:

<https://www.dhs.wisconsin.gov/diabetes/guidelines.htm> Oral Care: (1) Medical-Dental Team Referral

Form: <https://www.dhs.wisconsin.gov/publications/p49356-med-dent.pdf> (2) Diabetes: Screening

Tool for Inspection of Gums and Teeth: <https://www.dhs.wisconsin.gov/publications/p49356-gums.pdf> • Verhulst MJL, Teeuw WJ, Bizzarro S et al (2019). A rapid, non-invasive tool for

periodontitis screening in a medical care setting. *BMC Oral Health* (19) 87.

<https://doi.org/10.1186/s12903-019-0784-7> At:

<https://doi.org/10.1186/s12903-019-0784-7> At:

<https://bmcoralhealth.biomedcentral.com/articles/10.1186/s12903-019-0784-7> Abstract:

Background - Since periodontitis is bi-directionally associated with several systemic diseases, such as diabetes mellitus and cardiovascular diseases, it is important for medical professionals in a non-dental setting to be able examine their patients for symptoms of periodontitis, and urge them to visit a dentist if necessary. However, they often lack the time, knowledge and resources to do so. We aim to develop and assess “quick and easy” screening tools for periodontitis, based on self-reported oral health (SROH), demographics and/or salivary biomarkers, intended for use by medical professionals in a nondental setting. Methods - Consecutive, new patients from our outpatient clinic were recruited. A SROH questionnaire (8 questions) was conducted, followed by a 30 s oral rinse sampling protocol. A complete clinical periodontal examination provided the golden standard periodontitis classification: no/mild, moderate or severe periodontitis. Total periodontitis was defined as having either moderate or severe. Albumin and matrix metalloproteinase-8 concentrations, and chitinase and protease activities were measured in the oral rinses. Binary logistic regression analyses with backward elimination were used to create prediction models for both total and severe periodontitis. Model 1 included SROH, demographics and biomarkers. The biomarkers were omitted in the analysis for model 2, while model 3 only included the SROH questionnaire. The area under the receiver operating characteristic curves (AUROCC) provided the accuracy of each model. The regression equations were used to create scoring algorithms, composed of the remaining predictors, each with its own weight. Results - Of the 156 patients participating in this study, 67% were classified with total periodontitis and 33% had severe periodontitis. The models for total periodontitis achieved an AUROCC of 0.91 for model 1, 0.88 for model 2 and 0.81 for model 3. For severe periodontitis, this was 0.89 for model 1, 0.82 for model 2 and 0.78 for model 3. The algorithm for total periodontitis (model 2), which we consider valid for the Dutch population, was applied to create a freely accessible, web-based screening tool.

Conclusions - The prediction models for total and severe periodontitis proved to be feasible and accurate, resulting in easily applicable screening tools, intended for a non-dental setting. • Pumerantz AS, Bissett SM, Dong F, Ochoa C, Wassall RR, Davila H, Barbee M, Nguyen J, Vila P, Preshaw PM (2017) Standardized screening for periodontitis as an integral part of multidisciplinary management of adults with type 2 diabetes: an observational cross-sectional study of cohorts in the USA and UK. *BMJ Open Diabetes Res Care* 5(1):e000413 DOI: <http://dx.doi.org/10.1136/bmjdr-2017-000413> At: <https://drc.bmj.com/content/5/1/e000413> or <https://www.ncbi.nlm.nih.gov/pubmed/28761663> Abstract: Objective To determine prevalence and factors predictive of periodontitis by using a standardized assessment model in adults with type 2 diabetes. Research design and methods We performed an observational cross-sectional study to determine the burden of periodontitis in adults with type 2 diabetes attending urban, ambulatory referral centers in the USA and UK. Full-mouth probing was performed and periodontitis was diagnosed based on either a low (≥ 5 mm at ≥ 1 site) or high pocket probing-depth threshold (≥ 6 mm at ≥ 1 site). Results were stratified into a five-stage schema and integrated with other clinical variables into the novel Diabetes Cross-Disciplinary Index to function as a balanced health scorecard. Corresponding demographic and routinely collected health data were obtained and comparisons were made between patients with and without periodontitis. Multivariable logistic regression was performed to identify factors predictive of the presence or absence of periodontitis. Results Between our two cohorts, 253 patients were screened. Caucasians comprised $>90\%$ and Hispanic Americans $>75\%$ of the UK and US cohorts, respectively. Males and females were equally distributed; mean age was 53.6 ± 11 years; and 17 (6.7%) were edentulous. Of the 236 dentate patients, 128 (54.2%) had periodontitis by low threshold and 57 (24.2%) by high threshold. Just 17 (7.2%) were periodontally healthy. No significant differences in age, HbA1c, blood pressure, body mass index, low-density lipoprotein cholesterol, or smoking status (all $p > 0.05$) were identified between those with or without periodontitis (regardless of threshold) and none was found to be a significant predictor of disease. Conclusions Periodontitis is frequent in adults with type 2 diabetes and all should be screened. Periodontal health status can be visualized with other comorbidities and complications using a novel balanced scorecard that could facilitate patient-clinician communication, shared decision-making, and prioritization of individual healthcare needs. • Nomura Y, Okada A, Kakuta E, Gunii T, Kajiura S, Hanada N (2016). A new screening method for periodontitis: an alternative to the community periodontal index. *BMC Oral Health* 16:64. doi: [10.1186/s12903-016-0216-x](https://doi.org/10.1186/s12903-016-0216-x) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4937556/> Abstract: Background - Periodontal screening plays an important role in the prevention of periodontal disease and promotes an improvement in oral health-related quality of life. The World Health Organization's Community Periodontal Index should be carried out by well-trained dentists. However, the Community Periodontal Index is an invasive technique, and if used for periodontal screening, increases the cost of evaluation. In order to overcome these issues, we developed saliva tests for periodontal screening. The purpose of this study was to calculate the sensitivity and specificity of our method for measuring hemoglobin and lactate dehydrogenase levels in saliva. Methods - Inclusion criteria were adults aged over 20 years with at least 20 teeth remaining. The study population comprised 38 men and 54 women with a mean age of 50.03 years. Oral examinations were carried out by dentists, and the number of remaining teeth, presence or absence of calculus, bleeding on probing and pocket depth were recorded. In this study, periodontitis was defined according to the criteria of the Center for Disease Control and Prevention in partnership with the American Academy of Periodontology. In order to examine hemoglobin and lactate dehydrogenase levels in saliva, participants were instructed to chew on a standard-sized tasteless and odorless gum base for 5 min, during which time, stimulated whole saliva was

continuously collected. Results - The sensitivity and specificity for hemoglobin levels were 0.759 and 0.763, respectively, and 0.722 and 0.711, respectively, for lactate dehydrogenase levels. Combining these two tests, when samples tested positive for both hemoglobin and lactate dehydrogenase, the positive predictive value was 91.7 %. Conclusion Measuring hemoglobin and lactate dehydrogenase levels in saliva is a less invasive method than the Community Periodontal Index. Therefore, our saliva tests may be a viable alternative to the Community Periodontal Index for periodontal screening. • Overmyer KA, Rhoads T, Merrill AE, Ye Z, Westphall MS, Acharya A, Shukla S, Coon JJ (2020). Proteomics, lipidomics, metabolomics and 16S rDNA sequencing of dental plaque from patients with diabetes and periodontal disease. At: https://www.researchgate.net/publication/339519185_Proteomics_lipidomics_metabolomics_and_16S_rDNA_sequencing_of_dental_plaque_from_patients_with_diabetes_and_periodontal_disease. DOI: 10.1101/2020.02.25.963967 Available via license: CC BY-NC-ND 4.0 Description: Oral microbiome influences human health, specifically pre- and type 2 diabetes (Pre-DM/DM) and periodontal diseases (PD), through complex microbial interactions. To explore these relations, we performed 16S rDNA sequencing, metabolomics, lipidomics, and proteomics analyses on supragingival dental plaque collected from individuals with Pre-DM/DM (n=39), Pre-DM/DM and PD (n=37), PD alone (n=11), or neither (n=10). We identified on average 2,790 operational taxonomic units and 2,025 microbial and host proteins per sample and quantified 110 metabolites and 415 lipids. Plaque samples from PreDM/DM patients contained higher abundance of *Fusobacterium* and *Tannerella* vs. plaques from metabolically healthy. Phosphatidylcholines, plasmeyl-phosphatidylcholines, ceramides containing non-OH fatty acids, and host proteins related to actin filament rearrangement were elevated in plaques from PD vs. non-PD. Cross-omic correlation analysis enabled the detection of a strong association between *Lautropia* and mono-methyl phosphotidylethanolamine (PE-NMe), striking because synthesis of PE-NMe is uncommon in oral bacteria. Lipidomics analysis of in vitro cultures of *Lautropia mirabilis* confirmed the bacteria's synthesis of PE-NMe. This comprehensive analysis revealed a novel microbial metabolic pathway and significant associations of host-derived proteins with PD. • Gurav AN (2014). The association of periodontitis and metabolic syndrome. *Dent Res J (Isfahan)* 11(1): 1-10. DOI: 10.4103/1735-3327.127175 At: <https://www.ncbi.nlm.nih.gov/pubmed/24688553> Abstract: Metabolic syndrome (MS) is a condition, which constitutes a group of risk factors that occur together and increase the risk for Coronary Artery Disease, Stroke and type 2 diabetes mellitus. This disorder is found prevalent in the industrialized societies of the world in epidemic proportions. Periodontitis is an oral disease of microbial origin characterized by loss of attachment apparatus of tooth, resulting in edentulism if untreated. Periodontitis has been attributed to produce a low grade systemic inflammatory condition. The link of periodontitis to various systemic disorders has led to the evolution of a new branch termed as "periodontal medicine." Studies reviewed in the present paper have indicated a positive link between the MS and periodontitis and it is suggested that subjects displaying several components of MS should be submitted to periodontal examination. Present studies have displayed coherent relation between the two entities. This review will address the vicious association between MS and periodontitis, depicting the commonality of pathophysiological pathway between the two entities. Systematic reviews, meta-analysis addressing the concerned subject were screened. Whether the systematic periodontal therapy in individuals exhibiting MS has the potential to reduce the incidence of various adverse systemic complications remains a logical proposition. Further, longitudinal and controlled trials with a large population would be imperative to depict the robustness in the association between MS and periodontal disease in human subjects. • Shimpi N, Glurich I, Panny A, Acharya A (2019). Knowledgeability, attitude, and practice behaviors of primary care providers toward managing patients' oral health

care in medical practice: Wisconsin statewide survey. *J Am Dent Assoc* 150(10): 863-872. doi: 10.1016/j.adaj.2019.05.020. Epub 2019 Aug 22. At: <https://pubmed.ncbi.nlm.nih.gov/31446976/> Abstract: Background: In this study, the authors sought to explore the receptivity, preparedness, and rates of adoption of integrated medical-dental models of care (MOCs) in the practice setting among primary care providers (PCPs) treating patients with diabetes mellitus (DM). -- Methods: The authors conducted an anonymous statewide survey targeting PCPs across a range of Wisconsin-based practice settings to evaluate knowledgeability, attitude, practice behaviors, and perceived barriers to oral health screening in a medical setting. Qualitative analytical approaches included thematic analyses applied to evaluate the status of and barriers to integrated medical-dental MOC adoption. -- Results: The integrated medical-dental MOC adoption rate was 34%. Top perceived barriers to integrated medical-dental MOC adoption included insurance coverage (71%) and care access (70%). A total of 39% indicated competency for educating patients about the association between DM and periodontitis. Although 72% of PCPs indicated optimal periodicity for oral health assessment as frequent, 39% reported frequently conducting such assessments. -- Conclusions: Although PCPs indicate receptivity to integrated medical-dental MOCs, PCPs identify suboptimal education, lack of adequate training in oral-systemic disease assessment, and barriers to oral health care access as barriers to integrated medical-dental MOC adoption. -- Practical implications: Integrated medical-dental MOC adoption in care delivery to patients with DM remains below average. Interdisciplinary efforts and education are needed to address identified barriers to care integration. • Glurich I, Nycz G, Acharya A (2017). Status Update on Translation of Integrated Primary Dental-Medical Care Delivery for Management of Diabetic Patients. *Clin Med Res* 15(1-2): 21-32. doi: 10.3121/cmr.2017.1348. Epub 2017 Apr 3 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5572842/> Abstract: Escalating prevalence of both diabetes and periodontal disease, two diseases associated with bi-directional exacerbation, has been reported. Periodontal disease represents a modifiable risk factor that may reduce diabetes onset or progression, and integrated models of cross-disciplinary care are needed to establish and manage glycemic control in affected patients. An ad-hoc environmental scan of current literature and media sought to characterize factors impacting status of integrated care models based on review of the existing evidence base in literature and media surrounding: (1) current cross-disciplinary practice patterns, (2) epidemiological updates, (3) status on risk assessment and screening for dysglycemia in the dental setting, (4) status on implementation of quality metrics for oral health, (5) care model pilots, and (6) public health perspectives. The survey revealed: escalating prevalence of diabetes and periodontitis globally; greater emphasis on oral health assessment for diabetic patients in recent medical clinical practice guidelines; high knowledgeability surrounding oral-systemic impacts on diabetes and growing receptivity to medical-dental integration among medical and dental providers; increasing numbers of programs/studies reporting on positive impact of emerging integrated dentalmedical care models on diabetic patient healthcare access and health outcomes; a growing evidence base for clinically significant rates of undiagnosed dysglycemia among dental patients reported by point-of-care pilot studies; no current recommendation for population-based screening for dysglycemia in dental settings pending a stronger evidence base; improved definition of true periodontitis prevalence in (pre)/diabetics; emerging recognition of the need for oral health quality indicators and tracking; evidence of persistence in dental access disparity; updated status on barriers to integration. The potential benefit of creating clinically-applicable integrated care models to support holistic management of an escalating diabetic population by targeting modifiable risk factors including periodontitis is being recognized by the health industry. Cross-disciplinary efforts supported by

high quality research are needed to mitigate previously- and newly-defined barriers of care integration and expedite development and implementation of integrated care models in various practice settings. Implementation of quality monitoring in the dental setting will support definition of the impact and efficacy of interventional clinical care models on patient outcomes. • McKernan SC, Kuthy RA, Reynolds JC, Tuggle L, García DT (2018). Medical-Dental Integration in Public Health Settings: An Environmental Scan. At:

http://ppc.uiowa.edu/sites/default/files/ced_environmental_scan.pdf Executive Summary: Noncommunicable chronic diseases (NCDs) account for almost 90% of total deaths in the United States. The four most common NCDs—cardiovascular diseases, diabetes, cancers, and chronic respiratory diseases—share common risk factors, including cigarette use, alcohol use, and dietary behaviors associated with obesity and elevated blood sugar. The most common oral diseases—dental caries, periodontal disease, and oral cancer—also share these same risk factors. A coordinated approach to primary prevention, the “common risk factor approach,” argues that coordinated primary prevention of oral and systemic diseases will reduce programmatic costs, and increase efficiency and effectiveness. However, use and evaluation of this coordinated approach in primary prevention activities in the United States has not been well documented. This report describes the results of an environmental scan to identify, categorize, and describe examples of medical-dental integration in US public health settings. Findings are intended to inform public health officials and other stakeholders about existing programs and policies that encourage coordination and integration. Conclusion: Public health activities targeting oral health and chronic diseases operate at multiple levels, including public policy, community-level campaigns, health care delivery systems, and clinical interventions. Welldeveloped efforts were especially noted for environmental approaches targeting sugar-sweetened beverage consumption, state-level efforts targeting tobacco use and oral cancer, and co-location of medical and dental services. The lack of robust evaluation and effectiveness data surrounding most of the activities described in this report may hamper widespread implementation, sustainability, and stakeholder support • Acharya A, Cheng B, Koralkar R, Olson B, Lamster IB, Kunzel C, Lalla E (2018). Screening for diabetes risk using integrated dental and medical electronic health record data. *JDR Clin Trans Res* 3(2): 188-194. doi: 10.1177/2380084418759496. Epub 2018 Feb 26. At:

<https://www.ncbi.nlm.nih.gov/pubmed/29568804> • Jananni M, Sivaramakrishnan M, Mahendra J, Kuduruthullah S, Fatta MA, Khair MB (2019). Periodontitis presage pre-diabetes – A comparative study of glycemic control in non-diabetic population with and without periodontal disease. *Biomedicine* 39(4): 595- 598. Researchgate At:

https://www.researchgate.net/publication/339106881_Periodontitis_presage_pre-diabetes_-_A_comparative_study_of_glycemic_control_in_nondiabetic_population_with_and_without_periodontal_disease • Pack GD, Craven M, Acharya A (2020). A Secondary Analysis of Panoramic Radiographs Reveals Hotspots in the Maxillofacial Region Associated with Diabetes. At: https://www.researchgate.net/publication/341829999_A_Secondary_Analysis_of_Panoramic_Radiographs_Reveals_Hotspots_in_the_Maxillofacial_Region_Associated_with_Diabetes Abstract: Diabetes mellitus is the putative cause of a number of pathologies occurring in the bony and soft tissues of the maxillo-facial region and is known to exacerbate other oral diseases such as periodontitis. We present the first use of clinical panoramic radiographs for a secondary analysis of disease, with a focus on identifying hotspots in the maxillofacial region that are associated with diabetes. We developed a curated data set using Consensus Landmark Points (CLPs) and used that data to develop an analysis pipeline. This pipeline entailed automatic data cleansing, registration, and intensity normalization. The pipeline was used to process 7280 uncurated images that were subsequently analyzed using pixel-wise methods for a case/control study of patients with a history

of diabetes. We detected statistically significant clusters of pixels that demarcated anatomical hotspots specific to the diabetic patients • Hummel J, Phillips KE (2016). A Population Health Management Approach to Oral Health. *J Calif Dent Assoc* 44(3): 167-172.

<https://www.ncbi.nlm.nih.gov/pubmed/27044237> At:

https://www.cda.org/Portals/O/journal/journal_032016.pdf

Abstract: Clinical outcomes have been shown to be better, and total costs lower, when patients with chronic illness such as diabetes are managed using a population health strategy in a primary care setting that includes structured coordination of care with specialty services. This "population health management approach" offers a promising new vision for addressing oral disease as a chronic illness through a collaborative partnership between primary care teams and dental professionals • Azañeda D, Chambergó-Michilot D, Hernández-Vásquez V (2020). Associations between chronic conditions and oral health services utilization in older Peruvian adults: a pooled analysis of the Demographic and Health Survey 2015-2017. *Epidemiol Health* 42: e2020023. DOI: <https://doi.org/10.4178/epih.e2020023> At: <https://www.e-epih.org/journal/view.php?number=1084> Abstract: Objectives: This study was conducted to investigate the associations between chronic conditions (CCs) and oral health services utilization (OHSU) within the previous 6 months in older Peruvian adults (defined as those 60 years of age or more according to Peruvian law). Methods: An analytical cross-sectional study was performed based on the 2015-2017 Peruvian Demographic and Family Health Survey. Pooled data from 13,699 older adults were analyzed. A logistic regression model was used to analyze the associations between OHSU (dependent variable) and CCs (independent variables). Tobacco consumption, obesity, educational level, age, sex, welfare quintile, area of residence, having health insurance, and natural region of residence were included as covariates in the analysis. Results: The frequency of OHSU in older adults was 18.5% (95% confidence interval [CI], 17.8 to 19.3). The highest percentage point (%p) differences with regards to OHSU were found between the extreme categories of educational level (higher education vs. none or elementary school: +24.8%p) and welfare quintile (richest vs. poorest: +24.0%p). In the crude model, OHSU was associated with diabetes (odds ratio [OR], 1.46; 95% CI, 1.26 to 1.69), but this association disappeared after adjustment for covariates. Meanwhile, depression decreased the likelihood of OHSU (OR, 0.82; 95% CI, 0.72 to 0.95) in the adjusted model. Conclusions: The frequency of OHSU was low in older Peruvian adults. Regarding CCs, we found that depression independently decreased the likelihood of OHSU in the adjusted model. Our results may be useful for the development of policies aimed at achieving greater OHSU in older adults with CCs, especially in those with depression. • Seitz MW, Listl S, Bartols A, Schubert I, Blaschke K, Haux C, et al. Current Knowledge on Correlations Between Highly Prevalent Dental Conditions and Chronic Diseases: An Umbrella Review. *Prev Chronic Dis* 2019;16:180641. DOI: <http://dx.doi.org/10.5888/pcd16.180641> At: https://www.cdc.gov/pcd/issues/2019/18_0641.htm Abstract: Introduction -- Studies have investigated the relationships between chronic systemic and dental conditions, but it remains unclear how such knowledge can be used in clinical practice. In this article, we provide an overview of existing systematic reviews, identifying and evaluating the most frequently reported dental-chronic disease correlations and common risk factors. Methods -- We conducted a systematic review of existing systematic reviews (umbrella review) published between 1995 and 2017 and indexed in 4 databases. We focused on the 3 most prevalent dental conditions and 10 chronic systemic diseases with the highest burden of disease in Germany. Two independent reviewers assessed all articles for eligibility and methodologic quality using the AMSTAR criteria and extracted data from the included studies. Results -- Of the initially identified 1,249 systematic

reviews, 32 were included for qualitative synthesis. The dental condition with most frequently observed correlations to chronic systemic diseases was periodontitis. The chronic systemic disease with the most frequently observed correlations with a dental condition was type 2 diabetes mellitus (T2DM). Most dental–chronic disease correlations were found between periodontitis and T2DM and periodontitis and cardiovascular disease. Frequently reported common risk factors were smoking, age, sex, and overweight. Using the AMSTAR criteria, 2 studies were assessed as low quality, 26 studies as moderate quality, and 4 studies as high quality. Conclusion -- The quality of included systematic reviews was heterogeneous. The most frequently reported correlations were found for periodontitis with T2DM and for periodontitis with cardiovascular disease. However, the strength of evidence for these and other disease correlations is limited, and the evidence to assess the causality of these disease correlations remains unclear. Future research should focus on the causality of disease links in order to provide more decisive evidence with respect to the design of intersectoral care processes. • Hegde H, Shimpi N, Panny A, Glurich I, Christie P, Acharya A (2019). Development of non-invasive diabetes risk prediction models as decision support tools designed for application in the dental clinical environment. *Inf Med Unl* 17, 100254:1-9. doi: 10.1016/j.imu.2019.100254. Available at: <https://www.sciencedirect.com/science/article/pii/S2352914819302758> • Teeuw WJ Gerdes VEA, Loos BGG (2010). Effect of Periodontal Treatment on Glycemic Control of Diabetic Patients: A systematic review and meta-analysis. *Diabetes Care* 33(2): 421-427. At: <https://care.diabetesjournals.org/content/33/2/421> DOI: <https://doi.org/10.2337/dc09-1378>

ABSTRACTS

OSHR: Oral Microbiome and Cancer - Page 1 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. OSHR – Oral Microbiome and Cancer Introduction, The oral microbiome and cancer, contributed by Dr. Ingrid Glurich, Project Scientist I, Center for Oral and Systemic Health, Marshfield Clinic Research Institute, Marshfield, WI, USA: <https://marshfieldresearch.org/profiles/5891> The hard and soft surfaces in the oral cavity present a spectrum of habitats that are colonized by bacteria representing over 600 taxa with variable density in representation across respective oral niches (1). Collectively, these organisms represent the oral microbiota. A growing body of evidence supports an important role for the oral microbiota as potential contributors to promotion of both local and systemic oncogenesis. Increased oncogenic potential appears to be associated with establishment of dysbiosis in the oral cavity, including establishment of oral pathogens associated with induction of periodontal disease. Moreover, pathogenic mechanisms that support active contribution to oncogenesis by oral bacteria have been delineated. To date contributory mechanisms that promote oncogenesis have been broadly classified into three categories: 1) induction of local and systemic inflammation largely through upregulation of pro-inflammatory cytokines; activation of pathways that disrupt physiologic apoptosis and normal cell cycling while promoting susceptibility to cellular invasion; and 3) release of toxic and/or carcinogenic substances into the environment that promote oncogenesis. (2,3) Oral pathogens implicated in more localized cancers such as oral squamous cell carcinomas include: *Streptococcus* sp., *Peptostreptococcus* sp *Prevotella* sp., *Porphyromonas gingivalis*, and *Capnocytophaga gingivalis* (4-10). Increased carriage of periodontal pathogens including *Porphyromonas gingivalis* and *Fusobacterium nucleatum* among other oral bacteria, has also been implicated in oncogenesis of extraoral cancers including colorectal (11-15) orodigestive (16,17) and pancreatic cancers (18,19). Higher representation of *Capnocytophaga* and *Veillonella* has also

been reported in conjunction with lung cancers (20). References: 1. Dewhirst, FE, Chen T, Izard J, Paster BJ, Tanner AC, Yu WH, Lakshmanan A, Wade WG. The human oral microbiome. *J Bacteriol* 2010;192(19):5002-5017 doi:10.1128/JB.00542-10. <https://jb.asm.org/content/jb/192/19/5002.full.pdf> 2. Zhang Y., Wang X., Li H., Ni C., Du Z., Yan F. Human oral microbiota and its modulation for oral health. *Biomed. Pharmacother.* 2018;99:883–893. doi: 10.1016/j.biopha.2018.01.146. 3. Karpinski T. Role of oral microbiota in cancer development. *Microorganisms* 2019;7(1):20 doi: 10.3390/microorganisms7010020 4. Sasaki M., Yamaura C., Ohara-Nemoto Y., Tajika S., Kodama Y., Ohya T., Harada R., Kimura S. Streptococcus anginosus infection in oral cancer and its infection route. *Oral Dis.* 2005;11:151–156. doi: 10.1111/j.1601-0825.2005.01051.x. 5. Mager D., Haffajee A., Devlin P., Norris C., Posner M., Goodson J. The salivary microbiota as a diagnostic indicator of oral cancer: A descriptive, nonrandomized study of cancerfree and oral squamous cell carcinoma subjects. *J. Transl. Med.* 2005;3:27. doi: 10.1186/1479-5876-3-27. OSHR: Oral Microbiome and Cancer - Page 2 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. 6. Katz J., Onate M.D., Pauley K.M., Bhattacharyya I., Cha S. Presence of Porphyromonas gingivalis in gingival squamous cell carcinoma. *Int. J. Oral Sci.* 2011;3:209–215. doi: 10.4248/IJOS11075. 7. Pushalkar S., Ji X., Li Y., Estilo C., Yegnanarayana R., Singh B., Li X., Saxena D. Comparison of oral microbiota in tumor and non-tumor tissues of patients with oral squamous cell carcinoma. *BMC Microbiol.* 2012;12:144. doi: 10.1186/1471-2180-12-144. 8. Atanasova K.R., Yilmaz O. Looking in the Porphyromonas gingivalis cabinet of curiosities: The microbium, the host and cancer association. *Mol. Oral Microbiol.* 2014;29:55–66. doi: 10.1111/omi.12047. 9. Galvão-Moreira L.V., da Cruz M.C. Oral microbiome, periodontitis and risk of head and neck cancer. *Oral Oncol.* 2016;53:17–19. doi: 10.1016/j.oraloncology.2015.11.013. 10. Lee W.H., Chen H.M., Yang S.F., Liang C., Peng C.Y., Lin F.M., Tsai L.L., Wu B.C., Hsin C.H., Chuang C.Y., et al. Bacterial alterations in salivary microbiota and their association in oral cancer. *Sci. Rep.* 2017;7:16540. doi: 10.1038/s41598-017-16418-x. 11. Castellarin M., Warren R.L., Freeman J.D., Dreolini L., Krzywinski M., Strauss J., Barnes R., Watson P., Allen-Vercoe E., Moore R.A., et al. Fusobacterium nucleatum infection is prevalent in human colorectal carcinoma. *Genome Res.* 2012;22:299–306. doi: 10.1101/gr.126516.111. 12. Ahn J., Sinha R., Pei Z., Dominianni C., Wu J., Shi J., Goedert J.J., Hayes R.B., Yang L. Human gut microbiome and risk for colorectal cancer. *J. Natl. Cancer Inst.* 2013;105:1907–1911. doi: 10.1093/jnci/djt300. 13. Kostic A.D., Chun E., Robertson L., Glickman J.N., Gallini C.A., Michaud M., Clancy T.E., Chung D.C., Lochhead P., Hold G.L., et al. Fusobacterium nucleatum potentiates intestinal tumorigenesis and modulates the tumor-immune microenvironment. *Cell Host Microbe.* 2013;14:207–215. doi: 10.1016/j.chom.2013.07.007. 14. Kostic A.D., Gevers D., Pedamallu C.S., Michaud M., Duke F., Earl A.M., Ojesina A.I., Jung J., Bass A.J., Tabernero J., et al. Genomic analysis identifies association of Fusobacterium with colorectal carcinoma. *Genome Res.* 2012;22:292–298. doi: 10.1101/gr.126573.111. 15. Mima K., Cao Y., Chan A.T., Qian Z.R., Nowak J.A., Masugi Y., Shi Y., Song M., da Silva A., Gu M., et al. Fusobacterium nucleatum in colorectal carcinoma tissue according to tumor location. *Clin. Transl. Gastroenterol.* 2016;7:e200. doi: 10.1038/ctg.2016.53. 16. Ahn J., Segers S., Hayes R.B. Periodontal disease, Porphyromonas gingivalis serum antibody levels and orodigestive cancer mortality. *Carcinogenesis.* 2012;33:1055–1058. doi: 10.1093/carcin/bgs112. 17. Peters B.A., Wu J., Pei Z., Yang L., Purdue M.P., Freedman N.D., Jacobs E.J., Gapstur S.M., Hayes R.B., Ahn J. Oral microbiome composition reflects prospective risk for esophageal cancers. *Cancer Res.* 2017;77:6777–6787. doi: 10.1158/0008-5472.CAN-17-1296. 18. Mitsuhashi K., Nosho K., Sukawa Y., Matsunaga Y., Ito M., Kurihara H., Kanno S., Igarashi H., Naito T., Adachi Y., et al. Association of Fusobacterium species in pancreatic cancer tissues with

molecular features and prognosis. *Oncotarget* 2015;6:7209–7220. doi: 10.18632/oncotarget.3109. 19. Fan X., Alekseyenko A.V., Wu J., Peters B.A., Jacobs E.J., Gapstur S.M., Purdue M.P., Abnet C.C., Stolzenberg-Solomon R., Miller G., et al. Human oral microbiome and OSHR: Oral Microbiome and Cancer - Page 3 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. prospective risk for pancreatic cancer: A population-based nested case-control study. *Gut*. 2018;67:120–127. doi: 10.1136/gutjnl-2016-312580. 20. Yan X., Xinmin Y., Yang M., Liu J., Gao R., Hu J., Li J., Zhang L., Shi Y., Guo H., et al. Discovery and validation of potential bacterial biomarkers for lung cancer. *Am. J. Cancer Res.* 2015;5:3111–3122 e-collection. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4656734/pdf/ajcr0005-3111.pdf> Oral Microbiome Gao L, Xu T, Huang G, Jiang S, Gu Y, Chen F (2018). Oral microbiomes: more and more importance in oral cavity and whole body. *Protein Cell*. 2018 May; 9(5): 488–50 Published online 2018 May 7. doi: 10.1007/s13238-018-0548-1 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960472/> Abstract: Microbes appear in every corner of human life, and microbes affect every aspect of human life. The human oral cavity contains a number of different habitats. Synergy and interaction of variable oral microorganisms help human body against invasion of undesirable stimulation outside. However, imbalance of microbial flora contributes to oral diseases and systemic diseases. Oral microbiomes play an important role in the human microbial community and human health. The use of recently developed molecular methods has greatly expanded our knowledge of the composition and function of the oral microbiome in health and disease. Studies in oral microbiomes and their interactions with microbiomes in variable body sites and variable health condition are critical in our cognition of our body and how to make effect on human health improvement. Kilian M, Chapple ILC, Hannig M, Marsh PD, Meuric V, Pedersen AML, Tonetti MS, Wade WG, Zaura E (2016). The oral microbiome – an update for oral healthcare professionals M. Kilian. *Brit Dent J* 221: 657-666. DOI: 10.1038/sj.bdj.2016.865 At: <https://www.nature.com/articles/sj.bdj.2016.865.pdf?origin=ppub> Abstract: For millions of years, our resident microbes have coevolved and coexisted with us in a mostly harmonious symbiotic relationship. We are not distinct entities from our microbiome, but together we form a ‘superorganism’ or holobiont, with the microbiome playing a significant role in our physiology and health. The mouth houses the second most diverse microbial community in the body, harbouring over 700 species of bacteria that colonise the hard surfaces of teeth and the soft tissues of the oral mucosa. Through recent advances in technology, we have started to unravel the complexities of the oral microbiome and gained new insights into its role during both health and disease. Perturbations of the oral microbiome through modern-day lifestyles can have detrimental consequences for our general and oral health. In dysbiosis, the finely-tuned equilibrium of the oral ecosystem is disrupted, allowing disease-promoting bacteria to manifest and cause conditions such as caries, gingivitis and periodontitis. For practitioners and patients alike, promoting a balanced microbiome is therefore important to effectively maintain or restore oral health. This article aims to give an update on our current knowledge of the oral microbiome in health and disease and to discuss implications for modern-day oral healthcare. Lim Y, Totsika M, Morrison M, Punyadeera C (2017).. *Oral Microbiome: A New Biomarker Reservoir for Oral and Oropharyngeal Cancers*. *Theranostics* 7(17):4313-4321. doi:10.7150/thno.21804. At: <http://www.thno.org/v07p4313.htm> Abstract: Current biomarkers OSHR: Oral Microbiome and Cancer - Page 4 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. (DNA, RNA and protein) for oral cavity and oropharyngeal cancers demonstrate biological variations between individuals, rendering them impractical for clinical translation. Whilst these biomarkers originate from the host, there is not

much information in the literature about the influence of oral microbiota on cancer pathogenesis, especially in oral cancers. Oral microbiotas are known to participate in disease initiation and progression not only limited to the oral cavity, but also at other distant sites. Due to the close proximity of oral microbiota and oral cavity and oropharyngeal tumours, abundance changes in oral microbiota may provide useful information on tumourigenesis. This review aims to highlight information on the role of oral microbiota in oral cavity and oropharyngeal cancers. An in-depth analysis into the oral microbiota may provide a new avenue to diagnose and treat these patients. Keywords: biomarker, oral and oropharyngeal cancers, oral microbiome. Slocum C, Kramer C, Genco CA (2016). Immune dysregulation mediated by the oral microbiome: potential link to chronic inflammation and atherosclerosis. *J Intern Med* 280(1): 114–128. DOI: 10.1111/joim.12476 At: <https://pubmed.ncbi.nlm.nih.gov/26791914/> Abstract. Slocum C, Kramer C, Genco CA (Ora Inc., Andover, MA, USA; and Tufts University School of Medicine, Boston, MA, USA). Immune dysregulation mediated by the oral microbiome: potential link to chronic inflammation and atherosclerosis (Review). *J Intern Med* 2016; 280: 114–128. Cardiovascular disease is an inflammatory disorder characterized by the progressive formation of plaque in coronary arteries, termed atherosclerosis. It is a multifactorial disease that is one of the leading causes of death worldwide. Although a number of risk factors have been associated with disease progression, the underlying inflammatory mechanisms contributing to atherosclerosis remain to be fully delineated. Within the last decade, the potential role for infection in inflammatory plaque progression has received considerable interest. Microbial pathogens associated with periodontal disease have been of particular interest due to the high levels of bacteremia that are observed after routine dental procedures and every day oral activities, such as tooth brushing. Here, we explore the potential mechanisms that may explain how periodontal pathogens either directly or indirectly elicit immune dysregulation and consequently progressive inflammation manifested as atherosclerosis. Periodontal pathogens have been shown to contribute directly to atherosclerosis by disrupting endothelial cell function, one of the earliest indicators of cardiovascular disease. Oral infection is thought to indirectly induce elevated production of inflammatory mediators in the systemic circulation. Recently, a number of studies have been conducted focusing on how disruption of the gut microbiome influences the systemic production of proinflammatory cytokines and consequently exacerbation of inflammatory diseases such as atherosclerosis. It is clear that the immune mechanisms leading to atherosclerotic plaque progression, by oral infection, are complex. Understanding the immune pathways leading to disease progression is essential for the future development of anti-inflammatory therapies for this chronic disease. Glurich I, Acharya A, Brilliant MH, Shukla SK (2015). Progress in oral personalized medicine: contribution of 'omics'. *J Oral Microbiol* 7: 10.3402/jom.v7.28223 DOI: 10.3402/jom.v7.28223 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4561229/> Abstract: Background Precision medicine (PM), representing clinically applicable personalized medicine, proactively integrates and interprets multidimensional personal health data, including clinical, 'omics', and environmental profiles, into clinical practice. Realization of PM remains in progress. Objective OSHR: Oral Microbiome and Cancer - Page 5 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. The focus of this review is to provide a descriptive narrative overview of: 1) the current status of oral personalized medicine; and 2) recent advances in genomics and related 'omic' and emerging research domains contributing to advancing oral-systemic PM, with special emphasis on current understanding of oral microbiomes. Design A scan of peer-reviewed literature describing oral PM or 'omic'-based research conducted on humans/data published in English within the last 5 years in journals indexed in the PubMed database was conducted using mesh search terms. An

evidence-based approach was used to report on recent advances with potential to advance PM in the context of historical critical and systematic reviews to delineate current state-of-the-art technologies. Special focus was placed on oral microbiome research associated with health and disease states, emerging research domains, and technological advances, which are positioning realization of PM. Results This review summarizes: 1) evolving conceptualization of personalized medicine; 2) emerging insight into roles of oral infectious and inflammatory processes as contributors to both oral and systemic diseases; 3) community shifts in microbiota that may contribute to disease; 4) evidence pointing to new uncharacterized potential oral pathogens; 5) advances in technological approaches to 'omics' research that will accelerate PM; 6) emerging research domains that expand insights into host-microbe interaction including inter-kingdom communication, systems and network analysis, and salivaomics; and 7) advances in informatics and big data analysis capabilities to facilitate interpretation of host and microbiome-associated datasets. Furthermore, progress in clinically applicable screening assays and biomarker definition to inform clinical care are briefly explored. Conclusion Advancement of oral PM currently remains in research and discovery phases. Although substantive progress has been made in advancing the understanding of the role of microbiome dynamics in health and disease and is being leveraged to advance early efforts at clinical translation, further research is required to discern interpretable constituency patterns in the complex interactions of these microbial communities in health and disease. Advances in biotechnology and bioinformatics facilitating novel approaches to rapid analysis and interpretation of large datasets are providing new insights into oral health and disease, potentiating clinical application and advancing realization of PM within the next decade. Keywords: microbiota, precision medicine, 'omics', big data, biomarkers. Extraroral Cancer (Pancreatic, Breast, Colon/Colorectal, Esophageal, Lung, Renal, Liver) Wallis C (2020). New Player in Cancer's Spread: A commonplace mouth bacterium now is tied to metastasis of some tumors. *Sci Am* 323(4): 28. See also: <https://www.scientificamerican.com/article/deadly-spread-of-some-cancers-may-be-driven-by-a-common-mouth-microbe/> Casasanta MA, Yoo CC, Udayasuryan B, Sanders BE, Umaña A, Zhang Y, Peng H, Duncan AJ, Li L, Verbridge SS, Slade DJ (2020). *Fusobacterium nucleatum* host-cell binding and invasion induces IL-8 and CXCL1 secretion that drives colorectal cancer cell migration. *Sci Signaling* 641: eaba9157 DOI: 10.1126/scisignal.aba9157 At: <https://stke.sciencemag.org/content/13/641/eaba9157> Abstract: *Fusobacterium nucleatum* is implicated in accelerating colorectal cancer (CRC) and is found within metastatic CRC cells in patient biopsies. Here, we found that bacterial invasion of CRC cells and cocultured immune cells induced a differential cytokine secretion that may contribute to CRC metastasis. We used a OSHR: Oral Microbiome and Cancer - Page 6 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. modified galactose kinase markerless gene deletion approach and found that *F. nucleatum* invaded cultured HCT116 CRC cells through the bacterial surface adhesin Fap2. In turn, Fap2-dependent invasion induced the secretion of the proinflammatory cytokines IL-8 and CXCL1, which are associated with CRC progression and promoted HCT116 cell migration. Conditioned medium from *F. nucleatum*-infected HCT116 cells caused naïve cells to migrate, which was blocked by depleting CXCL1 and IL-8 from the conditioned medium. Cytokine secretion from HCT116 cells and cellular migration were attenuated by inhibiting *F. nucleatum* host-cell binding and entry using galactose sugars, L-arginine, neutralizing membrane protein antibodies, or fap2 deletion. *F. nucleatum* also induces the mobilization of immune cells in the tumor microenvironment. However, in neutrophils and macrophages, the bacterial-induced secretion of cytokines was Fap2 independent. Thus, our findings show that *F. nucleatum* both directly and indirectly modulates immune and cancer cell

signaling and migration. Because increased IL-8 and CXCL1 production in tumors is associated with increased metastatic potential and cell seeding, poor prognosis, and enhanced recruitment of tumor-associated macrophages and fibroblasts, we propose that inhibition of host-cell binding and invasion, potentially through vaccination or novel galactoside compounds, could be an effective strategy for reducing *F. nucleatum*-associated CRC metastasis. Sun J, Tang Q, Yu S, Xie M, Yanling X, Chen G, Chen L (2020). Role of the oral microbiota in cancer evolution and progression. DOI: <https://doi.org/10.1002/cam4.3206> At: <https://onlinelibrary.wiley.com/doi/full/10.1002/cam4.3206> Abstract: Bacteria identified in the oral cavity are highly complicated. They include approximately 1000 species with a diverse variety of commensal microbes that play crucial roles in the health status of individuals. Epidemiological studies related to molecular pathology have revealed that there is a close relationship between oral microbiota and tumor occurrence. Oral microbiota has attracted considerable attention for its role in in-situ or distant tumor progression. Anaerobic oral bacteria with potential pathogenic abilities, especially *Fusobacterium nucleatum* and *Porphyromonas gingivalis*, are well studied and have close relationships with various types of carcinomas. Some aerobic bacteria such as *Parvimonas* are also linked to tumorigenesis. Moreover, human papillomavirus, oral fungi, and parasites are closely associated with oropharyngeal carcinoma. Microbial dysbiosis, colonization, and translocation of oral microbiota are necessary for implementation of carcinogenic functions. Various underlying mechanisms of oral microbiota-induced carcinogenesis have been reported including excessive inflammatory reaction, immunosuppression of host, promotion of malignant transformation, antiapoptotic activity, and secretion of carcinogens. In this review, we have systemically described the impact of oral microbial abnormalities on carcinogenesis and the future directions in this field for bringing in new ideas for effective prevention of tumors. Robayo DAG, Hernandez RF, Eira AT, Kandaurova L, Juarez CL, Juarez CL, Juarez V, Cid-Arregui A (2020). Oral Microbiota Associated with Oral and Gastroenteric Cancer. *The Open Microbiol J* 14. DOI: 10.2174/1874285802014010001 At: <https://openmicrobiologyjournal.com/VOLUME/14/PAGE/1/FULLTEXT/> Abstract: When the normal microbiota-host interactions are altered, the commensal microbial community evolves to a dysbiotic status resulting in some species becoming pathogenic and acting synergistically in the development of local and systemic diseases, including cancer. Advances in genetics, OSHR: Oral Microbiome and Cancer - Page 7 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. immunology and microbiology during the last years have made it possible to gather information on the oral and gastrointestinal microbiome and its interaction with the host, which has led to a better understanding of the interrelationship between microbiota and cancer. There is growing evidence in support for the role of some species in the development, progression and responses to treatment of various types of cancer. Accordingly, the number of studies investigating the association between oral microbiota and oral and gastrointestinal cancers has increased significantly during the last years. Here, we review the literature documenting associations of oral microbiota with oral and gastroenteric cancers Teles FRF, Alawi F, Castilho RM, Wang Y (2020). Association or Causation? Exploring the Oral Microbiome and Cancer Links. *J Dent Res* (Online ahead of print.) At: <https://pubmed.ncbi.nlm.nih.gov/32811287/> DOI: 10.1177/0022034520945242 Abstract: The oral microbiota plays an important role in the human microbiome and human health, and imbalances between microbes and their hosts can lead to oral and systemic diseases and chronic inflammation, which is usually caused by bacteria and contributes to cancer. There may be a relationship between oral bacteria and oral squamous cell carcinoma (OSCC); however, this relationship has not been thoroughly characterized. Therefore, in

this study, we compared the microbiota compositions between tumor sites and opposite normal tissues in buccal mucosal of 50 patients with OSCC using the 16S rDNA sequencing. Richness and diversity of bacteria were significantly higher in tumor sites than in the control tissues. Cancer tissues were enriched in six families (Prevotellaceae, Fusobacteriaceae, Flavobacteriaceae, Lachnospiraceae, Peptostreptococcaceae, and Campylobacteraceae) and 13 genera, including *Fusobacterium*, *Alloprevotella* and *Porphyromonas*. At the species level, the abundances of *Fusobacterium nucleatum*, *Prevotella intermedia*, *Aggregatibacter segnis*, *Capnocytophaga leadbetteri*, *Peptostreptococcus stomatis*, and another five species were significantly increased, suggesting a potential association between these bacteria and OSCC. Furthermore, the functional prediction revealed that genes involved in bacterial chemotaxis, flagellar assembly and lipopolysaccharide (LPS) biosynthesis which are associated with various pathological processes, were significantly increased in the OSCC group. Overall, oral bacterial profiles showed significant difference between cancer sites and normal tissue of OSCC patients, which might be considered diagnostic markers and treatment targets. Our study has been registered in the Chinese clinical trial registry (ChiCTR1900025253, <http://www.chictr.org.cn/index.aspx>). Keywords: oral microbiota, oral squamous cell carcinoma, *Fusobacterium nucleatum*, *Prevotella intermedia*, *Peptostreptococcus stomatis*, 16S rDNA sequencing. Robayo DAG, Hernandez RF, Erika AT, Kandaurova L, Juarez CL, Juarez CL, Juarez V, Cid-Arregui A (2020). Oral Microbiota Associated with Oral and Gastroenteric Cancer. *Open Microbiol J* 14: 1-17. DOI: 10.2174/1874285802014010001 At: <https://openmicrobiologyjournal.com/VOLUME/14/PAGE/1/FULLTEXT/> Abstract: When the normal microbiota-host interactions are altered, the commensal microbial community evolves to a dysbiotic status resulting in some species becoming pathogenic and acting synergistically in the development of local and systemic diseases, including cancer. Advances in genetics, immunology and microbiology during the last years have made it possible to gather information OSHR: Oral Microbiome and Cancer - Page 8 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. on the oral and gastrointestinal microbiome and its interaction with the host, which has led to a better understanding of the interrelationship between microbiota and cancer. There is growing evidence in support for the role of some species in the development, progression and responses to treatment of various types of cancer. Accordingly, the number of studies investigating the association between oral microbiota and oral and gastrointestinal cancers has increased significantly during the last years. Here, we review the literature documenting associations of oral microbiota with oral and gastroenteric cancers. <https://www.dental.columbia.edu/news/how-common-oral-bacteria-makes-colon-cancermore-deadly> New York, NY (March 4, 2019) – Researchers at the Columbia University College of Dental Medicine have determined how *F. nucleatum* — a common oral bacteria often implicated in tooth decay — accelerates the growth of colon cancer. The study was published online in the journal *EMBO Reports*. The findings could make it easier to identify and treat more aggressive colon cancers. It also helps explain why some cases advance far more quickly than others, thanks to the same bacteria found in dental plaque. Colon cancer is the second leading cause of cancer death in the U.S. Researchers have long known that the disease is caused by genetic mutations that typically accumulate over the course of a decade. “Mutations are just part of the story,” says study leader Yiping W. Han, PhD, professor of microbial sciences at Columbia University’s College of Dental Medicine and Vagelos College of Physicians & Surgeons. “Other factors, including microbes, can also play a role.” At: Rubinstein MR, Baik JE, Lagana SM, Han RP, Raab WJ, Sahoo D, Dalerba P, Wang TC, Han YW (2019). *Fusobacterium nucleatum* promotes colorectal cancer by inducing Wnt/ β -catenin modulator Annexin A1. *EMBO Rep* (2019)20:e47638

<https://doi.org/10.15252/embr.201847638> At:

<https://www.embopress.org/doi/10.15252/embr.201847638> Mascitti M, Togni L, Troiano G, Alberto-Caponio VC, Gissi DB, Montebugnoli L, Procaccini M, Muzio LL, Santarelli A (2019). Beyond Head and Neck Cancer: The Relationship Between Oral Microbiota and Tumour Development in Distant Organs. *Front Cell Infect Microbiol* 9: 232. DOI: 10.3389/fcimb.2019.00232 At:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6607058/> Abstract: An altered oral microbiota has been linked with the development of several oral diseases, such as dental caries, periodontal disease, and oral stomatitis. Moreover, poor oral health has been linked to head and neck cancer, particularly oral cancer. In recent years a growing number of studies indicate that oral microbiota could be involved in the development of primary tumours outside of head and neck region. The aim of this article is to review the recent studies based on high-throughput technology to present evidences of a relationship between oral microbiota and “non-head and neck tumours.” Oral dysbiosis seem to be more pronounced in patients with tumours of gastrointestinal tract, in particular oesophageal, gastric, pancreatic, and colorectal cancers, paving the way for developing specific oral microbiota test to allow early cancer detection. Regarding other tumour types, the results are promising but highly preliminary and still debated. Currently, there are several factors that limit the generalization of the results, such as the small sample size, the lack of adequate clinical information about patients, the different sequencing techniques used, and biological sample heterogeneity. Although only at the beginning, the analysis of oral microbiota could be the next step in the evolution of cancer therapy and will help clinicians to develop individualised OSHR: Oral Microbiome and Cancer - Page 9 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. approaches to cancer prevention and treatment. Keywords: oral microbiota, oral microbiome, pancreatic cancer, gastrointestinal tract cancer, high-throughput sequencing. Maddi A, Sabharwal A, Violante T, Manuballa S, Genco R, Patnaik S, Yendamuri S (2019). The microbiome and lung cancer. *J Thorac Dis* 11(1): 280-291. DOI: 10.21037/jtd.2018.12.88 At:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6384374/> Abstract: It has become increasingly clear that we live in a symbiotic relationship with microbes within us. We are just beginning to unravel the nature and strength of this relationship and its impact on both physiology and by extension, pathology. While microorganisms have long been known to have carcinogenic potential, their role may have been underestimated. The knowledge of the role of the microbiome in carcinogenesis is rapidly evolving. This evolution has reached a tipping point with current omics technologies used for cataloguing the microbiome. The lung is an organ constantly exposed to the environment. It is now clear that the lung has a distinct microbiome and that this may influence the development of lung cancer. In addition, evidence suggests that this microbiome originates from the oral microbiome. This review summarizes current knowledge about the role of microbiome, especially the oral and lung microbiome in human lung cancer. The goal of the manuscript is to provide a summary of this rapidly evolving field while providing a context of the general role of the microbiome in carcinogenesis. In addition, a primer of the current technology used in evaluating the microbiome is provided to familiarize the practicing clinician with the experimental methods used to generate the information that will likely impact the field of lung cancer. Gerlovin H, Michaud DS, Cozier YC, Palmer JR (2019). Oral Health in Relation to Pancreatic Cancer Risk in African American Women. Downloaded from cebp.aacrjournals.org on March 29, 2019 *Cancer Epidemiol Biomarkers Prev*; 28(4), April 2019, At: <https://pubmed.ncbi.nlm.nih.gov/30923045/> DOI: 10.1158/1055-9965.EPI-18-1053 Abstract: Background: Incidence of pancreatic cancer is higher in African Americans than in U.S. whites. We hypothesized that poor oral health, disproportionately common in African Americans and associated with increased risk of pancreatic

cancer in several studies of predominantly white populations, may play a role in this disparity.

Methods: We examined the relation of self-reported measures of oral health (periodontal disease and adult tooth loss) in relation to pancreatic cancer incidence in the prospective Black Women's Health Study (BWHS). Cox proportional hazard analyses were used to calculate HRs of pancreatic cancer for women with periodontal disease, tooth loss, or both, relative to women who reported neither. Multivariable models adjusted for age, cigarette smoking, body mass index (BMI), type 2 diabetes, and alcohol consumption. Results: Participants aged 33 to 81 were followed for an average of 9.85 years from 2007 through 2016, with occurrence of 78 incidence cases of pancreatic cancer. Multivariable HRs for pancreatic cancer incidence were 1.77 [95% confidence interval (CI) 0.57- 5.49] for periodontal disease with no tooth loss, 2.05 (95% CI, 1.08-3.88) for tooth loss without report of periodontal disease, and 1.58 (95% CI, 0.70-3.57) for both tooth loss and periodontal disease. The HR for loss of at least five teeth, regardless of whether periodontal disease was reported, was 2.20 (95% CI, 1.11-4.33). Conclusions: The poor oral health experienced by many OSHR: Oral Microbiome and Cancer - Page 10 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. African Americans may contribute to their higher incidence of pancreatic cancer. Impact: Future research will assess associations between the oral microbiome and pancreatic cancer risk in this population. Al-Hebshi, N. N., Borgnakke, W. S., and Johnson, N. W. (2019). The microbiome of oral squamous cell carcinomas: a functional perspective. *Curr. Oral Health Rep.* 6, 145–160. doi: 10.1007/s40496-019-0215-5 At: https://www.researchgate.net/publication/344876587_Screening_of_HealthAssociated_Oral_Bacteria_for_Anticancer_Properties_in_vitro/references Jordão HW, McKenna G, McMEnamin, 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 Gastroenterol J* 7(9): 1241-1249. doi: 10.1177/2050640619858043. Epub 2019 Jun 8. At: <https://pubmed.ncbi.nlm.nih.gov/31700637/> 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. Lu H, Ren Z, Li A, Zheng HJ, Zhang CP (2019). Tongue Coating Microbiome Data Distinguish Patients With Pancreatic Head Cancer From Healthy Controls. *J Oral Microbiol* 9: 476. DOI: 10.1080/20002297.2018.1563409 .At: <https://pubmed.ncbi.nlm.nih.gov/30728915/> Abstract: Background: The microbiota plays a critical role in the process of human carcinogenesis. Pancreatic head carcinoma (PHC)-associated tongue coating microbiome dysbiosis has not yet been clearly defined. Objective: Our aim is to reveal the

bacterial composition shifts in the microbiota of the tongue coat of PHC patients. Design: The tongue coating microbiota was analyzed in 30 PHC patients and 25 healthy controls using 16S rRNA gene sequencing technology. Results: The microbiome diversity of the tongue coat in PHC patients was significantly increased, as shown by the Shannon, Simpson, inverse Simpson, Obs and incidence-based coverage estimators. Principal component analysis revealed that PHC patients OSHR: Oral Microbiome and Cancer - Page 11 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. were colonized by remarkably different tongue coating microbiota than healthy controls and liver cancer patients. Linear discriminant analysis effect size revealed that Leptotrichia, Fusobacterium, Rothia, Actinomyces, Corynebacterium, Atopobium, Peptostreptococcus, Catonella, Oribacterium, Filifactor, Campylobacter, Moraxella and Tannerella were overrepresented in the tongue coating of PHC patients, and Haemophilus, Porphyromonas and Paraprevotella were enriched in the tongue coating microbiota of healthy controls. Strikingly, Haemophilus, Porphyromonas, Leptotrichia and Fusobacterium could distinguish PHC patients from healthy subjects, and Streptococcus and SR1 could distinguish PHC patients from liver cancer patients. Conclusions: These findings identified the microbiota dysbiosis of the tongue coat in PHC patients, and provide insight into the association between the human microbiome and pancreatic cancer. Keywords: Miseq sequencing; Pancreatic head carcinoma; microbiome dysbiosis; tongue coat. Campbell MJ, McCune E, Johnson B, O'Meara, Heditsian D, Brain S, Esserman L (2019). Breast cancer and the human oral and gut microbiomes [abstract]. In: Proceedings of the American Association for Cancer Research Annual Meeting 2019; 2019 Mar 29-Apr 3; Atlanta, GA. Philadelphia (PA): AACR; Cancer Res 2019;79(13 Suppl): Abstract nr 2830. At: https://cancerres.aacrjournals.org/content/79/13_Supplement/2830 Vasilyeva D, Peters SM, Philipone EM, Yoon AJ (2018). Renal cell carcinoma metastatic to the maxillary gingiva: A case report and review of the literature. J Oral Maxillofac Pathol 22(Suppl 1): S102-S107. DOI: 10.4103/jomfp.JOMFP_69_17 At: <https://pubmed.ncbi.nlm.nih.gov/29491617/> Abstract: Tumor metastasis to the oral cavity is rare and is usually an indication of late-stage disease and poor prognosis. While, there are reports of renal cell carcinoma (RCC) metastatic to oral cavity, vast majority of them are to the jaw. Herein, we present a case of a 78-year-old woman with RCC metastasis limited to the oral soft tissue without any bone involvement. As the lesion solely involved maxillary gingiva, it clinically mimicked that of a pyogenic granuloma, which is a reactive, nonneoplastic condition. This case was further complicated as the patient was unaware of primary cancer and appeared to be in good physical health. Her oral metastasis marked the initial manifestation of an otherwise silent primary renal cancer. McKernan SC, Kuthy RA, Reynolds JC, Tuggle L, García DT (2018). Medical-Dental Integration in Public Health Settings: An Environmental Scan. At: http://ppc.uiowa.edu/sites/default/files/ced_environmental_scan.pdf Executive Summary: Noncommunicable chronic diseases (NCDs) account for almost 90% of total deaths in the United States. The four most common NCDs—cardiovascular diseases, diabetes, cancers, and chronic respiratory diseases—share common risk factors, including cigarette use, alcohol use, and dietary behaviors associated with obesity and elevated blood sugar. The most common oral diseases—dental caries, periodontal disease, and oral cancer—also share these same risk factors. A coordinated approach to primary prevention, the “common risk factor approach,” argues that coordinated primary prevention of oral and systemic diseases will reduce OSHR: Oral Microbiome and Cancer - Page 12 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. programmatic costs, and increase efficiency and effectiveness. However, use and evaluation of this coordinated approach in primary prevention activities in the United States has not been well

documented. This report describes the results of an environmental scan to identify, categorize, and describe examples of medical-dental integration in US public health settings. Findings are intended to inform public health officials and other stakeholders about existing programs and policies that encourage coordination and integration. Conclusion: Public health activities targeting oral health and chronic diseases operate at multiple levels, including public policy, community-level campaigns, health care delivery systems, and clinical interventions. Well-developed efforts were especially noted for environmental approaches targeting sugarsweetened beverage consumption, state-level efforts targeting tobacco use and oral cancer, and co-location of medical and dental services. The lack of robust evaluation and effectiveness data surrounding most of the activities described in this report may hamper widespread implementation, sustainability, and stakeholder support Flemer B, Warren RD, Barrett MP, Cisek K, Das A, Jeffrey IB, Hurley E, O’Riordan M, Shanahan F, O’Toole PW (2018). The oral microbiota in colorectal cancer is distinctive and predictive. *Gut* 67(8): 1454-1463. DOI: 10.1136/gutjnl-2017-314814 At: <https://pubmed.ncbi.nlm.nih.gov/28988196/> Abstract: Background and aims: Microbiota alterations are linked with colorectal cancer (CRC) and notably higher abundance of putative oral bacteria on colonic tumours. However, it is not known if colonic mucosa-associated taxa are indeed orally derived, if such cases are a distinct subset of patients or if the oral microbiome is generally suitable for screening for CRC. Methods: We profiled the microbiota in oral swabs, colonic mucosae and stool from individuals with CRC (99 subjects), colorectal polyps (32) or controls (103). Results: Several oral taxa were differentially abundant in CRC compared with controls, for example, *Streptococcus* and *Prevotellas* sp. A classification model of oral swab microbiota distinguished individuals with CRC or polyps from controls (sensitivity: 53% (CRC)/67% (polyps); specificity: 96%). Combining the data from faecal microbiota and oral swab microbiota increased the sensitivity of this model to 76% (CRC)/88% (polyps). We detected similar bacterial networks in colonic microbiota and oral microbiota datasets comprising putative oral biofilm forming bacteria. While these taxa were more abundant in CRC, core networks between pathogenic, CRC-associated oral bacteria such as *Peptostreptococcus*, *Parvimonas* and *Fusobacterium* were also detected in healthy controls. High abundance of *Lachnospiraceae* was negatively associated with the colonisation of colonic tissue with oral-like bacterial networks suggesting a protective role for certain microbiota types against CRC, possibly by conferring colonisation resistance to CRC-associated oral taxa and possibly mediated through habitual diet. Conclusion: The heterogeneity of CRC may relate to microbiota types that either predispose or provide resistance to the disease, and profiling the oral microbiome may offer an alternative screen for detecting CRC. Keywords: colonic bacteria; colorectal cancer; colorectal cancer screening; diet; tumour markers. Peters BA, Wu J, Pei Z, Yang L, Purdue MP, Freedman ND, Jacobs EJ, Gapstur SM, Hayhes RB, Ahn J (2017). Oral microbiome composition reflects prospective risk for esophageal cancers. *OSHR: Oral Microbiome and Cancer - Page 13 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. Cancer Res* 77(23): 6777-6787. DOI: 10.1158/0008-5472.CAN-17-1296 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5726431/> Abstract: Bacteria may play a role in esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC), although evidence is limited to cross-sectional studies. In this study, we examined the relationship of oral microbiota with EAC and ESCC risk in a prospective study nested in two cohorts. Oral bacteria were assessed using 16S rRNA gene sequencing in pre-diagnostic mouthwash samples from n=81/160 EAC and n=25/50 ESCC cases/matched controls. Findings were largely consistent across both cohorts. Metagenome content was predicted using PiCRUST. We examined associations between centered log-ratio transformed taxon or functional pathway abundances and risk using conditional

logistic regression adjusting for BMI, smoking, and alcohol. We found the periodontal pathogen *Tannerella forsythia* to be associated with higher risk of EAC. Further, we found that depletion of the commensal genus *Neisseria* and the species *Streptococcus pneumoniae* were associated with lower EAC risk. Bacterial biosynthesis of carotenoids was also associated with protection against EAC. Lastly, the abundance of the periodontal pathogen *Porphyromonas gingivalis* trended with higher risk of ESCC. Overall, our findings have potential implications for the early detection and prevention of EAC and ESCC. Keywords: oral microbiome, esophageal cancer, esophageal adenocarcinoma, esophageal squamous cell carcinoma, bacteria. Ramos A, Hemann MT (2017). Drugs, Bugs, and Cancer: *Fusobacterium nucleatum* Promotes Chemoresistance in Colorectal Cancer. *Cell* 170(3): 411-413. At:

<https://www.sciencedirect.com/science/article/pii/S0092867417308255> Yu TC, Guo F, Yu Y, Sun T, Ma D, Han J, Qian Y, Krycek I, Sun D, Nagarsheth N, Chen Y, Chen H, Hong J, Zou W, Fang JY (2017). *Fusobacterium nucleatum* Promotes Chemoresistance to Colorectal Cancer by Modulating Autophagy. *Cell* 170(3): 548-563.e16 At:

<https://www.sciencedirect.com/science/article/pii/S0092867417308152> Summary: Gut microbiota are linked to chronic inflammation and carcinogenesis. Chemotherapy failure is the major cause of recurrence and poor prognosis in colorectal cancer patients. Here, we investigated the contribution of gut microbiota to chemoresistance in patients with colorectal cancer. We found that *Fusobacterium* (*F.*) *nucleatum* was abundant in colorectal cancer tissues in patients with recurrence post chemotherapy, and was associated with patient clinicopathological characteristics.

Furthermore, our bioinformatic and functional studies demonstrated that *F. nucleatum* promoted colorectal cancer resistance to chemotherapy. Mechanistically, *F. nucleatum* targeted TLR4 and MYD88 innate immune signaling and specific microRNAs to activate the autophagy pathway and alter colorectal cancer chemotherapeutic response. Thus, *F. nucleatum* orchestrates a molecular network of the Toll-like receptor, microRNAs, and autophagy to clinically, biologically, and mechanistically control colorectal cancer chemoresistance. Measuring and targeting *F. nucleatum* and its associated pathway will yield valuable insight into clinical management and may ameliorate colorectal cancer patient outcomes. OSHR: Oral Microbiome and Cancer - Page 14 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. Nwizu NN, Marshall JR, Moysich K, Genco RJ, Hovey KM, Xiodan M, LaMonte JL, Wactawski-Wende J (2017). Periodontal Disease and Incident Cancer Risk among Postmenopausal Women: Results from the Women's Health Initiative Observational Cohort. *Cancer Epidemiol Biomarkers Prev* 26(8):1255-65. DOI:

10.1158/1055-9965.EPI-17-0212 At: <https://cebp.aacrjournals.org/content/26/8/1255> Freudenheim JL, Genco RJ, LaMonte MJ, Millen AE, Hovey KM, Mai X, Nwizu N, Andrews CA, Wactawski-Wende J (2016). Periodontal Disease and Breast Cancer: Prospective Cohort Study of Postmenopausal Women. *Cancer Epidemiol Biomarkers Prev* 25(1): 43-50. DOI: 10.1158/1055-9965.EPI-15-0750 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4713270/> Abstract:

Background Periodontal disease (PD) 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. PD was by self-report. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated by Cox proportional hazards, adjusted for breast cancer risk factors. Because the oral microbiome of those with PD 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. PD, reported by 26.1% of

women, was associated with increased breast cancer risk (HR 1.14, 95% CI 1.03 to 1.26), particularly among former smokers who quit within 20 years (HR 1.36; 95% CI 1.05 to 1.77). Among current smokers, the trend was similar (HR 1.32; 95% CI 0.83 to 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 to 21.79) and 10.90% (95% CI 10.31 to 28.94) for PD among former smokers quitting within 20 years and current smokers, respectively. Conclusion PD, 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. Keywords: Breast neoplasms, periodontal disease, postmenopausal women, inflammation, microbiome, epidemiology. Han P, Sun D, Yang J (2016). Interaction between periodontitis and liver diseases. *Biomed Rep* 5(3): 267-276. Published online 2016 Jul 18. doi: 10.3892/br.2016.718 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4998044/> Abstract: Periodontitis is an oral disease that is highly prevalent worldwide, with a prevalence of 30–50% of the population in developed countries, but only ~10% present with severe forms. It is also estimated that periodontitis results in worldwide productivity losses amounting to ~54 billion USD yearly. In addition to the damage it causes to oral health, periodontitis also affects other types of disease. Numerous studies have confirmed the association between periodontitis and systemic diseases, such as diabetes, respiratory disease, osteoporosis and cardiovascular disease. Increasing evidence also indicated that periodontitis may participate in the progression of liver diseases, such as non-alcoholic fatty liver disease, cirrhosis and hepatocellular carcinoma, as well as OSHR: Oral Microbiome and Cancer - Page 15 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. affecting liver transplantation. However, to the best of our knowledge, there are currently no reviews elaborating upon the possible links between periodontitis and liver diseases. Therefore, the current review summarizes the human trials and animal experiments that have been conducted to investigate the correlation between periodontitis and liver diseases. Furthermore, in the present review, certain mechanisms that have been postulated to be responsible for the role of periodontitis in liver diseases (such as bacteria, pro-inflammatory mediators and oxidative stress) are considered. The aim of the review is to introduce the hypothesis that periodontitis may be important in the progression of liver disease, thus providing dentists and physicians with an improved understanding of this issue. Whitmore SE, Lamont RJ; Goldman WE, ed. (2014). *Oral Bacteria and Cancer*. *PLoS Pathog* 10(3): e1003933. DOI: 10.1371/journal.ppat.1003933 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3968118/> Fan X, Alekseyenko AV, Wu J, Peters BA, Jacobs EJ, Gapstur SM, Purdue MP, Abnet CC, Solomon RS, Miller G, Ravel J, Hayes RB, Ahn J (2000). Human oral microbiome and prospective risk for pancreatic cancer: a population-based nested case-control study. *Gut* 67: 120-127. doi:10.1136/gutjnl-2016-312580 At: <https://gut.bmj.com/content/67/1/120.abstract> 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.

Oral Cancer, Head and Neck Cancer OSHR: Oral Microbiome and Cancer - Page 16 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. Fitzsimonds Z, Rodriguez,-Hernandez CJ, Bagaitkar J, Lamont RJ (2020). From Beyond the Pale to the Pale Riders: The Emerging Association of Bacteria with Oral Cancer. *J Dent Res* 99(6): 604- 612. DOI: 10.1177/0022034520907341 At: <https://pubmed.ncbi.nlm.nih.gov/32091956/> Abstract : Oral cancer, predominantly oral squamous cell carcinoma (OSCC), is the eighth-most common cancer worldwide, with a 5-y survival rate

Periodontal Disease and Chronic Systemic Disease

OSHR – PD/OH+Chronic Systemic Disease - Page 1 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. OSHR - Periodontal Disease/Oral Health and Chronic Systemic Illness General, Prevalence and Properties of Periodontal Disease Schmalz G, Ziebolz D (2020). Editorial, Special Issue "Oral Health and Systemic Diseases" Gerhard Schmalz and Dirk Ziebolz J Clin Med 9: 3156
doi:10.3390/jcm9103156 At:

https://www.researchgate.net/publication/344516094_Special_Issue_Oral_Health_and_Systemic_Diseases Summary: With an enormous prevalence worldwide, diseases of the oral cavity and respective tissues are a highly relevant global health issue. Beside of the oral health-related consequences of common oral diseases, like tooth loss, chewing deficiencies and quality of life impairment, oral and systemic disease interaction are apparent. Different systemic diseases and conditions have the potential to affect a risk of developing oral diseases, especially periodontitis; on the other hand, oral inflammation can have an effect on general health. Moreover, several general diseases are related to a potential risk of complications in dental therapy. Kang M-S, Lee D, Lee D-S, Lee S-A, Kim M-S, Nam S-H (2020). Effects of probiotic bacterium *Weissella cibaria* CMU on periodontal health and microbiota: a randomised, double-blind, placebo-controlled trial. BMC Oral Health 20(243). DOI: <https://doi.org/10.1186/s12903-020-01231-2> At:

<https://bmcoralhealth.biomedcentral.com/articles/10.1186/s12903-020-01231-2>. Abstract: Background: *Weissella cibaria* CMU (oraCMU) has been commercially available in the market for several years as oral care probiotics. The present study aimed to evaluate the effects of oraCMU-containing tablets on periodontal health and oral microbiota. Methods: A randomised, double-blind, placebo-controlled trial was conducted in 92 adults without periodontitis (20–39 years of age). All subjects received dental scaling and root planing, and were randomly assigned to either probiotic or placebo groups. The tablets were administered once daily for 8 weeks. Periodontal clinical parameters included bleeding on probing (BOP), probing depth (PD), gingival index (GI), and plaque index (PI). In addition, microbiota in the gingival sulcus were analysed. Results: BOP improved more in the probiotic group over 8 weeks. There were statistically significant differences in BOP of the maxilla buccal and lingual sites between the groups during the intervention (P 90% and Hispanic Americans >75% of the UK and US cohorts, respectively. Males and females were equally distributed; mean age was 53.6±11 years; and 17 (6.7%) were edentulous. Of the 236 dentate patients, 128 (54.2%) had periodontitis by low threshold and 57 (24.2%) by high threshold. Just 17 (7.2%) were periodontally healthy. No significant differences in age, HbA1c, blood pressure, body mass index, low-density lipoprotein cholesterol, or smoking status (all p>0.05) were identified between those with or without periodontitis (regardless of threshold) and none was found to OSHR – PD/OH+Chronic Systemic Disease - Page 15 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. be a significant predictor of disease. Conclusions Periodontitis is frequent in adults with type 2 diabetes and all should be screened. Periodontal health status can be visualized with other comorbidities and complications using a novel balanced scorecard that could facilitate patient– clinician communication, shared decision-making, and prioritization of individual healthcare needs. Glurich I, Nycz G, Acharya A (2017). Status Update on Translation of Integrated Primary DentalMedical Care Delivery for Management of Diabetic Patients. Clin Med Res 15(1-2): 21-32. doi: 10.3121/cmr.2017.1348. Epub 2017 Apr 3 At:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5572842/> Abstract: Escalating prevalence of both diabetes and periodontal disease, two diseases associated with bi-directional exacerbation, has

been reported. Periodontal disease represents a modifiable risk factor that may reduce diabetes onset or progression, and integrated models of cross-disciplinary care are needed to establish and manage glycemic control in affected patients. An ad-hoc environmental scan of current literature and media sought to characterize factors impacting status of integrated care models based on review of the existing evidence base in literature and media surrounding: (1) current cross-disciplinary practice patterns, (2) epidemiological updates, (3) status on risk assessment and screening for dysglycemia in the dental setting, (4) status on implementation of quality metrics for oral health, (5) care model pilots, and (6) public health perspectives. The survey revealed: escalating prevalence of diabetes and periodontitis globally; greater emphasis on oral health assessment for diabetic patients in recent medical clinical practice guidelines; high knowledgeableability surrounding oral-systemic impacts on diabetes and growing receptivity to medical-dental integration among medical and dental providers; increasing numbers of programs/studies reporting on positive impact of emerging integrated dental-medical care models on diabetic patient healthcare access and health outcomes; a growing evidence base for clinically significant rates of undiagnosed dysglycemia among dental patients reported by point-of-care pilot studies; no current recommendation for populationbased screening for dysglycemia in dental settings pending a stronger evidence base; improved definition of true periodontitis prevalence in (pre)/diabetics; emerging recognition of the need for oral health quality indicators and tracking; evidence of persistence in dental access disparity; updated status on barriers to integration. The potential benefit of creating clinicallyapplicable integrated care models to support holistic management of an escalating diabetic population by targeting modifiable risk factors including periodontitis is being recognized by the health industry. Cross-disciplinary efforts supported by high quality research are needed to mitigate previously- and newly-defined barriers of care integration and expedite development and implementation of integrated care models in various practice settings. Implementation of quality monitoring in the dental setting will support definition of the impact and efficacy of interventional clinical care models on patient outcomes. Teeuw WJ Gerdes VEA, Loos BGG (2010). Effect of Periodontal Treatment on Glycemic Control of Diabetic Patients: A systematic review and meta-analysis. *Diabetes Care* 33(2): 421-427. At: <https://care.diabetesjournals.org/content/33/2/421> DOI:: <https://doi.org/10.2337/dc09-1378>

OSHR – PD/OH+Chronic Systemic Disease - Page 16 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021.

Periodontal Disease and Diabetes 1 Duda-Sobczak A, Zozulinska-Ziolkiewicz D, Wyganowska-Swiatkowska M (2018). Type 1 Diabetes and Periodontal Health. *Clin Therapeut* 40(6): 823-827. DOI: <https://doi.org/10.1016/j.clinthera.2018.01.011> At: Abstract: It is well established that hyperglycemia affects periodontal outcomes. A body of evidence, predominantly over the past 20 years supports significant independent associations between periodontal disease and glycemic control or complications of diabetes. Association between periodontal tissue and hyperglycemia is possible through altered cellular immunity, increased proliferation of bacteria, microangiopathy, and formation of the advanced glycation end products. However, most studies focus solely on patients with type 2 diabetes or diabetes in general. There is still the paucity of data concerning patients with type 1 diabetes (T1D). Here, the authors consider the possible mechanisms linking periodontal disease with diabetes, focusing mainly on T1D and discuss possible diagnostic and therapeutic approaches. Duran-Merino D, Molina-Frechero N, Castañeda-Castaneira E, Gaona E, Reyes-Reyes RE , Tremillo-Maldonado O, del Muro-Delgado R , Juárez-López ML and Bologna-Molina R (2017). Relationship between Periodontal Disease and Type 1 Diabetes in Adolescents. *Ann Med & Health Sci Res* 7: 350-354. DOI: 10.1155/2015/379626 At: <https://www.amhsr.org/articles/relationship-between-periodontal-disease-and-type-1-diabetes-in->

adolescents.pdf Abstract: Aim: The aim of this study was to evaluate the prevalence and severity of periodontal disease (PD) in adolescents with type 1 diabetes mellitus (DM) and assess the relationship with the clinical and metabolic control of diabetes in adolescents. Material and Methods: A descriptive and analytical study was conducted in patients of both sexes who had a definite diagnosis of type 1 DM and diabetes duration of at least 3 years. An odontologist evaluated PD using the American Dental Association criteria. The measured glycosylated hemoglobin (HbA1c) levels revealed an association between PD and the duration and metabolic control of DM. Results: One hundred and one patients with an average age of 15.02 ± 1.216 years were studied; 59.4% were female. Adolescents with a shorter diabetes duration (3 to 5 years) had a lower prevalence of PD (65.6% versus 34.4%); and for those with a disease duration > 6 years, stages II-IV PD predominated (56.8%, $p < 0.001$), probing pocket depth ($P < 0.001$) and clinical attachment level ($P = 0.001$). Patients diagnosed for diabetes for shorter duration of time (4-7 years) showed bleeding index-disease severity correlation to be 1.760 ± 0.434 . Conclusion: Periodontal disease was more evident in type 1 diabetes mellitus patients and periodontal inflammation is greatly increased in subjects with longer disease course, poor metabolic control and diabetic complications. Keywords: Complications, HbA1c, metabolic control, periodontitis, type I diabetes. Periodontal Disease and Cardiovascular Diseases (CVDs) Coi SE, Sima C, Pandya A (2020). Impact of Treating Oral Disease on Preventing Vascular Diseases: A Model-Based Cost-effectiveness Analysis of Periodontal Treatment Among Patients With Type 2 Diabetes. *Diabetes Care* 43(3) : 563-571. DOI: <https://doi.org/10.2337/dc19-1201> At: <https://care.diabetesjournals.org/content/43/3/563.abstract> Abstract: OBJECTIVE Previous randomized trials found that treating periodontitis improved glycemic control in patients with type 2 diabetes (T2D), thus lowering the risks of developing T2D-related microvascular diseases and cardiovascular disease (CVD). Some payers in the U.S. have started covering nonsurgical periodontal treatment for those with chronic conditions, such as diabetes. We sought to identify the cost-effectiveness of expanding periodontal treatment coverage among patients with T2D. - RESEARCH DESIGN AND METHODS A cost-effectiveness analysis was conducted to estimate lifetime costs and health gains using a stochastic microsimulation model of oral health conditions, T2D, T2D-related microvascular diseases, and CVD of the U.S. population. Model parameters were obtained from the nationally representative National Health and Nutrition Examination Survey (NHANES) (2009–2014) and randomized trials of periodontal treatment among patients with T2D. - RESULTS Expanding periodontal treatment coverage among patients with T2D and periodontitis would be expected to avert tooth loss by 34.1% (95% CI -39.9, -26.5) and microvascular diseases by 20.5% (95% CI -31.2, -9.1), 17.7% (95% CI -32.7, -4.7), and 18.4% (95% CI -34.5, -3.5) for nephropathy, neuropathy, and retinopathy, respectively. Providing periodontal treatment to the target population would be cost saving from a health care perspective at a total net savings of \$5,904 (95% CI -6,039, -5,769) with an estimated gain of 0.6 quality-adjusted life years per capita (95% CI 0.5, 0.6). - CONCLUSIONS Providing nonsurgical periodontal treatment to patients with T2D and periodontitis would be expected to significantly reduce tooth loss and T2D-related microvascular diseases via improved glycemic control. Encouraging patients with T2D and poor oral health conditions to receive periodontal treatment would improve health outcomes and still be cost saving or cost-effective. Chang Y, Woo HG, Park J, Lee JS, Song TJ (2019). Improved oral hygiene care is associated with decreased risk of occurrence for atrial fibrillation and heart failure: a nationwide population- OSHR – PD/OH+Chronic Systemic Disease - Page 18 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. based cohort study. *Eur J Prev Cardiol*, doi: 10.1177/2047487319886018. [Epub ahead of print]. At:

<https://www.ncbi.nlm.nih.gov/pubmed/31786965> Patel J, Mowery D, Krishnan A, Thyvalikakath T (2018). Assessing Information Congruence of Documented Cardiovascular Disease between Electronic Dental and Medical Records. *AMIA Annu Symp Proc* 1442-1450. At: <https://www.ncbi.nlm.nih.gov/pubmed/30815189> Fagundes N C F, Almeida A P C P S C, Vilhena K F B, Magno M B, Maia L C, Lima R R (2019). Periodontitis as a risk factor for stroke: a systematic review and meta-analysis. *Vascular Health and Risk Management* 15: 519-532. Available at: <https://www.dovepress.com/periodontitis-asa-risk-factor-for-stroke-a-systematic-review-and-meta-peer-reviewed-article-VHRM> Patrakka O, Pienimäki JP, Tuomisto S, Ollikainen J, Tehtimäki T, Karhunen PJ, Martiskainen M (2019). Oral Bacterial Signatures in Cerebral Thrombi of Patients With Acute Ischemic Stroke Treated With Thrombectomy. *J Amer Heart Assn* 8: e012330. At: <https://www.ahajournals.org/doi/10.1161/JAHA.119.012330> Pillai RS, Iyer K, Spin-Neto R, Kothari SF, Nielsen JF, Kothari M (2018). Oral Health and Brain Injury: Causal or Casual Relation? *Cerebrovasc Dis Extra* 8(1): 1–15. Published online 2018 Jan 9. doi: 10.1159/000484989 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5836263/> Batty GD, Jun KJ, Mok Yejin, Lee SJ, Back JH, Lee S, Jee SH (2018). Oral health and later coronary heart disease: Cohort study of one million people. *Eur J Prev Cardiol* 25(6):598-605. Doi: 10- 1177/2047487318759112 At: <https://journals.sagepub.com/doi/pdf/10.1177/2047487318759112> Ishai A, Takx R, Abdelrahman A, El Kholly K, Van Dyke T, Tawakoi A (2018). Abstract 20033: Periodontal Disease Activity Independently Predicts Future Risk for Cardiovascular Events. *Circulation* 134, Supplement 1. https://www.ahajournals.org/doi/abs/10.1161/circ.134.suppl_1.20033 Allareddy V, Prakasam S, Rampa S, Stein K, Nalliah RP, Allareddy V, Venugopalan RS. (2017). Impact of Periapical Abscess on Infectious Complications in Patients Undergoing Extracorporeal Circulation Auxiliary to Open-Heart Surgical Procedures. *J Evid Based Dent Pract.* 2017 Mar;17(1):13-22. Jockel-Schneider Y, Heß J, Schlagenhauf U. (2016). Was Parodontitis und Herz-KreislaufErkrankungen verbindet. *wissen kompakt* 10, 95–102 (2016). <https://doi.org/10.1007/s11838-016-0025-8> At: <https://link.springer.com/article/10.1007/s11838-016-0025-8> Zusammenfassung: Parodontitis wie auch kardiovaskuläre Erkrankungen stellen in der Bevölkerung weit verbreitete Gesundheitsprobleme dar. Die Assoziation beider Erkrankungen ist durch zahlreiche Studien gut belegt. Die genauen Zusammenhänge sind allerdings nur fragmentarisch entschlüsselt. Die Frage, welche Auswirkungen die Elimination einer parodontalen Entzündung hat, ist ebenfalls nur wenig untersucht. Erste Ergebnisse weisen aber auf eine Dosis-Wirkungs-Beziehung beider Erkrankungen hin. Bokhari SAH, Khan AA, Leung WK, Wajid G (2015). Association of periodontal and cardiovascular diseases: South-Asian studies 2001–2012. *Indian Soc Periodontol* 19(5): 495-500. doi: 10.4103/0972-124X.157876. At: OSHR – PD/OH+Chronic Systemic Disease - Page 19 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. https://www.researchgate.net/publication/277978573_Association_of_periodontal_and_cardiovascular_diseases_South-Asian_studies_2001-2012 Abstract: Large proportion of Asian populations have moderate to severe periodontal disease and a substantial number are anticipated to be at high risk of cardiovascular diseases(CVD). This study reviews epidemiology and association of periodontal and CVDs from the South-Asian region. Observational studies and clinical trials published during January 2001–December 2012 focusing association between periodontitis and CVDs in South-Asian countries were retrieved from various databases and studied. Current evidence suggests that both periodontal and CVDs are globally prevalent and show an increasing trend in developing countries. Global data on epidemiology and association of periodontal and CVDs are predominantly from the developed world; whereas Asia with 60% of the world's population lacks substantial scientific data on the link between periodontal and CVDs. During the

search period, 14 studies (5 clinical trials, 9 case–controls) were reported in literature from South-Asia; 100% of clinical trials and 77% case–control studies have reported a significant association between the oral/periodontal parameters and CVD. Epidemiological and clinical studies from South-Asia validate the global evidence on association of periodontal disease with CVDs. However, there is a need for meticulous research for public health and scientific perspective of the Periodontal and CVDs from South-Asia. Fifer KM, Qadir S, Subramanian S, Vijayakumar J, Figueroa AL, Truong QA, Hoffman U, Brady TJ, Tawakoi A (2011). Positron emission tomography measurement of periodontal ¹⁸Ffluorodeoxyglucose uptake is associated with histologically determined carotid plaque inflammation. *J Am Coll Cardiol* 57(8):971-976. doi: 10.1016/j.jacc.2010.09.056

Periodontal Disease and Respiratory Diseases, including VAP, Covid-19 Zimmerman S, Sloan PD, Ward K, Wretman CJ, Stearns SC, Poole P, Preisser JS (2020). Effectiveness of a Mouth Care Program Provided by Nursing Home Staff vs Standard Care on Reducing Pneumonia Incidence: A Cluster Randomized Trial. *JAMA Network Open* 3(6): e204321 doi:10.1001/jamanetworkopen.2020.4321 At: <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2767357>

Abstract: IMPORTANCE Pneumonia affects more than 250 000 nursing home (NH) residents annually. A strategy to reduce pneumonia is to provide daily mouth care, especially to residents with dementia. **OBJECTIVE** To evaluate the effectiveness of Mouth Care Without a Battle, a program that increases staff knowledge and attitudes regarding oral hygiene, changes mouth care, and improves oral hygiene, in reducing the incidence of pneumonia among NH residents. **DESIGN, SETTING, AND PARTICIPANTS** This pragmatic cluster randomized trial observing 2152 NH residents for up to 2 years was conducted from September 2014 to May 2017. Data collectors were masked to study group. The study included 14 NHs from regions of North Carolina that evidenced proportionately high rehospitalization rates for pneumonia and long-term care residents. Nursing homes were pair matched and randomly assigned to intervention or control groups. **INTERVENTION** Mouth Care Without a Battle is a standardized program that teaches that mouth care is health care, provides instruction on individualized techniques and products for mouth care, and trains caregivers to provide care to residents who are resistant and in special situations. The control condition was standard mouth care. **MAIN OUTCOMES AND MEASURES** Pneumonia incidence (primary) and hospitalization and mortality (secondary), OSHR – PD/OH+Chronic Systemic Disease - Page 20 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. obtained from medical records. **RESULTS** Overall, the study enrolled 2152 residents (mean [SD] age, 79.4 [12.4] years; 1281 [66.2%] women; 1180 [62.2%] white residents). Participants included 1219 residents (56.6%) in 7 intervention NHs and 933 residents (43.4%) in 7 control NHs. During the 2-year study period, the incidence rate of pneumonia per 1000 resident-days was 0.67 and 0.72 in the intervention and control NHs, respectively. Neither the primary (unadjusted) nor secondary (covariate-adjusted) analyses found a significant reduction in pneumonia due to Mouth Care Without a Battle during 2 years (unadjusted incidence rate ratio, 0.90; upper bound of 1-sided 95% CI, 1.24; P = .27; adjusted incidence rate ratio, 0.92; upper bound of 1-sided 95% CI, 1.27; P = .30). In the second year, the rate of pneumonia was nonsignificantly higher in intervention NHs. Adjusted post hoc analyses limited to the first year found a significant reduction in pneumonia incidence in intervention NHs (IRR, 0.69; upper bound of 1-sided 95% CI, 0.94; P = .03). **CONCLUSIONS AND RELEVANCE** This matched-pairs cluster randomized trial of a mouth care program compared with standard care was not effective in reducing pneumonia incidence at 2 years, although reduction was found during the first year. The lack of significant results in the second year may be associated with sustainability. Improving mouth care in US NHs may require the presence and support of dedicated oral care

aides. Botros N, Iyer P, Ojcius DM (2020). Is there an association between oral health and severity of COVID-19 complications? *Biomed J* 43: 325-327. DOI: DOI: 10.1016/j.bj.2020.05.016 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7258848/pdf/main.pdf> Abstract: Most patients with severe complications from COVID-19 have underlying conditions such as obesity, diabetes, and hypertension. In parallel, there is growing evidence for a link between periodontitis and non-oral systemic diseases. The oral cavity is also a reservoir for respiratory pathogens, and patients with periodontal disease are more likely to develop hospital-acquired pneumonia than healthy individuals. We therefore hypothesize that improving oral health could decrease the severity of COVID-19 symptoms and reduce the associated morbidity. Dörfer C; Benz C; Aida J; Campard G (2017). The relationship of oral health with general health and NCDs: A brief review. *Int. Dent. J.* 67: 14–18. DOI: 10.1111/idj.12360 At: <https://pubmed.ncbi.nlm.nih.gov/29023744/> Abstract: Oral health is closely related to systemic health. Periodontitis, a chronic inflammatory disease which is highly prevalent worldwide, interacts with a variety of noncommunicable diseases (NCDs). It is a risk factor in the complex pathogenesis of diabetes mellitus and cardiovascular disease and plays a role in the development of endocarditis and recurrent pneumonia in elderly people. However, the available data may be interpreted in different ways, and more and better-designed studies are still needed to answer relevant questions about the causal role of periodontitis in NCDs. What is clear is that periodontitis contributes to the systemic inflammatory burden. As periodontitis shares many common risk factors with NCDs, close collaboration between physicians and dentists is needed to increase the chance of early detection and improve the prevention and control of these conditions Manger D, Walshaw M, Fitzgerald R, Doughty J, Wanyony KL, White S, Gallagher JE (2017). Evidence summary: the relationship between oral health and pulmonary disease. *Br Dent J* 222, OSHR – PD/OH+Chronic Systemic Disease - Page 21 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. 527–533. doi: <https://doi.org/10.1038/sj.bdj.2017.315> At: <https://www.nature.com/articles/sj.bdj.2017.315> Hue F, Xie H, Worthington HV, Furness S, Zhang Q, Li C, Cochrane Oral Health Group, Managing Eds. (2016). Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database Syst Rev* 10: CD008367. DOI: 10.1002/14651858.CD008367.pub3 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6460950/> Abstract: Background Ventilator-associated pneumonia (VAP) is defined as pneumonia developing in people who have received mechanical ventilation for at least 48 hours. VAP is a potentially serious complication in these patients who are already critically ill. Oral hygiene care (OHC), using either a mouthrinse, gel, toothbrush, or combination, together with aspiration of secretions, may reduce the risk of VAP in these patients. Objectives To assess the effects of oral hygiene care on incidence of ventilator-associated pneumonia in critically ill patients receiving mechanical ventilation in hospital intensive care units (ICUs). Search methods We searched the following electronic databases: Cochrane Oral Health's Trials Register (to 17 December 2015), the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library, 2015, Issue 11), MEDLINE Ovid (1946 to 17 December 2015), Embase Ovid (1980 to 17 December 2015), LILACS BIREME Virtual Health Library (1982 to 17 December 2015), CINAHL EBSCO (1937 to 17 December 2016), Chinese Biomedical Literature Database (1978 to 14 January 2013), China National Knowledge Infrastructure (1994 to 14 January 2013), Wan Fang Database (January 1984 to 14 January 2013) and VIP Database (January 2012 to 4 May 2016). We searched ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform for ongoing trials to 17 December 2015. We placed no restrictions on the language or date of publication when searching the electronic databases. Selection criteria We included randomised controlled trials (RCTs) evaluating the effects of OHC

(mouthrinse, swab, toothbrush or combination) in critically ill patients receiving mechanical ventilation for at least 48 hours. Data collection and analysis At least two review authors independently assessed search results, extracted data and assessed risk of bias in included studies. We contacted study authors for additional information. We pooled data from trials with similar interventions and outcomes. We reported risk ratio (RR) for dichotomous outcomes and mean difference (MD) for continuous outcomes, using random effects models unless there were fewer than four studies. Main results We included 38 RCTs (6016 participants). There were four main comparisons: chlorhexidine (CHX) mouthrinse or gel versus placebo/usual care; toothbrushing versus no toothbrushing; powered versus manual toothbrushing; and comparisons of oral care solutions. We assessed the overall risk of bias as low in five trials (13%), high in 26 trials (68%), and unclear in seven trials (18%). We did not consider the risk of bias to be serious when assessing the quality of evidence (GRADE) for VAP incidence, but we downgraded other outcomes for risk of bias. High quality evidence from 18 RCTs (2451 participants, 86% adults) shows that CHX mouthrinse or gel, as part of OHC, reduces the risk of VAP compared to placebo or usual care from 24% to about 18% (RR 0.75, 95% confidence intervals (CI) 0.62 to 0.91, $P = 0.004$, $I^2 = 35\%$). This is equivalent to a number needed to treat for an additional beneficial outcome (NNTB) of 17 (95% CI 9 to 50), which indicates that for every 17 ventilated patients in intensive care receiving OHC including chlorhexidine, one outcome of VAP would be prevented. There is no evidence of a difference OSHR – PD/OH+Chronic Systemic Disease - Page 22 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. between CHX and placebo/usual care for the outcomes of mortality (RR 1.09, 95% CI 0.96 to 1.23, $P = 0.20$, $I^2 = 0\%$, 14 RCTs, 2014 participants, moderate quality evidence), duration of mechanical ventilation (MD -0.09 days, 95% CI -1.73 to 1.55 days, $P = 0.91$, $I^2 = 36\%$, five RCTs, 800 participants, low quality evidence), or duration of intensive care unit (ICU) stay (MD 0.21 days, 95% CI -1.48 to 1.89 days, $P = 0.81$, $I^2 = 9\%$, six RCTs, 833 participants, moderate quality evidence). There is insufficient evidence to determine the effect of CHX on duration of systemic antibiotics, oral health indices, caregivers' preferences or cost. Only two studies reported any adverse effects, and these were mild with similar frequency in CHX and control groups.-- We are uncertain as to the effects of toothbrushing (\pm antiseptics) on the outcomes of VAP (RR 0.69, 95% CI 0.44 to 1.09, $P = 0.11$, $I^2 = 64\%$, five RCTs, 889 participants, very low quality evidence) and mortality (RR 0.87, 95% CI 0.70 to 1.09, $P = 0.24$, $I^2 = 0\%$, five RCTs, 889 participants, low quality evidence) compared to OHC without toothbrushing (\pm antiseptics). There is insufficient evidence to determine whether toothbrushing affects duration of mechanical ventilation, duration of ICU stay, use of systemic antibiotics, oral health indices, adverse effects, caregivers' preferences or cost. Only one trial (78 participants) compared use of a powered toothbrush with a manual toothbrush, providing insufficient evidence to determine the effect on any of the outcomes of this review. -- Fifteen trials compared various other oral care solutions. There is very weak evidence that povidone iodine mouthrinse is more effective than saline/placebo (RR 0.69, 95% CI 0.50 to 0.95, $P = 0.02$, $I^2 = 74\%$, three studies, 356 participants, high risk of bias), and that saline rinse is more effective than saline swab (RR 0.47, 95% CI 0.37 to 0.62, $P < 0.001$, $I^2 = 84\%$, four studies, 488 participants, high risk of bias) in reducing VAP. Due to variation in comparisons and outcomes among trials, there is insufficient evidence concerning the effects of other oral care solutions. Authors' conclusions OHC including chlorhexidine mouthwash or gel reduces the risk of developing ventilator-associated pneumonia in critically ill patients from 24% to about 18%. However, there is no evidence of a difference in the outcomes of mortality, duration of mechanical ventilation or duration of ICU stay. There is no evidence that OHC including both antiseptics and toothbrushing is different from OHC with antiseptics alone, and some weak

evidence to suggest that povidone iodine mouthrinse is more effective than saline/placebo, and saline rinse is more effective than saline swab in reducing VAP. There is insufficient evidence to determine whether powered toothbrushing or other oral care solutions are effective in reducing VAP. There is also insufficient evidence to determine whether any of the interventions evaluated in the studies are associated with adverse effects. Gupta A, Guopta A, Sing TK, Saxsena A (2016). Role of oral care to prevent VAP in mechanically ventilated Intensive Care Unit patients. *Saudi J Anesth* 10(1): 95-97. DOI: 10.4103/1658-354X.169484 Abstract: Scannapieco F (2006). Pneumonia in nonambulatory patients. The role of oral bacteria and oral hygiene. *J Am Dent Assoc* 137 Suppl: 21S-25S doi: 10.14219/jada.archive.2006.0400. At: <https://pubmed.ncbi.nlm.nih.gov/17012732/> Abstract: Background: Considerable evidence exists to support a relationship between poor oral health, the oral microflora and bacterial pneumonia, especially ventilator-associated pneumonia in institutionalized patients. Teeth or dentures have nonshedding surfaces on which oral biofilms (that is, dental plaque) form that are susceptible to colonization by respiratory pathogens. Subsequent aspiration of respiratory pathogens shed from oral biofilms into the lower airway OSHR – PD/OH+Chronic Systemic Disease - Page 23 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. increases the risk of developing a lung infection. In addition, patients may aspirate inflammatory products from inflamed periodontal tissues into the lower airway, contributing to lung insult. Types of studies reviewed: The author reviewed laboratory studies, clinical trials and review articles. Conclusions: A number of studies have shown that the mouth can be colonized by respiratory pathogens and serve as a reservoir for these organisms. Other studies have demonstrated that oral interventions aimed at controlling or reducing oral biofilms can reduce the risk of pneumonia in high-risk populations. Taken together, the evidence is substantial that improved oral hygiene may prevent pneumonia in vulnerable patients. Clinical implications: Institution of rigorous oral hygiene regimens for hospitalized patients and longterm-care residents may reduce the risk of developing pneumonia. Periodontal Diseases and Inflammatory Auto-Immune Dseases Lee YC, Jeong SJ, Eun Y-G, Song R, Oh IH (2020). Risk of autoimmune diseases in recurrent aphthous ulcer patients: A nationwide population study. *Oral Dis* doi:10.1111/odi.13659 At: <https://onlinelibrary.wiley.com/doi/abs/10.1111/odi.13659> Abstract: Objective To estimate the risk of developing autoimmune disease in patients diagnosed having recurrent aphthous stomatitis (RAS) through a nationwide population-based cohort study. Methods This study included two group of patients 'patients who had three or more episodes with aphthae diagnosed from their physician (RAS group) and a similar matched group of patients without aphthae (control group). Both groups were collected within the period of 2005-2007 from the Korean National Health Insurances claims database. Non-RAS cohort were matched after frequency matching. The final enrolled subjects were observed during a follow-up period from 2008 to 2015 and those who received autoimmune diseases diagnoses during follow-up were identified. The hazard ratio (HR) for developing autoimmune diseases was estimated. Results A total of 4,637 patients with RAS and 4,637 controls were included. The risk of overall autoimmune diseases was significantly increased in the RAS group. (adjusted HR (aHR), 1.19) With regard to each disease entity, patients with RAS showed an increased risk of Bechet's disease (31.16), systemic lupus erythematosus (SLE) (1.74), ankylosing spondylitis (AS) (1.47), gout (1.47), Hashimoto thyroiditis(1.42), Graves' disease (1.37). and rheumatoid arthritis (RA) (1.19). Conclusion RAS like lesion may be an early sign of systemic autoimmune disease, as it was associated with an increased risk of Graves' disease, Hashimoto thyroiditis, SLE, AS, gout, RA, and Bechet's disease from real world data. Busch M (2020). Mouth ulcers may be early sign of autoimmune disease. *DrBicuspid*. At: <https://www.drbuspid.com/index.aspx?sec=nws&sub=rad&pag=dis&itemID=327375>

Eriksson K, Fei G, Ludmark A, Benchimol D, Lee L, Hu Y, Kats A, Saevarsdottir S, Catrina AI, Klinge B, Andersson AF, Klaarskog L, Lundberg K, Jansson L, Yucel-Lidberg T (2019). Periodontal Health and Oral Microbiota in Patients with Rheumatoid Arthritis. *J Clin Med* 8(5). Pii: E60. doi: 10.3390/jcm8050630 At: <https://www.ncbi.nlm.nih.gov/pubmed/31072030> Lin C-Y, Tseng C-F, Liu J-M, Chuang H-C, Lei W-T, Liu LY-M, Yu Y-C, Hsu R-J (2019). Association between Periodontal Disease and Subsequent Sjögren's Syndrome: A Nationwide PopulationBased Cohort Study. *Int J Environ Res Public Health* 16(5): 771. DOI: 10.3390/ijerph16050771 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6427323/> Potempa J, Mydel P, Koziel J OSHR – PD/OH+Chronic Systemic Disease - Page 24 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. (2017). The Case for Periodontitis in the Pathogenesis of Rheumatoid Arthritis. *Nat Rev Rheumatol* 13(10): 606-620. doi: 10.1038/nrrheum.2017.132. Epub 2017 Aug 24. At: <https://pubmed.ncbi.nlm.nih.gov/28835673/> Abstract: Rheumatoid arthritis (RA), an autoimmune disease that affects ~1% of the human population, is driven by autoantibodies that target modified self-epitopes, whereas ~11% of the global adult population are affected by severe chronic periodontitis, a disease in which the commensal microflora on the tooth surface is replaced by a dysbiotic consortium of bacteria that promote the chronic inflammatory destruction of periodontal tissue. Despite differences in aetiology, RA and periodontitis are similar in terms of pathogenesis; both diseases involve chronic inflammation fuelled by proinflammatory cytokines, connective tissue breakdown and bone erosion. The two diseases also share risk factors such as smoking and ageing, and have strong epidemiological, serological and clinical associations. In light of the ground-breaking discovery that *Porphyromonas gingivalis*, a pivotal periodontal pathogen, is the only human pathogen known to express peptidylarginine deiminase, an enzyme that generates citrullinated epitopes that are recognized by anticitrullinated protein antibodies, a new paradigm is emerging. In this Review, the clinical and experimental evidence supporting this paradigm is discussed and the potential mechanisms involved in linking periodontitis to RA are presented. Skudutyte-Rysstad R, Slevolden EM, Hansen BF, Sandvik L, Ragnar-Preus HR (2014). Association between moderate to severe psoriasis and periodontitis in a Scandinavian population. *BMC Oral Health* 14: 139. Association between moderate to severe psoriasis and periodontitis in a Scandinavian population. Published online 2014 Nov 26. doi: 10.1186/1472-6831-14-139 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4280688/> Abstract: Background The aim of the present study was to compare the prevalence of periodontitis and alveolar bone loss among individuals with psoriasis and a group of randomly selected controls. Methods Fifty individuals with psoriasis and 121 controls completed a structured questionnaire, and were examined clinically and radiographically. Oral examination included numbers of missing teeth, probing pocket depth (PPD), clinical attachment level (CAL), presence of dental plaque and bleeding on probing, as well as alveolar bone loss from radiographs. Questionnaires requested information on age, gender, education, dental care, smoking habits, general diseases and medicament use. For adjustment for baseline differences between psoriasis individuals and controls the propensity score based on gender, age and education was computed using multivariate logistic regression. A subsample analysis for propensity score matched psoriasis individuals (n = 50) and controls (n = 50) was performed. Results When compared with controls, psoriasis individuals had significantly more missing teeth and more sites with plaque and bleeding on probing. The prevalence of moderate and severe periodontitis was significantly higher among psoriasis individuals (24%) compared to healthy controls (10%). Similarly, 36% of psoriasis cases had one or more sites with radiographic bone loss ≥ 3 mm, compared to 13% of controls. Logistic regression analysis showed that the association between moderate/severe periodontitis and psoriasis remained statistically significant

when adjusted for propensity score, but was attenuated when smoking was entered into the model. The association between psoriasis and one or more sites with bone loss ≥ 3 mm remained statistically significant when adjusted for OSHR – PD/OH+Chronic Systemic Disease - Page 25 of 28 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. propensity score and smoking and regularity of dental visits. In the propensity score (age, gender and education) matched sample (n = 100) psoriasis remained significantly associated with moderate/severe periodontitis and radiographic bone loss.

Conclusions Within the limits of the present study, periodontitis and radiographic bone loss is more common among patients with moderate/severe psoriasis compared with the general population.

This association remained significant after controlling for confounders. Üstün K, Sezer U, Kısacık B. et al. (2013). Periodontal Disease in Patients with Psoriatic Arthritis. *Inflammation* 36, 665–669

<https://doi.org/10.1007/s10753-012-9590-y> At:

<https://link.springer.com/article/10.1007/s10753-012-9590-y> Abstract: Rheumatological diseases and periodontal disease are both characterized by dysregulation of the host inflammatory response. The aim of this study was to determine the possible relationship between periodontitis and psoriatic arthritis (PsA). Fifty-one adults with PsA (27 men and 24 women; mean age 41.73 ± 11.27 years) and 50 age- and gender-balanced systemically healthy control subjects participated in the study. Participants' periodontal status as determined by probing pocket depth, clinical attachment loss (CAL), plaque index, and gingival index was evaluated. The CAL levels of the PsA group were significantly higher than those of the control group.

The Oral Microbiome and Cancer

OSHR: Oral Microbiome and Cancer - Page 1 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. OSHR – Oral Microbiome and Cancer Introduction, The oral microbiome and cancer, contributed by Dr. Ingrid Glurich, Project Scientist I, Center for Oral and Systemic Health, Marshfield Clinic Research Institute, Marshfield, WI, USA: <https://marshfieldresearch.org/profiles/5891> The hard and soft surfaces in the oral cavity present a spectrum of habitats that are colonized by bacteria representing over 600 taxa with variable density in representation across respective oral niches (1). Collectively, these organisms represent the oral microbiota. A growing body of evidence supports an important role for the oral microbiota as potential contributors to promotion of both local and systemic oncogenesis. Increased oncogenic potential appears to be associated with establishment of dysbiosis in the oral cavity, including establishment of oral pathogens associated with induction of periodontal disease. Moreover, pathogenic mechanisms that support active contribution to oncogenesis by oral bacteria have been delineated. To date contributory mechanisms that promote oncogenesis have been broadly classified into three categories: 1) induction of local and systemic inflammation largely through upregulation of pro-inflammatory cytokines; activation of pathways that disrupt physiologic apoptosis and normal cell cycling while promoting susceptibility to cellular invasion; and 3) release of toxic and/or carcinogenic substances into the environment that promote oncogenesis. (2,3) Oral pathogens implicated in more localized cancers such as oral squamous cell carcinomas include: *Streptococcus* sp., *Peptostreptococcus* sp *Prevotella* sp., *Porphyromonas gingivalis*, and *Capnocytophaga gingivalis* (4-10). Increased carriage of periodontal pathogens including *Porphyromonas gingivalis* and *Fusobacterium nucleatum* among other oral bacteria, has also been implicated in oncogenesis of extraoral cancers including colorectal (11-15) orodigestive (16,17) and pancreatic cancers (18,19). Higher representation of *Capnocytophaga* and *Veillonella* has also been reported in conjunction with lung cancers (20). References: 1. Dewhirst, FE, Chen T, Izard J, Paster BJ, Tanner AC, Yu WH, Lakshmanan A, Wade WG. The human oral microbiome. *J Bacteriol* 2010;192(19):5002-5017 doi:10.1128/JB.00542-10. <https://jb.asm.org/content/jb/192/19/5002.full.pdf> 2. Zhang Y., Wang X., Li H., Ni C., Du Z., Yan F. Human oral microbiota and its modulation for oral health. *Biomed. Pharmacother.* 2018;99:883–893. doi: 10.1016/j.biopha.2018.01.146. 3. Karpinski T. Role of oral microbiota in cancer development. *Microorganisms* 2019;7(1):20 doi: 10.3390/microorganisms7010020 4. Sasaki M., Yamaura C., Ohara-Nemoto Y., Tajika S., Kodama Y., Ohya T., Harada R., Kimura S. *Streptococcus anginosus* infection in oral cancer and its infection route. *Oral Dis.* 2005;11:151–156. doi: 10.1111/j.1601-0825.2005.01051.x. 5. Mager D., Haffajee A., Devlin P., Norris C., Posner M., Goodson J. The salivary microbiota as a diagnostic indicator of oral cancer: A descriptive, nonrandomized study of cancerfree and oral squamous cell carcinoma subjects. *J. Transl. Med.* 2005;3:27. doi: 10.1186/1479-5876-3-27. OSHR: Oral Microbiome and Cancer - Page 2 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. 6. Katz J., Onate M.D., Pauley K.M., Bhattacharyya I., Cha S. Presence of *Porphyromonas gingivalis* in gingival squamous cell carcinoma. *Int. J. Oral Sci.* 2011;3:209–215. doi: 10.4248/IJOS11075. 7. Pushalkar S., Ji X., Li Y., Estilo C., Yegnanarayana R., Singh B., Li X., Saxena D. Comparison of oral microbiota in tumor and non-tumor tissues of patients with oral squamous cell carcinoma. *BMC Microbiol.* 2012;12:144. doi: 10.1186/1471-2180-12-144. 8. Atanasova K.R., Yilmaz O. Looking in the *Porphyromonas gingivalis* cabinet of curiosities: The microbium, the host and cancer association.

Mol. Oral Microbiol. 2014;29:55–66. doi: 10.1111/omi.12047. 9. Galvão-Moreira L.V., da Cruz M.C. Oral microbiome, periodontitis and risk of head and neck cancer. *Oral Oncol.* 2016;53:17–19. doi: 10.1016/j.oraloncology.2015.11.013. 10. Lee W.H., Chen H.M., Yang S.F., Liang C., Peng C.Y., Lin F.M., Tsai L.L., Wu B.C., Hsin C.H., Chuang C.Y., et al. Bacterial alterations in salivary microbiota and their association in oral cancer. *Sci. Rep.* 2017;7:16540. doi: 10.1038/s41598-017-16418-x. 11. Castellarin M., Warren R.L., Freeman J.D., Dreolini L., Krzywinski M., Strauss J., Barnes R., Watson P., Allen-Vercoe E., Moore R.A., et al. *Fusobacterium nucleatum* infection is prevalent in human colorectal carcinoma. *Genome Res.* 2012;22:299–306. doi: 10.1101/gr.126516.111. 12. Ahn J., Sinha R., Pei Z., Dominianni C., Wu J., Shi J., Goedert J.J., Hayes R.B., Yang L. Human gut microbiome and risk for colorectal cancer. *J. Natl. Cancer Inst.* 2013;105:1907–1911. doi: 10.1093/jnci/djt300. 13. Kostic A.D., Chun E., Robertson L., Glickman J.N., Gallini C.A., Michaud M., Clancy T.E., Chung D.C., Lochhead P., Hold G.L., et al. *Fusobacterium nucleatum* potentiates intestinal tumorigenesis and modulates the tumor-immune microenvironment. *Cell Host Microbe.* 2013;14:207–215. doi: 10.1016/j.chom.2013.07.007. 14. Kostic A.D., Gevers D., Pedamallu C.S., Michaud M., Duke F., Earl A.M., Ojesina A.I., Jung J., Bass A.J., Tabernero J., et al. Genomic analysis identifies association of *Fusobacterium* with colorectal carcinoma. *Genome Res.* 2012;22:292–298. doi: 10.1101/gr.126573.111. 15. Mima K., Cao Y., Chan A.T., Qian Z.R., Nowak J.A., Masugi Y., Shi Y., Song M., da Silva A., Gu M., et al. *Fusobacterium nucleatum* in colorectal carcinoma tissue according to tumor location. *Clin. Transl. Gastroenterol.* 2016;7:e200. doi: 10.1038/ctg.2016.53. 16. Ahn J., Segers S., Hayes R.B. Periodontal disease, *Porphyromonas gingivalis* serum antibody levels and orodigestive cancer mortality. *Carcinogenesis.* 2012;33:1055–1058. doi: 10.1093/carcin/bgs112. 17. Peters B.A., Wu J., Pei Z., Yang L., Purdue M.P., Freedman N.D., Jacobs E.J., Gapstur S.M., Hayes R.B., Ahn J. Oral microbiome composition reflects prospective risk for esophageal cancers. *Cancer Res.* 2017;77:6777–6787. doi: 10.1158/0008-5472.CAN-17-1296. 18. Mitsuhashi K., Nosho K., Sukawa Y., Matsunaga Y., Ito M., Kurihara H., Kanno S., Igarashi H., Naito T., Adachi Y., et al. Association of *Fusobacterium* species in pancreatic cancer tissues with molecular features and prognosis. *Oncotarget* 2015;6:7209–7220. doi: 10.18632/oncotarget.3109. 19. Fan X., Alekseyenko A.V., Wu J., Peters B.A., Jacobs E.J., Gapstur S.M., Purdue M.P., Abnet C.C., Stolzenberg-Solomon R., Miller G., et al. Human oral microbiome and OSHR: Oral Microbiome and Cancer - Page 3 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. prospective risk for pancreatic cancer: A population-based nested case-control study. *Gut.* 2018;67:120–127. doi: 10.1136/gutjnl-2016-312580. 20. Yan X., Xinmin Y., Yang M., Liu J., Gao R., Hu J., Li J., Zhang L., Shi Y., Guo H., et al. Discovery and validation of potential bacterial biomarkers for lung cancer. *Am. J. Cancer Res.* 2015;5:3111–3122 e-collection. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4656734/pdf/ajcr0005-3111.pdf> Oral Microbiome Gao L, Xu T, Huang G, Jiang S, Gu Y, Chen F (2018). Oral microbiomes: more and more importance in oral cavity and whole body. *Protein Cell.* 2018 May; 9(5): 488–50 Published online 2018 May 7. doi: 10.1007/s13238-018-0548-1 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960472/> Abstract: Microbes appear in every corner of human life, and microbes affect every aspect of human life. The human oral cavity contains a number of different habitats. Synergy and interaction of variable oral microorganisms help human body against invasion of undesirable stimulation outside. However, imbalance of microbial flora contributes to oral diseases and systemic diseases. Oral microbiomes play an important role in the human microbial community and human health. The use of recently developed molecular methods has greatly expanded our knowledge of the composition and function of the oral microbiome in health and disease. Studies in oral microbiomes and their interactions with

microbiomes in variable body sites and variable health condition are critical in our cognition of our body and how to make effect on human health improvement. Kilian M, Chapple ILC, Hannig M, Marsh PD, Meuric V, Pedersen AML, Tonetti MS, Wade WG, Zaura E (2016). The oral microbiome – an update for oral healthcare professionals M. Kilian. *Brit Dent J* 221: 657-666. DOI: 10.1038/sj.bdj.2016.865 At: <https://www.nature.com/articles/sj.bdj.2016.865.pdf?origin=ppub>

Abstract: For millions of years, our resident microbes have coevolved and coexisted with us in a mostly harmonious symbiotic relationship. We are not distinct entities from our microbiome, but together we form a ‘superorganism’ or holobiont, with the microbiome playing a significant role in our physiology and health. The mouth houses the second most diverse microbial community in the body, harbouring over 700 species of bacteria that colonise the hard surfaces of teeth and the soft tissues of the oral mucosa. Through recent advances in technology, we have started to unravel the complexities of the oral microbiome and gained new insights into its role during both health and disease. Perturbations of the oral microbiome through modern-day lifestyles can have detrimental consequences for our general and oral health. In dysbiosis, the finely-tuned equilibrium of the oral ecosystem is disrupted, allowing disease-promoting bacteria to manifest and cause conditions such as caries, gingivitis and periodontitis. For practitioners and patients alike, promoting a balanced microbiome is therefore important to effectively maintain or restore oral health. This article aims to give an update on our current knowledge of the oral microbiome in health and disease and to discuss implications for modern-day oral healthcare. Lim Y, Totsika M, Morrison M, Punyadeera C (2017).. Oral Microbiome: A New Biomarker Reservoir for Oral and Oropharyngeal Cancers. *Theranostics* 7(17):4313-4321. doi:10.7150/thno.21804. At: <http://www.thno.org/v07p4313.htm>

Abstract: Current biomarkers OSHR: Oral Microbiome and Cancer - Page 4 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. (DNA, RNA and protein) for oral cavity and oropharyngeal cancers demonstrate biological variations between individuals, rendering them impractical for clinical translation. Whilst these biomarkers originate from the host, there is not much information in the literature about the influence of oral microbiota on cancer pathogenesis, especially in oral cancers. Oral microbiotas are known to participate in disease initiation and progression not only limited to the oral cavity, but also at other distant sites. Due to the close proximity of oral microbiota and oral cavity and oropharyngeal tumours, abundance changes in oral microbiota may provide useful information on tumourigenesis. This review aims to highlight information on the role of oral microbiota in oral cavity and oropharyngeal cancers. An in-depth analysis into the oral microbiota may provide a new avenue to diagnose and treat these patients. Keywords: biomarker, oral and oropharyngeal cancers, oral microbiome. Slocum C, Kramer C, Genco CA (2016). Immune dysregulation mediated by the oral microbiome: potential link to chronic inflammation and atherosclerosis. *J intern Med* 280(1): 114-128. DOI: 10.1111/joim.12476 At: <https://pubmed.ncbi.nlm.nih.gov/26791914/> Abstract. Slocum C, Kramer C, Genco CA (Ora Inc., Andover, MA, USA; and Tufts University School of Medicine, Boston, MA, USA). Immune dysregulation mediated by the oral microbiome: potential link to chronic inflammation and atherosclerosis (Review). *J Intern Med* 2016; 280: 114–128. Cardiovascular disease is an inflammatory disorder characterized by the progressive formation of plaque in coronary arteries, termed atherosclerosis. It is a multifactorial disease that is one of the leading causes of death worldwide. Although a number of risk factors have been associated with disease progression, the underlying inflammatory mechanisms contributing to atherosclerosis remain to be fully delineated. Within the last decade, the potential role for infection in inflammatory plaque progression has received considerable interest. Microbial pathogens associated with periodontal disease have been of particular interest due to the high levels of bacteremia that are observed after routine dental

procedures and every day oral activities, such as tooth brushing. Here, we explore the potential mechanisms that may explain how periodontal pathogens either directly or indirectly elicit immune dysregulation and consequently progressive inflammation manifested as atherosclerosis. Periodontal pathogens have been shown to contribute directly to atherosclerosis by disrupting endothelial cell function, one of the earliest indicators of cardiovascular disease. Oral infection is thought to indirectly induce elevated production of inflammatory mediators in the systemic circulation. Recently, a number of studies have been conducted focusing on how disruption of the gut microbiome influences the systemic production of proinflammatory cytokines and consequently exacerbation of inflammatory diseases such as atherosclerosis. It is clear that the immune mechanisms leading to atherosclerotic plaque progression, by oral infection, are complex. Understanding the immune pathways leading to disease progression is essential for the future development of anti-inflammatory therapies for this chronic disease. Glurich I, Acharya A, Brilliant MH, Shukla SK (2015). Progress in oral personalized medicine: contribution of 'omics'. *J Oral Microbiol* 7: 10.3402/jom.v7.28223 DOI: 10.3402/jom.v7.28223 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4561229/> Abstract: Background Precision medicine (PM), representing clinically applicable personalized medicine, proactively integrates and interprets multidimensional personal health data, including clinical, 'omics', and environmental profiles, into clinical practice. Realization of PM remains in progress. Objective OSHR: Oral Microbiome and Cancer - Page 5 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. The focus of this review is to provide a descriptive narrative overview of: 1) the current status of oral personalized medicine; and 2) recent advances in genomics and related 'omic' and emerging research domains contributing to advancing oral-systemic PM, with special emphasis on current understanding of oral microbiomes. Design A scan of peer-reviewed literature describing oral PM or 'omic'-based research conducted on humans/data published in English within the last 5 years in journals indexed in the PubMed database was conducted using mesh search terms. An evidence-based approach was used to report on recent advances with potential to advance PM in the context of historical critical and systematic reviews to delineate current state-of-the-art technologies. Special focus was placed on oral microbiome research associated with health and disease states, emerging research domains, and technological advances, which are positioning realization of PM. Results This review summarizes: 1) evolving conceptualization of personalized medicine; 2) emerging insight into roles of oral infectious and inflammatory processes as contributors to both oral and systemic diseases; 3) community shifts in microbiota that may contribute to disease; 4) evidence pointing to new uncharacterized potential oral pathogens; 5) advances in technological approaches to 'omics' research that will accelerate PM; 6) emerging research domains that expand insights into host-microbe interaction including inter-kingdom communication, systems and network analysis, and salivaomics; and 7) advances in informatics and big data analysis capabilities to facilitate interpretation of host and microbiome-associated datasets. Furthermore, progress in clinically applicable screening assays and biomarker definition to inform clinical care are briefly explored. Conclusion Advancement of oral PM currently remains in research and discovery phases. Although substantive progress has been made in advancing the understanding of the role of microbiome dynamics in health and disease and is being leveraged to advance early efforts at clinical translation, further research is required to discern interpretable constituency patterns in the complex interactions of these microbial communities in health and disease. Advances in biotechnology and bioinformatics facilitating novel approaches to rapid analysis and interpretation of large datasets are providing new insights into oral health and disease, potentiating clinical application and advancing realization of PM within the next decade.

Keywords: microbiota, precision medicine, 'omics', big data, biomarkers. Extroral Cancer (Pancreatic, Breast, Colon/Colorectal, Esophageal, Lung, Renal, Liver) Wallis C (2020). New Player in Cancer's Spread: A commonplace mouth bacterium now is tied to metastasis of some tumors. *Sci Am* 323(4): 28. See also: <https://www.scientificamerican.com/article/deadly-spread-of-some-cancers-may-be-driven-by-a-common-mouth-microbe/> Casasanta MA, Yoo CC, Udayasuryan B, Sanders BE, Umaña A, Zhang Y, Peng H, Duncan AJ, Li L, Verbridge SS, Slade DJ (2020). *Fusobacterium nucleatum* host-cell binding and invasion induces IL-8 and CXCL1 secretion that drives colorectal cancer cell migration. *Sci Signaling* 641: eaba9157 DOI: 10.1126/scisignal.aba9157 At: <https://stke.sciencemag.org/content/13/641/eaba9157> Abstract: *Fusobacterium nucleatum* is implicated in accelerating colorectal cancer (CRC) and is found within metastatic CRC cells in patient biopsies. Here, we found that bacterial invasion of CRC cells and cocultured immune cells induced a differential cytokine secretion that may contribute to CRC metastasis. We used a OSHR: Oral Microbiome and Cancer - Page 6 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. modified galactose kinase markerless gene deletion approach and found that *F. nucleatum* invaded cultured HCT116 CRC cells through the bacterial surface adhesin Fap2. In turn, Fap2-dependent invasion induced the secretion of the proinflammatory cytokines IL-8 and CXCL1, which are associated with CRC progression and promoted HCT116 cell migration. Conditioned medium from *F. nucleatum*-infected HCT116 cells caused naïve cells to migrate, which was blocked by depleting CXCL1 and IL-8 from the conditioned medium. Cytokine secretion from HCT116 cells and cellular migration were attenuated by inhibiting *F. nucleatum* host-cell binding and entry using galactose sugars, L-arginine, neutralizing membrane protein antibodies, or fap2 deletion. *F. nucleatum* also induces the mobilization of immune cells in the tumor microenvironment. However, in neutrophils and macrophages, the bacterial-induced secretion of cytokines was Fap2 independent. Thus, our findings show that *F. nucleatum* both directly and indirectly modulates immune and cancer cell signaling and migration. Because increased IL-8 and CXCL1 production in tumors is associated with increased metastatic potential and cell seeding, poor prognosis, and enhanced recruitment of tumor-associated macrophages and fibroblasts, we propose that inhibition of host-cell binding and invasion, potentially through vaccination or novel galactoside compounds, could be an effective strategy for reducing *F. nucleatum*-associated CRC metastasis. Sun J, Tang Q, Yu S, Xie M, Yanling X, Chen G, Chen L (2020). Role of the oral microbiota in cancer evolution and progression. DOI: <https://doi.org/10.1002/cam4.3206> At: <https://onlinelibrary.wiley.com/doi/full/10.1002/cam4.3206> Abstract: Bacteria identified in the oral cavity are highly complicated. They include approximately 1000 species with a diverse variety of commensal microbes that play crucial roles in the health status of individuals. Epidemiological studies related to molecular pathology have revealed that there is a close relationship between oral microbiota and tumor occurrence. Oral microbiota has attracted considerable attention for its role in in-situ or distant tumor progression. Anaerobic oral bacteria with potential pathogenic abilities, especially *Fusobacterium nucleatum* and *Porphyromonas gingivalis*, are well studied and have close relationships with various types of carcinomas. Some aerobic bacteria such as *Parvimonas* are also linked to tumorigenesis. Moreover, human papillomavirus, oral fungi, and parasites are closely associated with oropharyngeal carcinoma. Microbial dysbiosis, colonization, and translocation of oral microbiota are necessary for implementation of carcinogenic functions. Various underlying mechanisms of oral microbiota-induced carcinogenesis have been reported including excessive inflammatory reaction, immunosuppression of host, promotion of malignant transformation, antiapoptotic activity, and secretion of carcinogens. In this review, we have systemically described

the impact of oral microbial abnormalities on carcinogenesis and the future directions in this field for bringing in new ideas for effective prevention of tumors. Robayo DAG, Hernandez RF, Erika AT, Kandaurova L, Juarez CL, Juarez CL, Juarez V, Cid-Arregui A (2020). Oral Microbiota Associated with Oral and Gastroenteric Cancer. *The Open Microbiol J* 14. DOI:

10.2174/1874285802014010001 At:

<https://openmicrobiologyjournal.com/VOLUME/14/PAGE/1/FULLTEXT/> Abstract: When the normal microbiota-host interactions are altered, the commensal microbial community evolves to a dysbiotic status resulting in some species becoming pathogenic and acting synergistically in the development of local and systemic diseases, including cancer. Advances in genetics, OSHR: Oral Microbiome and Cancer - Page 7 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. immunology and microbiology during the last years have made it possible to gather information on the oral and gastrointestinal microbiome and its interaction with the host, which has led to a better understanding of the interrelationship between microbiota and cancer. There is growing evidence in support for the role of some species in the development, progression and responses to treatment of various types of cancer. Accordingly, the number of studies investigating the association between oral microbiota and oral and gastrointestinal cancers has increased significantly during the last years. Here, we review the literature documenting associations of oral microbiota with oral and gastroenteric cancers Teles FRF, Alawi F, Castilho RM, Wang Y (2020). Association or Causation? Exploring the Oral Microbiome and Cancer Links. *J Dent Res* (Online ahead of print.) At: <https://pubmed.ncbi.nlm.nih.gov/32811287/> DOI:

10.1177/0022034520945242 Abstract: The oral microbiota plays an important role in the human microbiome and human health, and imbalances between microbes and their hosts can lead to oral and systemic diseases and chronic inflammation, which is usually caused by bacteria and contributes to cancer. There may be a relationship between oral bacteria and oral squamous cell carcinoma (OSCC); however, this relationship has not been thoroughly characterized. Therefore, in this study, we compared the microbiota compositions between tumor sites and opposite normal tissues in buccal mucosal of 50 patients with OSCC using the 16S rDNA sequencing. Richness and diversity of bacteria were significantly higher in tumor sites than in the control tissues. Cancer tissues were enriched in six families (Prevotellaceae, Fusobacteriaceae, Flavobacteriaceae, Lachnospiraceae, Peptostreptococcaceae, and Campylobacteraceae) and 13 genera, including *Fusobacterium*, *Alloprevotella* and *Porphyromonas*. At the species level, the abundances of *Fusobacterium nucleatum*, *Prevotella intermedia*, *Aggregatibacter segnis*, *Capnocytophaga leadbetteri*, *Peptostreptococcus stomatis*, and another five species were significantly increased, suggesting a potential association between these bacteria and OSCC. Furthermore, the functional prediction revealed that genes involved in bacterial chemotaxis, flagellar assembly and lipopolysaccharide (LPS) biosynthesis which are associated with various pathological processes, were significantly increased in the OSCC group. Overall, oral bacterial profiles showed significant difference between cancer sites and normal tissue of OSCC patients, which might be considered diagnostic markers and treatment targets. Our study has been registered in the Chinese clinical trial registry (ChiCTR1900025253, <http://www.chictr.org.cn/index.aspx>). Keywords: oral microbiota, oral squamous cell carcinoma, *Fusobacterium nucleatum*, *Prevotella intermedia*, *Peptostreptococcus stomatis*, 16S rDNA sequencing. Robayo DAG, Hernandez RF, Erika AT, Kandaurova L, Juarez CL, Juarez CL, Juarez CL, Juarez V, Cid-Arregui A (2020). Oral Microbiota Associated with Oral and Gastroenteric Cancer. *Open Microbiol J* 14: 1-17. DOI: 10.2174/1874285802014010001 At: <https://openmicrobiologyjournal.com/VOLUME/14/PAGE/1/FULLTEXT/> Abstract: When the normal microbiota-host interactions are altered, the commensal microbial community evolves to a dysbiotic

status resulting in some species becoming pathogenic and acting synergistically in the development of local and systemic diseases, including cancer. Advances in genetics, immunology and microbiology during the last years have made it possible to gather information OSHR: Oral Microbiome and Cancer - Page 8 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. on the oral and gastrointestinal microbiome and its interaction with the host, which has led to a better understanding of the interrelationship between microbiota and cancer. There is growing evidence in support for the role of some species in the development, progression and responses to treatment of various types of cancer. Accordingly, the number of studies investigating the association between oral microbiota and oral and gastrointestinal cancers has increased significantly during the last years. Here, we review the literature documenting associations of oral microbiota with oral and gastroenteric cancers.

<https://www.dental.columbia.edu/news/how-common-oral-bacteria-makes-colon-cancermore-deadly> New York, NY (March 4, 2019) – Researchers at the Columbia University College of Dental Medicine have determined how *F. nucleatum* — a common oral bacteria often implicated in tooth decay — accelerates the growth of colon cancer. The study was published online in the journal *EMBO Reports*. The findings could make it easier to identify and treat more aggressive colon cancers. It also helps explain why some cases advance far more quickly than others, thanks to the same bacteria found in dental plaque. Colon cancer is the second leading cause of cancer death in the U.S. Researchers have long known that the disease is caused by genetic mutations that typically accumulate over the course of a decade. “Mutations are just part of the story,” says study leader Yiping W. Han, PhD, professor of microbial sciences at Columbia University’s College of Dental Medicine and Vagelos College of Physicians & Surgeons. “Other factors, including microbes, can also play a role.” At: Rubinstein MR, Baik JE, Lagana SM, Han RP, Raab WJ, Sahoo D, Dalerba P, Wang TC, Han YW (2019). *Fusobacterium nucleatum* promotes colorectal cancer by inducing Wnt/ β -catenin modulator Annexin A1. *EMBO Rep* (2019)20:e47638

<https://doi.org/10.15252/embr.201847638> At:

<https://www.embopress.org/doi/10.15252/embr.201847638> Mascitti M, Togni L, Troiano G, Alberto-Caponio VC, Gissi DB, Montebugnoli L, Procaccini M, Muzio LL, Santarelli A (2019). Beyond Head and Neck Cancer: The Relationship Between Oral Microbiota and Tumour Development in Distant Organs. *Front Cell Infect Microbiol* 9: 232. DOI: 10.3389/fcimb.2019.00232 At:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6607058/> Abstract: An altered oral microbiota has been linked with the development of several oral diseases, such as dental caries, periodontal disease, and oral stomatitis. Moreover, poor oral health has been linked to head and neck cancer, particularly oral cancer. In recent years a growing number of studies indicate that oral microbiota could be involved in the development of primary tumours outside of head and neck region. The aim of this article is to review the recent studies based on high-throughput technology to present evidences of a relationship between oral microbiota and “non-head and neck tumours.” Oral dysbiosis seem to be more pronounced in patients with tumours of gastrointestinal tract, in particular oesophageal, gastric, pancreatic, and colorectal cancers, paving the way for developing specific oral microbiota test to allow early cancer detection. Regarding other tumour types, the results are promising but highly preliminary and still debated. Currently, there are several factors that limit the generalization of the results, such as the small sample size, the lack of adequate clinical information about patients, the different sequencing techniques used, and biological sample heterogeneity. Although only at the beginning, the analysis of oral microbiota could be the next step in the evolution of cancer therapy and will help clinicians to develop individualised OSHR: Oral Microbiome and Cancer - Page 9 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for

International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. approaches to cancer prevention and treatment. Keywords: oral microbiota, oral microbiome, pancreatic cancer, gastrointestinal tract cancer, high-throughput sequencing. Maddi A, Sabharwal A, Violante T, Manuballa S, Genco R, Patnaik S, Yendamuri S (2019). The microbiome and lung cancer. *J Thorac Dis* 11(1): 280-291. DOI: 10.21037/jtd.2018.12.88 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6384374/> Abstract: It has become increasingly clear that we live in a symbiotic relationship with microbes within us. We are just beginning to unravel the nature and strength of this relationship and its impact on both physiology and by extension, pathology. While microorganisms have long been known to have carcinogenic potential, their role may have been underestimated. The knowledge of the role of the microbiome in carcinogenesis is rapidly evolving. This evolution has reached a tipping point with current omics technologies used for cataloguing the microbiome. The lung is an organ constantly exposed to the environment. It is now clear that the lung has a distinct microbiome and that this may influence the development of lung cancer. In addition, evidence suggests that this microbiome originates from the oral microbiome. This review summarizes current knowledge about the role of microbiome, especially the oral and lung microbiome in human lung cancer. The goal of the manuscript is to provide a summary of this rapidly evolving field while providing a context of the general role of the microbiome in carcinogenesis. In addition, a primer of the current technology used in evaluating the microbiome is provided to familiarize the practicing clinician with the experimental methods used to generate the information that will likely impact the field of lung cancer. Gerlovin H, Michaud DS, Cozier YC, Palmer JR (2019). Oral Health in Relation to Pancreatic Cancer Risk in African American Women. Downloaded from cebp.aacrjournals.org on March 29, 2019 *Cancer Epidemiol Biomarkers Prev*; 28(4), April 2019, At: <https://pubmed.ncbi.nlm.nih.gov/30923045/> DOI: 10.1158/1055-9965.EPI-18-1053 Abstract: Background: Incidence of pancreatic cancer is higher in African Americans than in U.S. whites. We hypothesized that poor oral health, disproportionately common in African Americans and associated with increased risk of pancreatic cancer in several studies of predominantly white populations, may play a role in this disparity. Methods: We examined the relation of self-reported measures of oral health (periodontal disease and adult tooth loss) in relation to pancreatic cancer incidence in the prospective Black Women's Health Study (BWHS). Cox proportional hazard analyses were used to calculate HRs of pancreatic cancer for women with periodontal disease, tooth loss, or both, relative to women who reported neither. Multivariable models adjusted for age, cigarette smoking, body mass index (BMI), type 2 diabetes, and alcohol consumption. Results: Participants aged 33 to 81 were followed for an average of 9.85 years from 2007 through 2016, with occurrence of 78 incidence cases of pancreatic cancer. Multivariable HRs for pancreatic cancer incidence were 1.77 [95% confidence interval (CI) 0.57- 5.49] for periodontal disease with no tooth loss, 2.05 (95% CI, 1.08-3.88) for tooth loss without report of periodontal disease, and 1.58 (95% CI, 0.70-3.57) for both tooth loss and periodontal disease. The HR for loss of at least five teeth, regardless of whether periodontal disease was reported, was 2.20 (95% CI, 1.11-4.33). Conclusions: The poor oral health experienced by many OSHR: Oral Microbiome and Cancer - Page 10 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. African Americans may contribute to their higher incidence of pancreatic cancer. Impact: Future research will assess associations between the oral microbiome and pancreatic cancer risk in this population. Al-Hebshi, N. N., Borgnakke, W. S., and Johnson, N. W. (2019). The microbiome of oral squamous cell carcinomas: a functional perspective. *Curr. Oral Health Rep.* 6, 145–160. doi: 10.1007/s40496-019-0215-5 At: https://www.researchgate.net/publication/344876587_Screening_of_HealthAssociated_Oral_Bacte

ria_for_Anticancer_Properties_in_vitro/references Jordão HW, McKenna G, McMenamin, 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 Gastroenterol J* 7(9): 1241-1249. doi: 10.1177/2050640619858043. Epub 2019 Jun 8. At: <https://pubmed.ncbi.nlm.nih.gov/31700637/> 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. Lu H, Ren Z, Li A, Zheng HJ, Zhang CP (2019). Tongue Coating Microbiome Data Distinguish Patients With Pancreatic Head Cancer From Healthy Controls. *J Oral Microbiol* 9: 476. DOI: 10.1080/20002297.2018.1563409 .At: <https://pubmed.ncbi.nlm.nih.gov/30728915/> Abstract: Background: The microbiota plays a critical role in the process of human carcinogenesis. Pancreatic head carcinoma (PHC)-associated tongue coating microbiome dysbiosis has not yet been clearly defined. Objective: Our aim is to reveal the bacterial composition shifts in the microbiota of the tongue coat of PHC patients. Design: The tongue coating microbiota was analyzed in 30 PHC patients and 25 healthy controls using 16S rRNA gene sequencing technology. Results: The microbiome diversity of the tongue coat in PHC patients was significantly increased, as shown by the Shannon, Simpson, inverse Simpson, Obs and incidence-based coverage estimators. Principal component analysis revealed that PHC patients OSHR: Oral Microbiome and Cancer - Page 11 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. were colonized by remarkably different tongue coating microbiota than healthy controls and liver cancer patients. Linear discriminant analysis effect size revealed that *Leptotrichia*, *Fusobacterium*, *Rothia*, *Actinomyces*, *Corynebacterium*, *Atopobium*, *Peptostreptococcus*, *Catonella*, *Oribacterium*, *Filifactor*, *Campylobacter*, *Moraxella* and *Tannerella* were overrepresented in the tongue coating of PHC patients, and *Haemophilus*, *Porphyromonas* and *Paraprevotella* were enriched in the tongue coating microbiota of healthy controls. Strikingly, *Haemophilus*, *Porphyromonas*, *Leptotrichia* and *Fusobacterium* could distinguish PHC patients from healthy subjects, and *Streptococcus* and SR1 could distinguish PHC patients from liver cancer patients. Conclusions: These findings identified the microbiota dysbiosis of the tongue coat in PHC patients, and provide insight into the association between the human microbiome and pancreatic cancer. Keywords: Miseq sequencing; Pancreatic head carcinoma; microbiome dysbiosis; tongue coat. Campbell MJ, McCune E, Johnson B, O'Meara, Heditsian D, Brain S, Esserman L (2019). Breast cancer and the human oral and gut microbiomes [abstract]. In: *Proceedings of the American Association for Cancer Research Annual Meeting 2019*; 2019 Mar 29-Apr 3; Atlanta, GA.

Philadelphia (PA): AACR; Cancer Res 2019;79(13 Suppl): Abstract nr 2830. At: https://cancerres.aacrjournals.org/content/79/13_Supplement/2830 Vasilyeva D, Peters SM, Philipone EM, Yoon AJ (2018). Renal cell carcinoma metastatic to the maxillary gingiva: A case report and review of the literature. *J Oral Maxillofac Pathol* 22(Suppl 1): S102-S107. DOI: 10.4103/jomfp.JOMFP_69_17 At: <https://pubmed.ncbi.nlm.nih.gov/29491617/> Abstract: Tumor metastasis to the oral cavity is rare and is usually an indication of late-stage disease and poor prognosis. While, there are reports of renal cell carcinoma (RCC) metastatic to oral cavity, vast majority of them are to the jaw. Herein, we present a case of a 78-year-old woman with RCC metastasis limited to the oral soft tissue without any bone involvement. As the lesion solely involved maxillary gingiva, it clinically mimicked that of a pyogenic granuloma, which is a reactive, nonneoplastic condition. This case was further complicated as the patient was unaware of primary cancer and appeared to be in good physical health. Her oral metastasis marked the initial manifestation of an otherwise silent primary renal cancer. McKernan SC, Kuthy RA, Reynolds JC, Tuggle L, García DT (2018). Medical-Dental Integration in Public Health Settings: An Environmental Scan. At: http://ppc.uiowa.edu/sites/default/files/ced_environmental_scan.pdf Executive Summary: Noncommunicable chronic diseases (NCDs) account for almost 90% of total deaths in the United States. The four most common NCDs—cardiovascular diseases, diabetes, cancers, and chronic respiratory diseases—share common risk factors, including cigarette use, alcohol use, and dietary behaviors associated with obesity and elevated blood sugar. The most common oral diseases—dental caries, periodontal disease, and oral cancer—also share these same risk factors. A coordinated approach to primary prevention, the “common risk factor approach,” argues that coordinated primary prevention of oral and systemic diseases will reduce OSHR: Oral Microbiome and Cancer - Page 12 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. programmatic costs, and increase efficiency and effectiveness. However, use and evaluation of this coordinated approach in primary prevention activities in the United States has not been well documented. This report describes the results of an environmental scan to identify, categorize, and describe examples of medical-dental integration in US public health settings. Findings are intended to inform public health officials and other stakeholders about existing programs and policies that encourage coordination and integration. Conclusion: Public health activities targeting oral health and chronic diseases operate at multiple levels, including public policy, community-level campaigns, health care delivery systems, and clinical interventions. Well-developed efforts were especially noted for environmental approaches targeting sugarsweetened beverage consumption, state-level efforts targeting tobacco use and oral cancer, and co-location of medical and dental services. The lack of robust evaluation and effectiveness data surrounding most of the activities described in this report may hamper widespread implementation, sustainability, and stakeholder support Flemer B, Warren RD, Barrett MP, Cisek K, Das A, Jeffrey IB, Hurley E, O’Riordan M, Shanahan F, O’Toole PW (2018). The oral microbiota in colorectal cancer is distinctive and predictive. *Gut* 67(8): 1454-1463. DOI: 10.1136/gutjnl-2017-314814 At: <https://pubmed.ncbi.nlm.nih.gov/28988196/> Abstract: Background and aims: Microbiota alterations are linked with colorectal cancer (CRC) and notably higher abundance of putative oral bacteria on colonic tumours. However, it is not known if colonic mucosa-associated taxa are indeed orally derived, if such cases are a distinct subset of patients or if the oral microbiome is generally suitable for screening for CRC. Methods: We profiled the microbiota in oral swabs, colonic mucosae and stool from individuals with CRC (99 subjects), colorectal polyps (32) or controls (103). Results: Several oral taxa were differentially abundant in CRC compared with controls, for example, *Streptococcus* and *Prevotellas* pp. A classification model of oral swab microbiota distinguished

individuals with CRC or polyps from controls (sensitivity: 53% (CRC)/67% (polyps); specificity: 96%). Combining the data from faecal microbiota and oral swab microbiota increased the sensitivity of this model to 76% (CRC)/88% (polyps). We detected similar bacterial networks in colonic microbiota and oral microbiota datasets comprising putative oral biofilm forming bacteria. While these taxa were more abundant in CRC, core networks between pathogenic, CRC-associated oral bacteria such as *Peptostreptococcus*, *Parvimonas* and *Fusobacterium* were also detected in healthy controls. High abundance of *Lachnospiraceae* was negatively associated with the colonisation of colonic tissue with oral-like bacterial networks suggesting a protective role for certain microbiota types against CRC, possibly by conferring colonisation resistance to CRC-associated oral taxa and possibly mediated through habitual diet. Conclusion: The heterogeneity of CRC may relate to microbiota types that either predispose or provide resistance to the disease, and profiling the oral microbiome may offer an alternative screen for detecting CRC. Keywords: colonic bacteria; colorectal cancer; colorectal cancer screening; diet; tumour markers. Peters BA, Wu J, Pei Z, Yang L, Purdue MP, Freedman ND, Jacobs EJ, Gapstur SM, Hayhes RB, Ahn J (2017). Oral microbiome composition reflects prospective risk for esophageal cancers. OSHR: Oral Microbiome and Cancer - Page 13 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. *Cancer Res* 77(23): 6777-6787. DOI: 10.1158/0008-5472.CAN-17-1296 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5726431/> Abstract: Bacteria may play a role in esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC), although evidence is limited to cross-sectional studies. In this study, we examined the relationship of oral microbiota with EAC and ESCC risk in a prospective study nested in two cohorts. Oral bacteria were assessed using 16S rRNA gene sequencing in pre-diagnostic mouthwash samples from n=81/160 EAC and n=25/50 ESCC cases/matched controls. Findings were largely consistent across both cohorts. Metagenome content was predicted using PiCRUST. We examined associations between centered log-ratio transformed taxon or functional pathway abundances and risk using conditional logistic regression adjusting for BMI, smoking, and alcohol. We found the periodontal pathogen *Tannerella forsythia* to be associated with higher risk of EAC. Further, we found that depletion of the commensal genus *Neisseria* and the species *Streptococcus pneumoniae* were associated with lower EAC risk. Bacterial biosynthesis of carotenoids was also associated with protection against EAC. Lastly, the abundance of the periodontal pathogen *Porphyromonas gingivalis* trended with higher risk of ESCC. Overall, our findings have potential implications for the early detection and prevention of EAC and ESCC. Keywords: oral microbiome, esophageal cancer, esophageal adenocarcinoma, esophageal squamous cell carcinoma, bacteria. Ramos A, Hemann MT (2017). Drugs, Bugs, and Cancer: *Fusobacterium nucleatum* Promotes Chemoresistance in Colorectal Cancer. *Cell* 170(3): 411-413. At: <https://www.sciencedirect.com/science/article/pii/S0092867417308255> Yu TC, Guo F, Yu Y, Sun T, Ma D, Han J, Qian Y, Krycek I, Sun D, Nagarsheth N, Chen Y, Chen H, Hong J, Zou W, Fang JY (2017). *Fusobacterium nucleatum* Promotes Chemoresistance to Colorectal Cancer by Modulating Autophagy. *Cell* 170(3): 548-563.e16 At: <https://www.sciencedirect.com/science/article/pii/S0092867417308152> Summary: Gut microbiota are linked to chronic inflammation and carcinogenesis. Chemotherapy failure is the major cause of recurrence and poor prognosis in colorectal cancer patients. Here, we investigated the contribution of gut microbiota to chemoresistance in patients with colorectal cancer. We found that *Fusobacterium* (F.) *nucleatum* was abundant in colorectal cancer tissues in patients with recurrence post chemotherapy, and was associated with patient clinicopathological characteristics. Furthermore, our bioinformatic and functional studies demonstrated that F. *nucleatum* promoted

colorectal cancer resistance to chemotherapy. Mechanistically, *F. nucleatum* targeted TLR4 and MYD88 innate immune signaling and specific microRNAs to activate the autophagy pathway and alter colorectal cancer chemotherapeutic response. Thus, *F. nucleatum* orchestrates a molecular network of the Toll-like receptor, microRNAs, and autophagy to clinically, biologically, and mechanistically control colorectal cancer chemoresistance. Measuring and targeting *F. nucleatum* and its associated pathway will yield valuable insight into clinical management and may ameliorate colorectal cancer patient outcomes. OSHR: Oral Microbiome and Cancer - Page 14 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. Nwizu NN, Marshall JR, Moysich K, Genco RJ, Hovey KM, Xiodan M, LaMonte JL, WactawskiWende J (2017). Periodontal Disease and Incident Cancer Risk among Postmenopausal Women: Results from the Women's Health Initiative Observational Cohort. *Cancer Epidemiol Biomarkers Prev* 26(8):1255-65. DOI: 10.1158/1055-9965.EPI-17-0212 At: <https://cebp.aacrjournals.org/content/26/8/1255>

Freudenheim JL, Genco RJ, LaMonte MJ, Millen AE, Hovey KM, Mai X, Nwizu N, Andrews CA, Wactawski-Wende J (2016). Periodontal Disease and Breast Cancer: Prospective Cohort Study of Postmenopausal Women. *Cancer Epidemiol Biomarkers Prev* 25(1): 43-50. DOI: 10.1158/1055-9965.EPI-15-0750 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4713270/> Abstract: Background Periodontal disease (PD) 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. PD was by self-report. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated by Cox proportional hazards, adjusted for breast cancer risk factors. Because the oral microbiome of those with PD 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. PD, reported by 26.1% of women, was associated with increased breast cancer risk (HR 1.14, 95% CI 1.03 to 1.26), particularly among former smokers who quit within 20 years (HR 1.36; 95% CI 1.05 to 1.77). Among current smokers, the trend was similar (HR 1.32; 95% CI 0.83 to 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 to 21.79) and 10.90% (95% CI 10.31 to 28.94) for PD among former smokers quitting within 20 years and current smokers, respectively. Conclusion PD, 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. Keywords: Breast neoplasms, periodontal disease, postmenopausal women, inflammation, microbiome, epidemiology. Han P, Sun D, Yang J (2016). Interaction between periodontitis and liver diseases. *Biomed Rep* 5(3): 267-276. Published online 2016 Jul 18. doi: 10.3892/br.2016.718 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4998044/> Abstract: Periodontitis is an oral disease that is highly prevalent worldwide, with a prevalence of 30–50% of the population in developed countries, but only ~10% present with severe forms. It is also estimated that periodontitis results in worldwide productivity losses amounting to ~54 billion USD yearly. In addition to the damage it causes to oral health, periodontitis also affects other types of disease. Numerous studies have confirmed the association between periodontitis and systemic diseases, such as diabetes, respiratory disease, osteoporosis and cardiovascular disease. Increasing evidence also indicated that periodontitis may participate in the progression of liver diseases, such as non-alcoholic fatty liver disease, cirrhosis and hepatocellular carcinoma, as well as OSHR: Oral Microbiome and Cancer

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affecting liver transplantation. However, to the best of our knowledge, there are currently no reviews elaborating upon the possible links between periodontitis and liver diseases. Therefore, the current review summarizes the human trials and animal experiments that have been conducted to investigate the correlation between periodontitis and liver diseases. Furthermore, in the present review, certain mechanisms that have been postulated to be responsible for the role of periodontitis in liver diseases (such as bacteria, pro-inflammatory mediators and oxidative stress) are considered. The aim of the review is to introduce the hypothesis that periodontitis may be important in the progression of liver disease, thus providing dentists and physicians with an improved understanding of this issue. Whitmore SE, Lamont RJ; Goldman WE, ed. (2014). Oral Bacteria and Cancer. PLoS Pathog 10(3): e1003933. DOI: 10.1371/journal.ppat.1003933 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3968118/> Fan X, Alekseyenko AV, Wu J, Peters BA, Jacobs EJ, Gapstur SM, Purdue MP, Abnet CC, Solomon RS, Miller G, Ravel J, Hayes RB, Ahn J (2000). Human oral microbiome and prospective risk for pancreatic cancer: a population-based nested case-control study. Gut 67: 120-127. doi:10.1136/gutjnl-2016-312580 At: <https://gut.bmj.com/content/67/1/120.abstract> 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. Oral Cancer, Head and Neck Cancer OSHR: Oral Microbiome and Cancer - Page 16 of 22 The Oral-Systemic Health Resource (OSHR) Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November, 2021. Fitzsimonds Z, Rodriguez-Hernandez CJ, Bagaitkar J, Lamont RJ (2020). From Beyond the Pale to the Pale Riders: The Emerging Association of Bacteria with Oral Cancer. J Dent Res 99(6): 604- 612. DOI: 10.1177/0022034520907341 At: <https://pubmed.ncbi.nlm.nih.gov/32091956/> Abstract : Oral cancer, predominantly oral squamous cell carcinoma (OSCC), is the eighth-most common cancer worldwide, with a 5-y survival rate.

The Medical Information Physicians Need.

EHR Integration and Physician's Data Needs - Page 1 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. OSHR - EHR Integration and Physician's OH Data Needs Donoff B (2019). The Challenge of Medical Dental Integration: Oral Health in Primary Care. At: <https://harkinstitute.drake.edu/wp-content/uploads/sites/103/2019/11/Donoff.pdf> Shea CM, Turner K, White BA, Zhu Y, Rozier RG (2018). Providers' preferences for pediatric oral health information in the electronic health record: a cross-sectional survey. *BMC Pediatr* 18(1): 5 DOI: 10.1186/s12887-017-0979-5 At: <https://pubmed.ncbi.nlm.nih.gov/29325519/> Abstract: Background: The majority of primary care physicians support integration of children's oral health promotion and disease prevention into their practices but can experience challenges integrating oral health services into their workflow. Most electronic health records (EHRs) in primary care settings do not include oral health information for pediatric patients. Therefore, it is important to understand providers' preferences for oral health information within the EHR. The objectives of this study are to assess (1) the relative importance of various elements of pediatric oral health information for primary care providers to have in the EHR and (2) the extent to which practice and provider characteristics are associated with these information preferences. Methods: We surveyed a sample of primary care physicians who conducted Medicaid well-child visits in North Carolina from August - December 2013. Using descriptive statistics, we analyzed primary care physicians' oral health information preferences relative to their information preferences for traditional preventive aspects of well-child visits. Furthermore, we analyzed associations between oral health information preferences and provider- and practice-level characteristics using an ordinary least squares regression model. Results: Fewer primary care providers reported that pediatric oral health information is "very important," as compared to more traditional elements of primary care information, such as tracking immunizations. However, the majority of respondents reported some elements of oral health information as being very important. Also, we found positive associations between the percentage of well child visits in which oral health screenings and oral health referrals are performed and the reported importance of having pediatric oral health information in the EHR. Conclusions: Incorporating oral health information into the EHR may be desirable for providers, particularly those who perform oral health screenings and dental referrals. Keywords: Dental health; Electronic health record; Medicaid; Oral health; Primary health care; Well child visit. Verhulst MJL, Teeuw WJ, Bizzarro S et al (2019). A rapid, non-invasive tool for periodontitis screening in a medical care setting. *BMC Oral Health* (19) 87. <https://doi.org/10.1186/s12903-019-0784-7> At: <https://bmcoralhealth.biomedcentral.com/articles/10.1186/s12903-019-0784-7> Abstract: Background - Since periodontitis is bi-directionally associated with several systemic diseases, such as diabetes mellitus and cardiovascular diseases, it is important for medical professionals in a non-dental setting to be able examine their patients for symptoms of periodontitis, and urge them to visit a dentist if necessary. However, they often lack the time, knowledge and resources to do so. We aim to develop and assess "quick and easy" screening tools for periodontitis, based on self-reported oral health (SROH), demographics and/or salivary biomarkers, intended for use by medical professionals in a non-dental setting. Methods - Consecutive, new patients from our outpatient clinic were recruited. A SROH questionnaire (8 questions) was conducted, followed by a 30 s oral rinse sampling protocol. A complete clinical periodontal examination provided the golden standard periodontitis classification: no/mild, OSHR - EHR Integration and Physician's Data Needs - Page 2 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. moderate or severe periodontitis. Total periodontitis was

defined as having either moderate or severe. Albumin and matrix metalloproteinase-8 concentrations, and chitinase and protease activities were measured in the oral rinses. Binary logistic regression analyses with backward elimination were used to create prediction models for both total and severe periodontitis. Model 1 included SROH, demographics and biomarkers. The biomarkers were omitted in the analysis for model 2, while model 3 only included the SROH questionnaire. The area under the receiver operating characteristic curves (AUROCC) provided the accuracy of each model. The regression equations were used to create scoring algorithms, composed of the remaining predictors, each with its own weight. Results - Of the 156 patients participating in this study, 67% were classified with total periodontitis and 33% had severe periodontitis. The models for total periodontitis achieved an AUROCC of 0.91 for model 1, 0.88 for model 2 and 0.81 for model 3. For severe periodontitis, this was 0.89 for model 1, 0.82 for model 2 and 0.78 for model 3. The algorithm for total periodontitis (model 2), which we consider valid for the Dutch population, was applied to create a freely accessible, web-based screening tool. Conclusions - The prediction models for total and severe periodontitis proved to be feasible and accurate, resulting in easily applicable screening tools, intended for a non-dental setting.

Shimpi N, Glurich I, Panny A, Acharya A (2019). Knowledgeability, attitude, and practice behaviors of primary care providers toward managing patients' oral health care in medical practice: Wisconsin statewide survey. *J Am Dent Assoc* 150(10): 863-872. doi: 10.1016/j.adaj.2019.05.020. Epub 2019 Aug 22. At: <https://pubmed.ncbi.nlm.nih.gov/31446976/> Abstract: Background: In this study, the authors sought to explore the receptivity, preparedness, and rates of adoption of integrated medical-dental models of care (MOCs) in the practice setting among primary care providers (PCPs) treating patients with diabetes mellitus (DM). -- Methods: The authors conducted an anonymous statewide survey targeting PCPs across a range of Wisconsin-based practice settings to evaluate knowledgeability, attitude, practice behaviors, and perceived barriers to oral health screening in a medical setting. Qualitative analytical approaches included thematic analyses applied to evaluate the status of and barriers to integrated medical-dental MOC adoption. -- Results: The integrated medical-dental MOC adoption rate was 34%. Top perceived barriers to integrated medical-dental MOC adoption included insurance coverage (71%) and care access (70%). A total of 39% indicated competency for educating patients about the association between DM and periodontitis. Although 72% of PCPs indicated optimal periodicity for oral health assessment as frequent, 39% reported frequently conducting such assessments. -- Conclusions: Although PCPs indicate receptivity to integrated medical-dental MOCs, PCPs identify suboptimal education, lack of adequate training in oral-systemic disease assessment, and barriers to oral health care access as barriers to integrated medical-dental MOC adoption. - - Practical implications: Integrated medical-dental MOC adoption in care delivery to patients with DM remains below average. Interdisciplinary efforts and education are needed to address identified barriers to care integration.

Shimpi N, Schwei K, Cooper S, Chyou P-H, Acharya A (2018). Understanding patients' oral health information needs. *J Amer Dent Assoc* 149(3): 184-190. DOI: <https://doi.org/10.1016/j.adaj.2017.09.051>

OSHR – EHR Integration and Physician's Data Needs - Page 3 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. Glurich I, Schwei KM, Lindberg S, Shimpi N, Acharya A (2018). Integrating Medical-Dental Care for Diabetic Patients: Qualitative Assessment of Provider Perspectives. *Health Promot Pract* 19(4): 531-541. DOI: 10.1177/1524839917737752 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5878963/> Abstract: Globally, periodontal disease and diabetes have achieved epidemic proportions and have become a top healthcare priority. Mutual bidirectional exacerbation of these conditions driven by underlying inflammatory processes has been demonstrated. Creation of cross-disciplinary integrated care delivery (ICD) models that

bridge the traditionally-siloed healthcare domains of dentistry and medicine are being advanced to improve management of both conditions. By engaging focus groups inclusive of both medical and dental providers and one-on-one interviews, this qualitative study investigated provider knowledgeability, receptiveness, and readiness to engage ICD and sought input from the medical/dental primary care practitioner participants on perceived opportunities, benefits, and challenges to achieving ICD models for patients with diabetes/prediabetes. Statewide regional representation and inclusivity of diverse practice settings were emphasized in soliciting participants. Thematic analysis of focus group and interview transcripts was undertaken to establish current state-of-the-art, gauge receptivity to alternative ICD models, and seek insights from practitioners surrounding opportunities and barriers to ICD achievement. Forty providers participated, and thematic analyses achieved saturation. Providers were well informed regarding disease interaction, receptive to ICD, including implementation of better screening and referral processes, and favored improving interdisciplinary communication inclusive of access to integrated electronic health records. Perceived barriers and opportunities communicated by participants for advancing ICD were documented. Acharya A, Cheng B, Koralkar R, Olson B, Lamster IB, Kunzel C, Lalla E (2018). Screening for diabetes risk using integrated dental and medical electronic health record data. *JDR Clin Trans Res* 3(2): 188-194. DOI: 10.1177/2380084418759496. Epub 2018 Feb 26. At: <https://www.ncbi.nlm.nih.gov/pubmed/29568804> Abstract: Undiagnosed diabetes and prediabetes present a serious public health challenge. We previously reported that data available in the dental setting can serve as a tool for early dysglycemia identification in a primarily Hispanic, urban population. In the present study, we sought to determine how the identification approach can be recalibrated to detect diabetes or prediabetes in a White, rural cohort and whether an integrated dental-medical electronic health record (iEHR) offers further value to the process. We analyzed iEHR data from the Marshfield Clinic, a health system providing care in rural Wisconsin, for dental patients who were ≥ 21 y of age, reported that they had never been told they had diabetes, had an initial periodontal examination of at least 2 quadrants, and had a glycemic assessment within 3 mo of that examination. We then assessed the performance of multiple predictive models for prediabetes/diabetes. The study outcome, glycemic status, was gleaned from the medical module of the iEHR based on American Diabetes Association blood test cutoffs. The sample size was 4,560 individuals. Multivariate logistic regression revealed that the best performance was achieved by a model that took advantage of the iEHR. Predictors included age, sex, race, ethnicity, number of missing teeth, percentage of teeth with at least 1 pocket ≥ 5 mm from the dental EHR, and overweight/obesity, hypertension, hyperlipidemia, and smoking status from the medical EHR. The model achieved an area under OSHR – EHR Integration and Physician’s Data Needs - Page 4 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That’s Come," November 2021. the receiver operating characteristic curve of 0.71 (95% confidence interval, 0.69-0.72), yielding a sensitivity of 0.70 and a specificity of 0.62. Across a range of populations, informed by certain patient characteristics, dental care team members can play a role in helping to identify dental patients with undiagnosed diabetes or prediabetes. The accuracy of the prediction increases when dental findings are combined with information from the medical EHR. Knowledge Transfer Statement: Prediabetes and diabetes often go undiagnosed for many years. Early identification and care can lead to improved glycemic outcomes and prevent wide-ranging morbidity, including adverse oral health consequences, in affected individuals. Information available in the dental office can be used by clinicians to identify those who remain undiagnosed or are at risk; the accuracy of this prediction increases when combined with information from the medical electronic health record. Keywords: dentists; hyperglycemia; periodontitis; prediabetic state; prevention & control; risk. Burgette JM, Preisser JS,

Rozier RG (2018). Access to Preventive Services Following the Integration of Oral Health into Early Childhood Education and Medical Care. *J Am Dent Assoc* 149(12): 1024-1031.e2 DOI: 10.1016/j.adaj.2018.07.019 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7239644/> The integration of oral health services into primary medical care developed in direct response to the high prevalence of dental caries and limited dental access experienced by many families. Multiple well-child visits occur during the first 3 years of life. Provision of preventive oral health services (POHS) such as checking on the development of the mouth, counseling on proper diet and the application of fluoride varnish is congruent with the goals of well-child visits. Support for this strategy has evolved over many years, and it now is considered an essential part of the well-child visits. Jones JA, Snyder JJ, Gesko DS, Helgeson MJ (2017). Integrated Medical-Dental Delivery Systems: Models in a Changing Environment and Their Implications for Dental Education. *J Dent Educ* 81(9): eS21-eS29. DOI: 10.21815/JDE.017.029 At: <https://pubmed.ncbi.nlm.nih.gov/28864800/> Abstract: Models and systems of the dental care delivery system are changing. Solo practice is no longer the only alternative for graduating dentists. Over half of recent graduates are employees, and more than ever before, dentists are practicing in groups. This trend is expected to increase over the next 25 years. This article examines various models of dental care delivery, explains why it is important to practice in integrated medical-dental teams, and defines personcentered care, contrasting it with patient-centered care. Systems of care in which teams are currently practicing integrated oral health care delivery are described, along with speculation on the future of person-centered care and the team approach. Critical steps in the education of dental and other health care professionals and the development of clinical models of care in moving forward are considered. This article was written as part of the project "Advancing Dental Education in the 21st Century." Keywords: dental care delivery; dental education; dental health services; electronic health record; health care systems; interprofessional practice; patient-centered care; person-centered care. Dolce MC, Haber J, SAVageau JA, Hartnett E, Riedy CA (2018). Integrating oral health curricula into nurse practitioner graduate programs: Results of a US survey. *J Am Assoc Nurse Pract* 30(11): 638-647, DOI: 10.1097/JXX.000000000000079 At: <https://pubmed.ncbi.nlm.nih.gov/30095671/> Abstract: Background and purpose: Nurse practitioners (NPs) are a significant segment of the US primary care workforce and have a OSHR – EHR Integration and Physician's Data Needs - Page 5 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. pivotal role in improving access to oral health (OH) care. The purpose of this research was to assess OH curricular integration in primary care NP programs and to examine factors that influence integration and satisfaction with graduates' level of OH competence. Methods: A cross-sectional, national survey of NP programs (N = 466) was conducted using an electronically distributed 19-item, self-administered questionnaire. Data analysis included univariate, bivariate, multivariate statistics, and logistic regression modeling. Conclusions: The large majority of pediatric, family, and adult-gerontology primary care programs are educating NP graduates about OH. Significant factors promoting integration and satisfaction with graduates' level of competence included the presence of a faculty champion and routine teaching by a dental professional or nondental OH expert. Implications for practice: With adequate OH education, NPs are ideally positioned to integrate OH and primary care services in practice, thereby, improving access to OH care. Schillinger D, McNamara D, Crossley S, Lyles C, Moffet HH, Sarkar U, Duran N, Allen J, Liu J, Oryn D, Ratanawongsa N, Karter AJ (2017). Review Article: The Next Frontier in Communication and the ECLIPPSE Study: Bridging the Linguistic Divide in Secure Messaging. *J Diabetes Res Article* ID 1348242 DOI: <https://doi.org/10.1155/2017/1348242> Health systems are heavily promoting patient portals. However, limited health literacy (HL) can restrict online

communication via secure messaging (SM) because patients' literacy skills must be sufficient to convey and comprehend content while clinicians must encourage and elicit communication from patients and match patients' literacy level. This paper describes the Employing Computational Linguistics to Improve Patient-Provider Secure Email (ECLIPPSE) study, an interdisciplinary effort bringing together scientists in communication, computational linguistics, and health services to employ computational linguistic methods to (1) create a novel Linguistic Complexity Profile (LCP) to characterize communications of patients and clinicians and demonstrate its validity and (2) examine whether providers accommodate communication needs of patients with limited HL by tailoring their SM responses. We will study >5 million SMs generated by >150,000 ethnically diverse type 2 diabetes patients and >9000 clinicians from two settings: an integrated delivery system and a public (safety net) system. Finally, we will then create an LCP-based automated aid that delivers real-time feedback to clinicians to reduce the linguistic complexity of their SMs. This research will support health systems' journeys to become health literate healthcare organizations and reduce HL-related disparities in diabetes care. Lamster IB, Wright NM (2017). Oral Health Care in the Future: Expansion of the Scope of Dental Practice to Improve Health. *J Dent Educ* 81(9): eS83-eS90. DOI: 10.21815/JDE.017.038 At: <https://pubmed.ncbi.nlm.nih.gov/28864808/> Abstract: The health care environment in the U.S. is changing. The population is aging, the prevalence of non-communicable diseases (NCDs) is increasing, edentulism is decreasing, and periodontal infection/inflammation has been identified as a risk factor for NCDs. These trends offer an opportunity for oral health care providers to broaden the scope of traditional dental practice, specifically becoming more involved in the management of the general health of patients. This new practice paradigm will promote a closer integration with the larger health care system. This change is based on the realization that a healthy mouth is essential for a healthy life, including proper mastication, communication, esthetics, and comfort. Two types of primary care are proposed: screenings for medical conditions that are directly affected by oral disease (and may modify the provision of OSHR – EHR Integration and Physician's Data Needs - Page 6 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. dental care), and a broader emphasis on prevention that focuses on lifestyle behaviors. Included in the former category are screenings for NCDs (e.g., the risk of cardiovascular disease and identification of patients with undiagnosed dysglycemia or poorly managed diabetes mellitus), as well as identification of infectious diseases, such as HIV or hepatitis C. Reducing the risk of disease can be accomplished by an emphasis on smoking cessation and dietary intake and the prevention of obesity. These activities will promote interprofessional health care education and practice. While change is always challenging, this new practice paradigm could improve both oral health and health outcomes of patients seen in the dental office. This article was written as part of the project "Advancing Dental Education in the 21st Century." Keywords: dental services; interprofessional practice; primary care; scope of practice. Braun PA, Cusick A (2016). Collaboration Between Medical Providers and Dental Hygienists in Pediatric Health Care. *J Evid Based Dent Pract* 16: Suppl: 59-67. DOI: 10.1016/j.jebdp.2016.01.017 At: <https://pubmed.ncbi.nlm.nih.gov/27236997/> Abstract: Basic preventive oral services for children can be provided within the medical home through the collaborative care of medical providers and dental hygienists to expand access for vulnerable populations. Background: Because dental caries is a largely preventable disease, it is untenable that it remains the most common chronic disease of childhood. Leveraging the multiple visits children have with medical providers has potential to expand access to early preventive oral services. Developing interprofessional relationships between dental providers, including dental hygienists, and medical providers is a strategic approach to symbiotically expand access to dental care. Alternative care delivery models that provide dental

services in the medical home expand access to these services for vulnerable populations. The purpose of this article is to explore 4 innovative care models aimed to expand access to dental care. Methods: Current activities in Colorado and around the nation are described regarding the provision of basic preventive oral health services (eg, fluoride varnish) by medical providers with referral to a dentist (expanded coordinated care), the colocation of dental hygiene services into the medical home (colocated care), the integration of a dental hygienist into the medical care team (integrated care), and the expansion of the dental home into the community setting through telehealth-enabled teams (virtual dental home). Gaps in evidence regarding the impacts of these models are elucidated. Conclusion: Bringing preventive and restorative dental services to the patient both in the medical home and in the community has potential to reduce long-standing barriers to receive these services, improve oral health outcomes of vulnerable patients, and decrease oral health disparities. Keywords: Integrated care; Medical; Medicaldental integration; Oral health; Preventive dentistry. Kalenderian E, Halamka JD, Spallek H (2016). An EHR with Teeth. *Appl Clin Inform* 7(2): 425–429. Published online 2016 May 25. doi: 10.4338/ACI-2015-09-LE-0124 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4941850/> McCarthy K (2016). Why dental health and general health should be linked through EHRs. At: <https://nuemd.com/news/2016/02/02/dental-health-general-health-should-be-linked-through-ehrs> If patients are really sick or have several health conditions, it's important for doctors and dentists to work together to provide patients with comprehensive care by communicating through shared messaging and exchanged notes. If children have several cavities at a young age, both dentists and doctors should recognize that health isn't a top priority at home and they should work to change it. Again, recognizing these somewhat minor issues early on can help prevent them later in the timeline and stop them from getting worse. While many providers are aggravated by the lack of interoperability, as this software improves both providers should work to keep each other in the loop and help find ways to care for their patients, together. Tinanoff N, Bernstein J, Varas C, Gebel C, Walter A, Garcia R (2015). Integration of Oral Health into Pediatric Medical Primary Care in Community Health Centers. At: <http://www.bu.edu/creedd/files/2016/05/Final-report-NIDCR-Protocol-11-013.pdf> AAFP (American Academy of Family Physicians) 2015: <http://www.aafp.org/news/health-ofthe-public/20151224oralhealth.html> and <http://www.aafp.org/patient-care/inform/oralhealth.html> Primary Care - <http://www.qualishealth.org/about-us/newsroom/press-releases/nationalconsensus-is-growing-for-integrating-oral-health-in-primary-care> HRSA (2014). IOHPCP (Integration of Oral Health and Primary Care Practice): <https://www.hrsa.gov/sites/default/files/hrsa/oralhealth/integrationoforalhealth.pdf> Horowitz AM, Robinson LA, Ng MW, Acharya A (2014). After Visit Summaries: A Tool Whose Time Has Come for Use in Dentistry. *NAM Perspectives* DOI: <https://doi.org/10.31478/201407b> At: <https://nam.edu/perspectives-2014-after-visit-summaries-a-tool-whose-time-has-come-for-use-in-dentistry/> In dentistry, an after visit summary (AVS) can be thought of in both the context of a standalone dental practice and as a combined summary integrating oral health-related information with medical information. In this commentary, the authors explore the AVS from both perspectives and make a case for considering the AVS as an important piece of the larger puzzle needed to improve oral health and general health literacy for all patients. -- The concept of providing patients with an AVS is gaining attention as a result of the electronic health record (EHR) incentive program commonly known as "meaningful use" (MU). MU is a part of the Health Information Technology for Economic and Clinical Health (HITECH) Act that went into effect in February 2009 (DesRoches et al,

2013). However, the authors believe that AVS remains a foreign concept among the vast majority of dental practices in the United States that are either not eligible for MU or not aware of it (Schroeder et al, 2013). OSHR – EHR Integration and Physician’s Data Needs - Page 8 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That’s Come," November 2021. Elangovan S, Hertzman-Miller R, Karimbux N, Giddon D (2014). A Framework for PhysicianDentist Collaboration in Diabetes and Periodontitis. Clin Diabetes 32(4): 188-192. DOI: 10.2337/diaclin.32.4.188 At:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4220595/> Offers Diagram: Diagrammatic illustration of healthy (A) and diseased (B) periodontium. The crown of the teeth is covered by enamel (1). Cementum covering the root (2), periodontal ligament (3), alveolar bone (4), and gingival attachment (5) are the four tissues that comprise the periodontium. In periodontitis subjects, dental plaque is usually seen attached to the root surface, which gets calcified over time (6), deep in the periodontal pocket (7). A periodontal probe is used clinically to diagnose periodontitis (8). on p. 189. [See above.] Mitchell-Royston L, Nowal A, Silverman J (2014).

Interprofessional Study of Oral Health in Primary Care. At:

https://www.aapd.org/assets/1/7/Dentaquest_Year_1_Final_Report.pdf Abstract: OBJECTIVES: 1. Collect information about oral health promotion in the primary care setting 2. Identify drivers to successful implementation of oral health promotion in the primary care setting 3. Learn which caries-risk assessment tools are being used in primary care and how they might be improved 4. Determine what parents/caregivers think about oral health care information presented by primary care providers METHODS: Six focus groups were conducted with primary care providers (17 pediatricians, 11 family medicine physicians, 10 nurse practitioners, and three physician assistants) currently conducting oral health promotion for children 0-12 years old. Participants represented various practice types: public (such as academic medical centers, free clinics, community health centers), private, HMOs, FQHCs, hospital based, and school based. Twelve practice observations were conducted in primary care facilities that are currently conducting oral health promotion for children 0-6 years old. Various practice types were represented: private, hospital/ academic, FQHCs, and faith based/volunteer. Within the 12 sites, the following providers were represented: 73 pediatricians, 51 family medicine physicians, 23 nurse practitioners, 26 physician assistants, 112 pediatric residents, 29 family medicine residents, 71 registered nurses and licensed practical nurses, and 131 medical assistants. RESULTS: Oral health care activities studied in the primary care sites visited were: caries-risk assessment, visual inspection/screening, fluoride varnish application, fluoride supplementation, oral health education and anticipatory guidance, and referral to a dentist. Information regarding oral health promotion obtained was in reference to: workflow, caries-risk assessment tools, documentation of oral health activities, payment for oral health services, challenges to implementing oral health promotion in the primary care setting, referral systems and relationships with dentists, and family/caregiver response. Suggestions for system improvement and simplification were also solicited. Drivers of successful implementation of oral health promotion reported and observed were: • Oral health champion(s) present, defined as someone motivated to make a change within the site and willing to work towards sustainability. • Oral health activities delegated throughout the healthcare team. • Oral health activities formally integrated into the work flow OSHR – EHR Integration and Physician’s Data Needs - Page 9 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That’s Come," November 2021. • Oral health prompts and questions included in the electronic health record (EHR): • Specific questions and/or prompts included in intake and exam screens • Order sets in EHR for dental referral and fluoride varnish automatically bundled together • Ability to analyze oral health related data for quality improvement (fluoride varnish application) 5 CONCLUSIONS:

Incorporating oral health activities into existing primary care workflows is difficult, but there is much that can be learned from this group of providers and practices who have implemented oral health promotion into the practice of primary care medicine, including the following:

- The impetus for integrating oral health promotion into the primary care practice varied from one site to another, however, in all instances, at least one person (i.e. oral health champion) had strong feelings about the importance of oral health and its relationship to systemic health.
- Successful integration of oral health promotion in primary care necessitates a team approach.
- Providers of all types reported a need for improved oral health instruction in professional training programs (e.g., MD, PA, NP, RN, LPN, MA, PharmD).
- Visual inspection was the most commonly identified caries-risk assessment tool by primary care providers.
- External support from recognized experts (e.g., Chapter Oral Health Advocates, American Academy of Pediatrics, Cavity-Free by Three,) was identified as extremely helpful to primary care providers in establishing an oral health program.
- Generally, if not paid for fluoride varnish applications, primary care providers will not provide this service to patients at well child visits.
- Caries-risk assessment tools are not utilized in their original versions and need to be simplified.
- Integration of caries-risk assessment tools and preventive strategies into the EHR makes implementation much easier and was reported as an essential step for consistent implementation, quality assurance and documentation.
- When practices were able to include oral health activities in their quality improvement efforts through EHR-generated reports, they reported an improvement in implementation and consistency.

Cohen LA (2013). Expanding the Physician's Role in Addressing the Oral Health of Adults. *Am J Public Health* 103(3): 408-412. DOI: 10.2105/AJPH.2012.300990 At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3673507/>

Many disadvantaged adults visit physicians or hospital emergency departments to receive relief from dental pain. Physicians also see patients with general questions or concerns about their oral health. Unfortunately, because physicians generally have received little oral health training, patients often do not receive comprehensive emergency services or appropriate counseling. -- This situation has begun to change, as there has been a growing sentiment among the dental and medical communities that better integration and coordination between medicine and dentistry would be beneficial. Reports from the Institute of Medicine and professional associations and foundations reflect the need for better integration. -- I have outlined the rationale for and progress toward expanding the physician's role in addressing the oral health of adults. Silk H, Deutchman M (2014) Offering Oral Health Services in Your Office: Health problems of the mouth can affect the whole patient, making primary care physicians a natural ally. *Fam Pract Manag* 21(4): 21-24 At: <https://www.aafp.org/fpm/2014/0700/p21.html>

OSHR – EHR Integration and Physician's Data Needs - Page 10 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. Hummel J, Gandara BK (2011). Health Information Exchange and Care Coordination of Diabetic Patients Between Medicine and Dentistry. *Diabetes Spectrum* 24(4): 205-210. DOI: <https://doi.org/10.2337/diaspect.24.4.205>

Inadequate coordination of care between dentists and medical doctors presents a barrier to comprehensive management of patients with diabetes. New technologies for managing and exchanging health data hold a promise of improved transfer of clinical information between specialties. The authors present a model of how information technology can be used to support standardized workflows in medicine and dentistry to optimize care coordination for patients with diabetes. [See left , Figure 2. Sample electronic form for sharing information between medical and dental providers, p. 209.

From Conclusion: Health information technology in itself is insufficient to improve coordination of care and health outcomes. Rather, information technology makes it possible for providers to improve care if they can redesign the way information is used to reduce fragmentation of services, particularly when care is delivered across a variety of settings. As noted above, evidence suggests

that fragmented care between medicine and dentistry can make treatment of patients with diabetes and periodontal disease less effective. -- For care coordination to be successful, primary care providers in medicine and dentistry must be accountable for establishing relationships with their counterparts and setting up an infrastructure for tracking patients whom they send to each other for consultation. Work in other specialties suggests that this type of care coordination requires organizational agreements that take into account the perspectives and needs of both types of providers. Finally, it requires the type of interconnectivity outlined here as an HIE.... The model presented in this article includes a workflow for interprofessional care by physicians and dentists with suggested key datasets that can be modified as needed and validated by its users. It is hoped that this model can be extended to the management of other diseases with oral and systemic interactions currently at OSHR – EHR Integration and Physician’s Data Needs - Page 11 of 12

Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. high risk for being lost in the gap between medicine and dentistry. At: <https://spectrum.diabetesjournals.org/content/24/4/205> Close K, Rozier RG, Zeldin LP, Gilbert AR (2010). Barriers to the adoption and implementation of preventive dental services in primary medical care. *Pediatrics* 125(3): 509-517. DOI: 10.1542/peds.2009-1008 At: <https://pubmed.ncbi.nlm.nih.gov/20123767/> Abstract: Objective: To determine the barriers to adopting preventive oral health procedures in medical primary care. -- Methods: Medical providers who participated in a Medicaid demonstration in North Carolina completed questionnaires reporting their experiences with providing preventive dental services for children from birth to 3 years of age. Eleven factors were established as possible obstacles to the adoption of an oral health program. After 12 months of participation in the Into the Mouths of Babes training program, providers (N = 231) from 49 pediatric practices and 28 family physician practices reported if any of the 11 factors had been an obstacle to adoption and, if so, whether these obstacles were overcome. Program adoption and implementation, defined as providing all of the services on a regular basis, were predicted by using logistic regression to analyze the responses from providers who reported 1 or more barriers, the number of barriers identified (knowledge, attitudes, and external factors), and the number that were overcome. -- Results: Program-adoption rates were high, with 70.3% of the participants providing dental services on a routine basis. Attitude and external factors were positively associated with adoption, particularly with difficulty in applying the varnish, integration of the dental procedures into practice, resistance among staff and colleagues, and dentist referral difficulties. From 40.4% to 61.5% of providers overcame these 4 most common barriers. Those who reported external barriers and were unable to overcome them were less likely to provide the services, compared with those providers who reported no barriers (odds ratio: 0.08 [95% confidence interval: 0.01-0.44]). -- Conclusions: The number of barriers to adopting preventive dental procedures in primary care medical practices is associated with implementation. A large proportion of these barriers can be overcome, leading to high adoption rates in a short amount of time. The barriers to adoption are similar to those identified in the literature on changing patient care, with the unique aspects of fluoride application to teeth. Interventions to promote preventive dental care in medical settings should rely heavily on empirical literature. Training physicians in preventive dentistry should identify and target potential barriers with information and options for introducing office-based systems to improve the chances of adoption. Rudman, WJ.; Hart-Hester S, Jones W, Warren A, Caputo N, Madison M (2010). Integrating Medical and Dental Records: A New Frontier in Health Information Management, *Journal of AHIMA* 81(10):36-39. <https://library.ahima.org/doc?oid=102372#.XdhqZehKiM8> Lieberthal B (2008). The Electronic Medical Record and the future of dentistry. *AAOMS Practice Management Notes*. At: https://www.aaoms.org/images/uploads/pdfs/2008_04_pmn.pdf Schleyer TK (2004).

Should dentistry be part of the National Health Information Infrastructure? J Am Dent Assoc 135(12): 1687–1695. PMID: 15646601. DOI: 10.14219/jada.archive.2004.0120 OSHR – EHR Integration and Physician's Data Needs - Page 12 of 12 Prepared for International Conference: "The integration of Primary Care in Dental Practice - A Time That's Come," November 2021. At: <https://pubmed.ncbi.nlm.nih.gov/15646601/> Abstract: Background: The National Health Information Infrastructure, or NHII, proposes to improve the effectiveness, efficiency and overall quality of health in the United States by establishing a national, electronic information network for health care. To date, dentistry's integration into this network has not been discussed widely. Methods: The author reviews the NHII and its goals and structure through published reports and background literature. The author evaluates the advantages and disadvantages of the NHII regarding their implications for the dental care system. Results: The NHII proposes to implement computer-based patient records, or CPRs, for most Americans by 2014, connect personal health information with other clinical and public health information, and enable different types of care providers to access CPRs. Advantages of the NHII include transparency of health information across health care providers, potentially increased involvement of patients in their care, better clinical decision making through connecting patient-specific information with the best clinical evidence, increased efficiency, enhanced bioterrorism defense and potential cost savings. Challenges in the implementation of the NHII in dentistry include limited use of CPRs, required investments in information technology, limited availability and adoption of standards, and perceived threats to privacy and confidentiality. Conclusions: The implementation of the NHII is making rapid strides. Dentistry should become an active participant in the NHII and work to ensure that the needs of dental patients and the profession are met. Practice Implications. The NHII has far-reaching implications on dental practice by making it easier to access relevant patient information and by helping to improve clinical decision making. The compilation of this bibliographic resource was contributed by Dr. Valerie J. H. Powell, Project on Clinical Data Integration, Department of Computer and Information Systems, Robert Morris University (RMU), Moon Township. Pennsylvania (2020). Disclaimer: Any viewpoint expressed in this document is not necessarily a viewpoint of RMU.

Oral Health and Geriatrics (Dementia and Alzheimer's)

Hakeem F, Bernabé E, Sabbah W (2020). Association Between Oral Health and Frailty Among American Older Adults. *J Amer Med Dir Assoc*. DOI: [10.1016/j.jamda.2020.07.023](https://doi.org/10.1016/j.jamda.2020.07.023) At: <https://www.researchgate.net/publication/343887741> Association Between Oral Health and Frailty Among American Older Adults Abstract: Objective We examined the association between tooth loss, periodontal diseases, and frailty among older American adults. Designs, Settings, and Participants Data from the National Health and Nutrition Examination Surveys (NHANES) 2011–2014 was used. We included 2368 community-dwelling adults aged 60 years and older. Frailty was measured with the 49-item frailty index. Oral health indicators included number of teeth and periodontal disease. A composite nutritional intake variable based on 13 micronutrients from the dietary assessment was created. Negative binomial regression was used to test the association between oral health and frailty. The first model was adjusted for age and gender, the second model was additionally adjusted for nutritional intake, and the third model was additionally adjusted for other covariates. Results For each additional tooth, the rate ratio (RR) for frailty was 0.99 [95% confidence interval (CI) 0.98–0.99] in the fully adjusted model. Similarly, participants with moderate-severe periodontitis had 1.08 RR (95% CI 1.02–1.14) for frailty index compared with participants with no periodontitis after adjusting for age, gender, and poor nutritional intake. The association lost significance in the fully adjusted model. Conclusions and Implications Oral health is associated with the frailty index, and nutritional intake appears to have a modest effect on the association. Periodontal disease has a weaker association with frailty compared with number of teeth. The findings highlight the importance of maintaining good oral health at older age and incorporating oral health indicators in routine geriatric assessments. Future research should investigate the role of potential mediating factors in this association.

Sabbah W (2020). *Gerodontology*. DOI: [10.1111/ger.12489](https://doi.org/10.1111/ger.12489) The association between number of teeth and physical function limitation among older adults in the USA. At: <https://www.researchgate.net/publication/343207032> The association between number of teeth and physical function limitation among older adults in the USA Abstract: Aim To examine the association between the number of teeth and physical function limitation (PFL), as an indicator of frailty, among older adults in the USA. Background Physical function limitation is common among the elderly and potentially associated with oral health, particularly the number of extracted teeth. Materials and Methods Data from the Behavioral Risk Factor Surveillance System 2014 (BRFSS, 2014), a cross-sectional national interview survey of US population, were analyzed. The number of participating older adults aged 65 and over was 158 962. The association between PFL, outcome and number of extracted teeth, demographic data, socio-economic status, smoking, general health, comorbidity conditions and body mass index (BMI) was assessed using logistic regression analyses. Results The prevalence of PFL was 28%. In the

fully adjusted model, the number of extracted teeth had a significant association with PFL: edentulous older adults had higher odds for PFL, (odds ratio [OR]:1.36; 95%CI: 1.22, 1.52). Similarly, those who lost 6 teeth or more but not all were likely to have PFL (OR 1.35: 95% CI: 1.23, 1.48). Conclusions There was a significant association between the number of extracted teeth and PFL among US older adults aged 65 and more, based on the data from BRFSS 2014. The findings indicate that losing teeth may be a potential risk for PFL.

Demmer ET, Norby FL, Lakshminarayan K, Walker KA, Pankow JS, Folsom AR, Mosley T, Beck J, Lutsey PL (2020). Periodontal Disease and Incident Dementia: The Atherosclerosis Risk in Communities Study (ARIC). *Neurology* 10.1212/WNL.0000000000010312. DOI: 10.1212/WNL.0000000000010312 At:

<https://n.neurology.org/content/early/2020/07/29/WNL.0000000000010312> Abstract:

Objective: To test the hypothesis that periodontal disease would be associated with increased risk for dementia and mild cognitive impairment (MCI) we prospectively assessed dementia/MCI outcomes following a baseline periodontal examination. **Methods:** Participants enrolled in the Atherosclerosis Risk in Communities Study with a clinical periodontal examination (or edentulous participants) at visit 4 (1996-1998; mean±SD age=63±6, 55% female, 21% black) and adjudicated dementia outcomes through 2016 were included (n=8,275). A subgroup of 4,559 participants had adjudicated dementia and MCI assessments at visit 5 (2011-2013). Participants received a full-mouth periodontal exam and were classified into periodontal profile classes (PPCs) based on the severity and extent of gingival inflammation and attachment loss. MCI and dementia were determined via neurocognitive testing, neurological exam and history, informant interviews, and brain MRI in a subset. Cox proportional hazards models regressed incident dementia on PPCs. Relative risk regression models were utilized for the composite of MCI/dementia. **Results:** The cumulative incidence and incidence density of dementia during follow-up (average=18.4 years) were 19% (n=1569) and 11.8 cases per 1,000 person-years. Multivariable adjusted hazard ratios (HRs) [95% CI] for incident dementia among participants with severe-PPC or edentulism (vs. periodontal healthy) were 1.22[1.01-1.47] and 1.21[0.99-1.48], respectively. For the combined dementia/MCI outcome adjusted risk ratios among participants with mild/intermediate-PPC, severe-PPC or edentulism (vs. periodontal healthy) were 1.22[1.00-1.48], 1.15[0.88-1.51] and 1.90[1.40-2.58]. Results were stronger among younger (≤62 years) participants, p-value for interaction=0.02. **Conclusion:** Periodontal disease was modestly associated with incident MCI and dementia in a community-based cohort of black and white participants.

Beydoun MA, Beydoun HA, Hossain S, El-Hajj ZW, Weiss J, Zonderman AB (2020). Clinical and Bacterial Markers of Periodontitis and Their Association with Incident All-Cause and Alzheimer's Disease Dementia in a Large National Survey. *J Alzheimers Dis* 75(1): 157-172. doi: 10.3233/JAD-200064. At: <https://pubmed.ncbi.nlm.nih.gov/32280099/> Abstract: Microbial agents including periodontal pathogens have recently appeared as important actors in Alzheimer's disease (AD) pathology. We examined associations of clinical periodontal and bacterial parameters with incident all-cause and AD dementia as well as AD mortality among US middle-aged and older adults. Clinical [Attachment Loss (AL); probing pocket depth (PPD)] and bacterial [pathogen immunoglobulin G (IgG)] periodontal markers were investigated in relation to AD and all-cause dementia incidence and to AD mortality, using data from the third National Health and

Nutrition Examination Surveys (NHANES III, 1988-1994) linked longitudinally with National Death Index and Medicare data through January 1, 2014, with up to 26 years of follow-up. Sex- and age-specific multivariable-adjusted Cox proportional hazards models were conducted. Among those ≥ 65 years, AD incidence and mortality were consistently associated with PPD, two factors and one cluster comprised of IgG titers against *Porphyromonas gingivalis* (*P. gingivalis*), *Prevotella melaninogenica* (*P. melaninogenica*) and *Campylobacter rectus* (*C. rectus*) among others. Specifically, AD incidence was linked to a composite of *C. rectus* and *P. gingivalis* titers (per SD, aHR = 1.22; 95% CI, 1.04-1.43, $p = 0.012$), while AD mortality risk was increased with another composite (per SD, aHR = 1.46; 95% CI, 1.09-1.96, $p = 0.017$) loading highly on IgG for *P. gingivalis*, *Prevotella intermedia*, *Prevotella nigrescens*, *Fusobacterium nucleatum*, *C. rectus*, *Streptococcus intermedius*, *Capnocytophaga Ochracea*, and *P. melaninogenica*. This study provides evidence for an association between periodontal pathogens and AD, which was stronger for older adults. Effectiveness of periodontal pathogen treatment on reducing sequelae of neurodegeneration should be tested in randomized controlled trials.

Gao SS, Chu CH, Young FYF (2020). Oral Health and Care for Elderly People with Alzheimer's Disease. *Int J Environ Res Public Health* 17(16): 5713. DOI: [10.3390/ijerph17165713](https://doi.org/10.3390/ijerph17165713) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7460333> Abstract: Ryder MI (2020).

Porphyromonas gingivalis and Alzheimer disease: Recent findings and potential therapies. *J Periodontol* **91 Suppl** 1:S45-S49 DOI: [10.1002/JPER.20-0104](https://doi.org/10.1002/JPER.20-0104) At:

<https://pubmed.ncbi.nlm.nih.gov/32533852/> Abstract: Epidemiological studies have identified an association between periodontitis and Alzheimer disease (AD); however, the nature of this association has been unclear. Recent work suggests that brain colonization by the periodontal pathogen *Porphyromonas gingivalis* may link these two inflammatory and degenerative conditions. Evidence of *P. gingivalis* infiltration has been detected in autopsy specimens from the brains of people with AD and in cerebrospinal fluid of individuals diagnosed with AD.

Gingipains, a class of *P. gingivalis* proteases, are found in association with neurons, tau tangles, and beta-amyloid in specimens from the brains of individuals with AD. The brains of mice orally infected with *P. gingivalis* show evidence of *P. gingivalis* infiltration, along with various neuropathological hallmarks of AD. Oral administration of gingipain inhibitors to mice with established brain infections decreases the abundance of *P. gingivalis* DNA in brain and mitigates the neurotoxic effects of *P. gingivalis* infection. Thus, gingipain inhibition could provide a potential approach to the treatment of both periodontitis and AD.

Freed M, Potetz L, Jacobson G, Neuman T (2019). Policy options for improving dental coverage for people on Medicare. At: <https://www.kff.org/medicare/issue-brief/policy-options-for-improving-dental-coverage-for-people-on-medicare/> Summary: Since its inception, Medicare, the national health insurance program for more than 60 million older adults and younger people with long-term disabilities, has explicitly excluded coverage of dental services, with limited exceptions. Some Medicare beneficiaries have access to dental coverage through other sources, such as Medicare Advantage plans, Medicaid, or private plans (either employer-sponsored retiree plans or plans purchased by individuals), but the scope of coverage under these plans varies widely and is typically quite limited. -- Nearly two-thirds of the Medicare population – 37 million beneficiaries – have no dental coverage at all. Cost concerns and lack of

dental coverage contribute to beneficiaries foregoing routine and other dental procedures. Lack of dental care can exacerbate chronic medical conditions, such as diabetes and cardiovascular disease, contribute to delayed diagnosis of serious medical conditions, and lead to preventable complications that sometimes result in costly emergency room visits.¹ As a result, there is ongoing interest in policy options to make dental care more affordable by broadening dental coverage for people on Medicare.² -- This issue brief begins with a review of dental coverage permitted under current Medicare law to set the context for understanding proposals that could improve oral health coverage for the Medicare population. It reviews a range of policy options that could make dental care more affordable, examines basic policy features associated with each proposal, and discusses potential implications for key stakeholders, including Medicare beneficiaries, taxpayers, insurers, and dental professionals. -- This brief describes five potential ways to strengthen oral health care for older adults (Table 1). The first two options would create a new dental benefit under Medicare: one would add dental benefits to Medicare Part B, and the other would establish a separate dental benefit under a new part of Medicare, similar in some ways to the Part D benefit for prescription drugs. The other three options would be expected to provide less help in improving dental coverage and reducing out-of-pocket costs for dental care, and would have a more limited impact on Medicare spending

Dominy SS, Lynch C, Ermini F, Benedyk M, Marczyk A, Konradi A, Nguyen M, Haditsch U, Raha D, Griffin C, Holsinger LJ, Arastu-Kapur S, Kaba S, Lee A, Ryder MI, Potempa B, Mydel P, Hellvard A, Adamowicz, Hasturk H, Walker GD, Reynolds EC, Faull RLM, Curtis MA, Dragunow M, Potempa J (2019). *Porphyromonas gingivalis* in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors. *Sci Adv* 5(1): eaau3333 DOI: 10.1126/sciadv.aau3333 Abstract: *Porphyromonas gingivalis*, the keystone pathogen in chronic periodontitis, was identified in the brain of Alzheimer's disease patients. Toxic proteases from the bacterium called gingipains were also identified in the brain of Alzheimer's patients, and levels correlated with tau and ubiquitin pathology. Oral *P. gingivalis* infection in mice resulted in brain colonization and increased production of A β ₁₋₄₂, a component of amyloid plaques. Further, gingipains were neurotoxic in vivo and in vitro, exerting detrimental effects on tau, a protein needed for normal neuronal function. To block this neurotoxicity, we designed and synthesized small-molecule inhibitors targeting gingipains. Gingipain inhibition reduced the bacterial load of an established *P. gingivalis* brain infection, blocked A β ₁₋₄₂ production, reduced neuroinflammation, and rescued neurons in the hippocampus. These data suggest that gingipain inhibitors could be valuable for treating *P. gingivalis* brain colonization and neurodegeneration in Alzheimer's disease.

Singhrao SK, Olsen I (2019). Assessing the role of *Porphyromonas gingivalis* in periodontitis to determine a causative relationship with Alzheimer's disease. *J Oral Microbiol* 11(1): 1563405. DOI: [10.1080/20002297.2018.1563405](https://doi.org/10.1080/20002297.2018.1563405) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6352933/> Abstract: Chronic periodontitis of 10 years' duration is reported to become a twofold risk factor for the development of Alzheimer's disease (AD). Periodontitis is modifiable, and this fits with the current action plan for preventing AD. However, until periodontitis, becomes acknowledged as a firm risk factor for AD, this risk will continue. Here, we put forward our own argument based on the current literature for *in vivo* infection-mediated periodontal disease models supporting the antimicrobial protection

hypothesis of AD and interventional studies supporting the causal links. Oral infections with *Porphyromonas gingivalis*, or introduction of its lipopolysaccharide (LPS), in various mouse models has demonstrated the development of key neuropathological hallmark lesions defining AD. These are extracellular amyloid-beta plaques, phosphorylated tau, neurofibrillary tangles, widespread acute and chronic inflammation, blood–brain barrier defects together with the clinical phenotype showing impaired learning and spatial memory. Live *P. gingivalis* and its LPS (commercial or from ‘microbullets’) are powerful peripheral and intracerebral inflammatory signalling initiators, and this has direct implications on memory and lesion development. Maintaining a healthy oral microbiome and managing periodontal disease with regular surveillance and good oral hygiene throughout life is likely to reduce the unnecessary burden of AD in some individuals. **Keywords:** Alzheimer’s disease, chronic periodontitis, cause, infection, *P. gingivalis*, lipopolysaccharide risk factor, intervention.

Alzforum (2019). An Antimicrobial Approach to Treating Alzheimer’s? At: <https://www.alzforum.org/news/research-news/antimicrobial-approach-treating-alzheimers>

Islas-Granillo H, Borges-Yañez SA, Navarrete-Hernández JdJ, Veras-Hernández MA, Casanova-Rosado JF, Minaya-Sánchez M, Casanova-Rosado AJ, Fernández-Barrera MÁ, Medine-Solís CE (2019). The presence of multimorbidity: a cross-sectional study. *Clin Interv Aging* 14: 219-224. doi: [10.2147/CIA.S170470](https://doi.org/10.2147/CIA.S170470) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6363395/> Abstract: **Purpose** The aim of this study was to determine whether there are differences in the distribution of various indicators of oral health among elderly people with and without multimorbidity (ie, two or more chronic diseases). **Subjects and methods** A cross-sectional, comparative study was conducted using a sample of Mexican elderly individuals aged ≥ 60 years. The average age of the cohort was 79.06 ± 9.78 years, and 69.1% were women. The variables indicating oral health were as follows: functional dentition, edentulism, hyposalivation, xerostomia, root caries and periodontitis. The multimorbidity variable was operationally categorized as follows: 0= subjects with no chronic disease or one chronic disease and 1= subjects with two or more chronic diseases. Questionnaires were used to collect information on various variables regarding general health. Likewise, the participants underwent a clinical oral examination. The analysis was performed using Stata 11.0. **Results** The overall prevalence of multimorbidity was 27.3%. The prevalences of various oral health indicators were as follows: without functional dentition 89.9%; hyposalivation 59.7%; edentulism 38.9% and self-reported xerostomia 25.2%. Dental caries were observed in 95.3% of the subjects, and the prevalence of severe periodontitis was 80%. We found a significant difference only in edentulism; its prevalence was higher among subjects with multimorbidity (55.3% vs 32.7%, $P=0.015$) than among those without multimorbidity. **Conclusion** The presence of edentulism in this sample of Mexican older adults was higher in subjects with multimorbidity. Multimorbidity and oral diseases constitute a true challenge in elderly people, because they affect quality of life and are associated with high health care costs.

Dörfer C; Benz C; Aida J; Campard G (2017). The relationship of oral health with general health and NCDs: A brief review. *Int. Dent. J.* 67: 14–18. DOI: [10.1111/idj.12360](https://doi.org/10.1111/idj.12360) At: <https://pubmed.ncbi.nlm.nih.gov/29023744/> Abstract: Oral health is closely related to systemic health. Periodontitis, a chronic inflammatory disease which is highly prevalent worldwide, interacts with a variety of noncommunicable diseases (NCDs). It is a risk factor in the complex

pathogenesis of diabetes mellitus and cardiovascular disease and plays a role in the development of endocarditis and recurrent pneumonia in elderly people. However, the available data may be interpreted in different ways, and more and better-designed studies are still needed to answer relevant questions about the causal role of periodontitis in NCDs. What is clear is that periodontitis contributes to the systemic inflammatory burden. As periodontitis shares many common risk factors with NCDs, close collaboration between physicians and dentists is needed to increase the chance of early detection and improve the prevention and control of these conditions.

Holmstrup P, Damgaard C, Olsen I, Klinge B, Flyvbjerg A, Nielsen CH, Hansen PR (2017). Comorbidity of periodontal disease: two sides of the same coin? An introduction for the clinician. *J Oral Microbiol.* 9(1):1332710. DOI: 10.1080/20002297.2017.1332710. PMID: PMC5508374. At: <https://pubmed.ncbi.nlm.nih.gov/28748036/> Abstract: Increasing evidence has suggested an independent association between periodontitis and a range of comorbidities, for example cardiovascular disease, type 2 diabetes, rheumatoid arthritis, osteoporosis, Parkinson's disease, Alzheimer's disease, psoriasis, and respiratory infections. Shared inflammatory pathways are likely to contribute to this association, but distinct causal mechanisms remain to be defined. Some of these comorbid conditions may improve by periodontal treatment, and a bidirectional relationship may exist, where, for example, treatment of diabetes can improve periodontal status. The present article presents an overview of the evidence linking periodontitis with selected systemic diseases and calls for increased cooperation between dentists and medical doctors to provide optimal screening, treatment, and prevention of both periodontitis and its comorbidities. **Keywords:** Alzheimer's disease; Parkinson's disease; Periodontitis; cardiovascular disease; comorbidity; low-grade inflammation; osteoporosis; periodontal disease; pneumonia; psoriasis; rheumatoid arthritis; type 2 diabetes.

Willink A, Schoen C, Davis K (2016). Dental Care And Medicare Beneficiaries: Access Gaps, Cost Burdens, And Policy Options. *Health Affairs* 35(12): [HTTPS://DOI.ORG/10.1377/HLTHAFF.2016.0829](https://doi.org/10.1377/hlthaff.2016.0829) At: <https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2016.0829> Abstract: Despite the wealth of evidence that oral health is related to physical health, Medicare explicitly excludes dental care from coverage, leaving beneficiaries at risk for tooth decay and periodontal disease and exposed to high out-of-pocket spending. To profile these risks, we examined access to dental care across income groups and types of insurance coverage in 2012. High-income beneficiaries were almost three times as likely to have received dental care in the previous twelve months, compared to low-income beneficiaries—74 percent of whom received no dental care. We also describe two illustrative policies that would expand access, in part by providing income-related subsidies. One would offer a voluntary, premium-financed benefit similar to those offered by Part D prescription drug plans, with an estimated premium of \$29 per month. The other would cover basic dental care in core Medicare Part B benefits, financed in part by premiums (\$7 or \$15 per month, depending on whether premiums covered 25 percent or 50 percent of the cost) and in part by general revenues. The fact that beneficiaries are forgoing dental care and are exposed to significant costs if they seek care underscores the need for action. The policies offer pathways for improving health and financial independence for older adults.

Yoshida M, Suzuki R (2016). Nutrition and oral status in elderly people. *Japan Dent Sci Rev* 50,1:9-14. <https://doi.org/10.1016/j.jdsr.2013.09.001> At: <https://www.sciencedirect.com/science/article/pii/S1882761613000562>

Gil-Montoya JA, Ferreira de Mello AL, Barrios R, Gonzales-Moles MA, Bravo M (2015). Oral health in the elderly patient and its impact on general well-being: a nonsystematic review. *Clin Interv Aging* 10:461-467. doi [10.2147/CIA.S54630](https://doi.org/10.2147/CIA.S54630) At: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4334280/> Abstract: Data on the oral health of the elderly depict a worrying situation, with an elevated prevalence of caries and moderate periodontal disease, frequent edentulism, and numerous cases of dry mouth and oral cancer. There is wide evidence that periodontitis is a risk factor for certain systemic diseases, and impaired oral health has been associated with mastication and nutritional problems, especially among the elderly, with highly negative effects on their quality of life. In this nonsystematic review, the authors discuss the importance of evaluating the oral health of the geriatric population in a comprehensive manner, beyond simple clinical assessments.

Carlson C, Merel SE, Yukawa M (2015). Geriatric syndromes and geriatric assessment for the generalist. *Med Clin North Am* 99(2): 263-279. DOI: 10.1016/j.mcna.2014.11.003. Epub 2015 Jan 10 At: <https://pubmed.ncbi.nlm.nih.gov/25700583/> Abstract: Geriatric assessment is an increasingly important area of outpatient medicine, given the unprecedented aging of the US population. Screening and evaluation for geriatric syndromes, particularly falls, urinary incontinence, frailty, and cognitive impairment, are crucial aspects of outpatient geriatric assessment. Innovative models of care are emerging to improve quality of care and enhance cost savings for the geriatric patient. High-value features of geriatric care systems include providing increased 24/7 access to care, a multidisciplinary team-based approach to care, performing medication reconciliation and comprehensive geriatric assessments, and integrating palliative care into treatment planning. **Keywords:** Care delivery systems; Frailty; Geriatric assessment; Geriatric syndromes; Primary care.

Dolce MC, Aghazadeh-Sanai N, Mohammed S, Fulmer TT (2014). Integrating Oral Health into the Interdisciplinary Health Sciences Curriculum. *Dental Clinics of North America* 58(4). DOI: [10.1016/j.cden.2014.07.002](https://doi.org/10.1016/j.cden.2014.07.002) At: <https://www.researchgate.net/publication/264385795> Integrating Oral Health into the Interdisciplinary Health Sciences Curriculum Abstract: Oral health inequities for older adults warrant new models of interprofessional education and collaborative practice. The Innovations in Interprofessional Oral Health: Technology, Instruction, Practice and Service curricular model at Bouvé College of Health Sciences aims to transform health professions education and primary care practice to meet global and local oral health challenges. Innovations in simulation and experiential learning help to advance interprofessional education and integrate oral health care as an essential component of comprehensive primary health care. The Program of All-Inclusive Care for the Elderly clinic is an exemplary model of patient-centeredness and interprofessional collaborative practice for addressing unmet oral health needs of its patient population.

Razak PA, Richard KMJ, Thankachan RP, Hafiz KAA, Kumar KN, Sameer KM (2014). Geriatric Oral Health: A Review Article. *J Int Oral Health* 6(6): 110-116. At:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4295446/> Abstract: Geller MC, Alter D (2012). The Impact of Dentures on the Nutritional Health of the Elderly. <http://www.jarcp.com/872-the-impact-of-dentures-on-the-nutritional-health-of-the-elderly.html>

Mysore AR, Aras MA (2012). "Understanding the psychology of geriatric edentulous patients." *Gerodontology*. <http://europepmc.org/abstract/MED/21707742>

Iacopino AM, Wathen WF (1993). Craniomandibular Disorders in the Geriatric Patient. *J Orofac Pain* 7(1): 38-53. At: <https://www.ncbi.nlm.nih.gov/pubmed/8467296> Abstract: This paper represents a general review of basic age-related changes that take place in the craniomandibular apparatus and the most frequently presenting conditions associated with craniomandibular disorders (CMD) in the elderly. The evaluation of geriatric patients with signs or symptoms of CMD must consider (1) normal age-related changes in the craniomandibular apparatus and their impact on both normal function and responses to stress; (2) the role of dentition status and dental prosthesis in CMD; and (3) the contribution of malignant disease, psoriasis, arthritic conditions, pseudogout, granulomatous vascular conditions, and metaplastic involvement of tissue to the pathosis of CMD. The clinician must also be aware of various effects of psychologic, sociologic, and biologic aspects of aging on the development of headache and atypical facial pain as components of CMD in the geriatric patient.