RESEARCH REPORTS
Clinical

Patient Stratification for Preventive Care in Dentistry

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J Dent Res DOI: 10.1177/0022034513492336

APPENDIX

METHODS

Participant Recruitment

In stage 1, no patient-level information was available to anyone other than the payer. Dental patients were identified for the study if they had insurance coverage by the payer through one employee group, had at least 15 consecutive years of dental claims data, and were age 34 through 55 yrs at the initial record. At completion of the study, 16 years' worth of claims data was available for analysis. Two groups of patients were excluded from the potential population if they had (a) a prior diagnosis of early periodontitis, since they inherently qualified for more than 2 preventive visits annually (*i.e*., presented with CDT codes associated with periodontal therapy: D4240, D4241, D4259, D4260, D4261, D4340, D4341, D4910), or (b) irregular preventive care, based on consistently less than 1 preventive visit annually during a six-year index period. Tooth loss data were available for the two excluded populations and are presented in the Results section to provide perspective on tooth loss in the study population.

Claims data were then searched to identify patients who habitually met *a priori* criteria for preventive dental visits twice annually or once annually during the index period, although all patients were covered for 2 preventive visits *per* year. The payer sent study information letters to the 25,452 patients who met all of the above criteria. If the patient was interested in learning more about the study and was willing to have his/her contact information provided to the University investigators, he/she had to return a signed release to the payer.

In stage 2, the names and addresses of the 9,927 individuals who expressed interest in participating were transmitted to the University investigators, who mailed enrollment kits. Kits included 2 buccal swabs for DNA collection, a consent form, and a study questionnaire. The questionnaire included a total of 18 main questions along with sub-questions related to age, gender, race/ethnicity, oral health, disease risk factors, alcohol consumption, and medication use. The results are included in the Table (main article). In total, 5,578 enrollment kits were returned, of which 5,291 were genotyped after removal of individuals whose submissions did not qualify (Fig. 1, main article). Of these, 5,117 had complete questionnaires and genetic information and were included in the final analysis.

Genotyping

SNP genotyping by a single base extension (SBE) method (Beckman Coulter, Brea, CA, USA) was run in a CLIA-certified molecular genetics laboratory (Interleukin Genetics, Waltham, MA, USA). Buccal swabs were processed with a commercially available DNA extraction method (Epicenter QuickExtract™ DNA). DNA concentrations were subsequently adjusted to a range compatible with multiplex polymerase chain-reaction (PCR) conditions. The SBE assay was run according to the manufacturer's protocol, hybridized to a 48-plex microarray plate, and read (SNPstream; Beckman Coulter). The allele calls from the automated reader were verified by a trained laboratory technologist according to laboratory quality assurance protocols. Validation plates (384 well) contained negative and positive controls, and study samples were genotyped in duplicate or triplicate to evaluate genotyping accuracy for IL-1 single-nucleotide polymorphisms (SNPs) located in the genes for IL-1α (IL1A) and IL-1β (IL1B) located on chromosome 2q13. Participants were classified as IL-1 genotype-positive or -negative by 2 versions of a composite genotype test. Version 1 was comprised of 2 SNPs, IL1A (+4845) (rs17561) and IL1B (+3954) (rs1143634), previously associated with severity or progression of periodontitis (Kornman *et al*., 1997; Karimbux *et al*., 2012). Version 2 included 3 SNPs, IL1B (-511) (rs16944), IL1B (-1464) (rs1143623), and IL1B (-3737) (rs4848306), in pre-defined patterns previously associated with expression levels of IL-1β and other inflammatory mediators (Rogus *et al.*, 2008) and a fourth SNP, IL1B (+3877) (rs1143633), previously associated with various disorders in Asians (Sasayama *et al.*, 2011) and Caucasians (Solovieva *et al.*, 2009). The primary analysis utilized the genotype version 1 as reported by the laboratory to classify risk. Some secondary analyses used the

version 2 genotype classification and are explicitly described as such when incorporated. Genotyping was performed in a CLIA-certified molecular genetics laboratory (Interleukin Genetics), and study oversight and sample accountability are described below.

Study Oversight and Sample Accountability

All materials sent to potential participants were bar-coded, and only pre-specified data management individuals at the University had access to the key that linked questionnaire data, genotyping results, and claims data. The payer had no access to genetic or questionnaire data at the patient level, and the genotyping laboratory had no access to any patient data other than the bar code identifier and the genetic results. Double entry was used to input key questionnaire fields. Genetic laboratory results were verified according to standardized quality assurance protocols, and compiled tables of genetic results were verified by two independent data monitors. All transformed database fields and all database merges were independently verified by two data monitors.

Participants with the primary endpoint of tooth loss during the 16-year period were identified by American Dental Association Current Dental Terminology (CDT) (American Dental Association, 2010) tooth extraction codes (D7010, D7140, or D7210). Secondary analyses of periodontal treatment costs used CDT codes including surgical, non-surgical, and local chemotherapeutic procedures for treatment of periodontitis (D4240, D4241, D4260, D4261, D4274, D44340, D4341, D4342, and D4381). Total costs of treatment were calculated based on all dental procedure costs submitted by the dentist during the observation interval.

Cost Models

To consider the potential influence of risk stratified preventive dental care for adults based on these findings, we constructed 3 cost models with different assumptions (Appendix Table 2). We included total costs of treatment, as provided by the dentist, with no consideration of claims actually paid. The reference model assumed 2 preventive visits for all patients, which defines the maximum exposure of the health care system under current prevention recommendations. The "minimum use, maximum risk" model assumed that all patients eligible for the current study received only 1 preventive visit annually. The "risk-based" model used frequency distributions of the current study, coverage for the genetic test, and 1, 2, or 3 preventive visits annually based on the number of risk factors. The risk-based model produces preventive care savings of more than $2.2 million, in contrast to the current model of biannual preventive visits for all patients. Assuming a population of 175 million covered adult lives (NDJDB Report, 2011), that translates to a potential savings of greater than $4.8 billion *per* year. Assumptions that shift all adults to only 1 preventive visit *per* year would produce a maximum cost savings of greater than $17.5 billion *per* year, but does not include expected later-year costs due to increased tooth loss. With various assumptions, cost savings *per* year to the health care delivery systems should reasonably be expected to fall between $4.8 and $17.5 billion *per* year.

RESULTS

Preventive Visit Frequency and Risk Factor Relationships to Costs

The mean total cost of periodontal procedures for study patients, which by protocol excluded those with a diagnosis of periodontitis, was very low (range, $172-$197; data not shown), with no difference by preventive frequency in either low-risk (LoR) ($p = .87$) or high-risk (HiR) patients ($p = .49$). Cumulative 16-year mean costs for all procedures ranged from $7,075 to $9,093, depending on risk status and preventive frequency (Appendix Table 2), and patients with 2 preventive visits had higher total costs than those with 1 visit for both LoR ($p < .001$) and HiR ($p < .001$) patients. One risk factor had no association with higher cumulative mean costs over 0 risk factors for patients with 1 preventive visit ($7,273 *vs*. $7,075, respectively; $p = .446$) or for those with 2 visits ($8,006 *vs*. $7,879, respectively; $p = .416$). Having 2 or 3 risk factors was related to higher costs compared with 0 risk factors for patients with 1 visit ($8,671 *vs*. $7,075, respectively; $p < .001$) and for those with 2 visits ($9,093 *vs.* $7,879, respectively; $p < .001$).

Having 2 or 3 risk factors also correlated with increased costs, in contrast to having 1 risk factor in patients with 1 visit ($8,671 *vs.* $7,273, respectively; $p = .001$) and 2 visits ($9,093 *vs*. $8,006, respectively; $p < .001$).

DISCUSSION

For adults without a history of periodontitis, regular dental recalls generally include a clinical examination and removal of bacterial deposits on the teeth to prevent periodontitis (PD). Recommendations for biannual preventive dental visits date back many years and were promoted widely in toothpaste commercials in the 1950s. The need for biannual preventive dental care for all adults is not supported by evidence (Sheiham, 1977; Beirne *et al.*, 2007; Clarkson *et al.*, 2009), and both the U.S. Centers for Disease Control and Prevention (Chronic Disease Prevention and Health Promotion, 2012) and the U.K. National Institute for Health and Clinical Excellence (Guide on dental recall, 2004) have recommended that dental recalls, which usually include preventive cleanings, be on the basis of individual patient needs. Recall frequency may be relevant to other oral health outcomes, such as dental caries and oral cancer, that may not be reflected in the endpoint of tooth loss, which is most commonly due to periodontitis after age 40 yrs (Murray *et al.,* 1996; Ong, 1996). Other studies show no advantage of biannual recalls for dental caries or oral cancer detection (Beirne *et al.*, 2007; Patel *et al.*, 2010). A subset of tooth loss did not respond to more frequent cleanings, regardless of risk status, suggesting that routine preventive care may not protect against certain causes of tooth loss.

It is likely that some LoR patients are misclassified, *e.g.*, undiagnosed diabetes or as-yet-unidentified risk factors, both of which may move some of the current LoR patients into the HiR category. Future improvements leading to risk reclassification may allow for further refinement of the group that is likely to respond well to 1 preventive visit annually.

It should also be noted that our study population was predominantly Caucasian (Table, main article). While smoking and diabetes have been associated with increased risk for periodontitis in all major ethnic populations, the primary IL-1 genotype used in this study is infrequent, therefore less informative, in Asian populations (Armitage *et al.*, 2000). For this reason, we also tested a second composite IL-1 genotype (version 2.0), which occurs frequently in all ethnic populations and is associated with elevated inflammatory biomarkers (Rogus *et al.*, 2008). Smoking timing and degree of exposure complicate relationships to health assessment. To reduce LoR misclassification, we considered "no relevant tobacco exposure" during the monitoring period to be "never smoked" or "none" for 10 years prior to data collection.

To address potential financial implications of these findings, we constructed cost models and compared risk-based costs using parameters derived from the current study with a reference model assuming maximum utilization of current prevention recommendations. Risk-based models project a $37 savings *per* patient/yr, including cost of genetic information, which translates to more than $2.2 million saved for the 5,117 patients during the study period (Appendix Table 3). These modest *per* patient/yr savings translate to $4.8 billion potentially saved *per* year for 175 million patients with dental insurance (NDJDB Report, 2011).

Dental costs in the U.S. reached $108 billion in 2010, increasing in parallel with medical costs (Chronic Disease Prevention and Health Promotion, 2012). Since many dental care needs are not symptomatic or urgent, they are often identified as part of a routine examination, which inherently leads to more costs with more visits, as seen in this study. The effects of the risk factors were also evident in costs, in that patients with 2 or 3 risk factors had higher costs, regardless of the frequency of preventive visits. Other measures, such as quality-adjusted tooth-years (Antczak-Bouckoms and Weinstein, 1987), and future studies on indirect savings from disease avoidance may provide additional perspective on the cost-effectiveness of risk-based prevention.

AUTHOR CONTRIBUTIONS

Dr. Giannobile was responsible for accuracy of the questionnaire and claims databases, and Dr. Doucette-Stamm was responsible for accuracy of the genotyping database. Dr. Giannobile had full access to all data in the study and assumes responsibility for data integrity and data analysis accuracy.

Study concept and design: Giannobile, Kornman
Statistical analysis: Braun, Giannobile
Analysis and interpretation of data: Giannobile, Kornman, Duff, Braun
Drafting of the manuscript: Giannobile, Kornman, Duff, Doucette-Stamm
Obtaining funding: Giannobile and Kornman
Study and database supervision: Giannobile, Caplis
Administrative or technical support: Caplis, Doucette-Stamm

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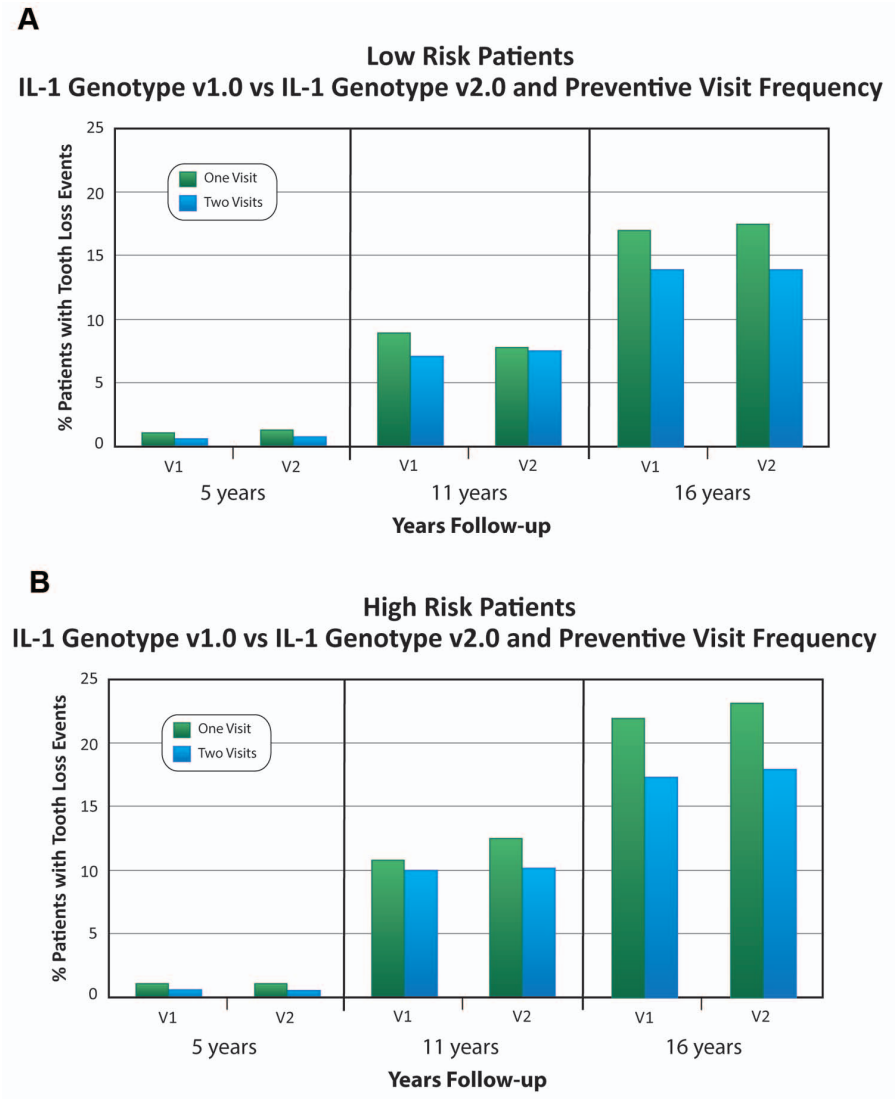

Appendix Figure. Effect of preventive visit frequency on tooth loss events. Individuals were evaluated for tooth loss at 5, 11, and 16 years by versions 1 and 2 of the IL-1 test and 1 visit or 2 visits *per* year. Low-risk individuals who had never smoked or had not smoked in the preceding 10 yrs, had no history of Type I or II diabetes, and were IL-1-negative are shown in **Panel A,** while high-risk individuals who met any one of these 3 criteria are shown in **Panel B**. Analysis of the data demonstrates that the use of either version of the IL-1 test to classify low- and high-risk patients provides the same results with regard to the relationship of the number of preventive visits and tooth loss.

Appendix Table 1. Tooth Loss Rates and Percentages of Patients Experiencing Events over Six-year Indexing Period

Number of Preventive Visits during Indexing Period	Employee Group 1			Employee Group 2		
	N (%)	Tooth Loss/ Person/yr	Patients with Tooth Loss (%)	N (%)	Tooth Loss/ Person/yr	Patients with Tooth Loss (%)
1 to 4	8,025 (18.6)	0.045	1,034 (12.9)	5,396 (29.1)	0.086	1,094 (20.3)
5 to 8	13,202 (30.7)	0.024	1,200 (9.1)	6,259 (33.8)	0.031	711 (11.4)
9	5,271 (12.2)	0.016	368 (7.0)	2,148 (11.6)	0.019	163 (7.6)
10 to 13	16,462 (38.2)	0.013	881 (5.4)	4,183 (22.6)	0.018	307 (7.3)
≥ 14	129 (0.3)	0.059	17 (13.4)	526 (2.8)	0.054	83 (15.8)
Totals	43,089 (100)	—	—	18,512 (100)	—	—

Appendix Table 2.

(a) Total Cost by Visits

	5 yrs	11 yrs	16 yrs
Low-risk			
1 preventive visit	$1,434	$4,314	$7,075
2 preventive visits	$1,703	$4,784	$7,879
p value	< .001	< .001	< .001
High-risk			
1 preventive visit	$1,554	$4,339	$7,557
2 preventive visits	$1,787	$4,949	$8,219
p value	< .001	< .001	< .001

(b) Total 16-year Cost by Risk Factors

Risk Factors	N	1 Preventive Visit			N	2 Preventive Visits		
0 RFs	732	$7,075	*p* = .446		1,686	$7,879	*p* = .416	
Any 1 RF	679	$7,273		*p* < .001	1,486	$8,006		*p* < .001
2 or 3 RFs	173	$8,671	*p* = .001		361	$9,093	*p* = .001	

Appendix Table 3. Implications of Patient Stratification on Cost Assumptions.

Reference Model: Recommendation of 2 Preventive Visits/yr

# Preventive Visits/yr	# Patients	Cost Year 1	Cost Year 2	Total Costs, 16 yrs
3	0		$0	
2	5,117[1]	$1,023,400[2]	$1,023,400	$16,374,400
1	0			$0
Cost of genetic information	0	—	—	$0
Total cost	$1,023,400	$1,023,400	$16,374,400	

Risk-base Model: Risk-based Assignment of Preventive Visit Frequency

# Preventive Visits/yr	# Patients	Cost Year 1; Including Cost of Genetic Information	Cost Year 2	Cost, 16 yrs
3	512[3]	$153,510	$153,510	$2,456,160
2	2,200	$440,062	$440,062	$7,040,992
1	2,405	$240,499	$240,499	$3,847,984
Cost of genetic information	5,117	$767,500[4]	—	$767,550
Total cost	$1,601,621	$834,071	$14,112,686	

Potential total one-year savings for 5,117 patients ($1,023,400-$834,071)[5]	$189,329	
Potential mean one-year savings *per* patient ($189,329/ 5,117)[5]	$37.00	
Potential total 16-year savings for 5,117 patients, including cost of genetic information ($16,374,400-$14,112,686)		$2,261,714
Potential total savings/yr for 175 million covered adults [([$2,261,714÷5,117 patients] ÷ 16 yrs) = savings/patient/yr * 175 million]		$4,834,375,000

Reference Model assumes the maximum financial exposure resulting from maximum utilization of services in a health care system that allocates resources to provide for 2 preventive dental visits *per* yr for all patients with regular dental visits.
Model Scenario 2 assumes the maximum financial exposure resulting from maximum utilization of services in a health care system that allocates resources to provide for preventive dental visits with a frequency based on an individual's number of risk factors for all patients with regular dental visits. The model assumes that patients with 0 risk factors will receive 1 annual preventive visit, those with 1 risk factor will receive 2 annual preventive visits, and those patients with 2 or 3 risk factors will receive 3 annual preventive visits. The proportion of patients in each risk factor category is the actual proportion observed in the study population.
[1]Number of patients in the study population who attended the dentist regularly for preventive dental care.
[2]Assumed cost of preventive care of $100 *per* visit.
[3]Number of patients with 1, 2, or 3 preventive visits *per* yr is based on distribution of study patients with 0, 1, and 2 or 3 risk factors, respectively.
[4]Assumed cost of genetic test of $150, once in lifetime.
[5]Represents only costs of preventive services, without cost of genetic information.