FACULTY OF DENTISTRY, UNIVERSITY OF THE WESTERN CAPE

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Department of Oral Medicine and Periodontics

Design of the Oral Medicine South Africa registry to facilitate surveillance of oral lesions and conditions in SA: Pilot results (2010-2022)

MChD

Oral Medicine and Periodontology

Theesan Ananda Vedan

2873945

Department of Oral Medicine and Periodontology

Tygerberg Hospital

Francie Van Zyl Drive, Parow, Cape Town

071 188 5909

theesanvedan@gmail.com

Declaration of Originality

Full names of student: **Theesan Ananda Vedan**

Student number: **2873945**

Topic/ Title of work: **Design of the Oral Medicine South Africa registry to facilitate surveillance of oral lesions and conditions in SA: Pilot results (2010-2022)**

Declaration

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Dedication

I dedicate this mini-dissertation to my wife, Gillian Moodley, friends and family, who have supported my career goals.

Acknowledgements

I thank Professor H. Holmes, Professor M.E. Engel (SA Medical Research Council) and Dr S. Mulder-Van Staden for supervising my project. I thank the **University of the Western Cape, the Faculty of Dentistry and the Department of Oral Medicine and Periodontology** for assisting me with the completion of this project. I thank the **Western Cape Department of Health** and the **National Health Laboratory Services** for allowing me access to medical records. I believe that the management of the **Tygerberg Dental Hospital, Mitchell's Plain Community Health Centre and Groote Schuur Hospital** will utilize the information contained in this mini-dissertation. I acknowledge **Mr Rezeen Daniels, Dr Mai Ahmed and Dr Rayan Hamid** for their assistance with data collection and database creation.

Contributions of co-authors

	Co-author		
Contribution	H. Holmes	Mark Engel	Sune Mulder Van Staden
Supervision	**X**	**X**	**X**
Concept development	**X**	**X**	**X**
Protocol development	**X**	**X**	**X**
Data use permission and approval	**X**	**X**	
Data analysis	**X**		
Statistical analysis			
Interpretation of results			
Manuscript preparation and review	**X**	**X**	**X**

Abstract

Background:

Aims: To establish the Oral Medicine database of South Africa (ORMSA). The database will be used to determine the range and frequency of diagnoses of oral medicine pathology in the Oral Medicine and Periodontology Department of the University of the Western Cape

Methods: This is a cross-sectional, retrospective analysis of patients presenting to the Tygerberg, Mitchells Plain and Groote Schuur Oral Medicine Clinic from 1 January 2010-1 January 2022. Data was obtained from collating histopathological reports and from a review of patient's folders. A RedCAP® database was created to capture data and export data for further analysis on STATA 14 (StataCorp. 2015).

Results: A total of 2021 patients and 2085 biopsy specimens were added to the database. The average age of patients was 42.8 years with a standard deviation of 19.7 (range: 1 month-89 years). Of these; 1087/2021 (53.7%) were women and 786/2021 (38.9%) were male (male: female ratio 1:1.38). The five most observed oral conditions were fibroepithelial hyperplasia 397/ 2085 (19%), squamous cell carcinoma 285/ 2085 (13.7%), pyogenic granulomas 199/ 2085 (9.5%), mucoceles 175/ 2085 (8.4%) and benign human papilloma virus induced lesions 120/ 2085 (12.2%).

Conclusion: This study led to the creation of the REDCap®-based ORMSA database. We described the epidemiology of oral lesions in a setting with a relatively high patient volume The reported frequencies of the most prevalent diagnoses were similar to those found in studies from comparable populations, with minor variations. Further research could be conducted to determine risk factors associated with the diverse pathological diagnoses.

Keywords: Prevalence, oral medicine, database, oral pathology

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List of Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ARV	Antiretroviral
CHC	Chronic Hyperplastic Candidiasis
DIGO	Drug-induced gingival overgrowth
FNA	Fine needle aspiration
GSH	Groote Schuur Hospital
HPV	Human Papilloma Virus
HIV	Human Immunodeficiency Virus
LIS	Laboratory Information System
MFOS	Maxillofacial and Oral Surgery
MPOHC	Mitchell's Plain Oral Health Centre
NHLS	National Health Laboratory System
OAF	Oral-antral fistula
OM	Oral medicine
OMP	Oral Medicine and Periodontology
ORMSA	Oral Medicine Database of South Africa
PMD	Potentially Malignant Disorders
REDCAP	Research Electronic Data Capture
SCC	Squamous Cell Carcinoma
TB	Tuberculosis
TBOHC	Tygerberg Oral Health Centre
TUGSE	Traumatic Ulcerative Granuloma with Stromal Eosinophilia
UWC	University of the Western Cape
WHO	World Health Organization

CHAPTER 1: INTRODUCTION

Oral medicine (OM) is a dental specialty that comprises of the clinical diagnosis and treatment of patients presenting with medical conditions that impact the oral and maxillofacial region. It includes the oral health management of medically complex patients (Han et al., 2022). The patients often present with a variety of oral lesions that have variable prognosis, depending on their benign or malignant nature. Management of these patients often involve collaboration with in a multidisciplinary team, with the OM specialist being at the interface to co-ordinate the management (Han et al., 2022).

Various studies in the developing and developed world have reported on the spectrum of oral medicine pathology prevalence (Villa et al, 2015; Kashif et al, 2020), which range from 10.8-81.3%. In general, malignant tumours comprised a small portion of these lesions, despite, being the most extensively researched entity (Feng et al., 2015, Kovač-Kavčič and Skalerič, 2000, Espinoza et al., 2003, Campisi and Margiotta, 2001). These studies suggest that further epidemiological information is required because the reported prevalence rates of different oral mucosal disorders within studies varied significantly, depending on the geographic location, population, participants, age, gender etc. In addition, oral mucosal lesions may have been stratified by the various aetiologies, anatomical site of presentation or description (by colour or appearance). This lack of standardization, results in misrepresentation of the actual prevalence and presentation of lesions in the oral cavity (Kansky et al., 2018). Knowledge of the disease burden and associated risk factors is vital to inform teaching curricula and for strategic planning and policy development in South Africa.

The University of the Western Cape (UWC) is the only dental school in the Western Cape province, which provided oral medicine services.

There is a dearth of information with regards to the overall disease burden of oral mucosal lesions/ soft tissue pathology within the public sector. In addition, there is a lack of standardized clinical record forms and electronic platforms suitable for the management of this sensitive information. The primary intention of this thesis is to develop ORMSA (Oral Medicine Registry of South Africa) database, for clinicians and researchers to understand the disease burden, associated risk factors and trends for oral medicine lesions. The database could further also serve to provide vital information to health officials and policymakers for education, prevention and treatment programmes The second objective is to report on the spectrum and pattern of histological diagnoses from oral soft tissue pathology specimens from the OM clinics at UWC dental faculty [Tygerberg Oral Health Centre (TBOHC), Mitchell's Plain Oral Health Centre (MPOHC) and Groote Schuur Hospital (GSH)]

ORMSA will focus on diseases/conditions and oral soft tissue pathology (clinical and laboratory) diagnosed in a defined population (TBOHC, GSH and MPOHC catchment area) and managed within a specific tertiary health care resource setting which health professionals can capture data relating to patient demographics, medical health status, oral health status, geographical location and treatment outcomes. This could provide a platform to assess disease burden and trends in various populations and analyse associations.

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CHAPTER 2: LITERATURE REVIEW

Oral medicine (OM) is defined as a discipline of dentistry concerned with the oral healthcare of medically complex patients, and it includes the diagnosis and management of conditions that affect the oral and maxillofacial region (Cohen, 2013). Patients who present to an OM clinic can demonstrate a broad spectrum of benign, potentially malignant (PMD), and malignant conditions (Goutzanis, 2022). The Fifth World Workshop in Oral Medicine confirmed the core clinical competencies in OM, which include the management of oral mucosal diseases, salivary dysfunction, oral manifestations of dermatoses, HIV, gastrointestinal, and rheumatic disease, and facial pain (Stoopler et al., 2011). However, the exact scope of OM is geographic specific. In South Africa, the scope of oral medicine has been defined as the diagnosis and management of diseases, disorders and anomalies that affect the oral and periodontal tissues, as well as the oral and peri-oral manifestations of systemic diseases according to evidence-based practices. (Fourie and Masenge, 2022) Temporomandibular joint disorders, behavioural and mental health issues have not been included in the South African OM scope (Fourie and Masenge, 2022).

Obtaining a diagnosis in OM involves a systematic approach that includes a thorough medical history, dental history, clinical examination, and appropriate diagnostic tests (Glick, 2015). Diagnostic tests used include radiographs, biopsy, salivary tests, bacterial and viral cultures, or blood tests (Naikmasur et al., 2009). The gold standard of diagnosing pathology in OM is a biopsy and a histopathological examination of the suspected lesion is essential to establish a definitive diagnosis. (Logan and Goss, 2010, Melrose et al., 2007). Histological examination is important to also determine evidence of malignancy, provide information on the clinical behaviour of the lesion and to give prognostic information, which directly impacts patient management. (Logan and Goss, 2010)

There are several types of oral biopsy techniques, including incisional biopsy, excisional biopsy, punch biopsy, and brush biopsy. The choice of technique mainly depends on the size and location of the lesion, the accessibility of the area, and the clinician's preference (Marx and Stern, 2012). In an incisional biopsy, only a portion

of the lesion is removed for examination. This technique is preferred when the lesion is large or involves a critical structure. The specimen is usually obtained using a scalpel or a biopsy punch (Marx and Stern, 2012).

In an excisional biopsy, the entire lesion is removed for examination (Marx and Stern, 2012). This technique is preferred when the lesion is small, benign and easily accessible lesions. In a punch biopsy, a small cylindrical piece of tissue is removed from the lesion (Marx and Stern, 2012). This technique is useful in diagnosing deep-seated lesions or those involving bone. In a brush biopsy, cells are collected from the surface of the lesion using a brush (Marx and Stern, 2012). This technique is useful in diagnosing superficial lesions or lesions that are difficult to access with other biopsy techniques (Marx and Stern, 2012). Recent advancements in oral biopsy techniques have focused on improving the accuracy and efficiency of the procedure. One such advancement is the use of laser-assisted biopsies, and molecular techniques in the analysis of biopsy specimens, (Chakraborty et al., 2019, Naikmasur et al., 2009)

Fine needle aspiration (FNA) is a minimally invasive procedure used to obtain a tissue sample from a suspicious salivary gland lesion (Wu and Burstein, 2004). The workflow for the diagnosis of these neoplasms involves clinical evaluation, imaging studies, FNA, histopathological examination, and molecular testing (Sood et al., 2016). During FNA, a thin needle is inserted, under anaesthesia into the gland, and cells are aspirated for examination (Wu and Burstein, 2004).

The National Health Laboratory Service (NHLS) is the largest diagnostic pathology service in the country and plays a major role in providing laboratory services to all public sector healthcare providers (NHLS, 2012). It supports and conducts health research, provides training for health science education in collaboration with medical facilities at universities and universities of technology (NHLS, 2012). TrakCare is a laboratory information system (LIS) used by the NHLS. It was implemented as a standardized LIS to streamline laboratory processes and enhance service delivery (NHLS, 2008). DisaLab is a legacy LIS used by the NHLS (Stevens, 2018). The Corporate Data Warehouse (CDW), is a national repository for all public health

hospitals in South Africa and contains data from DISALAB and TrakCare (Perovic, 2015).

Our study utilized REDCap® as a real-time clinical database to capture patient characteristics, presentation, diagnosis and outcomes. REDCap® was developed by Vanderbilt University in 2004 (project.redcap.org). REDCap® is a secure web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources (Harris et al.,2009, Harris et al., 2019). The components of REDCap® include the data collection form (which is analogous to the case report form), the study database, a query and monitoring system and analysis software. The REDCap® instrument consists of an electronic data collection form- which is used to enter data directly into the database. The data quality component consists of a query and monitoring system. Rules were run depending on specifications (Harris et al., 2019).

Prevalence studies of oral pathology are utilized to understand the epidemiology of oral pathology (Kelloway et al., 2014), and form an integral component of evidence-based medicine (Erasmus and Zemlin, 2009). A clinical electronic database is a tool that can be used to capture epidemiological information; they are structured collections of clinical data that is electronically accessible and stored (Beynon-Davies, 2017). These large databases are housed on computer clusters or cloud storage, whilst smaller clinical databases can be stored on a file system. (Beynon-Davies, 2017) Clinical databases facilitate health care workers to make better-informed clinical decisions in a shorter period of time resulting in more accurate diagnosis and more effective treatment (Nzabonimana et al., 2019).

A Google Scholar, MEDLINE and PubMed search using the terms “South Africa”, “prevalence” and “oral pathology” did not reveal many relevant results. Most publications, were international publications that reported the prevalence of oral pathology; and assessed a specific condition or lesion and were based on clinical

surveys or screenings and confined to specific age groupings (Kelloway et al., 2014, Jones and Franklin, 2006a, Jones and Franklin, 2006b, Mendez et al., 2012, Monteiro et al., 2017, Sixto-Requeijo et al., 2012).

A Kuwaiti study of lesions over an 18-year period, found that the most common diagnostic category was mucosal pathologies 205/ 697 (29.4%), odontogenic cysts 158/ 697 (22.7%) and reactive lesions 97/ 697 (13.9%) (Joseph et al., 2019). The three most common histopathological diagnoses were hyperkeratosis 70/697 (10%), dentigerous cysts 48/ 697 (6.8%), and mucoceles 44/ 697 (6.3%) (Joseph et al., 2019). Twenty-five malignant neoplasms were diagnosed; the majority in males. A significant association was observed between the age of the patient and the diagnosis ($P \leq 0.001$). The greatest incidence of oral lesions was in adults (in the fourth decade) and malignant lesions were more common in patients >50 years (Joseph et al., 2019). The study found that the mean age per diagnostic category was (in years): malignant tumour (51), mucosal pathology (45), reactive lesions (40), connective tissue disease (40), dental pathology (36), bone pathology (34), odontogenic cysts (30), odontogenic tumour (24) years and salivary gland disease (28) (Joseph et al., 2019). In a Nigerian study of 242 biopsies lesions taken between 2016- 2021, it was found that most oral lesions were located peripherally or centrally on the mandible and were mainly benign. The most common benign lesion was ameloblastoma 35/ 242 (14.5%), whereas the most common malignant lesion was squamous cell carcinoma (SCC) 19/ 242 (7.8%) (Fakuade et al., 2022).

A 2014 South African Study included 1,258 biopsies of children <16 years in the Maxillofacial and Oral Surgery (MFOS) department (Munsamy et al., 2011). Of all maxillofacial pathologies, pathology affecting the jaw bones made up the largest group, with odontogenic cysts and tumours predominating (Munsamy et al., 2011). The remaining pathology affected the oral/perioral soft tissues, salivary glands, and oral mucosa, in decreasing order of frequency. Of all the cases, 4.1% were malignant neoplasms, with Burkitt's lymphoma being the most prevalent malignancy (Munsamy et al., 2011). In a 2022, self-administered survey of 26 OM specialists, in South African private and academic practice, respondents estimated the most frequently observed lesions in clinical practice, are immune-mediated diseases (oral lichen

planus, mucous membrane pemphigoid, pemphigus vulgaris, recurrent aphthae, and erythema multiforme) are most frequently managed lesions (29.3%), followed by benign reactive neoplasms (26.5%), such as traumatic fibroma, fibrous epulis and pyogenic granuloma. Respondents stated that chemosensory disorders, such as altered taste perception, account for 1.5%, and oral mucosal disease as the presentation of systemic disease, accounted for 2.5% of lesions and conditions (Fourie and Masenge, 2022).

The literature review has highlighted the dearth and variability of data, both within a global and within the SA context. There has been only one South African study to date, which focussed on maxillofacial pathology in patients <16 years. Thus, South African data is needed through locally-based population-based studies documenting comprehensive diagnosis of oral medicine pathology.

The primary intention of this mini dissertation is to develop a REDCap® database for recording OM conditions at clinics managed by UWC. A retrospective, prevalence study of oral conditions presenting to the OM clinic, will assist clinicians with differential diagnosis, specify the relative prevalence of oral pathology in a subset of a population and allow for extrapolation to a wider populace. Epidemiological information will also guide the academic curriculum and assist with health resource planning and allocation. The epidemiological findings will also contribute to strengthening public health prevention programmes and public health education on risk factors for lesions, such as squamous cell carcinoma, submucous fibrosis and erythroplakia.

CHAPTER 3: METHODS

3.1. Aims and Objectives

3.1.1 Study Aim

To establish a database, from histopathological and clinical information, and to determine of the range and frequency of oral medicine pathology (from the Oral Medicine and Periodontology Department of TBOHC, MPHC and GSH).

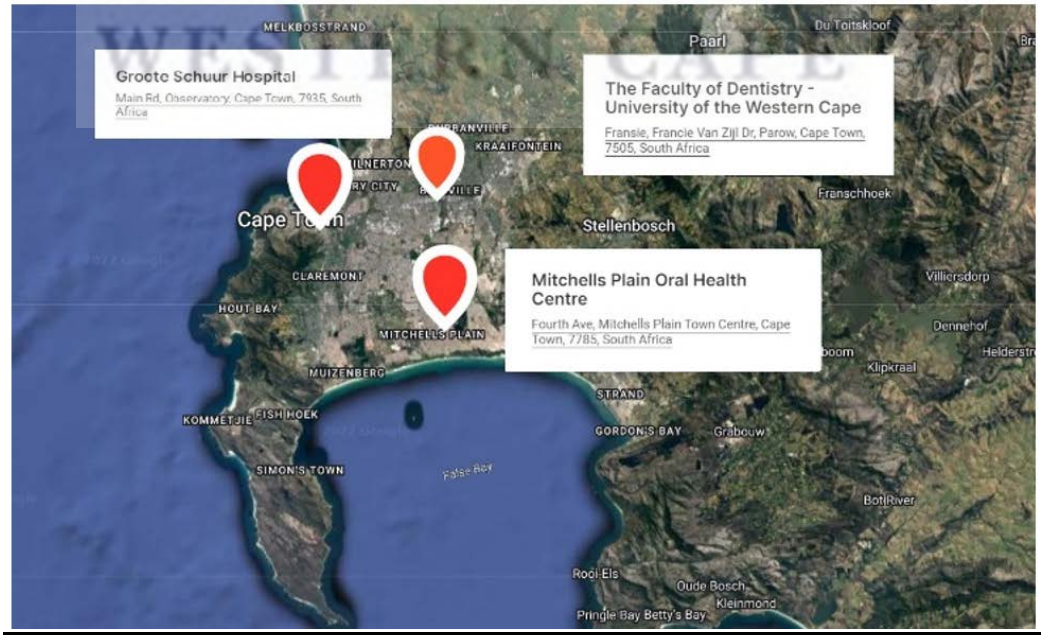
3.1.2 Study Objectives

1. To create a database which will record oral pathology
2. To provide an epidemiological description of oral medicine disease
3. To compare findings with similar studies

3.2 Study Design

This study made use of a retrospective cross-sectional analysis of patients presenting to the Oral Medicine and Periodontics Department from 1 January 2010-1 January 2022.

Figure 1: Map of the three sites included in the study, TBOHC, GSH and MPOHC



3.5 Sampling

We enrolled all consecutive patients, from whom biopsies were taken, at oral medicine postgraduate clinic between 1 January 2010-1 January 2022. Patient files that were located at the facilities and met the inclusion criteria, were included in the study.

3.3 Inclusion criteria

All histological reports submitted from the OM clinic of the Department of Oral Medicine and Periodontology to the NHLS, reporting clinical, histologic and epidemiological findings. Patient files that were located at the facilities and met the inclusion criteria, were included in the study. The study sites include: GSH, TBOHC and MPOHC; between 1 January 2010- 1 January 2022. The data of patients across irrespective of their race, age and gender were included in this study.

3.4 Exclusion criteria

Patients not meeting the inclusion criteria, duplicate entries and incomplete hospital records were excluded. These records were identified during the data collection process.

Database/registry creation and data collection and validation

Study data were collected and managed using REDCap® electronic data capture tools hosted at the University of the Western Cape. The REDCap® (Research Electronic Data Capture) platform was used to register the project, whereafter the online designer tool was used to customize the data capturing tools, as a collection of forms. These clinical case records were used to capture all the required data elements once role-based access was assigned to the researchers (TV, MA, RH). Input data was verified/crosschecked by HH.

Data Analysis

Data were exported in the Microsoft Excel format, which were imported into STATA 14 *(StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP)* for analysis. Data was cleaned before analysis. Descriptive statistics were used to summarize the epidemiology of oral specimens by person, place and time.

Overview of data management plan

1. **Data Collection**

The registry was populated by data obtained from the files oral medicine patients managed at the Oral Medicine Clinic and from laboratory reports obtained from the Corporate Data Warehouse.

2. **Ethics and Legal Compliance**

Ethics approval for the study was obtained from The University of the Western Capes Research and Ethics Committee (Appendix 1). Written permission to conduct this study, was obtained from the National Health Laboratory Services (Appendix 2) and the National Health Research Directorate (Appendix 3).

3. **Documentation and Metadata**

Use was made of a participant information leaflet (Appendix 4) which outlined the overview of the study for participants.

4. **Storage and Backup**

Data is stored on a password protected database hosted on a protected cloud server. User rights for the database are managed by ME, and role specific rights are granted to users.

5. **Selection and Preservation**

The data will be preserved for a minimum of 10 years and will be continued to be hosted on the secure UWC REDCap® server.

6. **Data Sharing**

Live data will only be accessible to TV, HH and ME. Other users may be included onto the database- and rights will be allocated according to the role of the user. Data will be disseminated in the form of journal articles and at academic conferences.

7. **Responsibilities**

The primary investigator TV, and supervisors HH, ME are primarily responsible for data management.

8. Resources

The project was self-funded. UWC's cloud storage servers were used to host the REDCap® database.

3.8 Ethical Approval

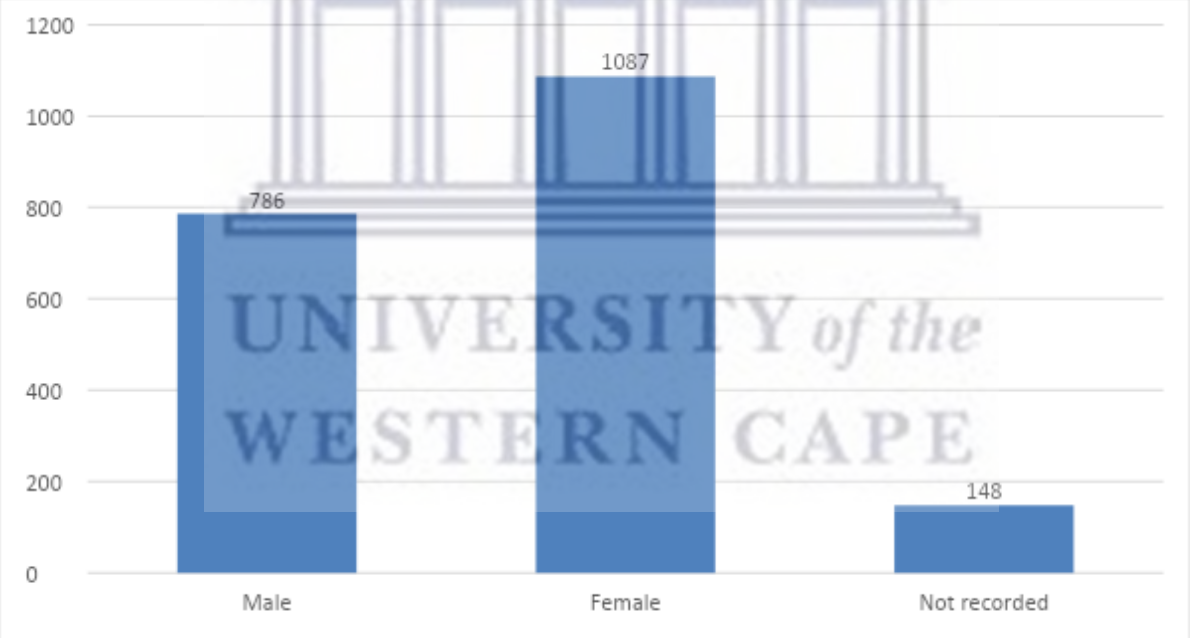
Ethical approval for the study was obtained from the University of the Western Cape's Research and Ethics Committee (BM21/6/25). Permission to access and utilize the histological reports was obtained from the National Health Research directorate and the National Health Laboratory Services (PR2225921).

CHAPTER 4:

RESULTS

A total of 2021 patients were included in this study, which was less than the total number of investigations (2085), indicating that in some cases more than one biopsy was taken for a patient. The average age of patients was 42.8 years with a SD of 19.7 (range: 1 month-89 years). In terms of distribution according to sex 1087/2021 (53.7%) were women and 786/2021 (38.9%) were men (male: female ratio 1:1.38). The average age for females was 42.7 ± 19.6 (SD), and the average age for males was 43.3 ± 20.3 (SD). A total of 148/2021 (7.3%) of patient's did not have sex recorded. Graph 1 shows the number of males, females and sex not recorded in the study. From the population; 1276/ 2021 (63.1%) of biopsies were taken at TBOHC, 545/ 2021 (26.9%) at GSH, and 200/ 2085 (9.9%) presented to MPOHC.

Figure 2: Males, females and sex not recorded in the study (N=2021)

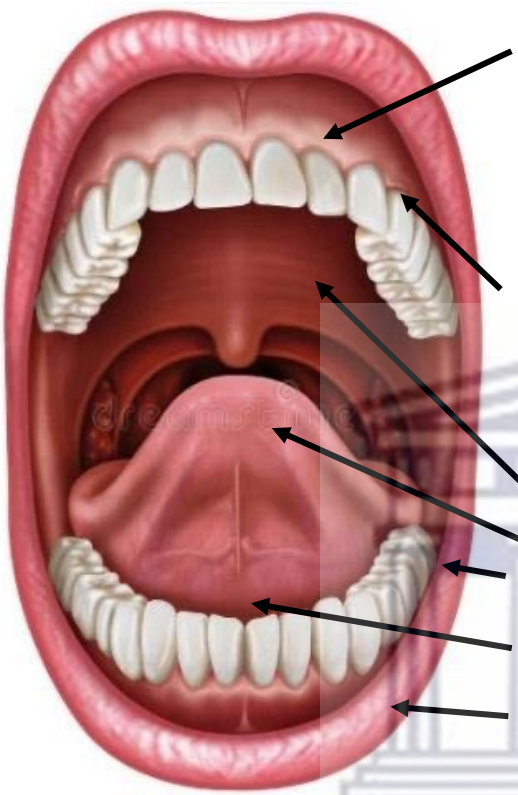


The most common biopsy technique was excisional biopsy 1283/ 2085 (61.5%), and other techniques were used for 804/ 2085 (38.5%) cases. The most frequent lesions observed were fibrous hyperplasia, 374/ 2085 of biopsies (17.9%); followed by SCC 284/ 2085 cases (13.6%). The third most common lesion was pyogenic granuloma 191/ 2085 (9.1%), followed by mucoceles, 167/ 2085 (8%). The prevalence of the diagnostic categories and their distribution is demonstrated in Table 1. The majority of OM conditions were classified as inflammatory/ reactive lesions, 1208/ 2085

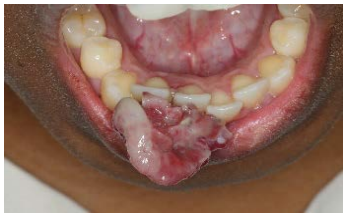
(57.9%). Epithelial and soft tissue neoplasms constituted 388/ 2085 (18.6%) of presentations and normal tissue was observed in 223/ 2085 (10.7%) of specimens. Inflammatory periapical lesions were found in 11/ 2085 (0.5%) of observations, developmental lesions 6/ 2085 (0.3%), and benign bone lesions 4/ 2085 (0.2%). The lesions were then classified according to diagnostic categories relevant to OM. The distribution of conditions was as follows: inflammatory and reactive lesions 1208/ 2085 (57.9%), epithelial and soft tissue neoplasms 388/ 2085 (18.6%), normal tissue 223/ 2085 (10.7%), potentially malignant 123/ 2085 (5.9%), autoimmune lesions 87/ 2085 (4.2%), odontogenic tumours, 54/ 2085 (2.6%), odontogenic cysts 24/ 2085 (1.2%), pigmented/ melanotic lesionsm16/ 2085 (0.8%), inflammatory periapical lesions 11/ 2085 (0.5%), developmental lesions 6/ 2085 (0.3%), and benign bone lesions 4/ 2085 (0.2%) (Table 1).

In our study, the gingiva 547/ 2085 (26.2%), the tongue 495/ 2085 (23.7%) and the buccal mucosa 326/ 2085 (15.6%) were the most frequently biopsied sites. The floor of the mouth was the least frequently biopsied site 31/ 2085 (1.5%) and 103/ 2085 (4.9%) of biopsies did not have a site specified. Figure 3 shows the distribution of biopsy sites in the sample.

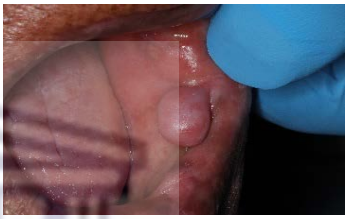
Figure 3: The intra-oral locations of biopsies taken (n = 2085)



A. Gingiva- (n=547) 26.2%



B. Buccal mucosa- (n=326) 15.6%



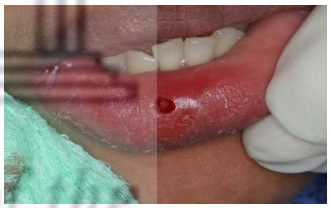
C. Palate: Hard- (n=86) 4.1%, Soft (n=36) 1.7%

D. Tongue- Lateral (n=180) 8.6%, dorsal (n=275) 13.2%, ventral (n= 40) 1.9%

E. Vestibule (n=112) 5.4%

F. Floor of the mouth (n=31) 1.5%

G. Lip (n=349) 16.7%



Unspecified: (n=103) 4.9%

* Stock image (Luengo, 2023) † Clinical pictures sourced from patients presenting to the Oral Medicine Clinic at the University of the Western Cape; who have consented for photographs.

Table 1: Distribution of the lesions according to diagnostic categories, N=2085

Diagnostic Category	No	%
Inflammatory/ Reactive lesions	1208	57.9
Epithelial and soft tissue neoplasms	388	18.6
Normal tissue	164	7.8
Potentially malignant lesions	123	5.8
Autoimmune lesions	87	4.2
Odontogenic tumours	54	2.6
Odontogenic cysts	24	1.2
Pigmented/ melanotic lesions	16	0.8
Inflammatory periapical lesions	11	0.5
Developmental lesions	6	0.3
Benign bone lesions	4	0.2
TOTAL	2085	100%

Benign lesions of the oral cavity accounted for 982/ 2085 (47%) of all biopsied lesions (Table 2). Fibroepithelial hyperplasia/ polyps accounted for 397/ 982 (40.3%), pyogenic granulomas 199/ 982 (20.3%), benign human papilloma virus (HPV) induced lesions 120/ 982 (12.2%), and peripheral odontogenic fibroma 27/ 982 (2.7%).

Table 2: Benign lesions of the oral cavity, N=982

Diagnosis	Total (n)	% group (n/N)	%total (n/2085)
Fibroepithelial hyperplasia/ polyp	396	40.3	13.7
Pyogenic granuloma	199	20.3	9.5
Total HPV induced lesions	120	12.2	5.7
Squamous papilloma's/ unspecified	*96*	*9.8*	*4.6*
Focal epithelial hyperplasia	*16*	*1.6*	*0.8*
Verruca vulgaris	*7*	*0.7*	*0.3*
Condyloma acuminatum	*1*	*0.1*	*0.05*
Lipoma	27	2.7	1.3
Peripheral odontogenic fibroma	27	2.	1.3
Traumatic fibroma	24	2.4	1.2
Ameloblastoma	20	2.0	1.0
Giant cell fibroma	22	2.2	1.1
Haemangioma	13	1.3	0.6
Pleomorphic adenoma	10	1.0	0.5
Kaposi's sarcoma	10	1.0	0.5
Benign giant cell tumours	8	0.8	0.4

Post extraction granuloma (granulation tissue)	7	0.7	0.3
Neurofibroma	7	0.7	0.3
Traumatic Ulcerative Granuloma with Stromal Eosinophilia	7	0.7	0.3
Peripheral ossifying fibroma	6	0.6	0.3
Benign vascular neoplasms	5	0.5	0.2
Fibro- osseous lesions	5	0.5	0.2
Leiomyoma	5	0.5	0.2
Cemento-ossifying fibroma	4	0.4	0.2
Melanotic macule	4	0.4	0.2
Oral focal mucinosis	4	0.4	0.2
Three occurrences of the following lesions were observed: Canalicular adenoma, Denture fissuratum, Lymphangioma, Granular cell tumour, Melanotic hyperplasia, Fibromatosis	18	1.8	0.9
Two occurrences of the following lesions were observed: Osteoma, Melanocytic naevus, Odontoma, Oral focal granulomatosis, Cemento osseous dysplasia, Fibrous dysplasia,	22	2	1.0

pigmented incontinence, amalgam tattoo, drug induced gingival overgrowth, Odontogenic myxoma, Traumatic neuroma			
One occurrence of the following lesions was observed: Verruciform xanthoma, Schwannoma, Basal cell adenoma, Benign mesenchymal neoplasm, Myoepithelioma, Smooth muscle neoplasm, Osseous choristoma, Peripheral dentinogenic ghost cell tumour, Hematoma, Graphite tattoo, Frictional keratosis, Basaloid salivary gland neoplasm	12	1.2	0.5
TOTAL	982	100%	47.1%

There were 330/ 2085 (15.8%) malignant lesions of the oral cavity. The majority of malignant lesions were SCC 285/ 2085 (13.7%) of the total biopsies and 285/ 330 (86.4%) of all malignant lesions. Lymphomas accounted for 12/ 330 (3.6%) and adenoid cystic carcinomas accounted for 7/ 330 (2.1%) of all malignant lesions. Table 3 shows a breakdown of the most observed malignant lesions of the oral cavity.

Table 3: Malignant lesions of the oral cavity, n=330

Diagnosis	Total (n)	% group (n/N)	%total (n/2085)
Squamous cell carcinoma	285	86.4	13.7
Lymphomas	12	3.6	0.6

Adenoid cystic carcinoma	7	2.1	0.3
Seborrheic keratosis	5	1.5	0.2
Polymorphous low-grade adenocarcinoma	5	1.5	0.2
Basal cell carcinoma	4	1.2	0.2
Clear cell carcinoma	3	0.9	0.1
Carcinoma in situ	2	0.6	0.1
Mucoepidermoid carcinoma	2	0.6	0.1
One occurrence of the following lesions was observed: Malignant melanoma, Malignant epithelial neoplasm, Osteosarcoma, Sarcoma, Verrucous carcinoma	5	1.5	0.2
TOTAL	330	100%	15.8%

There were 123/ 2085 (5.9%) lesions that could be classified as PMDs, utilizing the recommended definitions from the 2020 WHO Consensus report on the nomenclature and classification of oral PMDs. (Warnakulasuriya et al., 2021) Of these, 81/ 123 (65.9%) of specimens were classified as oral lichenoid disorders. Dysplastic lesions accounted for 18/ 123 (14.6%) of pathology. Of these; moderate epithelial dysplasia accounted for 10/123 (8.1%), severe epithelial dysplasia 5/ 123 (4%) and mild epithelial dysplasia 3/ 123 (2.4%). Table 4 provides a breakdown of lesions identified as PMD.

Table 4: Potentially malignant disorders, n= 123

Diagnosis	Total (n)	% group (n/N)	%total (n/2085)
Oral Lichenoid Disorders	81	65.9	3.9
Chronic hyperplastic candidiasis	12	9.8	0.6
Moderate epithelial dysplasia	10	8.1	0.5
Actinic keratosis	9	7.3	0.4
Severe epithelial dysplasia	5	4.1	0.2
Mild epithelial dysplasia	3	2.4	0.1
One occurrence of the following lesions was observed: Erythroplakia, Erythroleukoplakia, Proliferative Verrucous Leukoplakia	3	2.4	0.1
TOTAL	123	100%	5.9%

There were 235/ 2085 (11.3%) lesions that were classified as cysts of the jaw and oral tissue. Of this 175/ 235 (74.5%) were mucoceles, 11/ 235 (4.7%) were radicular cysts, 8/ 235 (3.4%) were ranulas and there were 8/ 235 (3.4%) unspecified odontogenic cysts of inflammatory origin.

Table 5: Cysts of jaw and oral tissue, n= 235

Diagnosis	Total (n)	% group (n/N)	%total (n/2085)
Mucoceles	175	74.5	8
Radicular cyst	11	4.7	0.5
Ranula	8	3.4	0.4
Odontogenic cyst of inflammatory origin with no further specification	8	3.4	0.4
Non-specific cyst	6	2.6	0.3
Odontogenic keratocyst	5	2.1	0.2
Epidermoid cyst	4	1.7	0.2
Dentigerous cyst	3	1.3	0.1
Two occurrences of the following lesions were observed: Traumatic bone cyst, Nasopalatine duct cyst, Epidermal inclusion cyst, Lateral periodontal cysts	8	3.4	0.4
One occurrence of the following lesions was observed: Dermoid cyst, Residual cyst, Eruption cyst, Inflammatory cyst, Paradental cyst, Pseudocyst, Salivary duct cyst	7	3.0	0.3

TOTAL	235	100%	11.3%

There were 175/ 2085 (8.4%) inflammatory lesions. Non-specific ulcers accounted for 67/ 175 (38.3%) of inflammatory lesions, 33/ 175 (18.9%) were chronic inflammation and 12/ 165 (6.9%) were classified as subacute inflammation.

Table 6: Inflammatory disease and autoimmune disease, n=175

Diagnosis	Total (n)	%group (n/N)	%total (n/2085)
Non-specific ulcer	67	38.3	3.2
Chronic Inflammation	33	18.9	1.6
Subacute inflammation	12	6.9	0.6
Periapical granuloma	9	5.1	0.4
Oral soft tissue abscess	8	4.6	0.4
Trauma (Unspecified)	7	4.0	0.3
Sialadenitis	6	3.4	0.3
Granulomatous inflammation	5	2.9	0.2
Inflammatory papillary hyperplasia	5	2.9	0.2
Ductal ectasia	5	2.9	0.2
Mucositis	4	2.3	0.2
Acute osteomyelitis	3	1.7	0.1
Erythema multiforme	3	1.7	0.1
Pemphigus vulgaris	3	1.7	0.1

One occurrence of the following lesions was observed: Blood clot, Stomatitis, Plasma cell mucositis, oral antral fistula, Acinar atrophy	5	2.9	0.2
TOTAL	175	100%	8.4%

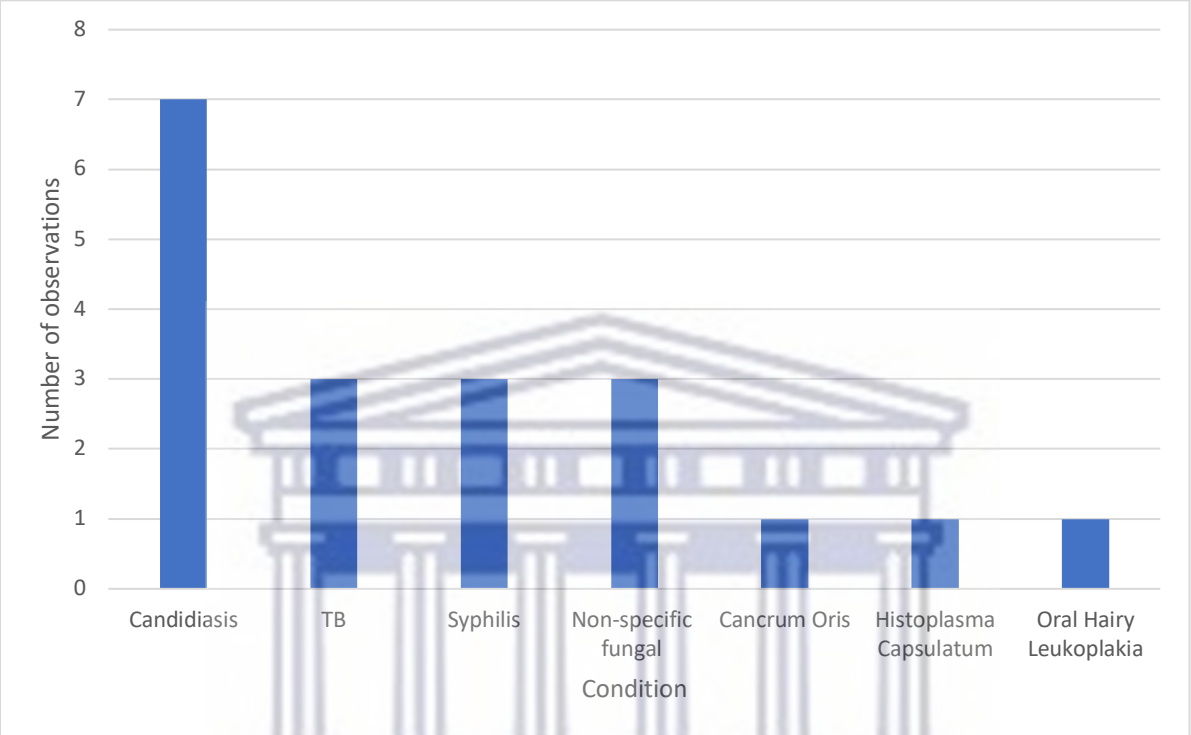
There were 164/ 2085 (7.8%) normal mucosa and non-diagnostic specimens. Of this, 110/ 164 (67.1%) had a non-specific histology. There were 36/ 164 (21.9%) lesions that were classified as normal, and 18/ 164 (11%) had no results.

Table 7: Normal mucosa/ non diagnostic specimen/ unspecified

Diagnosis	Total (n)	%group (n/N)	%total (n/2085)
Non-specific histopathological findings	110	67.1	5.3
Acanthosis	*46*	*28.0*	*2.2*
Hyperkeratosis	*43*	*26.2*	*2.1*
Parakeratosis	*11*	*6.7*	*0.5*
Hyperorthokeratosis	*5*	*3.0*	*0.2*
Acantholysis	*3*	*1.8*	*0.1*
Necrosis	*2*	*1.2*	*0.1*
Normal	36	28,0	2.2
No results- Non diagnostic specimen	18	21,3	1.7
TOTAL	164	100%	10.6%

There were 19/ 2085 (0.9%) biopsies- classified as 'other'. These lesions were bacterial, viral or fungal. From this 7/ 19 (36.8%) were candida, 3/ 19 (15.8%) were TB oral lesions, 3/ 19 (15.8%) were syphilitic and 3/ 19 (15.8%) were non-specific fungal lesions.

Figure 4: Bar graph showing other unclassified lesions, N=19



CHAPTER 5: DISCUSSION

During the 12-year period, 2085 specimens were processed by the OM department at three surveillance sites (averaging: 174 specimens/ year). This indicated that a high volume of oral biopsies was submitted to a diagnostic pathology service within the study period when compared with another study (64 specimens/ year) (Goutzanis, 2022). The rate was similar to a University of Queensland Oral Pathology study of 1, 0130 pathology specimens over 58 years (174 specimens/ year) (Ha et al., 2014). The study found that mucosal pathology was the most common pathology (37.2%), followed by odontogenic cysts (16.3%) and dental pathology (14.5%) (Ha et al., 2014). Queensland shares a similar population number and growth to the Western Cape. (Ha et al., 2014) (Statistics South Africa, 2022) The male to female ratio (1.38:1) of the study is comparable to a study of 44, 007 biopsies over a 30-year period in the UK (Franklin and Jones, 2006), a 2022 study of 545 biopsies in Greece (Goutzanis, 2022) and an analysis of 672 specimens in Spain (Sixto-Requeijo et al., 2012). We found a higher frequency of lesions in women, which is due to there being more women in our population.

The average age was 42.8 years with a SD of 19.7 (range: 1 month-89 years), and included children and thus differed from other studies, which excluded patients from different age categories. Some studies did not include patients <17 years (Franklin and Jones, 2006) and some only included the elderly (Souza et al., 2015). Other studies focused on paediatric patients (Sousa et al., 2002, Shulman, 2005). Nor have we focused on a particular condition or location, as in other studies (Buchner et al., 2010).

A total of 43 records were omitted from the study due to missing clinical data, and due to missing records on TrakCare. A South African study concluded that incomplete and missing records are an obstacle to record-based research as they compromise the validity and reliability (Mthethwa and Matjila, 2019). The availability of complete records plays a crucial role in oral biopsy prevalence studies (Charangowda, 2010). They provide accurate patient identification, a comprehensive medical history, assessment of risk factors, facilitate longitudinal monitoring, and enhance data

analysis. By ensuring the availability of complete dental records, researchers can improve the reliability and validity of their findings, leading to a more comprehensive understanding of oral conditions and their prevalence. (Charangowda, 2010)

In our study, the gingiva 547/ 2085 (26.2%), the tongue 495/ 2085 (23.7%) and the buccal mucosa 326/ 2085 (15.6%) were the most frequently biopsied sites. A 10-year retrospective study in India, found that the tongue was the most common site of oral lesions (18.8%), followed by the lips (15.9%) and floor of the mouth (15.5%) (Mohan and Padmakumar, 2017). Another study highlighted that the gingiva is a common site for many diseases affecting oral health, with the majority of gingival lesions being inflammatory (Montazer Lotf-Elahi et al., 2022). The floor of the mouth was the least frequently biopsied site 31/ 2085 (1.5%). The floor of the mouth is an anatomically difficult region to biopsy, and these lesions are often referred to the UWC MFOS department.

Inflammatory and reactive lesions comprised 1208/ 2085 (57.9%) of all lesions. Due to the frequent tissue damage, reactive lesions are frequently seen in the oral cavity. Systematic reviews or meta-analyses were not found on the prevalence of conditions falling into diagnostic categories. Weir et al. in the US conducted a review of 15,783 oral lesions over a period of 17.5 years and discovered that fibromas, periapical granulomas, mucoceles, and radicular cysts were the most prevalent reactive lesions seen in the oral cavity. In the study; 77% of observed lesions were inflammatory or reactive (Weir et al., 1987). In a Turkish study, inflammatory hyperplastic lesions constituted 1,000/ 1,198 (57.7%) of all lesions. Our proportion of inflammatory and reactive conditions to the total sample was similar to other studies.

Epithelial and soft tissue neoplasms accounted for 388/ 2085 (18.6%) of cases. This was markedly more than 9/ 231 (3. 9%) found in two Saudi Arabian teaching hospitals (Qannam and Bello, 2016) and 106/ 1218 (8.7%) (Alhindi et al., 2019). This could be explained by differences in the interpretation of the classification category. Normal tissue 164/ 2085 (7.8%) and autoimmune lesions were found in 87/ 2085 (4.2%) of presentations. The prevalence of oral mucosal involvement in immune-mediated

disorders varies according to the type of disease. Studies show that oral lichen planus is the most common immune-mediated disorder affecting the oral cavity, followed by pemphigus vulgaris and mucous membrane pemphigoid (Arisawa et al., 2008, Carvalho et al., 2011, Gonçalves et al., 2010, Jaafari-Ashkavandi et al., 2011, Leao et al., 2008). Interestingly, oral medicine specialists estimate that autoimmune disorders are managed most frequently (29.3%) in their clinics, followed by benign reactive neoplasms (26.5%) (Fourie and Masenge, 2022). We found that autoimmune disorders accounted for 4.2% and reactive lesions accounted for 57.9% of oral lesions. There are many possible reasons for this discrepancy including the inclusion of private practice experiences, recall bias and regional variations in pathology and regional referral patterns.

There are significant regional differences in the prevalence of odontogenic tumours. While they comprise 1% of all oral pathology in North America, it is as high as 19% in African countries (Regezi et al., 1978, Olaitan et al., 1993). Odontogenic cysts amounted to 24/ 2085 (1.2%) of oral pathology. The reported prevalence rates of odontogenic cysts in different populations range from 3.45%- 54.6% (Açikgöz et al., 2012, Johnson et al., 2014). It is important to note that the reported prevalence rates of odontogenic cysts may not reflect the true prevalence, as many lesions are diagnosed based on clinical and radiological information rather than histopathological (Ruslin et al., 2022). Additionally, the prevalence of odontogenic cysts may vary depending on the geographic location and ethnicity of the population studied (Katheriya, 2021, Mello et al., 2019).

Pigmented/ melanotic lesions accounted for 16/ 2085 (0.8%) of oral conditions. The finding is similar to a retrospective cross-sectional study conducted in Thailand, where oral pigmented lesions were found in 241/ 45175 (0.5%) of lesions diagnosed over a 20-year period (Dhanuthai et al., 2022). Another Jordanian study found that over a one-year period; oral pigmented lesions were present in 386/ 1275 (30.2%) patients (Hassona et al., 2016). The relative low number of inflammatory periapical lesions 11/2085 (0.5%), developmental lesions 6/ 2085 (0.3%), and benign bone lesions 4/2085 (0.2%) can be attributed to the fact that these lesions are generally managed by the MFOS discipline at the faculty.

The majority of diagnoses were benign 982/ 2085 (47.1%). Fibroepithelial hyperplasia/ fibroepithelial polyps were the most common lesions with 396/ 982 (40.3%). Fibroepithelial hyperplasia was the most common diagnosis, a finding similar to two other studies that assessed at the range and frequencies of histologically diagnosed oral lesions (Wan and Savage, 2010, Monteiro et al., 2017). Malignant lesions accounted for 330/ 2085 (15.8%) of all biopsied lesions. SCC was the most common malignancy of the oral cavity, appearing mostly on the tongue and lower lip. In our study SCC amounted to 285/ 330 (86.4%) of all malignant lesions (13.7% of total). This was higher than in other studies where SCCs accounted for 2% of all specimens (6/ 306 specimens) (Mujica et al., 2008), 5.4% in 2675 samples (Skinner et al., 1986), 1% in 205 samples. SCCs accounted for a greater percentage of all malignancies than other studies (66.1%) (Franklin and Jones, 2006).

In oral conditions that can be termed as potentially malignant; oral lichen planus and oral lichenoid reactions were grouped together as oral lichenoid diseases (OLD) (Cortés Ramírez et al., 2009, Aguirre Urizar, 2008). OLDs accounted for 81/ 123 (65.9%) of PMDs and 81/ 2085 (3.9%) of the total. This finding is similar to 3.5% found in 12068 participants of the Northern Finland Birth Cohort (Oivio et al., 2020). A major controversy surrounding chronic hyperplastic candidiasis (CHC) is whether this oral lesion has a malignant transformation potential (Lorenzo-Pouso et al., 2022). We classified CHC as a PMDs due to its inclusion in the 2017 World Health Organization (WHO) classification of head and neck tumours. (Grandis and WHO, 2017). However, the WHO 2020 working group for oral cancer did not include CHC for inclusion within the PMDs due to its insufficient evidence for malignant potential (Zhang et al., 2021). CHC was found in 12/ 123 (9.8%) of PMDs and 12/ 2085 (0.6%) of all biopsies. This finding is similar to 0.5% obtained from a Chinese cohort study of patients seen over a 6-year period. (Zhang et al., 2021)

The combination of cytological and architectural defects that suggest a potential for malignant transformation constitutes the histological diagnosis of epithelial dysplasia, (Speight, 2007). Although epithelial dysplasia is not considered a malignancy, it is a

PMD. It was found that 18/ 2085 (1%) of biopsy specimens were dysplastic. From these: moderate epithelial dysplasia accounted for 10/ 2085 (0.5%), severe epithelial dysplasia 3/ 2085 (0.1%) and mild epithelial dysplasia 3/ 2085 (0.1%).

Mucoceles represent the most diagnosed condition within the category of 'Cysts of the jaw and oral tissue'- with 175/ 235 (74.5%) and 175/ 2085 (8.6%) of all patient's observed. Similar findings were reported from a 2007, Thai study of paediatric biopsy specimens, which found mucoceles in 169/ 1251 (13.5%) of biopsy specimens (Dhanuthai et al., 2007). Several studies have reported that in the category of inflammatory/reactive lesions is the most common category with mucocele being the most frequently encountered oral lesion (Sousa et al., 2002, Jones et al., 2006, Skinner et al., 1986). Radicular cysts accounted for 9/ 2085 (3.8%) of jaw cysts. This was substantially lower than a Turkish prevalence study, which found that radicular cysts were the most biopsied lesion 216/ 475 (45.5%), followed by dentigerous cysts 77/ 475 (16.2%) (Hosgor et al., 2019).

Non-specific ulcers accounted for 67/2085 (3.2%), chronic Inflammation tallied 33/2085 (1.6%) and subacute inflammation 12/2085 (0.6%), respectively. This was less than another study where normal tissue accounted for 9% of the biopsies (Das and Das, 1993). Non-specific histological results 110/ 2085 (5.3%). There were 18/ 2085 (0.8%) nondiagnostic specimens. Reasons for non-diagnostic samples include: sampling errors (tissue that is not an accurate representation of the entire lesion); insufficient diagnostic material; the presence of obscuring inflammation; artifacts; and diagnostic (pathologist) discordance (different pathologists assigned for examination and final resection with different thresholds for diagnosing dysplastic and cystic lesions). (Chen et al., 2016)

Of the bacterial, viral and fungal infections: candidiasis accounted for 7/ 19 (36.8%) of cases, tuberculosis (TB) 3/ 19 (15.8%), 3/ 19 syphilis cases (15.8%) and 3/ 19 (15.8%) non-specific fungal diagnoses. The number of biopsied candida lesions may be an underrepresentation of the true prevalence of candida lesions in the population,

due to the fact that lesions are not always investigated using special tests and more likely to be sent for exfoliative cytology.

It must be mentioned that distinguishing extra-osseus from intra-osseus pathologies in some instances were a challenge, given the nature of clinical data / reporting and the processing of specimens. Creating an oral medicine specific database would thus help to ensure that future epidemiologic studies include pathology managed by the oral medicine department.

CHAPTER 6: LIMITATIONS

A constraint of the study was sample generalizability and representativity, which must be taken into consideration while analysing the study's results. During the study, we discovered that specimens from the MPOHC were grouped together with specimens from TBOHC, due to logistical arrangements. We thus could not differentiate specimens sent from MPOHC and TBOHC. We were not able to access files from all patients who attended the MPOHC and GSH OM clinic. We also excluded oral pathology diagnosed by other departments, other facilities and private facilities in the region. We reported on oral pathology that may lie outside the scope of OM in South Africa. This may be due to specimens from MFOS and OM that were sometimes pooled together.

The dental faculty keeps files for a period of five years; thereafter files are discarded- thus it was impossible to capture records of all patients who presented at the sites. Additionally, due to incomplete and missing data, patient files were excluded from the research during the data gathering procedures. These factors affect the generalizability and representativity.

Direct comparisons of the prevalence of patients presenting with lesions to an OM clinic are difficult due to regional differences in classifications of lesions, and differences in the scope or OM practitioners and MFOS practitioners. Despite all of these drawbacks, the results of this study are consistent with other research projects carried out globally to describe the epidemiology of oral conditions presenting in OM clinics.

It is important to note that the current study reflects the burden of disease as it relates to oral mucosal biopsies, and excludes the burden due to oral mucosal pathologies not subjected to biopsy. Nevertheless, the relatively small number of these (>100/2035) are unlikely to have skewed the results.

CHAPTER 7:

CONCLUSION

This study sought to design a REDCap®-based ORMSA database to facilitate an understanding of the epidemiology of oral lesions in a setting with a relatively high volume of patients. Pilot results of biopsied lesions indicate that the majority of diagnoses were benign and inflammatory/reactive in nature. The reported frequencies of the most prevalent diagnoses were similar to those found in studies from comparable populations, with minor variations. Further research could be conducted to determine risk factors associated with the diverse pathological diagnoses.

In summary, this study advocates implementing the routine use of the REDCap® based ORMSA record system and computerizing patient records, to enhance the department's record-keeping process. It further recommends the minimum set of variables required to provide a clinic-pathological derived diagnosis. Thus, ORMSA will be a valuable resource that can be used to describe the epidemiology of oral lesions in other OM facilities in South Africa and we wish to expand the scope of the project to cover a larger catchment area.

Appendix 1: Modification of WHO 2017 Classification of Head and Neck Tumours

Inflammatory/ Reactive lesions	Squamous papilloma, pleomorphic adenoma, monomorphous tubular adenoma, sialadenoma papilliferum, cemento-ossifying fibroma, giant cell fibroma, fibroepithelial hyperplasia/ polyp/epulis, denture fissuratum, traumatic fibroma, lipoma, leiomyoma, angioleiomyoma, haemangioma, pyogenic granuloma, post extraction granuloma, lymphangioma, venous lake, granular cell tumour, melanocytic naevus, melanotic macule, ameloblastic fibroma, odontoma, central and peripheral giant cell granuloma, peripheral odontogenic fibroma, peripheral ossifying fibroma, focal epithelial hyperplasia, verruca vulgaris, condyloma acuminatum, haematoma, verruciform xanthoma, actinic keratosis
Epithelial and soft tissue neoplasms	Carcinoma in situ, oral squamous cell carcinoma, primary intraosseous squamous cell carcinoma, oral carcinoma cuniculatum, acinic cell carcinoma, clear cell carcinoma, aggressive osteoblastoma, embryonal rhabdomyosarcoma, undifferentiated carcinoma, benign vascular neoplasms, neurofibroma, Kaposi's sarcoma, oral focal mucinosis, schwannoma, canalicular adenoma, fibromatosis, basal cell adenoma, myoepithelioma
Normal tissue	No histological abnormalities noted
Inflammatory periapical lesions	Periapical granuloma, periapical abscess, periapical scars, cemento osseous dysplasia

Odontogenic tumours	Benign Odontogenic Tumours: Epithelial Origin- 1-Ameloblastoma, conventional 2-Ameloblastoma, unicystic type 3-Ameloblastoma, extraosseous/ peripheral type 4-Metastasizing (malignant) ameloblastoma 5-Squamous odontogenic tumour 6-Calcifying epithelial odontogenic tumour 7-Adenomatoid odontogenic tumour Mesenchymal Origin- 1-Odontogenic fibroma 2-Odontogenic myxoma/myxofibroma 3-Cementoblastoma ossifying fibroma-Cemento-4 Mesenchymal) Origin-Mixed Epithelial- 1-Ameloblastic fibroma 2-Primordial odontogenic tumor 3-Odontomas (and ameloblastic fibro-odontoma) 4-Compound type 5-Complex type 6-Dentinogenic ghost cell tumor Malignant Odontogenic Tumours 1-Ameloblastic carcinoma 2-Primary intraosseous carcinoma, NOS 3-Sclerosing odontogenic carcinoma 4-Clear cell odontogenic carcinoma 5-Ghost cell odontogenic carcinoma 6-Odontogenic carcinosarcoma 7-Odontogenic sarcomas
Odontogenic cysts	Radicular cyst, dentigerous cyst, residual cyst, periapical cyst, odontogenic keratocyst, calcifying odontogenic cyst, eruption cyst
Benign bone lesions	Osteoid osteoma, simple bone cyst, osteochondroma, fibrous dysplasia, eosinophilic granuloma, osteoblastoma, chondroblastoma, aneurysmal bone cyst, fibro-osseous lesions, choristoma, peripheral dentinogenic ghost cell tumour

Pigmented/ melanotic lesions	Amalgam/ graphite/ lead, melanotic macule, nevus, malignant melanoma, post inflammatory pigmentation, physiological pigmentation, smokers melanosis, HIV associated, Albright's, Petuz Jeghers syndrome
Autoimmune lesions	Behcet's disease, Pemphigus, Pemphigoid, Rheumatoid arthritis, Sjogren's syndrome, Systemic Erythematous Lupus, Discoid Lupus Erythematosus
Developmental lesions	Dentigerous cyst, eruption cyst, gingival cyst, lateral periodontal cyst, calcifying odontogenic cyst, glandular odontogenic cyst
Other	Not otherwise specified
Non-diagnostic specimen	Specimens cannot be processed due to clinical or processing errors.

Appendix 2: University of the Western Cape ethics approval

UNIVERSITY of the WESTERN CAPE

60 YEARS of hope, action & knowledge

12 October 2021

Dr TA Vedan and Dr H Holmes
Oral Medicine and Periodontology
Faculty of Dentistry

Ethics Reference Number: BM21/6/25

Project Title: Design of the Oral Medicine South Africa registry to facilitate surveillance of oral medicine lesions and conditions in SA: Pilot results (2010-2020).

Approval Period: **12 October 2021 – 12 October 2024**

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project and the requested amendment to the project.

Any further amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report annually by 30 November for the duration of the project.

For permission to conduct research using student and/or staff data or to distribute research surveys/questionnaires please apply via:
https://sites.google.com/uwc.ac.za/permissionresearch/home

The permission letter must then be submitted to BMREC for record keeping purposes.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

NHREC Registration Number: BMREC-130416-050

FROM HOPE TO ACTION THROUGH KNOWLEDGE.

Appendix 2: National Health Laboratory Services Ethical Approval

NATIONAL HEALTH LABORATORY SERVICE

Academic Affairs and Research
Modderfontein Road, Sandringham, 2031
Tel: +27 (0)11 386 6155
Fax: +27 (0)11 386 6296
Email: babatyi.kgokong@nhls.ac.za
Web: www.nhls.ac.za

05 July 2022

Applicant: Theesan Vedan
Institution: University of Western Cape
E-mail Address: theesanvedan@gmail.com
Cell: 071 188 5909

Project Title: Prevalance of oral soft tissue lesions seen at UWC dentistry oral medicine clinics (2010-2021) and design of the ORMSA registry to facilitate surveillance and trends of oral medicine
Reference Number: PR2225921

Research Application Type(s):
1. Request for Data

RE: APPROVAL LETTER: REQUEST TO ACCESS NHLS RESOURCES FOR RESEARCH PURPOSES

This letter serves to advise that the application requesting permission to conduct the above-mentioned research using the listed NHLS resources has been reviewed and **"Approved"**. Please note that the approval is granted on the condition that you comply with the NHLS Research Material and Data Access Policy and requirements stated below.

1. All material and data requested shall be used as per the research protocol submitted to the NHLS and as approved by the relevant Health Research Ethics Committee (HREC) in South Africa.
2. Access to the NHLS material and/or data shall be limited to the minimum required for successful completion of the approved study and shall be made available ***without patient names***.
3. Confidentiality shall be maintained at the participant and institutional level and there shall be no disclosure of personal information or confidential information.
4. The material and/or data obtained from the NHLS shall be anonymised and not, for any reason, be used to track or recruit patients as no pre-approval/consent is obtained from patients.
5. Processes shall be discussed with the relevant NHLS departments (i.e. Corporate Data Warehouse (CDW), NHLS Laboratory Management, Operations Office, etc.) and agreed upon.
6. Any amendments to the study requirements, including the use of the material and/or data for purposes not initially disclosed to the NHLS) shall be cleared by an approved HREC and submitted to the NHLS for approval via the AARMS system – https://aarms.nhls.ac.za.
7. The NHLS shall be acknowledged as a source of material and/or data in any output, such as abstracts and journal articles, emanating from the project.
8. A final report of the research study and any published output resulting from this study shall be submitted to the NHLS via AARMS

Please note that this letter constitutes approval by the NHLS Academic Affairs and Research Office. The NHLS entities tasked with providing the material and/data may have additional requirements for access. Data related queries may be directed to NHLS CDW, email: zarina.sabat@nhls.ac.za; contact number: 011 386 6074 and sample related queries (if applicable) shall be directed to the relevant business manager.

pp. Dr. Babatyi Malope-Kgokong

Dr Babatyi Malope-Kgokong 05/07/2022
National Manager: Academic Affairs and Research

Appendix 3: National Health Research Database Ethics Approval

Appendix 4: Participant Information Leaflet

ORMSA

UNIVERSITY of the WESTERN CAPE

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

Protocol for the design of the ORMSA registry and a retrospective audit of clinical oral mucosal lesions presenting to the department of Oral Medicine and Periodontology

To be signed by:	All participants who are 18 years or older at enrolment or turn 18 years during the follow-up period. Participants should be contacted leading up to their 18th birthday to be re-consented.
Note:	All participants < 18 years but ≥ 7 years or capable of understanding the informed consent process must sign an **assent form for minors.**

What are we doing?

We are collecting information about people attending the Department of Oral Medicine and Periodontics.

Why am I reading this document?

We would like your permission to collect and store some information from you.

What are we asking of you?

- We would like to copy the results of any hospital tests carried out as part of your normal care, for example special pictures of your mouth.
- We think in the future this could teach us more about caring for our patients.

What is the *ORMSA Registry*?

- It is a special place where we keep information from people who attended the Department of Oral Medicine and Periodontology
- Only specific people are allowed to see that information.
- You will **not** be asked to pay to for having your information stored, and similarly you will get **no** money if you agree to having the information stored.

What will we do with your information?

- Your information will be stored, together with information from other patients who attended the Department of Oral Medicine and Periodontics.
- Your information will be used to help us understand more about how to manage patients and treat disease in the future.
- We would like to keep your information for 15 years.

Who will see the information you give us?

- Your information will only be shared with those working on the ORMSA Registry.
- We may share some of the information (without any of your personal details) with other scientists for future investigations into how to help the prevention and treatment of disease.

ORMSA

- All future investigations would need to get special approval and permission before using the shared information.

How will we protect your privacy?

- To protect your privacy, we will use a code instead of your name. We will only use this code on your sample and information about yourself. We will do our best to keep the code private. It is possible that someone could find out your name, but this is very unlikely to happen.
- Your name, date of birth or other identifying features will never be published or shown without your permission.

How long will we keep your information and samples for?

- We would like to keep your information for a total of 15 years (from the time we first got permission from you).
- You can ask for the information to be removed from the repository a at any time, even if you agree to have them included now.

Participation

- Your participation in the ORMSA is voluntary (your decision). This means:
  - You can decide whether or not your information continue to be stored in the ORMSA Registry
  - You will still receive the same medical treatment whether you agree or not.
  - You are allowed to change your mind at any time, all you need to do is phone Dr Theesan Vedan at +27 71 11 88 5909

If I choose to consent, what good or bad things could happen?

- Agreeing to be in the ORMSA Registry will not help you directly, but we hope it will benefit others in the future.
- Nothing bad or good will happen to you if you let the information be in the ORMSA Registry.
- There is a small chance that if someone may try to, they could find out who you are, but we are going to do our best to make sure this cannot happen.
- Your data will never be sold.

Is there something else you would like to know?

- If you have any questions, please contact Dr Theesan Vedan at +27 71 11 88 5909
- The ORMSA Registry is registered with the University of the Western Cape's Human Research Ethics Committee (HREC REF: New number).
- If you have any questions about your rights or welfare, or any ethical concerns with your information and samples being stored in the ORMSA Registry you may contact the UWC Human Research Ethics Committee:

ORMSA

I consent to the following:

	Please Circle:
1. I give permission for my information (data) to be collected and stored anonymously in the ORMSA for 15 years.	YES / NO
2. I give permission for routine hospital test results to be included in the ORMSA Registry for 15 years.	YES / NO
3. I give permission for my **data** to be shared anonymously with other researchers and investigators doing ethically approved research.	YES / NO

I have read the information, or it has been read to me. I have had the chance to ask questions about it and I understand with the answers I was given. I agree voluntarily and understand that I have the right to change my mind without this affecting my medical care.

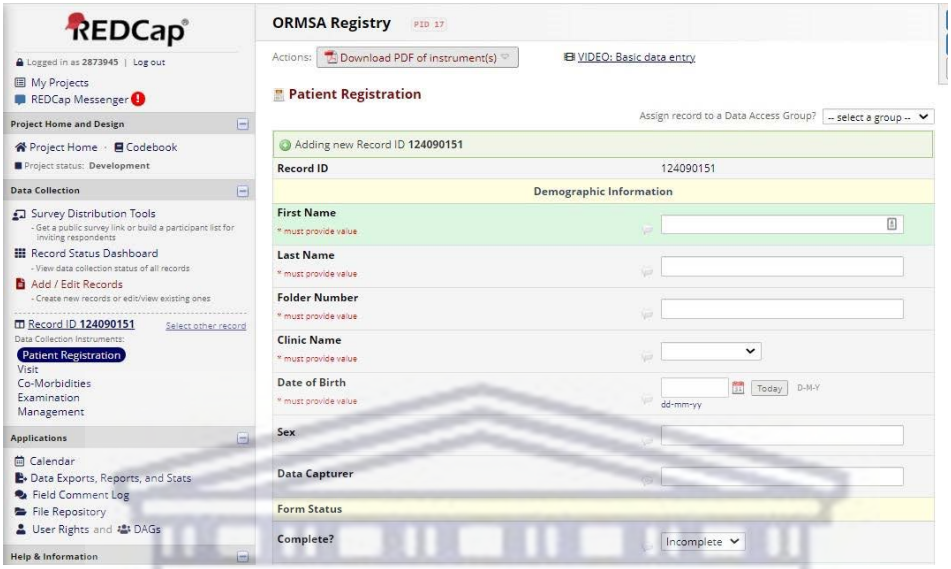
Signed

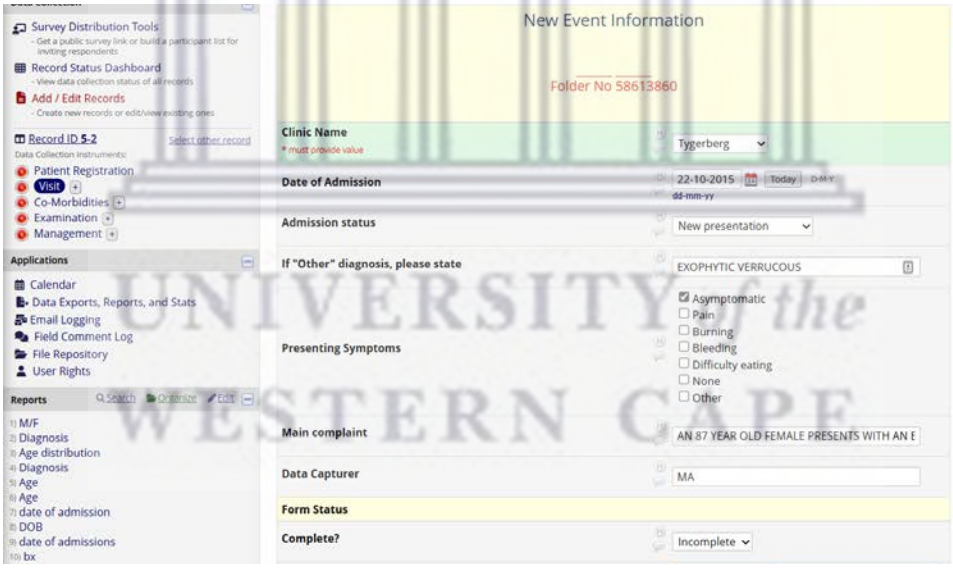
Participant:	Investigator:
Signature:	Signature:
Date:	Date:

Witnesses 1. _____

2. _____

Appendix 5: Screenshots of the ORMSA REDCap® based database





Appendix 6: Turn it in score

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