Research Article

Drug-Induced Xerostomia: The Physical, Mental, and Economic Impact

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ABSTRACT

Background: Many medications utilized in the United States (US) cause xerostomia (dry mouth); however, the costs and Quality Of Life (QOL) reduction associated with this side effect remains to be determined.

Objective: To estimate the annual dental expenditures and quality of life burden attributable to chronic use of medications that cause xerostomia in the US adult population.

Methods: This was a cross-sectional retrospective analysis evaluating prescribed medications in 2019 as reported by the Medical Expenditure Panel Survey. Medications were organized in 2 groups: medications with and without documentation of xerostomia. The treatment group included the US non-institutionalized adult population with chronic use of xerostomia causing medications. The control group included the rest of the US non-institutionalized adult population. Dental visits per year, total annual dental expenditures, and annual self-pay (out-of-pocket) dental expenditures were compared between treatment and control populations. Health related physical and mental quality of life scores were also compared.

Results: Those in the treatment group exhibited a 33.3% higher expected rate of dental visits per year. Treatment populations also incurred higher dental expenditures $523.830/year vs. $315.78/year (p<0.001), and self-expenditures $266 vs. $131/year (p<0.001). Importantly, the treatment arm has lower physical and mental health, are older and sicker, thus, an adjusted analysis was necessary. Following the adjusted analysis, the difference of 1.3 (p<0.001) for physical and 2.0 (p<0.001) for mental summary scores remained.

Conclusion: This study shows that medications that cause xerostomia result in higher dental costs and have a negative impact on physical and mental health.

Keywords: Polypharmacy; Mouth; Mental health; Dental utilization

INTRODUCTION

Xerostomia (dry mouth) has been shown to affect up to 46% of Americans, especially the older adult population [1]. Xerostomia, the subjective feeling of dry mouth is a common oral adverse medication reaction [2]. Polypharmacy, being on multiple medications, is an independent risk factor for xerostomia is polypharmacy [3]. Thus, it is logical to suggest that taking more than one medication with evidence of causing "xerostomia" may result in a compounded effect [4].

Xerostomia is a broad term that can be further delineated based on the degree in which saliva production is diminished. This level of delineation is not performed when documentation of side effects occurs in most clinical trials. The reporting provides the presence of the side effect with or without prevalence. For example, on

the first page of the package insert (prescribing information) for venlafaxine extended release, the most common adverse events are listed as "adverse reactions (incidence >5% and at least twice the rate of placebo): nausea, somnolence, dry mouth..." The exact incidence of dry mouth is later reported as 14.8% in one of the venlafaxine clinical trials [5].

Xerostomia left untreated will impact a patient's quality of life due to symptoms such as impaired swallowing, difficulty with speech, and poorer oral hygiene. Xerostomia is associated with additional complications such as candidiasis, dental carries, glossitis, impaired fit of dentures, and halitosis [6]. Leaving xerostomia untreated can lead to a subsequent decline in dental, physical, and mental health.

There have been studies to examine drug-induced xerostomia; however, evaluating the dental utilization and cost, as well as

physical and mental QOL for adults in the United States has not been determined [7]. This study aims to obtain a better grasp on how likely the use of prescribed medications that can lead to xerostomia are contributing to dental utilization, expenditures and impacting physical and/or mental health.

METHODOLOGY

Medications prescribed in 2019 were organized into two groups: medications with no documentation of xerostomia, and documentation of xerostomia as indicated in a side effect profile. From a later group a subset of medications with documented >1% prevalence of xerostomia was identified and used for sensitivity analysis. The treatment group of this study included the US non-institutionalized adult (18 years and older) population with chronic use of xerostomia causing medications. Chronic use was defined as either 3 unique prescriptions or 90 day-supply per year of xerostomia causing medications. The control group included the rest of the US non-institutionalized adult population. The number of dental visits per year, total annual dental expenditures, and annual self-pay out-of-pocket dental expenditures were compared between treatment and control populations. Health related physical and mental quality of life as measured by Physical Component Score and Mental Component Score (PCSMCS) of VR-12 instrument were also compared.

Data source

The Medical Expenditure Panel Survey (MEPS) is a comprehensive data source sponsored by the Agency for Healthcare Research and Quality (AHRQ) [8]. It provides data representing the United States non-institutionalized civilians through the lens of patients, families, third-party providers, medical professionals, and employers. Each entity aids to provide an accurate portrayal of medical resource usage. Some specifics applicable to this study include the MEPS medical provider component that comprises detailed information from pharmacies that validate pharmacy events and expenditures. Additional components gathered include demographic, socioeconomic, health conditions (as represented *via* ICD codes), insurance coverage status, and utilization and associated expenditures of health care services. The physical and mental health status is also measured by Veterans RAND-12 Item Health Survey, VR-12 (formerly known as SF12).

Variables of interest

The main independent variable of interest was an indicator variable that identifies MEPS respondents who have been prescribed medications associated with xerostomia. This identification required an analysis of all the prescribed medications, with the most up to date list provided in MEPS for the year 2019. Each medication was reviewed utilizing prescribing information (package inserts) and the Clinical Pharmacology drug database to determine if the drug had documentation of xerostomia as a side effect. From a later group a subset of medications with documented >1% prevalence of xerostomia was identified and used for sensitivity analysis.

Additional characteristics important in evaluating the association between xerostomia-causing drugs and outcomes (dental expenditures, physical and mental health) included age, sex, race, ethnicity, insurance, family income, annual comorbidity burden, education, and health status.

Statistical analysis

Statistical analyses with regression methods that differed by the type of outcome variable were utilized. Each outcome variable was regressed on indicator variable for the use of drug that causes xerostomia (yes or no) socio demographic and health status or comorbidity burden variables (Table 1).

The adjusted analysis used a negative binomial regression for dental visits. A negative binomial regression is a well-suited method for count outcomes and is robust to over dispersion issues commonly present in these types of variables. Generalized Linear Model (GLM) with log link and Poisson distribution were used for dental expenditures. Healthcare expenditures commonly exhibit right skewness with a significant number of individuals having zero expenditure. A log transformation of data helps to solve the skewness problem; however, logarithm of zero is not defined, and more complex measures are needed for the regression analysis. GLM estimates the logarithm of expected expenditures and is a robust to both skewness and cluster of zero observations. In addition, the modified Park test suggested that Poisson distribution for the errors is the most suitable for the current data [9]. Finally, linear regression was used for physical and mental health component scores. These scores are normalized to have a mean zero and standard deviation of 10 in general adult population and simple linear regression is an appropriate method for these variables. Indicator variable for the treatment population was included in regression analysis controlling for (1) socioeconomic: insurance coverage, family income level, educational attainment, (2) demographics: age, gender, race, ethnicity, and (3) comorbidity burden: number of unique International Classification of Diseases (ICD) 10 codes reported during the years.

RESULTS

Dental visits

For those on chronic medications with documentation of xerostomia as a side effect, an increase in the utilization of dental visits was exhibited. Adults exposed to xerostomia causing medications had 1.33 (p-value <0.001) times higher expected rate of annual dental visits than those not prescribed these medications. This translates into 0.3 additional dental visits per year after adjusting for confounding variables such as age, gender, race, ethnicity, dental insurance coverage, family income level, education physical and mental health status. The unadjusted visits analysis resulting in an increase of 0.39 (p-value <0.001) visits per year.

Dental expenditures

Treatment group also incurred higher dental expenditure costs $523.830/year vs. $315.78/year (p<0.001), and self-paid expenditures $266 vs. $131/year (p<0.001). The adjusted analysis further confirms addition financial burden of xerostomia (Table 2).

After adjusting for confounding variables, the generalized linear model reveled that xerostomia-associated group spent and additional $133 per year on dental services, including the additional $63 out of pocket amount (Table 3).

Table 1: Demographic, and socioeconomic variables stratified by treatment and control groups.

	N	Drug induced xerostomia group	No drug induced xerostomia group	p-value
Age	28,510	54,526	31,919	0
# of unique ICD-10 codes reported during the year	28,512	5,689	1,104	0
Age groups				
Age 18-24	2,238	0.041	0.116	0
Age 25-34	3,404	0.071	0.171	0
Age 35-44	3,464	0.1	0.139	0
Age 45-54	3,443	0.148	0.113	0
Age 55-64	3,828	0.207	0.088	0
Age 65-74	3,209	0.2	0.043	0
Age 75-84	1,690	0.114	0.015	0
Age 85+	677	0.049	0.006	0
Gender				
Male	13,659	0.444	0.514	0
Female	14,853	0.556	0.486	0
Race				
White	21,302	0.816	0.739	0
Black	4,325	0.109	0.137	0
American Indian	261	0.009	0.008	0.677
Asian	1,587	0.039	0.078	0
Multiple race reported	1,037	0.027	0.038	0.001
Ethnicity				
Hispanic	6,562	0.11	0.224	0
Non-Hispanic	21,950	0.89	0.776	0
Dental insurance coverage				
No dental insurance	15,640	0.569	0.467	0
Full year dental ins. coverage	10,089	0.365	0.453	0
Part of a year dental ins. coverage	1,952	0.065	0.081	0.001
Health insurance coverage				
Private insurance	16,988	0.627	0.689	0
Public insurance	9,414	0.355	0.224	0
Uninsured	2,110	0.018	0.087	0
Family income status				
Poor-negative	4,775	0.119	0.117	0.695
Near poor	1,481	0.044	0.043	0.696
Low income	4,104	0.127	0.131	0.462
Middle income	8,139	0.276	0.3	0
High income	10,013	0.434	0.408	0.007
Educational attainment				
No degree	3,517	0.114	0.098	0.001
GED	934	0.039	0.023	0
High school	9,122	0.391	0.277	0
Other degree	2,036	0.106	0.068	0
Bachelor	4,022	0.175	0.15	0
Master	1,959	0.092	0.07	0
Doctorate	483	0.021	0.017	0.021

Table 2: Unadjusted results for dental health.

	N	Drug induced xerostomia group	No drug induced xerostomia group	p-value
Number of dental visits per year	28,512	1.286	0.896	0
Total annual dental expenditures (in $ of 2021)	28,512	523.83	315.788	0
Total annual self-paid dental expenditures (in $ of 2021)	28,512	266.1	131.389	0
Physical summary score	17,780	45.091	53.655	0
Mental summary score	17,786	50.211	53.613	0

Table 3: Adjusted results for dental health.

	Regression coefficient	Marginal effect	p-value
Number of dental visits per year	1.33	0.3	0
Total annual dental expenditures (in $ of 2021)	0.32	133.05	0
Total annual self-paid dental expenditures (in $ of 2021)	0.31	62.96	0.001
Physical summary score	-1.33	-1.33	0
Mental summary score	-2	-2	0

Physical health

The xerostomia-associated group had 8.56 and 3.40 (p-value<0.01) lower physical and mental summary scores. Respondents in the xerostomia-associated group were older and sicker (more ICD codes, older age) and an adjusted analysis was necessary to estimate the direct financial burden of xerostomia. The regression analysis of health status variables showed 1.33 and 2.0 (p-value <0.001) lower physical and mental scores respectively for the xerostomia group.

For those on chronic use of medications with documentation of xerostomia as side effect, an increase in the utilization of dental visits was exhibited. Annual dental visits average at 1.286 and 0.896 in the treatment and control groups respectively (p<0.001). After adjusting for control variables adults on the xerostomia group had 33.3% higher expected rate of annual dental visits (0.3 more visit per year) compare to the non-xerostomia group. Treatment population also incurred higher dental expenditures $523.830/year vs. $315.78/year (p<0.001), and self-expenditures $266 vs. $131/year (p<0.001). After controlling for socioeconomic, demographic and comorbidity burden variables annual dental expenditures and self-expenditures are $133 and $63 respectively higher for the xerostomia compared to non-xerostomia group.

Unadjusted physical score of the treatment group was 45.091 in comparison to 53.655 in the non-xerostomia group. Following the adjusted analysis, the difference of 1.3 (p<0.001) remained, indicating that the physical health in the treatment group was poorer. Finally, the mental health summary score for the treatment and control groups were 50.211 and 53.613 respectively. This resulted in an unadjusted difference of 3.4 (p<0.001). After an adjusted analysis, a difference of 2.0 remained indicating that dry mouth may have a bigger impact on the mental health than physical health.

DISCUSSION

The magnitude of physical and mental health burden of drug-induced xerostomia is bigger than the burden of an additional ICD 9 code. In particular, drug-induced xerostomia is equivalent to two additional ICD for physical score and four additional ICD codes for mental score component. This emphasizes the importance of recognition and appropriate management of drug-induced xerostomia. It is already accepted that the quality of life of patients can be significantly impacted by poor oral health. Our study provides supporting evidence that individuals on drugs associated with xerostomia have poorer physical and mental health than individuals not taking medications associated with this poor oral health outcome. Furthermore, when comparing physical and mental health scores, mental health is impacted to a higher extent, supporting other studies outlining how oral health is important for mental health and QOL.

Examples of why drug-induced xerostomia can have such a negative impact on both mental and physical health include the negative impact of dentures fitting, leading to pain and discomfort, dysarthria, dysphagia, low self-esteem and social withdrawal [10-12]. Additionally it can be a risk for new and recurrent dental carries.1 Unfortunately, even though drug-induced xerostomia is associated with extensive adverse outcomes, as evidenced by our study and other supporting studies, it remains under reported and under treated [13].

For the sensitivity analysis a more parsimonious treatment group was defined as adults that have chronic use of medications with >1% prevalence of xerostomia. This population was compared to the non-xerostomia group. The results were similar to the original analysis, thus, even medications with reported low prevalence of xerostomia have significant burden on health and dental expenditures.

CONCLUSION

Many medications are associated with causing xerostomia. Our study highlights that individuals taking these medications have higher dental expenditures, and poorer physical and mental health. This study shows that medications that cause xerostomia result in higher dental utilization and costs and have a negative impact on both physical and mental health.

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