Burning Mouth Syndrome: a demographic and comorbid condition case series

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A thesis

submitted in partial fulfillment of the

requirements for the degree of:

Masters of Science in Dentistry

University of Washington

2014

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Program Authorized to Offer Degree:

Oral Medicine

To those that keep questioning…
regardless of preferred media

ACKNOWLEDGEMENTS

The Committee: This thesis was made possible due to the professional guidance of Dr. Michael Martin, my committee chair and mentor- he has always had my back and I will always be thankful he got me into this mess. I am also fortunate to have Dr. Mark Drangsholt and Dr. Edmond Truelove as my committee members- their experience, knowledge, and drive for evidence-based approaches have left me with an inescapable appreciation for research.

Clinical Faculty: I am very much grateful to the other clinical faculty for their years of instruction, patience, and guidance- Dr. Beatrice "Bea" Gandara (my OMed mom, yes- if I ever get hitched you'll be invited!), Dr. Earl Sommers (maybe I'll get back to that art stuff now?), Dr. Mark Schubert (someday I'll mush too, I'm the one from Alaska!), Dr. Stuart Taylor (seriously, OMed & Radiology?), Dr. Marijoyce Leynes (You prove it can be done on the "outside"!), Dr. Karen Manookin (your kindness and smile have always been appreciated!), & Dr. Rolf Christensen ("We're all mad here"- Cheshire Cat).

The Doctors: Dr. Sue Coldwell - the "sweetness" of your taste demos won't be forgotten, I need to steal some of those & Dr. Linda LeResche- I don't know if I'll ever really love stats, but I appreciate its importance- thanks for trying to unmuddy the murky!

First Encounters: (our frontline in OMCS) Liliya Gutnyk-Merrill, Natalie Stepanyuk, & Edgar Mesina- you've never led me astray and were always helpful and kind, much respect for the daily grind you guys do!

The Ladies Behind the Curtain: (Administration) Dalila Sebring & Hazel Valdez- you both helped make my life easier in so many ways, I cannot thank you enough!

Co-Residents: Dr. Lakshmi (Mitreyi) Gorugantula, Dr. Sumeia Werfalli, Dr. David Ryan Dean, Dr. Dina Moustafa Hammouda, Dr. Rania Abasaeed- It was a pleasure and honor to get to know you all, I look forward to seeing where we all go in life!

My Family & Friends: You guys remind me what life is all about!
I Love You ALL So Much!

The Radiology Crew: Its been fun & mayhap you have not escaped me…

The Missing: If you aren't named and you feel you should be you're likely right! A million apologies if I have left you out - it was highly unintentional! I hope you already know how appreciative I am.

ABSTRACT

Significance: Burning mouth syndrome (BMS) is known to be a highly adverse oral condition that is generally chronic in duration with an substantial uncertainty regarding the clinical presentation, etiologic factors, and descriptive characterization of the condition.

Purpose: Characterize our BMS population and identify most common demographic and comorbid conditions.

Methods: Case Series: Retrospective Chart Review, Level of Evidence 4. Review of existing University of Washington Oral Medicine Clinical Services patient charts with ICD-9 codes 782.0, 529.6: N=107.

Result Highlights for Female Patients (N=95):

Demographics: Female:Male = 9:1, Principal ethnicity: Caucasian 77%, Mean Age = 57.

Complaint Characterizations: *Burning location*- 73-83% tongue, 34-50% anterior palate and lips, 10-17% gingiva and dorsal tongue, 01-06% posterior tongue, teeth, and buccal mucosa. *Burning onset from event*: 12.6% after local anesthetic use. *Duration of burning*: mean of 69 weeks. *Recurrence pattern*: 37.9% constant. *Change since onset*: 21.1% unchanged. *Pain VAS%:* Aversiveness 65.1%, Intensity 50.2%.

Current Treatment: 50.5% clonazepam, 16.8% topical steroid, 11.6% antifungals, 10.5% maxillary stent, 10.5% membrane stabilizer Rx, 7.4% Sialogogue, and 4.2% for behavior modification, capsaicin, and stress reduction.

Comorbid Conditions (≥ 20%): Xerostomia 35.8%, Candida 21.1%, Bad Taste 29.5%, Post-menopausal 72.6%, Vaginal Dryness 20%, Sleep Disturbance 45%, Anxiety 36.8%, Depression 29.5%, Depression & Anxiety 20%, Hypothyroidism 20%.

Conclusions: Because of prevalence it seems reasonable to investigate the possibility of subclinical or untreated hypothyroid conditions. To address the psychological and quality of life factors involved with BMS, including quality of life assessments such as the SCL-90-R or impact questionnaires with all new patient databases would help early identification of possible conditions detrimental to a faster and more positive outcome and help to steer referral for beneficial treatment modalities.

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INTRODUCTION

Background

Burning Mouth Syndrome (BMS) is sometimes called Burning Mouth Disorder, stomatopyrosis, orodynia, glossodynia, and glossitis.[1,2] The characteristic clinical presentation is a patient reporting spontaneous burning of the anterior two thirds of the tongue (72%) and may also include the hard palate (25%) and lips (24%).[1, 3, 4] These symptoms can be acute or chronic, are usually bilateral, and are symmetrical across the midline.[5] The prevalence of BMS in the scientific literature has been reported to be between 0.7% - 5% in the general population[6], and escalating to a substantial 12 - 18% in postmenopausal females.[2] BMS has been shown to be associated with a reduced general quality of life as well as a reduced oral-health-related quality of life.[7-9]

The diagnosis of BMS is one of exclusion since BMS can present secondary to other pathology; because of this there are two types of BMS, primary and secondary.[11] With primary BMS there is no known cause and no morphologic changes or parafunctional habits that can be identified.[1, 12] Secondary BMS is usually associated with xerostomia, candida, hypersensitivities, parafunctional habits, nutritional deficiency, other mucosal diseases, and possibly psychogenic factors.[13-19] Research shows an increased risk for BMS in those with diabetes[20] and a higher instance of hypothyroidism has been found in those with BMS.[21] Patients with BMS also have been shown to demonstrate a greater degree of sleep disturbance than controls.[22] There is also a well-known female predilection for BMS and most cases present in peri- or postmenopausal women.[1, 23] Female to male BMS diagnosis is reported to be around 7:1 but also has been shown to be as high as 33:1, with 90% being perimenopausal.[1, 13, 14, 24]

Contributing factors to BMS range from local factors (e.g. dry mouth), systemic factors (e.g. reflux), and psychosocial factors (e.g. depression).[11] The table below lists local, systemic and psychosocial factors.

Table 1. From Balasubramaniam (2009).[11]

Table 1. Local, systemic and psychosocial factors which may be responsible for oral burning

Local	Systemic	Psychosocial
Dry mouth • hyposalivation • xerostomia	Haematinic disorders • vitamin B group • iron • folate • zinc	Psychological disorders • depression • anxiety • somatization
Taste alterations	Autoimmune type connective tissue • Sjögren's syndrome • sicca • systemic lupus erythematosis	Personality profiles • neurotisicism • extraversion • openness • conscientiousness
Oral infection • fungal • bacterial • viral	Gastroesophageal reflux disease	
Oral mucosal diseases • lichen planus • benign migratory glossitis • hairy tongue • fissured tongue	Endocrine-related disorders • diabetes • thyroid disorders • hormone deficiencies	
Oral parafunction	Medication side effects • tricyclic antidepressants • ACE inhibitors	
Oral galvanism	Central nervous system disorders • multiple sclerosis • Parkinson's disease • trigeminal neuralgia	
Poorly designed dentures	Idiopathic focal conditions • oro-cervical • uro-genital	
Allergic reactions • dental products • food products		

Because of the diversity of possible etiologies for BMS, current treatment modalities for BMS are also quite varied and include: electroconvulsive therapy,[25] behavior modification,[26] counseling,[27] prescription medications (topical and systemic anesthetics & antidepressants, anxiolytics, anticonvulsants, antifungals),[2, 13, 24, 28-30] saliva stimulation,[31] and capsaicin,[13] among others. Alternative methods are being researched as well, such as acupuncture[32] and herbal compounds like catuama, a "revitalizer".[30]

SIGNIFICANCE

Burning mouth syndrome is known to be a highly adverse oral condition that is generally chronic in duration with a substantial uncertainty regarding the clinical presentation, etiologic factors, and descriptive characterization of the condition. The clinical presentation can vary, and case-series of all types of BMS have not commonly been published. The relatively high prevalence of BMS combined with the negative impact to quality of life makes describing BMS as a valuable to step to better understanding the clinical spectrum, possible subtypes, and precipitating factors.

PURPOSE

The purpose of the study was to characterize the UW OMCS BMS patient population and help determine associations with local, regional, and systemic factors. Points of interest in the demographics were used such as gender ratio, age, and reports of burning complaints as well as comorbid conditions. The goal was to check that generalizable treatment methods were supported as well as to provide a possible expansion of the list of "red flags" for providers. The general aim of the study was to develop a clinical phenotype of the UW OMCS BMS patient population through the collection of existing data. The specific aims included 1. Identification of the demographic status of the clinical BMS population and comparison to those prior reports in the scientific literature; 2. Identification of comorbid conditions in the clinical BMS population and comparison to that reported in the scientific literature; and 3. Identification of the most commonly reported anatomical "cluster" of locations of burning in our BMS population.

IRB COMPLIANCE:

The study design and protocol were approved by the Institutional Review Board (IRB) at the Human Subjects Division (HSD), University of Washington School of Dentistry (UWSOD).

MATERIALS & METHODS

Sample Population and Criteria for Selection

A "waiver of requirement for HIPPA authorization" was obtained to screen existing UW OMCS patient records in the UW School of Dentistry EHR that had ICD-9 codes 782.0 and 529.6. All data was gathered from existing patients of record since the launch of AxiUm EHR software on July 1st of 2009. The subjects made up a convenience sample of patients with BMS in UW OMCS. It was estimated that there were 250 unique charts with BMS coded in AxiUm since its launch via an ICD-9 code analysis. The working diagnosis of BMS identified in chart records within AxiUm was based on ICD-9 codes: 782.0 "disturbance of sensation" such as burning used for BMS, and 529.6 for "glossodynia". The inclusion criterion included only a working diagnosis of BMS identified in chart records within AxiUm based on ICD-9 codes 782.0 and 529.6. The exclusion criterion was simply patient age. If the subject was <18 years old their data would not be collected. Both Primary and Secondary BMS patients were reviewed for this study.

A data abstraction sheet was developed and is shown in table 2. It consisted of gathering data from the clinical mucosal or pain questionnaire given at the first patient

visit along with existing charts notes, electronic drug prescription lists, and the stand-alone Symptom Checklist 90 Revised (SCL-90-R).

Data Abstraction Sheet Development

Table 2: Data in EHR for Collection:

Existing mucosal or pain databases o The initial intake health history forms o Demographics o Comorbid conditions o Characterization of complaint ▪ Location within the oral cavity / lips ▪ Onset ▪ Duration ▪ Pain scales, VAS %
Existing chart notes- New Patient Assessment o Date of BMS in Differential o Used to validate and supplement mucosal or pain database information o Databases are extensive health history forms
EHR o Current prescription lists o Referrals o Incoming & Outgoing
SCL-90-R form o Anxiety o Depression o Somatization with Pain o Somatization without Pain

The SCL-90-R is an instrument that helps evaluate a broad range of psychological problems and symptoms of psychopathology. Clinical psychologists, psychiatrists, and professionals in mental health, medical, and educational settings, as well as for research purposes use the SCL-90-R, which allows calculation of somatization, obsessive-compulsive symptoms, interpersonal sensitivity, depression, anxiety, hostility, phobic-anxiety, paranoid ideation, and psychoticism. For this study we calculated scores for anxiety, depression, and somatization both with and without pain as all of these have been shown to be significantly associated with BMS. [10]

The search terms used prior to collecting data are listed in Table 3 below. Knowing what data were generally available in the EHR in (Table 2), along with typical BMS complaints found in the literature, and possible comorbid conditions of interest from clinical experience and the scientific literature allowed construction of specific areas of interest were included in the development of the Data Abstraction sheet (Figure 1). The study design is classified as a case-series retrospective chart review with some follow-up data; overall level of evidence of four. Detailed steps in how data was collected to populate the abstraction sheet are provided in Appendix B.

Table 3: Search terms used to gather population statistics and literature for review. Search preformed on UW libraries linked PubMed search engine.

Initial search terms	Additional terms
BMS Burning mouth Comorbid burning mouth Comorbid BMS BMS demographic Northwest BMS Washington BMS Burning mouth demographic United states burning mouth Northwest burning mouth Washington burning mouth Seattle burning mouth Seattle BMS (United states BMS: limited to "last 5 years" and "human" which resulted zero results dealing with burning mouth- mostly results dealt with bare metal stents)	Hypothyroid burning mouth syndrome Hypothyroid BMS Salivary dysfunction Taste dysfunction Hormone/Menopause Tobacco use Reflux/GERD Candida Menopause / Sleep Sleep disturbance BMS sleep OLP BMMP/MMP
*Terms last searched 30Oct2013 **Additional literature was found within article bibliographies	*Terms last searched 05June2014

Statistical Analysis

All analyses were done with SPSS v19. Although the total sample size was 107, the number of males was only 12; therefore many analyses were performed on females only for an N=95. Descriptive statistics were calculated for patient demographics, characterization of complaint, and comorbid conditions. Additional analysis with ANOVA, chi-square analysis, linear regression, K-cluster analysis was performed as appropriate to assess the strength of associations.

RESULTS

Within the time constraints of the study, it was possible to review 174 charts. After reviewing 174 charts and eliminating charts for missing forms, diagnoses that were not BMS, or inability to access charts (purged paper charts or locked EHR), 107 subjects remained. Reasons and occurrences for omission are listed in Appendix C. A majority (85%) of patients in our study had more than one visit to the clinic for evaluation and care. This helps to assure that the most accurate diagnosis codes were being used and included within the study. A summary of findings can be viewed in Tables 4 & 5 below.

Table 4: Summary of Results – Excluding Comorbid Conditions

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		Female	Male
Gender	%	89	11
Mean Age	Years	57	54
Location of Burning %	Palate Anterior	49.5	50
	Palate Posterior	0	0
	Tongue Tip	73.7	50
	Tongue Anterior	82.1	67.7
	Tongue Posterior	4.2	0
	Tongue Lat Right	80	58.3
	Tongue Lat Left	82.1	50
	Tongue Dorsal	10.5	16.7
	Lips	34.7	41.7
	Gingiva	16.8	25
	Cheeks	6.3	8.3
	Teeth	1.1	0
	>1 additional	4.2	0
Burning Onset %	Post-LA	12.6	8.3
	Post-Surgery	8.4	0
	Post-Trauma	0	8.3
	Post-Rx Change	2.1	0
Duration of Burning	Mean # of weeks	69.4	231.9

Ethnicity %	Caucasian	77	
	Asian	9	
	Hispanic	3	
	Af/Amer	1	
	Amr Ind/AK Native	1	
	Unknown	9	
		Female	Male
Recurrence Pattern %	Constant	37.9	41.7
	Recurs Daily	22.1	41.7
	Unanswered	20.0	8.3
	Several X Daily	8.4	8.3
	1st Episode	4.2	0.0
	Recurs Weekly	3.2	0.0
	Recurs Monthly	3.2	0.0
	Several X Year	1.1	0.0
	Less than yearly	0.0	0.0
Change since Onset %	Unchanged	21.1	25.0
	Unanswered	18.9	8.3
	Worse	17.9	41.7
	Slightly Improved	11.6	8.3
	Was Worse now Better	8.4	8.3
	Slightly Worse	7.4	0.0
	Was Better now Worse	6.3	0.0
	Much Improved	3.2	0.0
	Much Worse	3.2	8.3
	Improved	2.1	0.0
Pain VAS%	% of Scale		
	Mean Aversiveness	65.1	68.6
	Mean Intensity	50.2	57.3

Table 5: Comorbid Conditions in Female Study Population

Table 5: Comorbid Conditions in Female Study Population					
Percent Positive Responses					
Hormonal Status	Pre-Meno	14.7	Post-Meno	72.6	
	Peri-meno	11.6	Taking HRT	26.3	
Psych Rx	SSRI	14.7	Taste Change	Bad	29.5
	2 Diff Rx	6.3		Increased	14.7
	Benzo	3.2		Reduced	13.7
	3 or more	3.2			
	ADHD	1.1	Mucosal History	Xerostomia	35.8
	Bipolar	1.1		Candida	21.1
	Other Antidep	1.1		OLP	9.5
	Unanswered	1.1		Geo Tongue	4.2
				Sjögren's	1.1
Endorsement Anx & Dep	Anxiety	36.8		BMMP	0
	Depression	29.5			
	Both	20	Vaginal Symptoms	Itch	4.2
				Dryness	20
Diabetes	I & II	5.3		Ulcerations	0
Sleep	Disturbance	45	Thyroid	Hypothyroid	20

Demographics

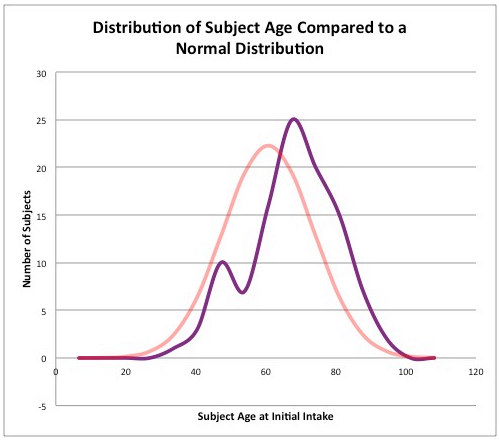
Gender-

The gender ratio of female to male patients seen at UW OMCS for BMS is close to 9:1. This is much closer to the literature stating female to male ratio is 7:1 [1] than the literature claiming a higher female proportion of 33:1 [14]. For the demographics results both male and female statistics will be represented in the figures presented and are available for overview in the summary tables (Tables 4 & 5), but as there were only 12 Male subjects and 95 female subjects the focus will be on the females in the study population.

Age-

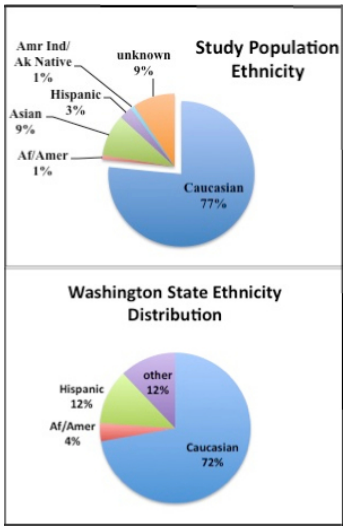
The mean ages (in years) of our patients were 57 and 54 for females and males respectively. The maximum ages were in the 9th decade with majority falling between the 5th and 8th decades (Figure 1). These data match a 2013 review of BMS noting BMS rarely affects those younger than 30, and has a usual occurrence of between the 5th and 7th decades. [5, 33]

Figure 1: Age Distribution of Patients at Initial Intake.



Ethnicity-

Figure 2: Ethnicity Distributions



Ethnicity percentages in the literature are highly subject to variation depending on study population geographic location. As depicted in Figure 2, UW OMCS had a majority (77%) Caucasian sample which has a similar distribution to Washington state's majority (72% Caucasian) as a whole. [34]

Complaint Characterization

Burning Location-

Because the abstraction sheet did not include the location initially, "tongue tip" was created for data analysis and was counted if the patient reported a combination of anterior and lateral sides of tongue together, or if the tip of tongue was described in the initial chart note as a burning location. The majority of female subjects reported burning in the anterior and left lateral tongue with an 82.11% reporting rate, followed by lateral right tongue at 80%, and tongue tip with 73.7%. Complaints for the anterior palate at 49.5%, and lips at 34.7% were the next highest reported. Following anterior/lateral tongue, anterior palate, and lips, the next burning locations were gingiva at 16.8% and dorsal tongue at 10.5%. Teeth and cheeks had the lowest burning rates of 1.1% to 6.3% respectively. The posterior palate did not have a single report of burning in our sample population. These percentages are illustrated in Figures 3 & 4 on the following page.

Figure 3: % Complaint distribution of Location of Oral Burning as reported in Mucosal Database and during Initial Intake for female and male patients.

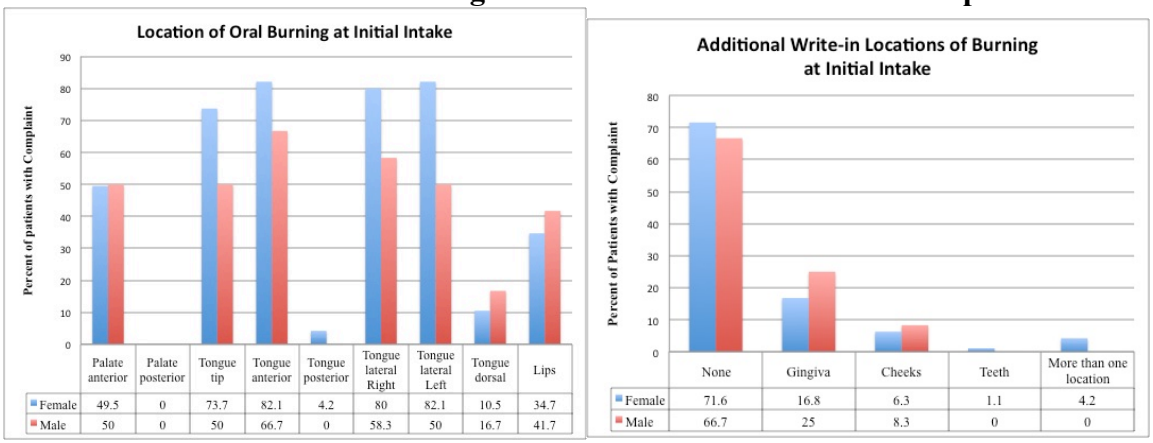
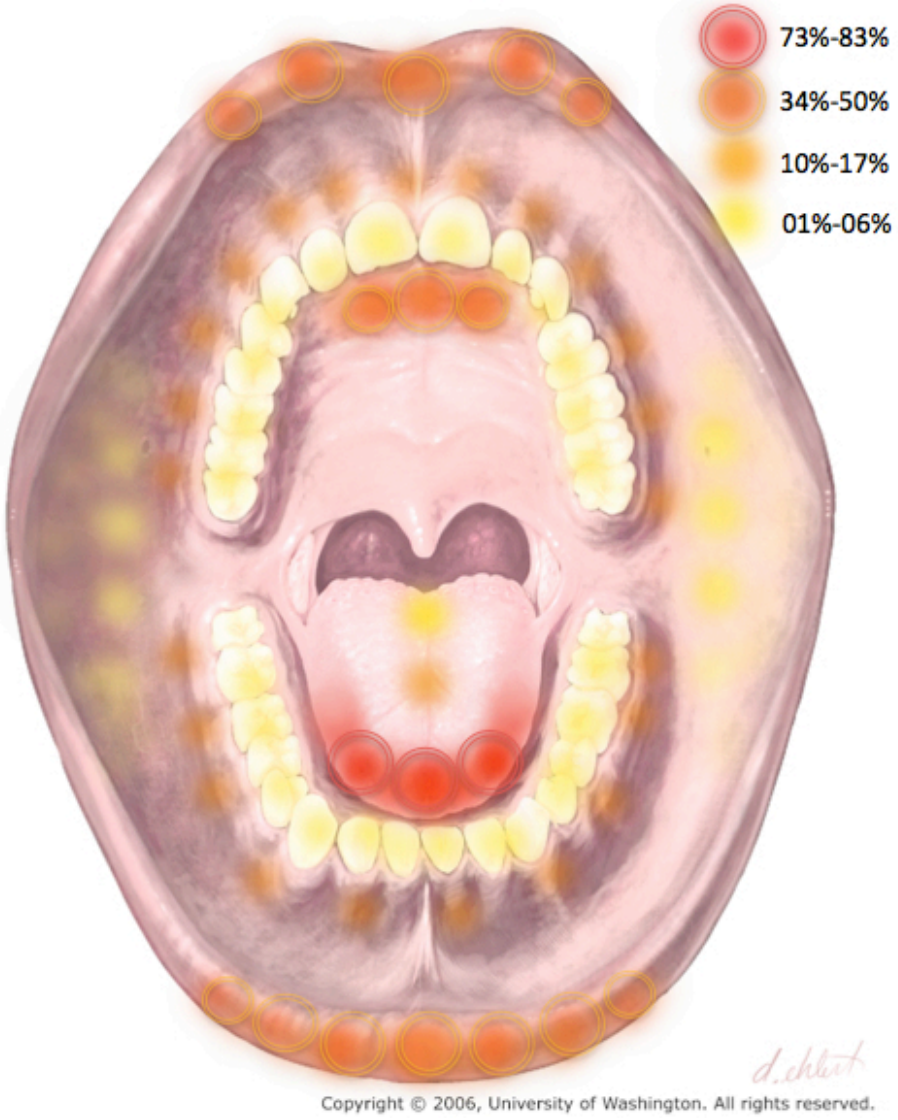


Figure 4: Female (N%) Burning Complaint Location at Initial Intake



Burning Onset-

Within our study there were only 12 males subjects, and one male individual reflects a inordinately high appearing prevalence of 8.3%; because of this, the discussion will be focused on the female population. The majority of patients did not have onset of symptoms following one of the four events investigated: local anesthetic use, surgery, trauma, or a change in medications. Slightly over twelve percent of female subjects reported onset of symptoms following the use of local anesthetic. The next most prevalent were: following surgery (8.4%) and a change in medications (2.1%). Female subjects did not report onset after trauma, though we recognize that surgery is a form of controlled trauma, the surgeries were usually described in our initial assessment, and one case that was omitted from the study had onset of symptoms following a vehicular accident- so we are fairly confident occurrences were adequately differentiated by the clinician at time of intake.

Burning Duration-

The burning duration at initial intake for the males averages over 231 weeks whereas the females averaged just fewer than 70 weeks. There were two males with much longer duration of burning times than the longest female duration. One was 520 weeks and one 1, 040 weeks. If the male subject with 1,040 weeks is excluded, the mean duration for males is 142 weeks. If both the subject with 520 weeks and the subject with 1,040 weeks are excluded, the mean duration is 94.9 weeks. The maximum burning duration for the females was reported at 416 weeks, or 8 years, with the shortest duration at intake was reported at 2 weeks.

Recurrence pattern of pain-

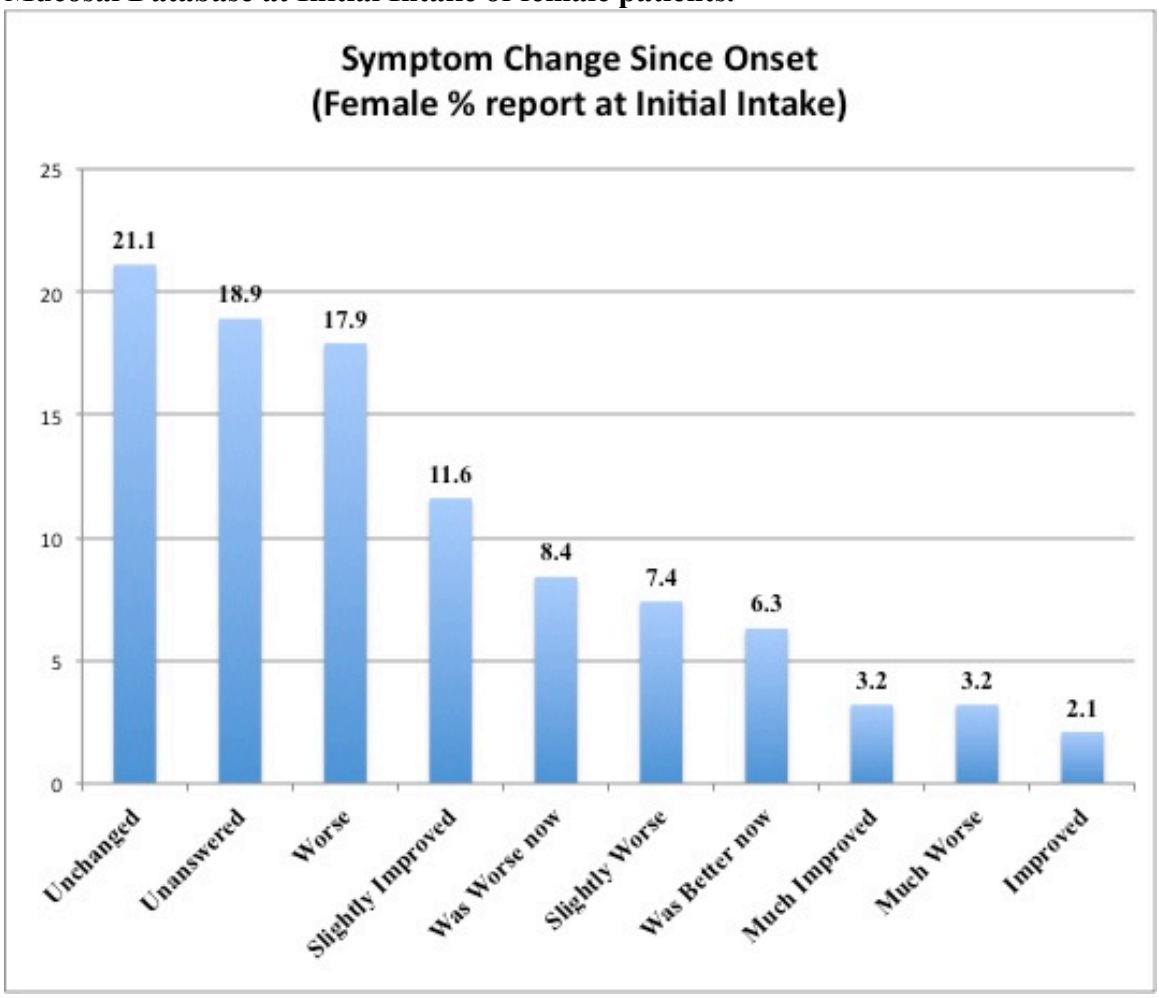
In the new patient intake Mucosal Database patients are asked to choose a "Recurrence Pattern of Pain." They are given nine options ranging between "constant" to "recurs daily/monthly" to " first episode". If a patient chose more than one option, the choice that illustrated a more constant or persistent pattern was recorded. Females reported constant pain most often with 37.9% of subjects, followed by "recurs daily" (22.1%), and surprisingly, data entered as missing was 3rd with 20% of the study group leaving that particular part of the mucosal database unanswered. The next most common pattern, reporting at 8.4% was "recurs several times daily," followed by "first episode" (4.2%), "recurs weekly" and "recurs monthly" both with (3.2%), and lastly "several times a year (1.1%). The option for "recurs less than yearly" was not chosen by any of our female subjects. Male subjects tied two times with 41.7% reporting "constant" and "daily," followed by 8.2% "recurs several times daily" and "unanswered". There were not enough male patients to have more recurrence patterns to report the likely variation that exists as demonstrated in the female population.

Change since onset-

As depicted below in Figure 5, the reported change in symptoms since onset varied dramatically. As in the section for "Recurrence Pattern of Pain", patients are given a variety of options to choose from to describe their "Symptom Change Since Onset." Choices range between "unchanged" to "improved" to "much worse." The highest reporting rate for females in this category was "unchanged" at 21.1%, followed by "unanswered", with 18.9% of females leaving the inquiry blank. The option of "worse"

was next with 17.9% reporting, followed by “improved” with 11.6% of the population. The remaining 48.4% were distributed unequally between the remaining categories. Male patients most often reported that their symptoms were “worse” since onset, at 41.7%, followed by “unchanged” with 25%. Of the remaining four subjects, one did not answer the question and the other three chose (one each) “much worse”, “slightly improved”, and “was worse now better.”

Figure 5: Complaint distribution of Symptom Change Since Onset as reported in Mucosal Database at Initial Intake of female patients.

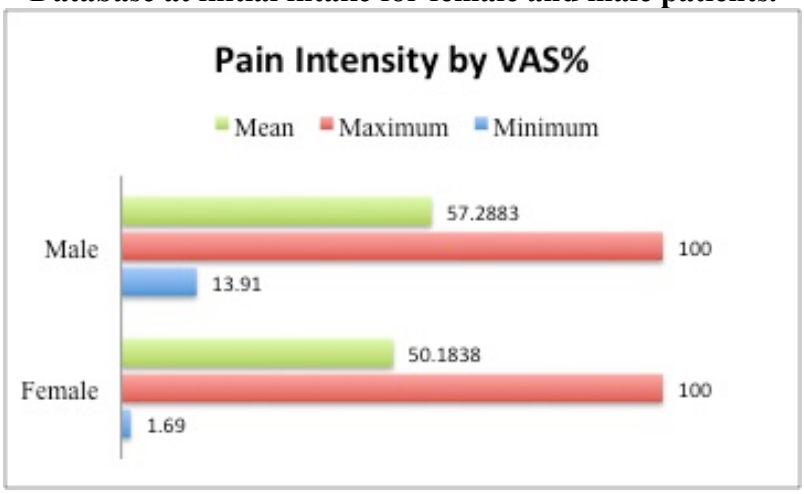


Pain Aversiveness and Intensity-

Pain Aversiveness and Pain Intensity ratings were recorded in the Mucosal Database on a Visual Analog Scale (VAS). Because screen resolution varies, and paper printouts do not always match 100mm (as per the usual format of a VAS), measures were taken as VAS% of the line presented on the questionnaire. Reports were recorded for VAS% by measuring the length of the line to the left of the mark made by the patient, then dividing it by the total length of the VAS line to give the VAS%.

Females and males showed a similar mean in "Aversiveness", averaging 65.11% and 68.57% respectively. Both genders included subjects that reported 100% on the VAS scales, but females showed a significantly smaller minimum at 3.12% compared to the male minimum of 27.27%, this discrepancy may possibly be explained by the small N=12 of the male sample. While no literature was found on the terms "Pain Aversiveness" and BMS, our findings for " Pain Intensity" (as seen below in Figure 6) comes very close to the findings of Komiyama (2012) who reported a mean VAS of "Pain Intensity" of BMS patients to be 6.96±2.11. [35]

Figure 6: Complaint distribution of Pain Intensity VAS% as reported in Mucosal Database at initial intake for female and male patients.



TREATMENT

The current treatments or therapies listed in the subject charts were quite diverse, likely reflecting the many etiologies of BMS as well as that several clinicians were providing care, and that care was delivered at different time-points in patient symptom presentation or in the patient's seeking of care, as seen in the variation of "burning duration" discussed earlier. Table 6 lists the treatments in decreasing order of most prescribed to the female study population.

Table 6: Percent of patients reporting the listed Treatments at most current visit for BMS.

Treatment Percent	Female	Male
Clonazepam	50.5	50
Topical steroid	16.8	8.3
Antifungal	11.6	16.7
Stent	10.5	0
Membrane stabilizer	10.5	0
Saliva Rx	7.4	0
Behavior Modification	4.2	8.3
Capsaicin	4.2	0
Decrease stress	4.2	0
TCA	3.2	16.7
Non-Rx saliva stim	3.2	0
Ref for psych	3.2	8.3
Chlorohexidine	2.1	8.3
Night guard	2.1	16.7
d/c products	2.1	0
Consult PCC	2.1	0
Lorazepam	1.1	0
Ref QST	1.1	0
Vitamin testing	1.1	0
Vitamin supplement	1.1	0
SSRI	1.1	0
Ambien	1.1	0
Analgesic	1.1	8.3
Tizanidine	1.1	0
Reflux/GERD	0	8.3
Only fluoride	0	8.3

SELF-REPORTED COMORBID CONDITIONS IN FEMALES

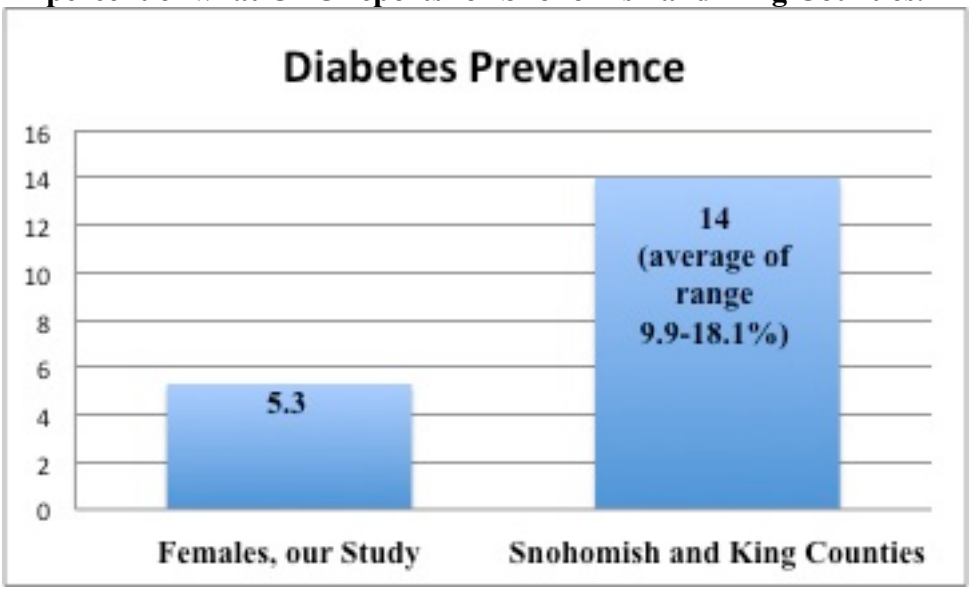
Reflux-

Self-reported Reflux in our study population had a high prevalence of 50.5%, which aligns with the report of BMS patients being 2-3.5 times more likely to have gastrointestinal diseases (e.g. gastritis, reflux, flatulence) than control patients. [36]

Diabetes-

Self-reported Diabetes percentage in our population of females was 5.3% (Figure 7); this is below the average 6.3-9% male and female diabetes rates in 2010 for King and Snohomish counties reported by the CDC. [37] Considering the average age of our female study patients was 57, the county statistics for males and females ages 45-74 years old increases to between 9.9-18.1%, [37] actually increasing the difference from our study population.

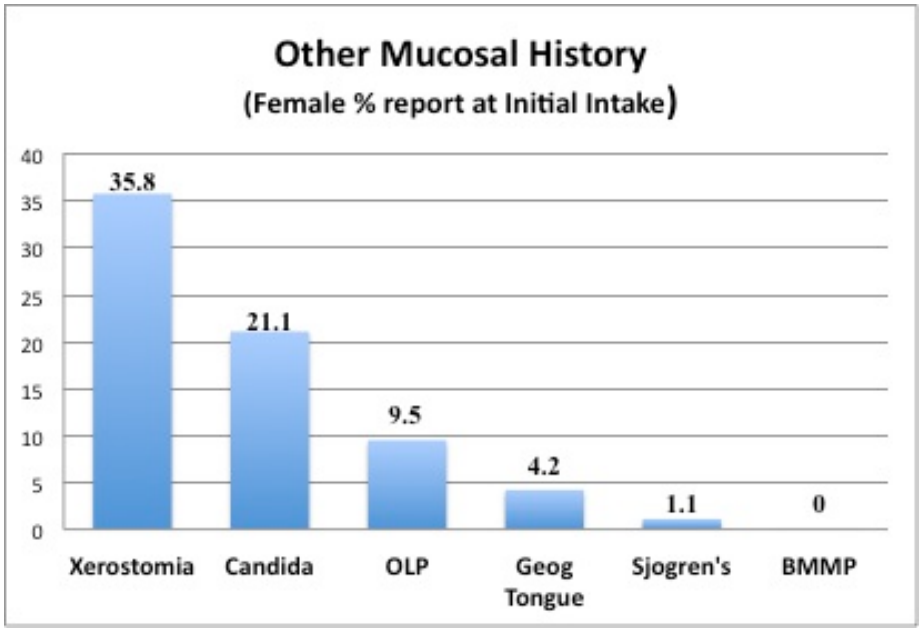
Figure 7: Percentage of female patients reporting DM and average percent of what CDC reports for Snohomish and King Counties.



Mucosal Conditions-

Figure 8 below depicts the percentages of the female study population reporting mucosal conditions at initial intake. Results are discussed separately following the figure.

Figure 8: Percentage of female patients reporting other mucosal conditions at initial intake.



- **Xerostomia**: 35.8% of our subjects reported dry mouth or xerostomia. Netto et al (2010) reported a 15.6% prevalence of dry mouth in their study population,[36] which is close to the reported 14.5% in Mignogna et al (2011) study.[17] Much like our study Netto et al (2010) took 32 records at their School of Dentistry diagnosed with BMS and recorded prevalence of xerostomia that appeared in their charts, whereas Mignogna et al (2011) examined 124 BMS patients in an "Oral Medicine Unit" and oral symptoms were collected by both an oral medicine specialist and general dentist.[36] [17] One explanation for our population reporting the high level of 35.8% was that dry mouth or xerostomia occurrence was not delineated between current or historical

at initial intake, also unstimulated and stimulated sublingual salivary flows decrease as female goes from pre→peri→post menopausal. [38, 39]

- **Candida**: While it is not necessarily illustrative of symptomatic infection, carriage rates were shown to be 53% in 30-45 year olds, and 59% in those over 60 in Kleinegger et al (1996). [40] While we recognize it is not equivalent to carriage rates, the majority of patients had no physical findings that would support a diagnosis of oral candidiasis and reports less than half that prevalence in actual yeast infection. Some variation in populations are expected as Kleinegger et al (1996) also writes that candida percentage reports vary widely depending on age, immune status, medications, and that intensity of yeast carriage increases with age. [40]

- **OLP**: Bombeccari et al (2011) as well as Baccaglini et al (2013) reported that OLP occurs in 1%-2% of the general population. [41, 42] Our study population had a much higher prevalence at 9.5%.

- **Sjögren's**: Primary Sjögren's syndrome has a prevalence of about 0·5% in the general population, [43] our female study population's prevalence is 1.1%. A positive correlation has been reported between salivary flow rate and the sensation of burning mouth in the elderly. [44]

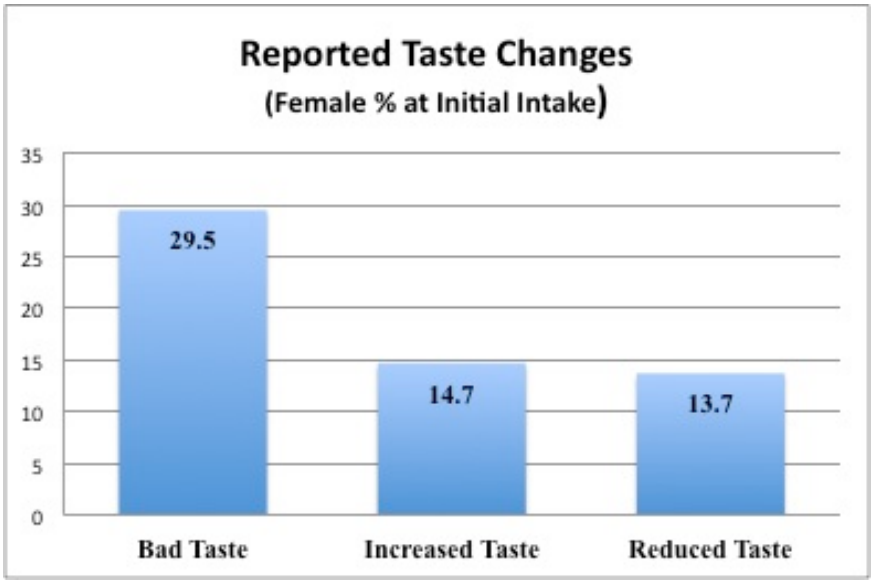
- **Geographic Tongue**: Ching et al (2012) studied the prevalence of geographic tongue in BMS patients. Within Ching et al (2012) BMS group, 22.7% of the female subjects were diagnosed with geographic and fissured tongue (GFT), which was near twice the percent of control female group at 12.9%. [18] Our female population had a much lower prevalence of 4.2%.

- **BMMP**: Xu et al (2013) lists the prevalence of mucous membrane pemphigoid to be 0.8 to 2 per million which supports why we did not have an occurrence of benign mucous membrane pemphigoid (BMMP) reported within our study group. [45]

Taste Changes-

Glazar et al (2010) found no correlation between hypo-salivation and taste disturbance in the elderly. [44] While this is not necessarily suggestive of a BMS and taste changes correlation as Glazar et al (2010) were not investigating BMS, but with 35.8% of our female study population reporting xerostomia it is not something to be ignored. Netto et al (2010) study found a 6.3% incidence of taste changes in their BMS study population. While having a relatively small N of 32 it does illustrate occurrence. Figure 9 below illustrates the rates of "Bad Taste", "Increased Taste", and "Reduced Taste" found in our study. Patients were able to choose one, all or none of the options within the initial intake health history (mucosal database).

Figure 9: Percent of female patients reporting taste changes at initial intake.

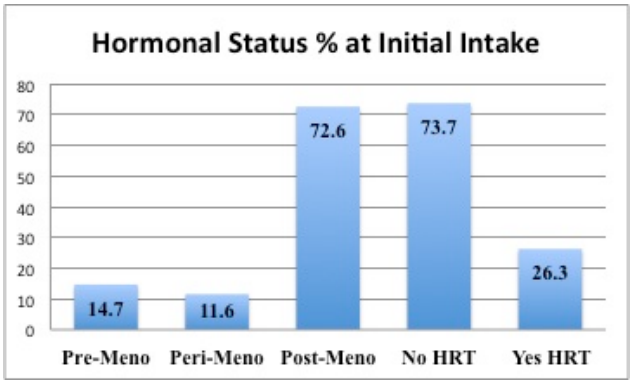


Tobacco use-

Tobacco use was reported in 2.1% for the female study population. This is considerably less than the 5.8% to 40.8% reported for females in 2012.[46] This low self-reported use may indicate the higher socio-economic status of the clinic population that we studied.

Hormonal Status-

Figure 10: Female patient hormonal status at initial intake: Premenopausal, peri-menopausal, post-menopausal as well as reported use of Hormone Replacement Therapy (HRT).



The general prevalence of BMS in prior studies is between 0.7%-5%[6] and escalating to a substantial 12-18% in postmenopausal females.[2] The dramatic increase is reflected in our population as 72.6% of our females reported being post-menopausal. HRT was not associated with any change in symptoms, this finding is in agreement with literature that also reports that mouth pain and dry mouth symptoms were not alleviated with use of HRT in their study population.[47]

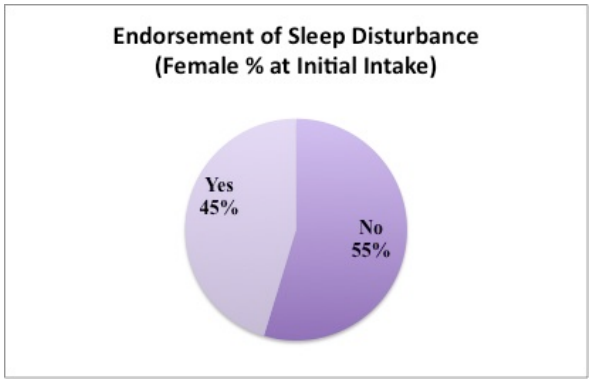
Vaginal Symptoms-

Vaginal dryness, poor sleep, and depression are reported to worsen during the menopausal transition.[48] Twenty percent of our patients reported a complaint of vaginal dryness, 4.2% reported vaginal itch, and there was no reporting of vaginal ulcerations. These statistics may be artificially low from patients not truthfully reporting vaginal symptoms for an "oral medicine" appointment. From Simon et al (2013); vaginal dryness was reported by 85% of women who had finished their menses at least 5years prior:

> "Most women (80%) considered vaginal discomfort to negatively impact their lives, particularly with regard to sexual intimacy (75%), ability to have a loving relationship (33%), and overall quality of life (25%); women also felt that it made them feel old (36%) and affected their self-esteem (26%). Of those with symptoms, 37% did not consult any healthcare professional, and 40% waited 1 year or more before doing so."[49]

Sleep Disturbance-

Figure 11: Percentage of female patient endorsement of sleep disturbance at initial intake.



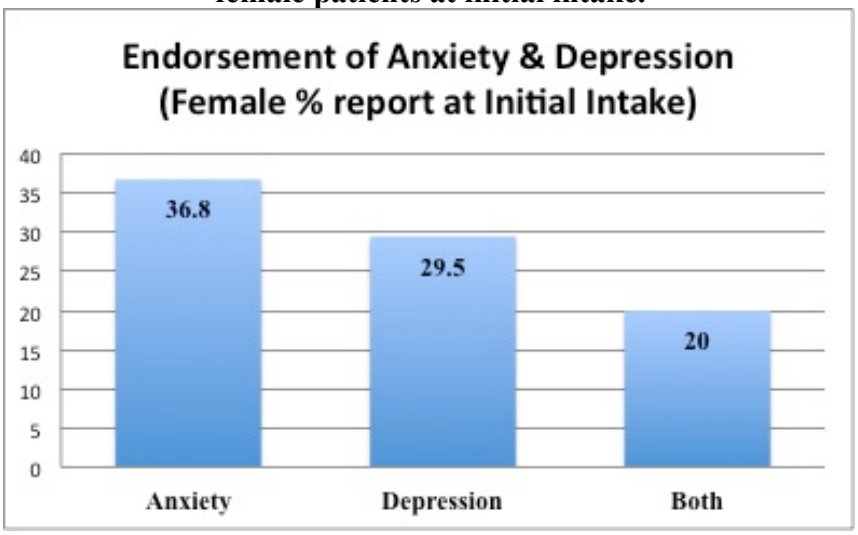
Our female population endorsed a 45% prevalence in sleep disturbance. This matches literature showing positive correlation between BMS and sleep dysfunction.[22] This also closely matches the reported 46-48% of US women aged 40 to 64years that report sleep problems.[50] Within current literature from Xu et al (2014) there appears to be a correlation of hormonal changes and sleep, specifically with Asian

and white women both having an increased rate of sleep disturbance at the perimenopausal and postmenopausal stage. [51] Ornat et al (2014) also reported in their mid-aged female study population that disturbed sleep was related to somatic menopausal-related symptoms. [52] Researchers also found that 56% of menopausal women demonstrated a primary sleep disorder and recommend that patients suspected of having these disorders be referred to a sleep disorders center. [50, 53]

Depression & Anxiety-

Anxiety and Depression are prominent comorbidities with BMS that are often underappreciated by the patients themselves. Our data corresponds with prior literature showing statistically significant higher levels of depression and anxiety in BMS patients. [15, 16, 35, 54] Anxiety was endorsed by 36.8% of our female BMS patients, depression by 29.5%, and 20% endorsed having both anxiety and depression. The fields are not mutually exclusive in that the 20% endorsing both anxiety and depression are part of the total percentages within the separate anxiety and depression fields.

Figure 12: Percent endorsement of anxiety and depression of female patients at initial intake.



Psychiatric Prescription-

Sixty-eight percent of our study population did not report having any psychiatric prescriptions. The itemization for those percentages in our study group of being prescribed medications is: SSRI (14.7%), two different medications (6.3%), benzodiazepine (3.2%), three or more medications (3.2%), ADHD (1.1), bipolar (1.1%), and other antidepressants (1.1%). Our study population demonstrates two times more SSRI (14.7%) prescriptions, and 1/10th the Benzodiazepine (3.2%) use than Souza's 2012 report of BMS treatments.[55] Souza (2012) did report a 3.3% bipolar diagnosis percentage, which is 3x higher than those prescribed bipolar medications in our study population. [54] These deviations do illustrate variability in treatment modalities across populations.

ANALYSIS OF ASSOCIATIONS

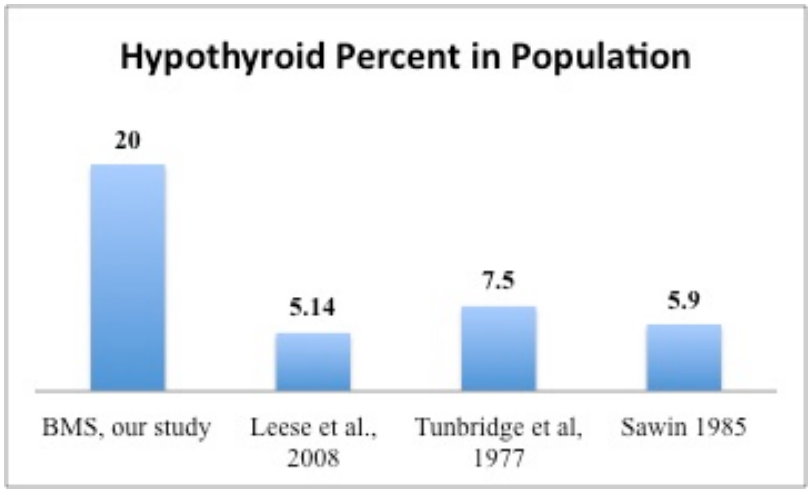
BMS Duration-of-Burning with Anxiety & Depression-

An ANOVA (Appendix D) was completed looking for a relationship between endorsement of anxiety and duration of burning, and endorsement of depression and duration of burning. The significance is 0.077 for anxiety and 0.156 for depression. This analysis shows that with an increase in the duration of burning, anxiety endorsement "approaches significance" by also increasing in prevalence. Depression statistics do not show any statistically significant association with duration of burning in our BMS study population.

BMS with Hypothyroidism-

Our female study population reported a 20% prevalence of having hypothyroidism. As seen in Figure 13, this is a considerably higher prevalence from that reported in general populations in three separate studies. Leese et al (2008) and Tunbridge et al (1977) included all age females, whereas the Sawin (1985) statistic is limited to 65-75yo females.[55-57] Though our patients were taking medications for their hypothyroid, patients taking thyroid medication may not be in normal range as the Colorado Thyroid Disease Prevalence Study found that only 60% of patients taking thyroid medication were within normal range of TSH.[58] It is also noted that subclinical hypothyroidism prevalence increases with age especially with women,[59] however HRT with estrogen does not seem to effect thyroid disease states.[58] Femiano et al (2008) found that subjects with thyroid alterations present with BMS symptoms and that hypothyroidism could be responsible for oral burning and therefore suggests that testing thyroid function be part of the diagnostic process for BMS.[21]

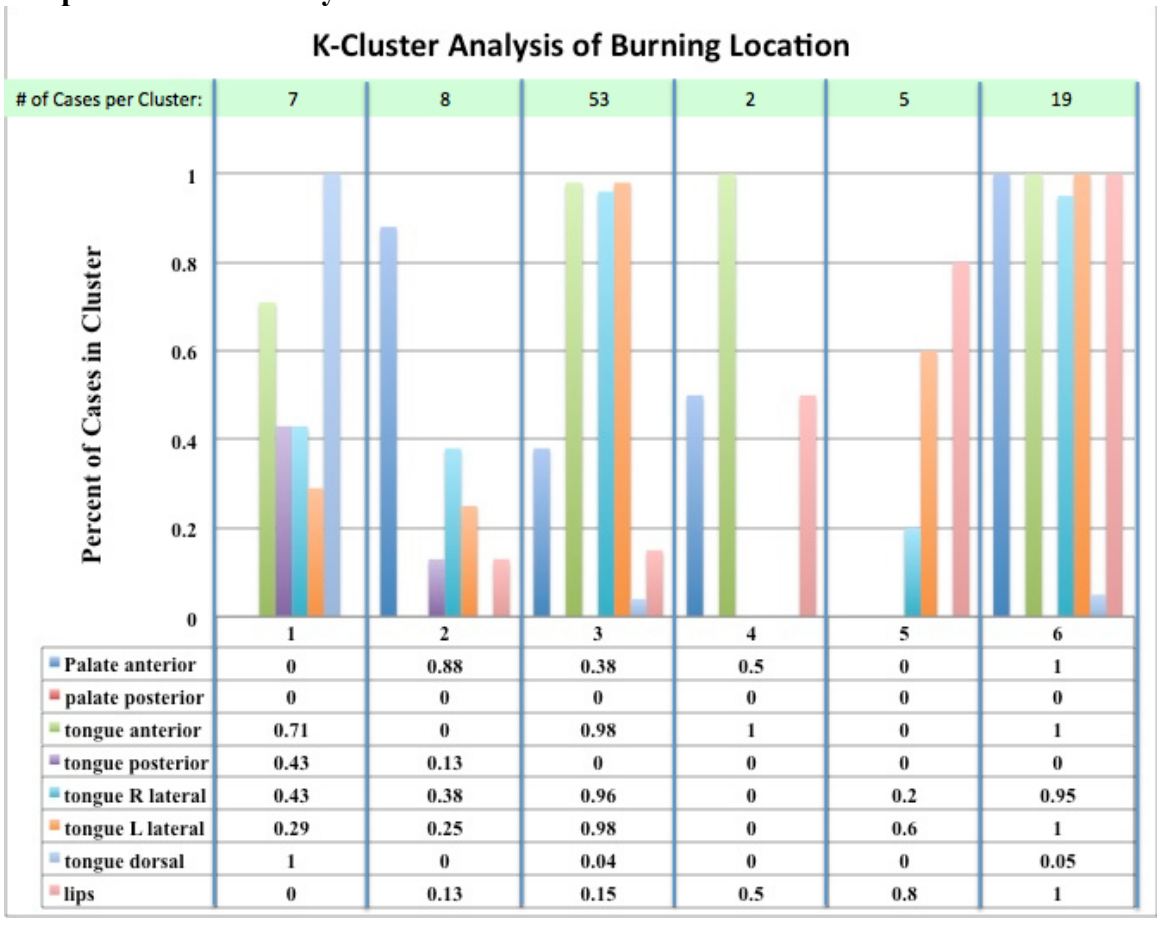
Figure 13: Percent of female patients reporting hypothyroid conditions at initial intake.



K-Cluster analysis of Burning Location-

The numbers of clusters were tested and no greater cluster correlation was found beyond the 6 clusters- a greater number of clusters investigated yielded smaller case numbers per cluster. Except the two examples in the chart, no other cluster had greater than 10 cases. The analysis shows there is no statistical significant association of patients having both anterior tongue and anterior palate complaints concurrently as 38 patients noted anterior tongue without anterior palate and 40 patients had both complaints. Likewise, only 7 patients complained of anterior palate burning without anterior tongue burning and 9 patients reported neither location.

Figure 14: K-Cluster analysis of burning location demonstrating no statistical significant association of patients having both anterior tongue and anterior palate complaints concurrently.



# of Cases per Cluster:	7	8	53	2	5	19
	1	2	3	4	5	6
Palate anterior	0	0.88	0.38	0.5	0	1
palate posterior	0	0	0	0	0	0
tongue anterior	0.71	0	0.98	1	0	1
tongue posterior	0.43	0.13	0	0	0	0
tongue R lateral	0.43	0.38	0.96	0	0.2	0.95
tongue L lateral	0.29	0.25	0.98	0	0.6	1
tongue dorsal	1	0	0.04	0	0	0.05
lips	0	0.13	0.15	0.5	0.8	1

We repeated the K-cluster analysis including the additional write-in locations of "cheeks", "teeth" and "gingiva". The "teeth" location appeared in only a single cluster, and represented only a single subject in that cluster. "Cheeks" appeared in 3 clusters, but represented only 2 subjects in 2 of the clusters, and a single subject in the third cluster. "Gingiva" was more robust, appearing in 4 clusters. However, this variable was represented only between 10 (representing only a single subject) to 21% of the time in any given cluster.

These analyses show that the tongue location has the highest prevalence rate in burning although the overall location patterns may be patient specific and multifactorial. Whether complaints arise from infection, traumas, salivary dysfunction, parafunction, to altered thyroid function (discussed more later), the tongue is highly mobile; used for taste, ingestion, communication, and therefore susceptible to sensory alterations and possibly heightened patient awareness and monitoring.

Correlations of Taste Disturbance-

As shown in Appendix E, a Pearson's Correlation was run on the data for our three variables on taste disturbance: "bad taste", "increased taste", and "reduced taste". It was shown that bad taste is very significantly correlated with increased taste with a P=0.014. Bad taste is not significantly correlated with reduced taste (P=0.159), nor is reduced taste significantly correlated with increased taste (P=0.367).

Conditions without Statistically Significant Associations-

Several statistics were analyzed for association. Table 7 below lists statistics that showed no statistically significant associations with BMS, within each complaint, as a comorbid condition.

Table 7: Comorbid Conditions without Statistically Significant Associations

No significant findings associated with BMS	No significant findings found between
Autoimmune disorders Vitamin deficiencies Sleep apnea *separate from sleep disturbance Dentate status Gastritis Other neurologic diseases Hypersensitivities SCL-90-R Scores, missing data *not part of most mucosal databases	Duration of burn o Pain intensity o Pain aversiveness o Salivary status Pain intensity o Location of burning o Taste changes o Salivary disturbance o Age Taste changes o Locations of burning Hypothyroid o Sleep disturbance, and reflux o Pain intensity o Burning location

Our linear regression shown in Appendix F shows that there was no association between pain complaints when compared to the duration of burning at initial intake. This does not match data showing difference in pain complaint of acute vs. chronic BMS, Komiyama et al (2012) showed acute symptoms had a statistically significant higher pain intensity in acute vs. chronic (>6mo) BMS,[35] however the average length of "duration of burn" in our population is nearly four times that of what was already considered chronic pain which could explain this difference.

DISCUSSION

Matches to existing literature-

Our study demographics did not deviate from expected for the following variables; subject age at onset, gender, and ethnicity corresponded to existing literature. From complaint characterization reports, location of oral burning and pain intensity also matched previous studies. Treatments utilized for our subjects also matched the variety found in literature. There were several comorbid conditions that did not deviate from BMS populations noted in the literature, among these are: anxiety, depression, taste changes, reflux, and BMMP. Sleep disturbance matched literature as having a higher prevalence in BMS patients, but this can also be attributed to hormonal changes as well as the increased rates of anxiety and depression as these conditions can contribute to sleep disturbances. There were too few completed SCL-90-R forms within the historical charts for significant analysis to be completed as this survey was only included in the "pain" intake health history and was just in the last few years added to the "mucosal" intake health history. The prevalence of endorsed anxiety and how it approached a significant association with duration of burning could be better evaluated with consistent SCL-90-R surveys as our database might not be capturing an accurate prevalence from patient endorsement. Heightened response to stimuli as well as worry from chronic conditions can also help to explain this association. Although hypothyroid conditions have been associated in literature prior to this study it was not something that was actively investigated at UW OMCS so the results, while not novel, are noteworthy. Femiano et al (2008) hypothesized that those with a larger number of fungiform papillae can be predisposed to taste phantoms and idiopathic oral burning: "hypothyroidism could

act as a negative factor for the maturation of fungiform papillae, with reduction in taste, the release of inhibition on the somatic-sensorial sensitivity of the trigeminal nerve in subjects with a larger number of taste papillae, and the subsequent onset of oral burning (tongue, palate, lip)."[60] Wood-Allum & Shaw (2014) also speculate that "Alteration in the levels of circulating thyroid hormones may produce a new neurologic complication, exacerbate a pre-existing neurologic problem, or unmask a subclinical neurologic problem."[61] It is reasonable then that patients presenting with recalcitrant BMS symptoms should be evaluated for possible thyroid dysfunction.

Lower than Existing Literature -

A few of our comorbid conditions had a lower prevalence than existing literature. Diabetes, geographic tongue, candida, and smoking percent were all lower than reports on normal populations. It is interesting that candida was lower, mostly due to the age of onset of our subjects would usually correspond with much higher candida infections rates considering expected dry mouth issues from medications as well as hormonal changes affecting salivary flow. Smoking percentage may have been lower in reporting than reality because current smoking status was not differentiated from being and "ever" smoker. A possible reason geographic tongue had a much lower prevalence in our study is that because of geographic tongue's benign nature, while doing a problem focused exam - clinicians may not have been recording a diagnosis for its presence.

Higher than Existing Literature-

The complaint characterization of duration of burning was higher than literature. It has been reported that BMS complaints last 4 to 6 months,[5] but clinically we have

seen the presentation last much longer and this is reflected in our study- the average female duration was 70 weeks or 17.5 months at initial intake. From our mucosal history statistics xerostomia, OLP, and Sjögren's had higher prevalence than their corresponding literature. We believe our OLP endorsement prevalence within the patient EHR is likely overrepresented because UW OMCS is a tertiary referral center that sees an extraordinary number of persons with OLP.

Study Limitations-

Some limitations to this study include sample size, time-points, and ambiguity on current or historical conditions in health histories. Our study is a relatively small study with a convenience sample of only the UW OMCS clinical services; this can certainly affect generalizability to broader populations. The study was limited to essentially two time-points; initial intake and last visit. Treatment variation and pain complaints could be investigated further and more information could be extrapolated with changes in time if more clinical visits were reviewed. Without differentiation between changes of therapy over time, and ambiguity in health history questions, some data was not defined as historical or currently-experiencing such as smoking habits, mucosal conditions, sleep disturbances, depression, and anxiety. A future study may show more deviations from literature if Primary BMS is differentiated from Secondary BMS.

Study Strengths-

A strength of the study was using a standard data collection form populated by a single investigator; this helped to insure consistency and accuracy of data throughout.

Though recall changes were not actively researched through visit progress, 85% of the study population had at least two appointments. Patient recall was a strength as this helps to narrow the possibility that the initial diagnosis was incorrect and that the study group contained actual BMS patients. The population, though relatively small and limited to one clinic patient pool, still had strengths because of the clinic utilized. The UW OMCS receives referrals region wide in Washington State and has a diverse and highly experienced clinical staff; for these reasons confidence is increased in accurate diagnoses and usual treatments methods that can assist population generalizability.

CONCLUSIONS

The multifactorial aspect to BMS diagnosis and treatment make it an almost limitless topic for investigation. The study found some traditional factors often discussed as associated with BMS not associated in our population suggesting that there are likely several mechanisms that may contribute to the presentation of BMS. On the other hand our findings of associations of BMS with thyroid dysfunction, reflux, behavioral changes offers opportunities to further consider central, metabolic, and behavioral mechanisms that may trigger or maintain BMS. The diverse treatment methods also identified in our review of patients enrolled in the study also suggest that several mechanisms of approach to treatment are feasible depending on the under etiologic and sustaining factors. The study performed here lays helpful groundwork for future research. Increasing awareness of the conditions deviating form normal populations will help construct a more descriptive and accurate clinical phenotype that is generalizable across a broader population. Better understanding of the categorization of differences in BMS subtypes

and matching those subtypes to treatment outcomes may also enlighten physiological mechanism, behavioral mechanisms and treatment strategies. Eventually, better characterization of the BMS population may reveal mechanisms for recognition of those at high risk for onset and offer primary or secondary methods of prevention. One condition to consider would be thyroid dysfunction. It seems reasonable to investigate the possibility of subclinical or untreated hypothyroid in patients presenting with BMS symptoms. To strengthen clinical services and address the psychological and quality of life factors involved with BMS, including quality of life assessments such as the SCL-90-R or quality of life impact questionnaires with all new patient databases would help early identification of possible conditions detrimental to a faster and more positive outcome. Patient education on the associations BMS has with hormonal changes, anxiety, depression, and sleep dysfunction may help alleviate the feelings of helplessness and shed some light on the seemingly ominous manifestation BMS can often impress on patients. Increasing a patient's understanding of BMS may encourage them to seek counseling and be open to stress reduction behavior modification that could increase quality of life and possibly reduce symptom severity, an effect that I think any healthcare provider would gladly assist a patient in achieving.

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SUPPLEMENTAL MATERIAL

Appendix A
Data Abstraction Sheet

Appendix B
Detailed steps in data collection process with populating abstraction sheet fields.

Appendix C
Reasons for omissions of charts.

Appendix D:
ANOVA Analysis between duration of burning and endorsement of anxiety and endorsement of depression

Appendix E:
Correlations of Taste Disturbance

Appendix F:
Pain complaints and duration of burning at initial intake

Appendix A: Data Abstraction Sheet

Subject ID: _____ Date Data collected_____

<table>
<tr><td colspan="2">Working diagnosis of BMS- date first in record (mm/dd/yyyy):</td></tr>
<tr><td colspan="2">Number of appointments until diagnosis of BMS:</td></tr>
<tr><td colspan="2">Last visit on record DDx and Date (mm/dd/yyyy):</td></tr>
<tr><td colspan="2">Most current therapies recorded:</td></tr>
<tr><td>Gender □Female □Male

Ethnicity:</td><td>Diabetes
Type I □Yes □No
Type II □Yes □No
Other Mucosal (circle)
Vaginal: Itching
Dryness Ulcers</td></tr>
<tr><td>Birth Year (yyyy):
Age:

Decade: 1-2-3-4-5-6-7-8-9-10</td><td>Salivary dysfunction
Too much □Yes □No
Too little □Yes □No
Tobacco use
□Yes □No</td></tr>
<tr><td>Hormonal
Menopausal: □Pre □peri □post □NA
HRT □Yes □No
Reduction of symptoms with HRT □Yes □No</td><td>Dysgeusia
Bad Taste □Yes □No
Increased taste sensitivity □Yes □No
Reduced taste sensitivity □Yes □No</td></tr>
<tr><td>Burning
Location
□Palate – anterior ½ □ posterior ½ □
□Tongue – anterior ½ □ posterior ½ □
Lateral R□ L□ Dorsum □
□Lips □Other: _____
Duration in weeks: _____
Onset: After LA injection □Yes □No
After Surgery □Yes □No
After trauma □Yes □No
After change in Rx □Yes □No</td><td>Contact Hypersensitivities (allergy)
Intraoral □Yes □No – if yes kind: _____
Extraoral □Yes □No – if yes kind: _____
Dental Mat Patch Test completed □Yes □No
Positive response materials:
Change since onset:

Recurrence pattern of pain:</td></tr>
<tr><td>Pain scales VAS %
Pain Aversiveness rating:

Pain Intensity rating:</td><td>SCL-90-R scores
Anxiety:
Depression:
Somatization- w/ pain: _____ w/o pain: _____
Psych Rx □Yes □No - if yes, kind:</td></tr>
<tr><td>Vitamin Deficiency □Yes □No
If yes, which and level:</td><td>Sleep
Sleep disturbance □Yes □No
Apnea □Yes □No - if yes: C-pap □Yes □No</td></tr>
<tr><td>Mucosal Diseases
OLP □Yes □No BMMP □Yes □No
Geographic tongue □Yes □No
Xerostomia □Yes □No Sjögren's □Yes □No
Candida □Yes □No</td><td>Other autoimmune
RA □Yes □No
LE □Yes □No
Other □Yes □No
if yes, which:
GI/Liver/Kidney
Reflux □Yes □No
Gastritis □Yes □No
Kidney dis. □Yes □No
Liver Dx(hep) □Yes □No</td></tr>
<tr><td>Dentate Status: Partial edent □Max □Mand
Max RPD □Yes □No Mand RPD □Yes □No
Edentulous □Yes □No Max CD □Yes □No
Mand CD □Yes □No</td><td>Other neuro Dx
MS □Yes □No Epilepsy □Yes □No
Neuralgia □Yes □No Bells palsy □Yes □No
Other □Yes □No if yes, which:</td></tr>
</table>

Appendix B: Data Collection

Steps used with abstraction sheet:

Open Chart number in EHR.

1. Confirm diagnosis of BMS exists within record.
2. Locate forms.
    - Confirm available "mucosal" or "pain" database in EHR.
    - Confirm clinical notes are present in EHR.
    - Request physical chart if initial visit prior to EHR launch.
    - Elimination of subject if other diagnoses are recorded and BMS is taken off of differential.
3. Using mucosal or pain databases and initial and most current clinical notes to record positive responses throughout.
    - Record date BMS first appeared in a differential diagnosis.
        - Check how many visits this diagnosis took to appear for the pain complaint visit.
    - Check last note and date for most current therapies.
        - Check EHR prescriptions tab to supplement or confirm note.
        - Record dates and therapies.
        - Excluded if BMS eliminated
    - Open mucosal or pain database.
        - Use "New Patient Assessment" note to supplement database if there is missing information in database.
    - Record patient age at time of initial differential of BMS is used.
        - EHR automatically reports current age, adjust if seen in prior year.
    - Continue with all other fields.
4. If data is missing or unrecognizable enter "999".
5. Tobacco use: "yes" only if current.
6. Add-ons, not specifically listed in abstraction sheet.
    - Provider code
        - recorded in UL corner as an add-on to form.
    - Thyroid Status:
        - Recorded in bottom middle of sheet as an add-on.
        - Recorded as:
            - "WNL" for within normal limits if no disorder reported.
            - "Hypo" for hypothyroid.
            - "Hyper" for hyperthyroid.
            - Rx and type recorded if documented medication is being taken for a thyroid condition.
7. Clarification for database specific question numbers:
    - Question 8: locations of pain,
        - Use patient assessment to confirm burning locations as some locations circled are not always "burning" locations.
        - Tongue "tip" recorded as a combination of anterior ½ + Lateral R&L

        - Any other burning locations use write-in area.
    - Measure question 9: “Pain aversiveness rating”
        - Mark line length in millimeters and record percentage.
        - If ambiguously marked, measure to middle of mark.
    - Measure question 10: “Pain intensity rating”
        - Mark line length in millimeters and record percentage .
        - If ambiguously marked, measure to middle of mark.
    - Question 22: SCL-90-R
        - Calculate values and record.
        - if no SCL-90-R on record check to see if anxiety or depression are endorsed in database or initial intake and record within box.
    - Question 25: Medications
        - check medication list to determine if psychiatric meds are being taken or if there are additional prescriptions indicating need for further research into chart notes for missing information in database.

Appendix C: Reasons for Omission of charts.

Reasons for Omission	Total
Purged or Locked Charts	27
Missing Forms	17
TNP/AFP	9
Lesion Present	5
Myofascial Pain	4
Numbness	2
AO	1
Post-surgical Neuropathy	1
Glossitis	1
Total Charts Omitted	67

Appendix D: ANOVA Analysis between duration of burning (dur_burn) and endorsement of anxiety (endorc_anx) and endorsement of depression (endorc_dep).

Between-Subjects Factors

		N
endorc_anx	.00	53
	1.00	30
endorc_dep	.00	59
	1.00	24

Tests of Between-Subjects Effects

Dependent Variable:dur_burn

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	29185.850[a]	3	9728.617	1.286	.285
Intercept	320511.910	1	320511.910	42.353	.000
endorc_anx	24255.372	1	24255.372	3.205	.077
endorc_dep	15523.102	1	15523.102	2.051	.156
endorc_anx * endorc_dep	930.023	1	930.023	.123	.727
Error	597839.379	79	7567.587		
Total	1056146.000	83			
Corrected Total	627025.229	82			

a. R Squared = .047 (Adjusted R Squared = .010)

Appendix E: Correlations of Taste Disturbance

Correlations of Taste Disturbance				
		Bad Taste	Increased Taste	Reduced Taste
Bad Taste	Pearson Correlation	1	.252*	0.146
	Sig. (2-tailed)		0.014	0.159
	N	95	95	95
Increased Taste	Pearson Correlation	.252*	1	0.094
	Sig. (2-tailed)	0.014		0.367
	N	95	95	95
Reduced Taste	Pearson Correlation	0.146	0.094	1
	Sig. (2-tailed)	0.159	0.367	
	N	95	95	95
*. Correlation is significant at the 0.05 level (2-tailed).				

Appendix F: Pain complaints and duration of burning at initial intake

Linear regression showing no difference in pain complaint of acute vs. chronic BMS by mapping duration of burning against pain intensity and aversiveness.