

The Relationship Between Cardiovascular Xerogenic Medication Intake and the Incidence of Crown/Root Restorations

Gerardo Maupomé, BDS, MSc, PhD; Dawn Peters, PhD; William A. Rush, PhD; D. Brad Rindal, DDS; B. Alex White, DMD, DrPH

Abstract

Objectives: This retrospective, longitudinal cohort study quantified the strength of the association between xerogenic cardiovascular medication use and dental restorations, using the latter as a proxy measure for dental caries experience. **Methods:** Study data were collected from 11 years of electronic clinical/pharmacy records in two large dental group practices associated with managed care organizations (MCO). Records were extracted for all members who were at least 55 years old at the end of the 11 year window, and had at least 48 months of concurrent dental, medical, and pharmacy coverage. The authors identified 4,448 individuals whose only xerogenic medication exposure was to drugs treating a cardiovascular condition. This group was compared to a group not taking any medications ($n=1,183$), and a group taking medications with no known xerostomic side effect ($n=5,622$). Poisson regression compared restoration incidence and mean restoration rates among the three groups. **Results:** MCO members taking cardiovascular or non-xerogenic medications had higher restoration incidence and mean restoration rates than individuals taking no medications. A small difference in mean restoration rate between the non-xerogenic medication group and the cardiovascular drug group was observed; no significant difference in restoration incidence was seen between these two groups. **Conclusions:** This study provides objective quantification of cardiovascular medication's long-term effects on increased restorations in older adults. When grouped under a single category labeled "cardiovascular," drugs with effects targeting the cardiovascular system did not appear to unequivocally lead to higher restorative experiences.

Key Words: xerostomia, restorations, cardiovascular, cardiovascular drugs, caries, rates, incidence

Introduction

Xerostomia, a reduction in salivary flow resulting in a subjective feeling of mouth dryness, is more common in adults, especially older adults. Xerostomia can result from a number of causes, (1) including autoimmune diseases, head and neck radiation (2), depression (3;4) anxiety, dehydration, and long-term use of medications affecting the autonomic nervous system (5-7). Aging does not affect salivary gland function *per se*. The frequency of medication use that influences salivary flow, however, does increase with

age (8)(9-11). Saliva serves an important protective function due to its remineralizing, antibacterial, and buffering actions (11).

Many commonly prescribed drugs have anticholinergic properties that block parasympathetic salivary gland stimulation (12). Anticholinergic medications have long been identified as contributing to xerostomia, and subsequent dental crown and root caries (13), with one or the other preferentially associated with the number of xerogenic medications taken (14). Reduced salivary flow can cause

chronic discomfort, functional problems, rapid caries progression, intensification of periodontal problems, and increased risk for oral candidiasis. A decrease in saliva's cleansing properties permits bacterial growth and adherence, leading to increased dental plaque accumulation. The same principle is responsible for the inadequate buffering of bacterial acids, which causes caries progression (15). Some studies, however, have failed to find such associations when salivary flow rate was examined, or when repeated cross-sectional assessments were attempted (16-19).

The intake of prescription medications increases with age, with more than 75% of persons aged 65 and older taking at least one prescription medication (20). Having at least one cardiovascular condition is common across all ages. The American Heart Association estimates that 61,800,000 Americans have cardiovascular disease, which can include high blood pressure, coronary heart disease, stroke, birth defects of the heart and blood vessels, or congestive heart failure. Recent reports found that 50 million Americans have high blood pressure, 12.6 million have coronary heart disease, and 4.6 million have suffered stroke (21). Even though an accurate estimate of cardiovascular drug use is difficult to attain, it is generally accepted that long-term cardiovascular drug use is very frequent, even after accounting for substantial under-medication of chronic conditions.

Send correspondence to: Dr. Gerardo Maupomé, Oral Health Research Institute, Department of Preventive and Community Dentistry, Indiana University / Purdue University at Indianapolis School of Dentistry, 415 Lansing Street, Indianapolis, IN 46202-2876. Phone: (317) 274-5529; Fax: (317) 274-5425. E-mail address: gmaupome@iupui.edu. Dr. Maupomé is affiliated with the Oral Health Research Institute, Department of Preventive and Community Dentistry, Indiana University / Purdue University at Indianapolis School of Dentistry and with the Center for Health Research, Portland, OR. Professor Peters is affiliated with the Department of Public Health and Preventive Medicine, Oregon Health and Sciences University, Portland, OR. Dr. Rindal is affiliated with the Health Partners Research Foundation, Bloomington, MN. Dr. White is affiliated with Delta Services of Massachusetts, Boston, MA. Source(s) of support: NIDCR 1R01DE013730-01 and K25-DE014093. Manuscript received 10/02/04; returned to authors for revision 8/14/05; final version accepted for publication 9/12/05. No reprints will be available.

Some studies have failed to quantitatively estimate anticholinergic medication's effect on outcomes directly relevant to observed dental status (16,17). Other studies have measured drug use at one, or two points in time (14,18), and then assumed that drug use was continuous between the two time points. There is a need to accurately quantify the effect of such medications by resorting to large, population-based, longitudinal assessments of the relationships between xerogenic medication usage and caries experience. The present study offers an investigation into the effect of xerogenic medications used to treat cardiovascular conditions on caries experience, aiming to quantify its long-term impact on restorative services in a population with good access to restorative care.

Methods

This retrospective, longitudinal cohort study's design and undertaking followed the guidelines for ethically conducting studies at the organizations where data were collected.

Managed care organizations members—description and eligibility. The study was conducted using electronic medical, dental, and pharmacy records within two large dental group practices associated with medical managed care organizations (MCO). One MCO is a staff model group practice consisting of 60 general dentists and specialists that provides both pre-paid and fee-for-service dental and oral-care services in 16 dental clinics located throughout the Twin Cities metropolitan area of Minnesota. It provides care for approximately 100,000 members. About 70% of the dentists' compensation is salary, with the remainder being related to production and other plan incentives (including adherence to clinical guidelines). Dentist supervisors do random audits to determine if the risk assigned and interventions prescribed make sense based on the clinical information. The second MCO is similar, except that it is made up of about 120 general dentists and specialists that supply dental services

through 16 dental clinics located in Southeast Washington State and Northern Oregon, with about 170,000 dental members at any one time. While design and enactment of clinical guidelines is also undertaken largely under the supervision of the group practice, it is only recently that plan incentives (again, with a substantial component of adherence to clinical guidelines) have replaced a small fraction of otherwise salaried practitioners.

Virtually all members obtained prescriptions through their MCO pharmacy benefits as the insurance coverage reduces the cost of most prescribed medications. MCO members at both sites were required to fulfill the following criteria for inclusion in the study. First, they had to be 55 years of age or older on 12/31/2000. Second, they had both dental and medical coverage with pharmacy benefits for an overlapping period of at least 48 consecutive months. Third, this period had to fall between 1990 and 2000. If a potential subject had more than one eligible period during this interval, only the earliest period was used. Contiguous gaps in coverage up to ninety days were not considered breaks in coverage. Due to differences in enrollment stability between the two sites, there were substantial differences in the length of eligibility periods by site (Table 1). Age distributions of MCO members by site are shown in Table 2.

Variable construction. MCO members taking xerogenic medications used to treat cardiovascular conditions composed one of the study groups. Two additional control groups were selected. The first consisted of MCO members without any pharmacy fills during the study period. These were included to control for a possible undetermined influence of being on any other non-xerogenic medication. The second control group had a history of medication use, but no exposure to the medications on the study xerogenic list. This group was included to control for xerostomic effects that might not be directly ascribable to xerogenic medications.

TABLE 1
Distribution of MCO members by site and length of eligibility

Length in Years	Eligibility Counts (Percentages)	
	Site 1	Site 2
4	1,433 (27%)	2,097 (9%)
5	2,430 (47%)	1,962 (9%)
6	383 (7%)	1,974 (9%)
7	629 (12%)	1,837 (8%)
8	231 (4%)	1,471 (6%)
9	71 (1%)	1,446 (6%)
10	39 (1%)	12,266 (53%)
Total	5,216	23,053

TABLE 2
Distribution of MCO members by age and by study site

Age	Eligibility Counts (Percentages)	
	Site 1	Site 2
55-59	2,072 (40%)	6,952 (30%)
60-64	1,367 (26%)	4,840 (21%)
65-69	814 (16%)	3,312 (14%)
70-74	524 (10%)	2,758 (12%)
75-79	241 (5%)	2,294 (10%)
80-84	116 (6%)	1,439 (6%)
85-89	42 (1%)	921 (4%)
90-94	18 (<1%)	403 (2%)
95-99	18 (<1%)	111 (<1%)
100-104	4 (<1%)	22 (<1%)
105-109	0	1 (<1%)
Total	5,216	23,053

Classification of xerogenic and non-xerogenic medications. The classification of xerogenic medications relied on three approaches. The *first approach* categorized drugs based on anticholinergic mechanisms (22; 23). The *second approach* assembled lists of drugs that were known to have xerogenic potential—either by their clinical manifestations, with special attention to dry mouth (18),(24) or because they were so classified based on their pharmacodynamics (25). An internal medicine specialist, a psychiatrist, and two pharmacists reviewed these lists before they were merged into a single list. The *third approach* conducted an electronic search for any drug with a reported xerostomic side effect rates of 3% or greater in the 2002 Physician's Desk Reference™ (PDR) (26). While crude, such an arbitrary threshold is set by

TABLE 3
Distributions of cardiovascular drug classes (GPI) and of MCO members
taking xerogenic medications by GPI class

GPI Class Code	Description	Count of Drugs in Each GPI Class	Count of Members Taking Drugs in Each GPI Class
3310	Beta Blockers Non-Selective	5	424
3320	Beta Blockers Cardio-Selective	4	2,488
3330	Alpha-Beta Blockers	1	15
3400	Calcium Blockers	8	578
3510	Antiarrhythmics Type I-A	4	79
3520	Antiarrhythmics Type I-B	2	2
3530	Antiarrhythmics Type I-C	3	44
3540	Antiarrhythmics Type III	1	71
3610	ACE Inhibitors	5	1,356
3615	Angiotensin II Receptor Antagonist	4	104
3620	Adrenolytic Antihypertensives	10	491
3640	Vasodilators	3	18
3710	Carbonic Anhydrase Inhibitors	2	58
3720	Loop Diuretics	4	606
3750	Potassium Sparing Diuretics	3	154
3760	Thiazides	7	1,585
3910	Bile Sequestrants	2	359
3920	Fibric Acid Derivatives	2	442
3940	HMG CoA Reductase Inhibitors	6	1,397
3950	Misc. Antihyperlipidemics	2	7
4030	Impotence Agents	2	486

current standards of reporting industrial specifications. To obtain a final classification for data analysis, we created a subset of medications that included all drugs that were derived from *approaches one, two, or three*. This final list contained 190 different putative xerogenic medications used by the study population. Each medication was coded by Generic Product Identifier (GPI)TM group and class for clustering by usage. Among subjects taking xerogenic medications, only those taking xerogenic drugs used to manage cardiovascular conditions were included in the present study.

The rationale for identifying medications with a xerostomic effect was twofold. The first was to exclude any patients on xerogenic medications from the control population. The second was to identify a sub-population whose only xerogenic medication experience was with the drug group of interest—in this case, cardiovascular drugs. Cardiovascular medications not determined to be xerogenic were not excluded from the “non xerogenic medicine group.” Cardiovascular medications included in the study

were identified on the xerogenic drug list and had a GPI group code of 33, 34, 35, 36, 37, 39, or 40. The number of MCO members having prescriptions in each of the cardiovascular drug classes is presented in Table 3.

To reduce the impact of cardiovascular xerogenic medications use prior to the eligibility period, any MCO members with a xerogenic cardiovascular fill within the first 100 days of initial eligibility were excluded. This period was chosen because less than 1% of cardiovascular drug fills or refills were for greater than 100 days. This criterion excluded 1,232 patients.

The effect of non-prescription, over-the-counter (OTC) medications was considered for incorporation to the analysis plan, but the authors decided against it. While subject to substantial recall bias in the absence of documented dispensings (in particular in the context of frequency of use/dose), the default assumption was that use of OTC drugs could be expected to be reasonably similar across all study groups. Because many OTC medications are occasionally used by

some people, or used as needed depending on symptoms or other considerations, long-term stable dosages would be unlikely to have a major xerostomic impact but would be exceedingly difficult to incorporate to the analysis plan.

Data assumptions, data manipulation, and statistical analysis. To obtain a proxy for caries activity, events were restricted to occurrences of amalgam or resin restorations. A chart audit of 517 MCO member records at site two found that 62% of all restorations were associated with primary or recurrent caries. As “all restorations” included crowns, it could be reasonably assumed that this percentage would be even higher if restricted to amalgams and resins. While the experience of resin and amalgam restorations cannot be considered a perfect representation of caries activity, we assume that the great majority of carious lesions that reached a restorable stage in the opinion of the treating dentist would be treated with resin and amalgam restorations in these MCOs, environments which provide good access to care.

Data were entered and analyzed in SAS8.2®. Dental procedure-coding systems from both sites were translated into a single common structure to create common data structures for analysis. Final analyses were undertaken fitting Poisson regression models (details included in description of model results).

Restoration incidence rates in Poisson regression models. The authors first examined whether the *restoration incidence rate* for individuals exposed to cardiovascular xerogenic medications was greater than that for those exposed to only non-xerogenic medications and those exposed to no medications. This analysis used Poisson regression, controlling for age, gender, and study site. The response was a binary variable (1=yes, 0=no) for the occurrence of any restoration during the study period. Poisson regression analysis was used because it allows an adjustment for the varying observation (eligibility) periods among the MCO members. The observation period used in this Poisson

analysis was the time from study entry for each individual (first day for which member had both dental and medical coverage between 1990 and 2000) until his/her first restoration. For individuals with no restorations, the observation period consisted of the time from study entry until the end of the members' eligibility within the study period. The model estimates the restoration incidence rate among members as a function of drug exposure, age, gender, and study site.

Restoration rates in Poisson regression models. The authors considered a Poisson model for the mean restoration rate to further explore the relationship between cardiovascular medication exposure and restorations. The response variable was the total number of restorations observed during the eligibility period, rather than the binary variable considered above for looking purely at incidence. Individual eligibility lengths were included in the model to estimate the *restoration rate* (number of restorations/eligibility time).

Results

Basic results. Fifty-six percent of MCO members at site one were male, compared to 57% at site two. Members at site two were also slightly older (65.3 vs. 62.7 years of age; $p < 0.0001$).

Cardiovascular drugs represented 42% of the xerogenic medications this project examined. Members were exposed to 21 cardiovascular, xerogenic

drug classes (Table 3). While exposure to multiple cardiovascular drug types was common, we felt that we had insufficient numbers in each drug type groups to conduct disaggregated analyses. No effort was made to do a sub-analysis for each cardiovascular drug type.

The study populations started with 5,216 eligible subjects in site 1, and 23,053 in site 2. Total study subjects excluded because of other xerogenic medications were 1,992 and 13,792. An additional 87 and 1,145 subjects were excluded due to medication fills in the first 100 days. This resulted in final study populations of 3,137 and 8,116 in sites 1 and 2, respectively, for a total of 11,253 subjects. Of these, there were 1,183 subjects with no exposure to prescription medication (584 at site 1 and 599 at site 2) and 5,622 subjects (1,747 at site 1 and 3,875 at site 2) with only non-xerogenic prescription medications dispensings. Finally, the MCO members whose only xerogenic medication exposure was to one or more of the cardiovascular drugs on the xerogenic list consisted of 4,448 individuals (806 at site 1 and 3,642 at site 2). Fifty-nine percent of the MCO members taking xerogenic cardiovascular medications were male. Their average age was 67 years. The first control group of MCO members with no pharmacy fills was 67% male and had a mean age of 62 years. The second control group of MCO members

with a history of medication use, but no exposure to the medications on the study xerogenic list was 52% male and had a mean age of 63 years.

Restoration incidence rates in Poisson regression models. The authors first considered a model with main effects of age, exposure group, gender, and site as well as all pair wise interactions with exposure group. Finding no pair-wise interactions with exposure group (exposure*age $p = 0.8005$, exposure*gender $p = 0.5847$, exposure*site = 0.2698), the study presents results from the main effects model (Table 4).

The incidence rate for restorations was approximately 28% greater for those dispensed xerogenic cardiovascular drugs than those with no medication dispensings, suggesting a xerostomic effect of the cardiovascular medications. The non-xerogenic medication group and the cardiovascular medication group rates were not significantly different. The estimated incidence rates, per year, were 0.20, 0.27, and 0.26 for the no medication, non-xerogenic medication, and the cardiovascular xerogenic medication groups, respectively.

Restoration rates in Poisson regression models. When modeling mean restoration rate as a function of age, exposure group, gender and age, along with all pair-wise interactions with exposure group, the authors found no evidence that the effect of exposure depended on either site

TABLE 4
Poisson regression results for estimation of restoration incidence rates as a function of exposure group, gender, site, and age (N = 11,249)

Effect	P-value for Testing Effect	Estimated Ratio of Restoration Incidence Rates Adjusted for Covariates	95% Confidence Interval for Estimated Restoration Incidence Rate Ratio
Exposure	<0.0001		
Cardiovascular Medications relative to No Medications	<0.0001	1.28	(1.15, 1.43)
Cardiovascular Medications Relative to Non-Xerogenic Medications	0.5090	0.98	(0.92, 1.04)
Non-Xerogenic Medications Relative to No Medications	<0.0001	1.31	(1.18, 1.45)
Gender: Male/Female	0.0230	1.07	(1.01, 1.14)
Site: 2/1	0.5438	1.02	(0.95, 1.09)
Age*	0.5338	0.99	(0.95, 1.03)

*The estimated ratio for age refers to the estimated incidence rate of restorations for individuals of a given age relative to individuals 10 years younger after adjustment for covariates.

TABLE 5
Poisson regression results for estimation of mean restoration rates as a function of
exposure group, gender, site, and age (N = 11,253)

Effect	p-value Testing Effect	Estimated Ratio of Mean Restoration Rates Adjusted for Covariates	95% Confidence Interval for for Estimated Restoration Rate Ratio
Cardiovascular Medications Relative to No Medications		(1.3344)(1.0015) ^{age}	
	For example:		
	Age=65: <0.0001	1.47	(1.35, 1.60)
	Age=75: <0.0001	1.49	(1.28, 1.73)
Cardiovascular Medications Relative to Non-Xerogenic Medications		.7755(1.0049) ^{age}	
	Age=65: 0.0020	1.07	(1.02, 1.11)
	Age=75: 0.0002	1.12	(1.06, 1.19)
Non-Xerogenic Medications Relative to No Medications		(1.7206)(0.9966) ^{age}	
	Age=65: <0.0001	1.38	(1.27, 1.50)
	Age=75: 0.0003	1.33	(1.14, 1.56)
Gender: Male/Female	<0.0001	1.25	(1.20, 1.30)
Site: 2/1	<0.0001	1.35	(1.28, 1.42)

($p=0.2363$) or gender ($p=0.9766$). The authors did find some evidence ($p=0.0329$) that the effect of cardiovascular drug exposure, relative to non-xerogenic medication exposure, depends on the individual's age. Table 5 presents results from the model containing the three main effects and the interaction between age and exposure group. Comparing the CVD drug exposure group to the non-xerogenic medication group, in particular, we find that the estimated relative rate ratio is approximately .7755 (1.0049)^{age}, so that the greater the age, the larger the relative rate ratio.

To illustrate the age interaction (i.e., the effect of age on the relative rate ratio), we display the estimated rate ratio separately for individuals of two different ages. For individuals who are 65 years of age this ratio is approximately 1.07 (95% CI: 1.02, 1.11), for individuals 75 years of age the estimated rate ratio is 1.12 (95% CI: 1.06, 1.19). For completeness, Table 5 presents the estimated relative rate ratios for each pair of exposure groups. The relative rate ratio for the xerogenic vs. non-xerogenic medication group varies only slightly with age. In general, for individuals 55 and over, the estimated restoration rate for the cardiovascular medication group is over 40% greater than that for the no medication group. Both site and gender had a significant effect on

mean restoration rate. Collapsing across age, site, and gender, the mean restoration rates are estimated to be 0.50, 0.69, and 0.73 for the no medication group, the non-xerogenic medication group, and the cardiovascular medication group, respectively.

Discussion

The present analyses evaluated the overall delivery of dental restorations (a proxy for caries experience) to MCO members undergoing different medication regimes. During the lengthy follow-up, MCO members taking cardiovascular medications or non-xerogenic medications had higher restoration incidence rates and higher mean restoration rates than individuals taking no medications. The differences in restoration incidence, however, were non-significant when the groups on xerogenic cardiovascular drugs were compared with the group on non-xerogenic drugs. Differences for mean restoration rates were of borderline significance.

The strongest effect identified through the analyses may be ascribed to using any medication (classified as xerogenic cardiovascular drugs or otherwise). While the authors have seen such differences when jointly examining the effects of anti-depressant medications (27) with other classes of medications without xerostomic side effects, the present

analyses led to different results. The latter have failed to clearly tease out the effect of cardiovascular drugs from other non-xerogenic medications. These results suggest the impact of xerogenic medication regime on level of restorative services' delivery may be significant, but this effect could not be separated from the effects of medications that are not supposed to induce xerostomia, or from the underlying conditions that gave rise to the use of cardiovascular drugs.

As past literature reports have highlighted this trend, the lack of effects differentiation between the cardiovascular medication regime and the non-xerogenic (as per the study's classification) medication regime for either restoration incidence and mean restoration rates (Tables 4 and 5) was not completely unexpected. This lack of differentiation may be generally grouped into pharmacological and behavioral. First, the lack of a universally accepted drug classification based on their xerogenic potential is a substantial problem. A number of factors should be taken into account when appraising the effect of drugs when grouped in a large variety of drugs labeled "cardiovascular," such as the one used for this study. (Incidentally, the diversity of drugs classified as anti-depressants in our previous report (27) was much smaller than the cardiovascular drugs pres-

ently used (Table 3). These factors include whether synergistic interactions between prescription drugs (and/or OTC drugs) lead to a stronger or weaker xerogenic effect when using more than one drug within the same GPI class. A person could also have been exposed to a drug with xerogenic potential, and then given a drug with a different xerogenic potential as older formulations were phased out, side-effects occurred, a tolerance developed, and so on. Further, the inconsistent direction of drug effects is compounded by the fact that drugs' xerogenic potential are poorly reported in the pharmaceutical industry specifications, which essentially summarizes xerostomic effects in rudimentary categories. Finally, the group using non-xerogenic medication might have been unknowingly contaminated with medications having xerogenic side effects that fell outside our classification.

Secondly, a complementary explanation from a behavioral perspective suggests people with cardiovascular diseases have poorer health behaviors — antecedent or simultaneous to their current conditions and medications. While some of these behaviors may have been a matter of lifestyle, other behaviors may limit the range of choices. For example, having competing priorities between dental and medical conditions forces the individual to seek clinical care in terms of perceived importance. As a result, a person with an "important" disease may not have time to be as dedicated to oral hygiene practices or recommended dental recall adherence, compared to another person who would not need to juggle lab tests, clinical appointments, buy drugs, or engage in non-cariogenic diets in his/her daily life. A separate analysis (data not reported here) found that patients with diabetes not only had higher caries counts, but also reduced dental visit rates (28). These choices are framed within an environment of realistic perceptions of individual-level restorative and preventive services (i.e., when directly asked, patients know what type of treatment needs they have and where their problems

lie (29)). Limited to a secondary analyses, however, the authors could not ascertain whether oral health behaviors differed between the three study groups.

Alternatively, the no medication group might be healthier (orally and medically) than the non-xerogenic medication and CVD medication usage groups, resulting in an overall lower risk of developing caries. While the mechanics are unknown, some cardiovascular conditions may be indirectly related to poorer oral health without a pharmacologic component. This explanation applies to the disabling consequences of cardiovascular disease manifestations, as would be the case for survivors of cerebrovascular incidents. A separate report investigating chronic conditions associated with oral features (30) found that diagnosed, non-fatal stroke was the only cardiovascular disease linked to increased number of decayed teeth, and to an increased ratio of decayed-to-present teeth. While not always explicitly dissociated from the larger class of cardiovascular diseases when investigated in relation to oral health, strokes are not commonly associated with tooth decay. Most of the attention in the literature related to stroke and oral health appears to focus on periodontal status (31-33), with mixed results (31;34;35). The exact mechanism directly linking caries and stroke remains unclear, except for speculations suggesting that stroke survivors lack the manual dexterity to brush or floss.

Due to the hypothesized relationship between periodontitis and certain cardiovascular conditions, the authors assume that some study participants' restored caries — root caries specifically — could have been associated with their cardiovascular conditions, and not only with their use of cardiovascular medications. Recessed gingiva is a pre-condition for caries on the root surfaces. On one hand, cardiovascular diseases' association with poor periodontal status has been extensively investigated (34;36-39), with some studies (31-33;35;40-43) suggesting that poor periodontal health precedes cardiovas-

cular disease independent of cardiovascular risk factors. On the other hand, the feasibility of a link between cardiovascular disease and periodontal problems has been questioned (43). Data for restorations placed on the tooth's root or crown, however, were available for only one study site, and this was only for the second half of the study period. This deficiency in the dataset precluded us from undertaking root-specific and crown-specific analyses. The present results fail to distinguish between their relative contributions to overall caries experience.

Methodological considerations.

As most participants were white, employed (or lived in a household whose head was employed), and had dental insurance, the present findings are not directly generalizable to other population groups. Certain methodological limitations and strengths are relevant to the study. 1) It is worthwhile emphasizing that overall restorative services' delivery is a reasonable, yet imperfect proxy for caries risk in these large study populations. The authors do not know, for example, what proportion of caries was treated with tooth extractions. They also do not know if non-cavitated carious lesions exhibit different patterns from the lesions that were deemed restorable. 2) This study was not able to tease out what effect (if any) cardiovascular diseases have on the development of restoration or caries rates on the root surfaces through increasing root exposure as the gingiva recedes, as opposed to the xerostomic effect of the medication used to treat cardiovascular diseases. The reasons for the association of cardiovascular diseases and oral health in adult groups are not clear (40). Follow-up research elucidating the longitudinal course of oral and cardiovascular health and dental interventions is needed.

Perhaps more importantly, 3) the study was conducted within two MCOs in three states of the US. Such an environment reduced deviations in services sought and rendered due to access-to-care problems, which probably reduced the variability of diagnostic and clinical approaches

that one could reasonably expect from dentists who are not affiliated with a group practice nor adhere to guidelines set by the group, and were salaried by the group practice – thus operating under different rules for compensation for individual clinical services, such as the more common fee-for-item payment schedule. The MCO environment poses, however, another interesting paradox: While having dental insurance may remove some obstacles that prevent a patient from obtaining dental care, it is reasonable to assume that some of the sickest patients may have had the hardest time obtaining it (dentists may have been unwilling to treat them as outpatients, patients might have mobility problems to reach dental offices, and so on). These factors may have lead to the restoration rate being differentially underestimated in these patients.

While prescription drugs use (xerogenic and non-xerogenic) may be related to the increased experience of restorative services in this population, the authors were unable to unequivocally establish a pharmacologic pathway for the xerogenic effects of a large and diverse group of cardiovascular drugs. Other factors appeared to play a role of uncertain importance. No recommendations with regard to public health policies appear warranted at this point in time. Further work is required to investigate the individual effects of smaller subgroups of cardiovascular drugs and continue building the body of reliable evidence on the association between drugs, specific drug classes, and dental caries.

Acknowledgements

The authors wish to gratefully acknowledge the support and expert advice from Drs. Ling Han, Marian S. McDonagh, Norman D. Muilenberg, Keith Griffin, and Craig Fleming. Responsibility for statements derived from the drug classification should not under any circumstances be ascribed to Drs. Han, McDonagh, Muilenberg, Griffin, or Fleming. Also, the authors would like to acknowl-

edge the contributions of Jeff Showell and Olga Godlevsky in obtaining the appropriate databases.

Source of Funding

This study was funded by the National Institute for Dental and Craniofacial Research Grant 1R01DE 013730-01. Dr Peters' time at the Kaiser Permanente Center for Health Research was funded by grant # K25-DE014093 from the NIDCR.

References

1. Guggenheimer J, Moore PA. Xerostomia: etiology, recognition and treatment. *J Am Dent Assoc* 2003; 134(1):61-69.
2. Nagler RM, Baum BJ. Prophylactic treatment reduces the severity of xerostomia following radiation therapy for oral cavity cancer. *Arch Otolaryngol Head Neck Surg* 2003; 129(2):247-250.
3. Friedlander AH, Friedlander IK, Gallas M, Velasco E. Late-life depression: its oral health significance. *Int Dent J* 2003; 53(1):41-50.
4. Anttila SS, Knuuttila ML, Sakki TK. Depressive symptoms as an underlying factor of the sensation of dry mouth. *Psychosom Med* 1998; 60(2):215-218.
5. Smith RG, Burtner AP. Oral side-effects of the most frequently prescribed drugs. *Spec Care Dentist* 1994; 14(3):96-102.
6. Vissink A, Panders AK, Gravenmade EJ, Vermey A. The causes and consequences of hyposalivation. *Ear Nose Throat J* 1988; 67(3):166.
7. Navazesh M. Salivary gland hypofunction in elderly patients. *J Calif Dent Assoc* 1994; 22(3):62-68.
8. Baum BJ. Evaluation of stimulated parotid saliva flow rate in different age groups. *J Dent Res* 1981; 60(7):1292-1296.
9. Tylenda CA, Ship JA, Fox PC, Baum BJ. Evaluation of submandibular salivary flow rate in different age groups. *J Dent Res* 1988; 67(9):1225-1228.
10. Ship JA, Baum BJ. Is reduced salivary flow normal in old people? *Lancet* 1990; 336(8729):1507.
11. Ship JA, Pillemer SR, Baum BJ. Xerostomia and the geriatric patient. *J Am Geriatr Soc* 2002; 50(3):535-543.
12. Handelman SL, Baric JM, Espeland MA, Berglund KL. Prevalence of drugs causing hyposalivation in an institutionalized geriatric population. *Oral Surg Oral Med Oral Pathol* 1986; 62(1):26-31.
13. Papas AS, Joshi A, MacDonald SL, Maravelis-Splagounias L, Pretara-Spanedda P, Curro FA. Caries prevalence in xerostomic individuals. *J Can Dent Assoc* 1993; 59(2):171-179.
14. Thomson WM, Slade GD, Spencer AJ. Dental caries experience and use of prescription medications among people aged 60+ in South Australia. *Gerodontology* 1995; 12(12):104-110.
15. Slome BA. Rampant caries: A side effect of tricyclic antidepressant therapy. *Gen Dent* 1984; 32(6):494-496.
16. Persson RE, Izutsu KT, Treulove EL, Persson R. Differences in salivary flow rates in elderly subjects using xerostomatic medications. *Oral Surg Oral Med Oral Pathol* 1991; 72(1):42-46.
17. Saunders RH, Handelman SL. Effects of hyposalivatory medications on saliva flow rates and dental caries in adults aged 65 and older. *Spec Care Dentist* 1992; 12(3):116-121.
18. Thomson WM, Spencer AJ, Slade GD, Chalmers JM. Is medication a risk factor for dental caries among older people? *Community Dent Oral Epidemiol* 2002; 30(3):224-232.
19. Janket SJ, Jones JA, Rich S, Meurman J, Garcia R, Miller D. Xerostomic medications and oral health: The Veterans Dental Study (part I). *Gerodontology* 2003; 20(1):41-49.
20. Chrischilles EA, Foley DJ, Wallace RB, Lemke JH, Semla TP, Hanlon JT et al. Use of medications by persons 65 and over: data from the established populations for epidemiologic studies of the elderly. *J Gerontol* 1992; 47(5):M137-M144.
21. American Heart Association. Heart disease and stroke statistics - 2004 update. Dallas: American Heart Association, 2004.
22. Summers WK. A clinical method of estimating risk of drug induced delirium. *Life Sci* 1978; 22(17):1511-1516.
23. Han L, McCusker J, Cole M, Abrahamowicz M, Primeau F, Elie M. Use of medications with anticholinergic effect predicts clinical severity of delirium symptoms in older medical inpatients. *Arch Intern Med* 2001; 161(8):1099-1105.
24. Sreebny LM, Valdini A, Yu A. Xerostomia. Part II: Relationship to nonoral symptoms, drugs, and diseases. *Oral Surg Oral Med Oral Pathol* 1989; 68(4):419-427.
25. Hardman JG, Limbird LE, Goodman-Gilman A. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 10th ed. 2001.
26. Physicians' Desk Reference. 56th ed. Medical Economics Company, Inc., 2002.
27. Rindal DB, Rush WA, Peters D, Maupome G. Antidepressant xerogenic medications and restoration rates. *Community Dent Oral Epidemiol* 2005; 33(1):74-80.
28. Diabetes and caries. 82nd General Session of the International Association for Dental Research. Honolulu, HI. 2004.
29. Maupome G, Peters D, White BA. Use of clinical services compared with patients' perceptions of and satisfaction with oral health status. *J Public Health Dent* 2004; 64(2):88-95.
30. Maupome G, Gullion CM, White BA, Wyatt CC, Williams PM. Oral disor-

- ders and chronic systemic diseases in very old adults living in institutions. *Spec Care Dentist* 2003; 23(6):199-208.
31. Morrison HI, Ellison LF, Taylor GW. Periodontal disease and risk of fatal coronary heart and cerebrovascular diseases. *J Cardiovasc Risk* 1999; 6(1):7-11.
 32. Joshipura KJ, Hung HC, Rimm EB, Willett WC, Ascherio A. Periodontal disease, tooth loss, and incidence of ischemic stroke. *Stroke* 2003; 34(1):47-52.
 33. Wu T, Trevisan M, Genco RJ, Dorn JP, Falkner KL, Sempos CT. Periodontal disease and risk of cerebrovascular disease: the first national health and nutrition examination survey and its follow-up study. *Arch Intern Med* 2000; 160(18):2749-2755.
 34. Grau AJ, Bugge F, Ziegler C, Schwarz W, Meuser J, Tasman AJ et al. Association between acute cerebrovascular ischemia and chronic and recurrent infection. *Stroke* 1997; 28(9):1724-1729.
 35. Beck J, Garcia R, Heiss G, Vokonas PS, Offenbacher S. Periodontal disease and cardiovascular disease. *J Periodontol* 1996; 67(10 Suppl):1123-1137.
 36. Syrjanen J, Peltola J, Valtonen V, Iivanainen M, Kaste M, Huttunen JK. Dental infections in association with cerebral infarction in young and middle-aged men. *J Intern Med* 1989; 225(3):179-184.
 37. Mattila KJ, Nieminen MS, Valtonen VV, Rasi VP, Kesaniemi YA, Syrjala SL et al. Association between dental health and acute myocardial infarction. *BMJ* 1989; 298(6676):779-781.
 38. Mattila KJ, Valle MS, Nieminen MS, Valtonen VV, Hietaniemi KL. Dental infections and coronary atherosclerosis. *Atherosclerosis* 1993; 103(2):205-211.
 39. Arbes SJ, Jr., Slade GD, Beck JD. Association between extent of periodontal attachment loss and self-reported history of heart attack: an analysis of NHANES III data. *J Dent Res* 1999; 78(12):1777-1782.
 40. DeStefano F, Anda RF, Kahn HS, Williamson DF, Russell CM. Dental disease and risk of coronary heart disease and mortality. *BMJ* 1993; 306(6879):688-691.
 41. Mattila KJ, Valtonen VV, Nieminen M, Huttunen JK. Dental infection and the risk of new coronary events: prospective study of patients with documented coronary artery disease. *Clin Infect Dis* 1995; 20(3):588-592.
 42. Joshipura KJ, Rimm EB, Douglass CW, Trichopoulos D, Ascherio A, Willett WC. Poor oral health and coronary heart disease. *J Dent Res* 1996; 75(9):1631-1636.
 43. Hujoel PP. Does chronic periodontitis cause coronary heart disease? A review of the literature. *J Am Dent Assoc* 2002; 133 Suppl:31S-36S.:31S-36S.