

Winter 5-1-2019

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Danevin Putrus
ez1183@wayne.edu

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Recommended Citation

Putrus, Danevin, "Xerostomia: A Comprehensive Review" (2019). *Honors College Theses*. 53.
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Xerostomia: A Comprehensive Review

Danevin Putrus

Wayne State University

Winter 2019

Abstract

This thesis will be highlighting the condition known as Xerostomia. Xerostomia is the condition also known as “dry mouth”. This condition affects many people all throughout the world with symptoms causing bad breath, discomfort, difficulty speaking and many other. The seriousness of this condition can lead to cardiovascular disease, dementia, respiratory infections, diabetes mellitus, rheumatoid arthritis, and even cancer (Absolutedental.com). Currently there is not any one specific solution for the condition although many have been proposed. Throughout the thesis I will closely examine former research studies, current solutions proposed, and propose my own study and solution based on research and evidence gathered.

Xerostomia can be defined in numerous different ways, however its most renowned definition is the subjective complaint of oral dryness (Morzavi et. al). Xerostomia may be a secondary symptom of other complications, namely dehydration leading to salivary glands producing less saliva than usual, as well as side effects from prescribed medication, aging, certain cancer therapies, nerve damage, and smoking. Symptoms directly related to xerostomia include the subjective feeling of thickened saliva, bad breath, sore throat, as well as dry tongue. More threatening complications rooting from xerostomia include mouth sores, malnutrition, yeast infections, and increased plaque, tooth decay, and gum disease. Research on xerostomia is constantly growing, and researchers are learning more about it each day. The first article highlighted in this comprehensive review is *Xerostomia, Etiology, Recognition, and Treatment (2003) (Guggenheimer et. al)* whereby a group of clinicians established a cornerstone for what xerostomia is, and its treatment through systematic review of prior research articles. This article will serve as a streamline for the more specific research articles to follow. The second article that will be highlighted in this review is *Risk Factors, Hyposalivation, and Impact of Xerostomia on oral health-related quality of life (2016) (Niklander et. al)* whereby a group of Brazilian oral researchers explained Xerostomia in light of the impact it has in everyday life through its symptoms. Finally, the last article that will be highlighted in this review is *Diagnosis and Management of Xerostomia and Hyposalivation (2015) (Villa et. al)* whereby researchers explained potential management techniques involved in treating Xerostomia through numerous systematic methodologies. The purpose of this comprehensive analysis is to illustrate a potential solution for xerostomia, primarily by addressing what exactly makes it problematic, and then evaluating and reaching a solution.

The problem at hand is that xerostomia leads to symptoms ranging from simple bad breath to yeast infections and gum disease in different contexts, regarding both social and ethical differences. Xerostomia is difficult to treat because its prevalence is difficult to determine, as it varies between different geographical zones, age groups, and sex differences. Epidemiological studies report its prevalence to range from 0.9% all the way to 64.8% (Niklander et. al). I am a pre-dental student at Wayne State University, and I see cases of Xerostomia on a daily basis through my clinical work. Xerostomia is an important topic to cover because I personally see cases that are treated well in certain patients using certain intervention strategies, that may not necessarily work in other patients, that my dentist recommends. There is a discrepancy in how exactly xerostomia is treated in different individuals. The purpose of this comprehensive review is to analyze these issues sprouting from this disease, and evaluate the solutions proposed by the researchers in subsequent studies.

In our first article, *Xerostomia, Etiology, Recognition, and Treatment (2003)*, clinicians James Guggenheimer and Paul A. Moore composed an Index Medicus-generated systematic review of renowned scientific reports of xerostomia in dental and medical literature spanning the past 20 years (1983-2003). The literature chosen was on the basis of xerostomia related to the disciplines of oral medicine, pathology, pharmacology, epidemiology, gerodontology, dental oncology, immunology, rheumatology, and the physiology behind salivary function and its relation to xerostomia-like symptoms (Guggenheimer et. al). The basis for this systematic review included was that many clinicians encounter symptoms of xerostomia in patients after taking certain medications and in patients with certain connective tissue or immunological disorders that have been treated via radiation. Additionally, xerostomia often is associated with Sjögren's syndrome, a condition that involves dry mouth and dry eyes and that may be accompanied by

rheumatoid arthritis or a related connective tissue disease (Guggenheimer, et. al) Clinicians hypothesized that when xerostomia is the result of a reduction in salivary flow, significant oral complications may occur.

After reviewing the articles, these clinicians found significant data to match their hypothesis. Guggenheimer et. al begins by explaining that xerostomia usually develops when the amount of the saliva within the oral mucous membrane is reduced, however, symptoms may occur without noticeable decrease in salivary gland function. With this review, these clinicians established that the most frequently reported reason behind patients' xerostomia like symptoms is due to medications with xerostomia-like side effects. Major complications involved in their symptoms included dental caries as well as difficulty using dentures. The authors then explain that although xerostomia's effects may be manageable by some treatments, there is no one universal cure to it. Different successfully documented management techniques collected by these reviews included three categories; palliative recommendations, saliva substitutes, and cholinergic drugs. Palliative recommendations included the use of alcoholic beverages and mouth rinses, humidifiers when sleeping, salivary slow stimulants such as sugarless chewing gum, XyliFresh, sugarless hard candies, and Salix Lozenges (Guggenheimer et. al). Saliva substitutes included over the counter solutions including contents of carboxymethyl or hydroxymethylcellulose. Popular saliva substitutes authors noted through collective review included Moi-Stir, MouthKote, ORALBalance, Salivart, and Xero-Lube. Cholinergic drugs were documented last, primarily because these are the only group of xerostomia management techniques that cannot be used in patients with heart disease, as they alter cardiac conduction frequencies. Some of these medications include Cevimeline and Pilocarpine (Guggenheimer et.

al). These clinicians also stressed the importance and benefits of using fluorides in management of xerostomia secondary to radiation therapy of the head and neck areas of the body.

The main takeaway from this article were the clinically proven best remediation of xerostomia-like symptoms, as well as the secondary effects that it may have sprouted from. Clinicians explained that the ideal best management techniques for xerostomia consist of “rigorous attention to personal oral hygiene, strict adherence to a noncariogenic diet, placement of sealants, and the application of topical fluorides” (Guggenheimer et. al). This is important to take note of because understanding the causes of xerostomia and the proper medicinal management techniques will always be second to simply keeping up with personal attention to oral health. This, along with the fact that xerostomia management techniques vary from patient to patient, gives the cornerstone for the rest of this thesis.

In the second article, *Risk Factors, Hyposalivation, and Impact of Xerostomia on oral health-related quality of life (2017)*, researchers Sven Niklander, Laura Veas, Cristina Barrera, Flavio Fuentes, Giuliana Chiappini, and Maureen Marshall of The University of Andres Bello sought to explain the impact Xerostomia related symptoms on patients’ oral health quality of life through normalized questionnaires and subsequent testing of salivary flow rate (Niklander et. al). The basis for conduction of this study was rooted in many different ideologies. Primarily, researchers explained that saliva is an often-forgotten essential fluid in the human body, and do not seek help for it until it affects other basic everyday functions, such as speaking and eating. Xerostomia was defined in this study as “the subjective sensation of dry mouth which is usually correlated with hyposalivation”, and hyposalivation was defined as “objectively low salivary flow rates”. However, it must be known because many patients have dry mouth sensation with normal salivary flow rate, xerostomia does not necessarily correlate causation. Researchers in

this study described the most common factors that have been associated with xerostomia including more than 400 medications with dry-mouth as common side effect, psychological conditions such as stress and anxiety, salivary gland disorders such as Sjögren's Syndrome, and head and neck radiotherapy (Niklander et. al). Some reports also added that age in and of itself acts as a risk factor for xerostomia, even furthering the discrepancies that come with how the disease is acquired and treated. The researchers quoted Field et. al when explaining that both medication use, and age independently increased the chances of Xerostomia development by approximately 1.24 times for every ten years of age (Field et. al in Niklander). The same article also explained that there is an almost four times greater prevalence of xerostomia development in patients taking medications (28%) as compared with patients who do not (7.5%). One can subsequently beg the question, are the elderly only at a higher chance of acquiring xerostomia because they have a higher chance of taking medication? The answer is not known. The negative impact that xerostomia has on patients is very detrimental in terms of comfort. This study explained that patients with this disease may complain about a variety of different things, ranging from an abnormal taste in the mouth, to dysphagia and even a burning sensation.

Although both salivary flow rate and prevalence of xerostomia have been widely studied in prior studies, such as the first article we reviewed, the aim of this second article was to determine xerostomia-related frequency, factors, and salivary flow rates of oral health related quality of life (OHRQoL) in patients attending the Universidad Andrés Bello School of Dentistry Clinic in Viña del Mar, Chile, conducted on a Chilean population between April and November of 2014. The conducted study consisted of 566 patients, calculated with a 90% power, a confidence level of 95%, and an estimated prevalence of 15%, and a standard error of 5%. Data was acquired in the form of a questionnaire including the following variables: gender, age,

systemic diseases, menopause, drugs (type, number, and time of use), smoking habits (measured by cigarettes consumed per day) and presence of Xerostomia. (Niklander et. al). Patients were subsequently asked “how often do you feel that your mouth is dry?” and could answer between three options: sometimes, usually, or always, to determine if xerostomia was present. Patients who responded to this question with “usually” or “always” were patients who were assumed to be suffering from xerostomia. The researchers then sought to measure severity in patients who were categorized as having xerostomia using a visual analogue scale (VAS) consisting of a horizontal line with two marks, 0 and 10, labeled at each extreme. Zero reflected no xerostomia and ten reflected the most severe case of xerostomia (Niklander et. al).

Next, researchers sought to evaluate oral health related quality of life using a fourteen-item questionnaire used to measure including the following self-reported domains: functional limitation, physical pain, psychological discomfort, physical incapacity, psychological incapacity, social incapacity, and social disadvantage. The scale ranged from 0-56, with lower scores representing a satisfactory perception of an individual’s oral conditions, and a higher satisfaction and better quality of life (Niklander et. al). To determine salivary flow rate, 35 of the 61 patients who fell into the category of having Xerostomia underwent a case control study. The reason behind not adding all of the patients who had Xerostomia to go through with the case study because they had other diseases associated with them that may have skewed results. 35 patients without xerostomia were then assigned as a control group, chosen by using a simple-random method. The patients in both groups were instructed to refrain from eating, drinking, smoking, and engaging in oral hygiene activities for two hours every morning and were always tested in the same room under synonymous conditions. Researchers analyzed salivary flow rate, or, sialometry, using the “spitting” method whereby patients were instructed to spit into a tube

for five minutes and their saliva was collected by using a graduated syringe and subsequently quantified as “non-stimulated” saliva. Next, both groups of patients were instructed to chew on a 15mm x 10mm wax cube for one minute at their own pace to stimulate their salivary glands. Again, saliva was collected by using graduated syringe, but this saliva was termed “stimulated”. This was important because there needed to be a baseline for salivary gland activation in both sets of patients to be able to relate them to everyday life experiences. People go through phases during their everyday lives where they have active or inactive salivary glands, and xerostomia must be addressed in both contexts.

The results of this study showed many different things. Primarily, the average age of the study population was 46 years old, and the study included 386 women and 180 men. Xerostomia was prevalent in 61 patients of the study; 50 women and 11 men. Another key takeaway from this study included the fact that the highest prevalence of xerostomia was by patients aged 68-77 years old, with the second highest prevalence being from age group of 78-83 years old, signifying that elderly patients were much more prone to having xerostomia. Furthermore, researchers concluded that out of the 566 patients involved in the study, 240 reported taking some type of medication on a daily basis, and 61 of these patients had Xerostomia-like symptoms. Collectively, the chances of having xerostomia increased 1.01 times for every one-year increment after normalizing the data. Data also showed that the chance of having xerostomia increased by 1.12 times for every additional medication being taken (Niklander et al). The data after being normalized showed that there was no significant difference in salivary flow rate in patients complaining of xerostomia, and patients who are not. This suggests that complaining of xerostomia may not have low salivary gland activity, just as the researchers originally stated in their introduction.

This study also explains that xerostomia is subjective, in that symptoms vary from one patient to another, rather than being able to be objectified by simply measuring salivary gland activity. This study also reiterates some of the key dynamics regarding xerostomia, including that one becomes at higher risk through old age, taking consistent medication, and is more prevalent in women rather than men. Through survey administration, the researchers in this study also concluded that dry mouth, or, Xerostomia, is a condition that can certainly affect overall health-related quality of life (OHRQoL). Hopcraft et al. explains that patients with severe xerostomia are 2.3-4.9 times more likely to have a negative experience, and negative impact on quality of life. There is already research done regarding Xerostomia affecting OHRQoL in many different ways, namely by affecting taste sensation, mood, and even speech impairment. In an overview, this study did a wonderful job of illustrating the common trends prevalent in patients with xerostomia, as well as furthering the claim that xerostomia is subjectively determined by the patient themselves and cannot be diagnosed by a dentist, and or any researcher. Many problems can arise from such a situation. Not all patients in the United States are also healthcare professionals themselves, therefore leaving them choices of several daunting tasks of either self-diagnosing themselves and doing the research to treat themselves or going to their oral health care professional and explaining their symptoms. This is problematic for many different reasons. Primarily, most people understand the symptoms of the common cold, but not many people, if any, understand the potential side effects or symptoms of xerostomia. As we learned in the prior article, *Xerostomia, Etiology, Recognition, and Treatment (2003) (Guggenheimer et. al)*, xerostomia has many complications that arise and can worsen exponentially over time if left untreated. Although the common cold certainly has more potentiality for dangerous secondary diseases, xerostomia must still be treated, nonetheless. While it is fair for patients who are not

trained in a background of oral health to assume that bodily sicknesses may pose a higher threat than oral sicknesses, they are also not entirely correct as well. Poor oral health leads to cardiovascular disease, dementia, respiratory infections, diabetes mellitus, rheumatoid arthritis, and even cancer (Absolutedental.com). The first step toward helping patients treat their Xerostomia to prevent subsequent complications is primarily to make the patients aware that they are dealing with something threatening. Why would anybody go out of their way to prevent something that, to their knowledge, is not dangerous? The third article that will be highlighted is *Diagnosis and Management of Xerostomia and Hyposalivation (2015) (Villa et. al)*, which deals with furthering the diagnosis of xerostomia, as well as potential treatment techniques tested in a laboratory will touch on this subject.

Now that we have comprised a cornerstone for Xerostomia the prevalence and trends associated, our third and final study deals primarily with testing the many different management techniques that have been accepted in oral healthcare to its time. Researchers in this study described xerostomia as a burden dealt with by many individuals, affecting things like speech, chewing, swallowing, and general well-being (Villa et. al). Researchers also explained that a frequent cause of hyposalivation leading to the feeling of xerostomia includes a variety of many different medications, including anticoagulants, antidepressants, antihypertensives, antiretrovirals, hypoglycemics, levothyroxine, multivitamins, non-steroidal anti-inflammatory drugs, and even basic steroid inhalers (Villa et. al unpublished data, 2014). Villa and his colleagues subsequently explained that because many different trends have been established in likelihood of having xerostomia, such as this medication use and age, their study was aimed at exploring the current state of management and treatment of xerostomia instead. The main criteria assessed in their study was prevalence of hyposalivation in diagnosing patients with xerostomia.

The methodology of this review was dense, as the researchers explained that dry-mouth symptoms cannot be the only criteria for a comprehensive analysis. Therefore, numerous different surveys were brought into play. The data collected by researchers showed that the most constant questionnaires used to assess criteria for xerostomia included statements like; rate the dryness inside your mouth, rate the dryness of your lips, and rate how easy it is for you to swallow solid foods (Villa et. al). These were all taken from questionnaires from prior researchers such as Fox, Thomas, van der Putten, as well as Eisbruch. Researchers explained that these questions, when previously tested in Dutch dental clinics, showed the highest correspondence with patients actually having Xerostomia. The reality is, one patient will answer a question based on one instance in time, whereas another may answer the question based on a collective review of all of their symptoms over the years. The key, as Villa and his colleagues explained in their analysis, is to administer the questionnaire to patients who have a collective understanding of what the questions are asking and normalize the data to eliminate outliers. Most questionnaires administered to patients, as researchers explained, can be useful in studying xerostomia, regardless of the exact terminology used. Researchers also explained that a key component in properly diagnosing xerostomia includes a very thorough medicinal background check, as patients could potentially be at much higher risk depending on the medication they have been taking.

The researchers then shifted gears to studying the best possible mechanism for quantifying salivary flow rate, in order to make sure patients are not exaggerating during questionnaires, as well as for future research experiments and clinical testing. These researchers, similarly, to Niklander and his colleagues in *Risk Factors, Hyposalivation, and Impact of Xerostomia on oral health-related quality of life (2017)* also explained that salivary flow testing

of stimulated and non-stimulated saliva poses the best mechanism for consistent results. One other example presented by researchers came from Leal et. al and involved collecting saliva using reweighed cotton rolls placed at the ducts of major salivary glands, and then reweighing them after collection time for stimulated and non-stimulated saliva. The results would be quantified after comparing the differing weights of the two sets of cotton balls in clinic. Lastly, saliva could be collected by using a graduated absorbent strip placed on the floor of the mouth and results would be collected after one, two and three minutes (Niklander et. al). The problem with this technique, however, is the normalization methods to compare to other research studies done. Another method highlighted included using a micropipette and absorbent filler paper collected in units of $\mu\text{L}/\text{min}/\text{cm}^2$ of mucosal area, most commonly known as the “Periotron” method. However, this method includes specific laboratory equipment that is not prevalent in all dental offices, making consistency an apparent issue. The last method highlighted by researchers in this study described a rather novel method of collecting data named the “spitting and suction method” which involved giving the patient an unflavored gum base or paraffin wax weighing approximately 1-2 grams for one minute, or administering a solution of 2% citric acid on the sides of the tongue for 30 minutes, and collecting saliva using a graduated cylinder for five minutes. This form of testing may bring about the most accurate results, however, the time and supervision that must be set aside to achieve consistency in results is too difficult and costly for it to be used on a regular basis to diagnose xerostomia. The most consistent means of comparing the data provided by stimulated and non-stimulated saliva to assess for xerostomia is therefore through use of Saliometry, or salivary flow testing.

Villa and his colleagues then sought to find the most practical means of treating Xerostomia in patients. Strategies that have been adopted within the past years include methods

that reduce a patient's secondary symptoms sprouting from Xerostomia, or simply increasing salivary flow rate. Simple ways to achieve these include proper hydration, increased night-time humidity, avoidance of crunchy foods, and use of sugar-free gums/candy (Villa et. al).

Researchers also included certain medications that seek to increase the fluids inside of the mucosal glands, including simple mucosal lubricants, and saliva stimulants and substitutes.

These medications are termed "sialogogues" and their main purpose is to increase salivary flow rate. Researchers collecting data from a variety of different sources explain that the two most used sialogogues are pilocarpine and cevimeline, as they are both US Food and Drug Administration Approved. They are administered for three months at a time in patients, and include many side effects including; excessive sweating, cutaneous vasodilatation, emesis, nausea, diarrhea, persistent hiccup, bronchoconstriction, hypotension, bradycardia, increased urinary frequency, and vision problem (Villa et. al). Neither medication should be administered if the patient has underlying cardiovascular problems, chronic respiratory problems including asthma or chronic pulmonary disease (CPD).

A more conservative approach to xerostomia management include intraoral topical agents rather than pilocarpine and cevimeline due to their side effects. Some of these agents include things like chewing gum, certain sprays, and even candy. Studies show that sialogogue spray containing 1% malic acid shows incredible results in patients with Xerostomia induced secondary to antidepressant or antihypertensive medication, however, these have been shown to cause enamel erosion in some cases (Villa et. al). Simple solutions that are readily attainable from most convenience shops include the use of sugar-free chewing gum and candy due to their remarkable ability to decrease mucosal friction and increase saliva secretion. Alternative substitutes include simply using mouthwash and the right toothpaste for your specific

teeth/mouth. However, the problem with this method is that patients must originally seek guidance from their dentists on which mouthwash and toothpastes are correct for their teeth, and then continue using them on their own without any apparent negatives if they stop. Regelink et. al reported that saliva substitutes are not effective in patients with reasonable stimulated salivary flow (Villa et. al).

From the three articles we have reviewed above, we can take away many important clinical remediations and prevalence statistics for xerostomia. Primarily, in the first article, *Xerostomia, Etiology, Recognition, and Treatment (2003) (Guggenheimer et. al)*, we saw a cornerstone for the subsequent articles to follow. This article explained that when xerostomia is the result of a reduction in salivary flow, significant oral complications may occur. One major complication included hindering the patient's overall health related quality of life, which is the major psychological impairment involved with xerostomia. Some medications that clinicians James Guggenheimer and Paul A. Moore explained may help alleviate symptoms of xerostomia included the use palliative recommendations such as rinsing the mouth, salivary flow stimulants such as sugarless chewing gum, and saliva substitutes such as over the counter solutions of hydroxy-methylcellulose. These clinicians concluded the article by explaining that although xerostomia may be rooted in similar pathology in some patients to others, not one universal cure for every patient is known to this day.

In the second article, *Risk Factors, Hyposalivation, and Impact of Xerostomia on oral health-related quality of life (2017)*, researchers Sven Niklander, Laura Veas, Cristina Barrera, Flavio Fuentes, Giuliana Chiappini, and Maureen Marshall of The University of Andres Bello examined the impact of overall health related quality of life on patients with xerostomia, as well as risk factors involved. This article acted as a streamline from the first article by taking the

objective fact that patients with xerostomia show substantially greater decline in overall oral health related quality of life and tested it using questionnaires. Hopcraft et al. explained that patients with severe xerostomia are 2.3-4.9x more likely to have a negative experience, and negative impact on quality of life by affecting namely taste sensation, mood, and speech impairment. This study showed that xerostomia is typically more prevalent in women than men, and that the highest prevalence of xerostomia was in elderly patients as opposed to younger patients. Researchers in this study also explained that over 25% (61/240) of patients who reported taking any type of medication on a daily basis showed xerostomia-like symptoms, and that the normalized data showed a 1.01x increase per year, and were further increased by an additional 1.12x after every additional medication that was taken. A majority of these patients included a progressive decline in their overall health related quality of life. The researchers in this article concluded by explaining that because there was no difference in control patients' salivary flow rate compared to patients with xerostomia, xerostomia is subjective and varies heavily from one patient to another, rendering managing techniques difficult to assess on a one-patient visit.

Our third article, *Diagnosis and Management of Xerostomia and Hyposalivation (2015)* (Villa et. al) explained that although there are many widely applicable methods for obtaining and quantifying salivary flow rate in patients with xerostomia, only basic sialometry would be able to be shared in laboratories to compare data in a consistent manner. The purpose of research is to quantify results to share and collaborate with colleagues in an endless effort to reach meaningful results, and that cannot be achieved using different measurement tools. The researchers then subsequently explained the results of their experiment attempting to find the most practical means of alleviating xerostomia in patients. These results showed that sialogogue spray

containing 1% malic acid showed the best results in stimulating salivary gland production, namely in patients suffering from extreme xerostomia secondary to anti-depressive medication. These sprays work well at stimulating salivary flow rate but come at a cost because erosion and dental caries are usual side-effects. Simpler solutions, and more practical if done more consistently, included using sugar-free chewing gum and candy due to their ability to decrease mucosal friction and increase saliva secretion.

These studies showed us many different aspects of xerostomia. We see where xerostomia is most prevalent, how salivary flow rate is ideally quantified, risk factors involved, and even potential alleviation methods. The word “potential is used because there is not a universal alleviation method capable of being applied to all patients. However, after analyzing the articles in this passage and incorporating Biology and Histology background knowledge from my education at Wayne State University, I will attempt to draw a plausible solution to xerostomia. The mouth contains an oral mucosal layer lining the inside of it that contains stratified squamous epithelium. The lining mucosa covers the span of the cheeks to the inside of the lips, including the buccal mucosa, labial mucosa, and alveolar mucosa. Specialized mucosa covers the taste bud areas near the dorsal end of the tongue. There are also three pairs of major salivary glands located dorsal and ventral to your jaw: the parotid, sublingual, and submandibular glands. Additional minor glands are found near the tip of the mouth near the outside of the lips, most well-known for salivary secretion. The activity, or lack thereof these glands are the main determining factor behind xerostomia. Drawing knowledge from the classes I have taken at Wayne State University will help me present my solution.

When I learned about the HIV/AIDS epidemic in my Evolution class at my university, I was in shock. The fact that there was a disease capable of turning one’s immune system against

itself changed my entire perspective about the human body. Subsequently, we were taught of a method that had very high success rates in treating HIV/AIDS; The Highly Active Antiretroviral Therapy (HAART) Method. The HAART method was originally brought to light when researchers became more aware of the disease's pathology. This method was central on the idea that if the virus adapted to one medication at one time, administration of a "cocktail" mix of many different medications may slow the virus' adaptation rate, and ultimately alleviate symptoms. Combination therapy important to the idea of HAART because HIV/AIDS' methodology lacks proofreading enzymes; thus, genetic variation is highly favored. HAART decreases the patient's symptoms of HIV/AIDS while also maintaining integrity of the immune system and preventing infections that may lead to death. A flurry of entry inhibitors, nucleotide reverse transcriptase inhibitors, and protease inhibitors swarm the body to simultaneously deny the body of producing more enzymes that deny immune system responses. Quality of retention/decrease of symptoms in a pool of AIDS patients over the course of four years was greater than 80% according to a study done by Brenda Crabtree-Ramirez in a population of Mexican clinic patients in 2010 (*Effectiveness of Highly Active Antiretroviral Therapy (HAART) Among HIV-Infected Patients in Mexico (Crabtree-Ramirez) (2010)*). Although the repercussions of HIV/AIDS are certainly greater than those of xerostomia, both diseases can be looked at in a similar light. Both diseases are difficult to treat in different groups of patients, and do not have one prominent universal alleviation method or cure. Both diseases also differ in social terms, namely from the population that acquire them and between men and women. Lastly, the diseases are similar because the best way of alleviating symptoms sprout from the patients themselves; xerostomia is best alleviated by patient consistency with their oral health at home, and HIV/AIDS is best alleviated by consistent use of all HAART medications simultaneously, or

even worse forms of the virus begin to form. I believe that alleviating symptoms of xerostomia in a cocktail-like “HAART” method would show remarkable results in patients because of the similarities they both show.

The first step of this would include a more recent collective review of all studies done in xerostomia spanning the course of the past 20 years, similarly to what James Guggenheimer did in the first reviewed article, *Xerostomia, Etiology, Recognition, and Treatment (2003)*. After assembling a recent basis for what medications have been applied in successful xerostomia experiments in the past, the screening process would begin. I would attempt to attain a sample size of 500 men and 500 women from different ethnic backgrounds to participate in this study and offer payment for taking a questionnaire that would be primarily administered. The questionnaire would include statements relating to overall health related quality of life, and xerostomia-like symptoms and patients would answer on a five-point scale with answers: strongly disagree, disagree, neutral, agree, strongly agree. Patients who would answer agree or strongly agree to the statements regarding having xerostomia would be considered for the second screen.

The drug screen would test which medications are consistently used in patients considered for the study and be quantified. Four groups would be present after the drug screen: man taking consistent medication, women taking consistent medication, men not taking consistent medication, and women not taking consistent medication. This would allow for a greater diversity in results during primary and secondary testing stages and maximizes internal validity by eliminating confounding variables, and also provide control groups. Generalizing the data would be easier when the experiment is finished. I would anticipate more women than men to be involved in the study because women are more prone to worry about their dental and

medical health and would thus be more prone to join a study like this. This would be balanced by asking substantially more people to sign up for the study than expected participants to ultimately reach an even split between all four groups. Salivary flow rate would be measured by basic sialometry to ensure generalization to other research labs. When eligible participants reach this stage, they will be asked to partake in the sialometry test for both stimulated and non-stimulated saliva production and the data will be quantified. After a baseline sialometry value is established, any patients who fall below the “basic” threshold will be placed in their own sub-group within one of the four main groups in an effort to view their results compared to patients who suffer objectively higher amounts of salivary gland dysfunction.

Alleviation techniques would be administered to the control group in a methodical manner; sialogogue spray containing 1% malic acid for three days, followed by palliative alleviation for three days, and lastly use of salivary stimulants (sugar free gum/hard candy) for three days. Alleviation techniques for the test group would entail a different “HAART-method” technique. Participants in this group will undergo a flurry of alleviation techniques all at once for nine days. These techniques will involve consistent sialogogue spray containing 1% malic acid, palliative alleviation and salivary stimulants for a nine-day span. Participants in this study would be required to brush their teeth twice a day, and record anything they may have ingested that could have led to excessive xerostomia-like symptoms that day, or lack thereof. This will be done by giving them a list of food/drink to add, as well as include any social tobacco use. These patients will come in during 5pm every day to have their stimulated and non-stimulated salivation rate tested by basic sialometry. The results will be quantified and compared to the opposing group. Test group participants will answer a short survey at the end of the study to

determine whether or not their symptoms felt alleviated, and if they would consider taking their regiment for an even longer time than originally.

After this primary study is done, the data will be examined on whether or not “HAART-method” showed greater salivary flow rates and improved overall health related quality of life as compared to control subjects. Constraints that may be apparent during this phase of the study would include difficulty deciding which alleviation techniques consistently work well with others. Collective review of studies at during part one of the study would help comprise a database of what treatment techniques have shown great increase in salivary flow rate on their own. Trial and error techniques will be continually done until a select successful combination is reached for all four groups. After these trials, a baseline would be comprised for treatment of xerostomia in smaller populations and would later be adapted into larger-scale research studies until the ideal combination of alleviation techniques are found. When more participants begin hearing about the study and the theoretical success of it, different groups will be established. Groups including consistent tobacco users, or xerostomia-like side effects secondary to radiation and nerve damage. The data would be able to be generalized to other institutions would which ultimately increase consistency.

The key however, to a study like this, is patient agreement. The patient must be fully aware that alleviation use will be applied in a daily manner, because that has been proven by prior experiments as the most effective way to a patient of their xerostomia-like symptoms. Without consistency in place, deeming the most effective combination would be rather impossible, and show many different confounding variables including potentially the use of specific brands of toothpaste and humidifier temperature, if those were chosen by prior articles. This would be another constraint to the study which could be resolved by supplying all patients

with similar palliative care techniques, however, something of this caliber could quickly expend many resources, especially when techniques are being chosen using a trial-and-error methodology.

Xerostomia can be defined in numerous different ways, however its most renowned definition is the subjective complaint of oral dryness (Morzavi et. al). Xerostomia may be a secondary symptom of other complications, namely dehydration leading to salivary glands producing less saliva than usual, as well as side effects from prescribed medication, aging, certain cancer therapies, nerve damage, and smoking. The three articles that were primarily reviewed in this thesis showed evidence of an ongoing and worsening problem, in our current modern day and age: xerostomia. *Xerostomia, Etiology, Recognition, and Treatment (2003)* (Guggenheimer et. al) explained xerostomia from a basic perspective, outlining subjectivity in the world of oral health care complaints and simple treatment techniques noted in past scientific articles. *Risk Factors, Hyposalivation, and Impact of Xerostomia on oral health-related quality of life (2017)* (Niklander et. al) evaluated the impact of xerostomia to everyday overall health related quality of life and contextual differences in xerostomia regarding old age and sex differences. Finally, *Diagnosis and Management of Xerostomia and Hyposalivation (2015)* (Villa et. al) gave clinicians an inside view of more specific management techniques including sialogogue spray containing 1% malic acid. These three articles, when taken together, help support the idea that xerostomia as a very life-hindering disease, as well as raise different solutions that work in some patients, but not others.

After review of these three articles, I believe a “HAART-method” type of alleviation techniques would effective in treating patients with xerostomia because of the similarity of the two diseases: both are difficult to alleviate due to variable genotypical differences in the patients

who acquire them, and both are difficult to alleviate because alleviation relies on the patients' own consistent administration. The "HAART-method" of treatment would show incredible internal validity and generalization to the population and attempt to consistently treat xerostomia in patients beginning in a small population, to later grow all across the United States.

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