ASSESSING FRAILTY AND CHRONIC DISEASE IN CONTEMPORARY HUMAN SKELETAL REMAINS

by

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DEDICATION

In Loving Memory of my dad, Mark E. Mundine, who always had my back.
I hope I made you proud.

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I would like to thank my amazing, strong, and caring mother, Vel Mundine, for always being my number one supporter and pushing me to be the best. She has always been there to pick me up when I fell. To my sister, Lisette, and my brother, Erick, for being the best big sister and brother that anyone can ask for. I am grateful always to have you both in my corner. To my brothers-in-law, Ricardo and Joe, I am grateful for you both! You both are kind, hilarious and we could not have gotten through 2020 without y'all. To my nephew, Trip, and my niece, Erabella, I love you both, always!

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LIST OF ABBREVIATIONS

Abbreviation	Description
BMI	Body Mass Index
CDC	Center for Disease Control and Prevention
CVD	Cardiovascular Disease
DISH	Diffuse Idiopathic Skeletal Hyperostosis
DJD	Degenerative Joint Disease
DoHaD	Developmental Origins of Health and Disease
SES	Socioeconomic Status
SFI	Skeletal Frailty Index
TXSTDSC	Texas State Donated Skeletal Collection

I. INTRODUCTION

Many studies in biological anthropology have focused on stress and frailty, but most are bioarcheological cases, and the causes and effects of skeletal frailty are often not well understood (DeWitte DeWitt and Stojanowski., 2015). For this research, I will be examining stress and frailty in contemporary human skeletal remains using a modified version of the Skeletal Frailty Index (SFI) developed by Marklein et al. (2016). North American historians define contemporary as post-World War II, 1945 to present (Maier 2001). This research uses the historical definition of contemporary to discuss contemporary skeletal remains. The SFI was originally used to assess frailty indicators on bone in medieval monastic and non-monastic skeletal remains. While SFI may be appropriate for working with historic and bioarcheological remains, it can not be applied to most contemporary human populations since it includes indicators usually not present in most contemporary humans (e.g., rickets, syphilis, cribra orbitalia, etc.). As a result, I will be modifying the SFI indicators that are not applicable to use on contemporary humans and will be adding additional indicators that are more reflective of contemporary populations.

Researchers have linked hardship during fetal development to chronic diseases that occur in later life (Gowland 2015). Epigenetic evidence has shown that environmental stresses begin *in utero* and can pass on to children in ways that can affect health for many generations (Forrest 2004). Many studies have assessed environmental stressors' effect on bones with research focused on cranial asymmetry, bone morphology, bone density, long bone growth, vertebral canal size, and isotopic analysis (Weisensee and Spradley 2018, Agarwal 2016, Hendrickson et al. 2018, Azcorra et al. 2013, Watts 2011). CT scans have

been used to examine the trabecular bone to assess bone mineral density (Garvin 2016). Additionally, stable isotope analysis is being used to study individuals' dietary habits to see if their dietary habits correlate with chronic disease frailty (O'Brien 2016). However, as important as these studies are, there are potentially other skeletal indicators that can be used to assess the link between stress, frailty, and chronic diseases. This research aims to identify additional markers of skeletal frailty that might correlate with frailty, chronic disease, and stress.

Frailty

Bergman et al. (2007) identify frailty as "...the increased vulnerability to stressors due to impairments in multiple, inter-related systems that lead to a decline in homeostatic reserve and resiliency" (Bergman et al. 2007: pp 2). For the purpose of this research, a more basic definition will be used to define frailty as "...a loss of ability to adapt to stress because of diminished functional reserves" (Weiss 2011:1). Studies have shown a link between frailty and chronic disease as a prime indicator of a person's health pattern over time and in later life (Weiss 2011). Researchers estimate that frailty affects about 20-50% of older hospitalized patients and an estimated 15% of higher frailty occurrence among older adults 65 years and older (Bandeen-Roche et al., 2015; Hogan et al., 2017). There is an increased interest in frailty research, but there are contradictory ideas of frailty's definition and criteria (Bergman et al., 2007).

Chronic Disease

Chronic disease is a common topic in health research due to the increasingly high numbers of individuals developing a chronic disease in contemporary populations. The Centers for Disease Control and Prevention (CDC) broadly defines chronic disease as:

"...conditions that last a year or more and require ongoing medical attention or limit activities of daily living or both" (CDC 2019). Chronic disease is one of the leading causes of disability and death in the United States (CDC 2019). The CDC identifies major chronic diseases as heart disease, stroke, cancer, tooth decay, arthritis, and diabetes. The factors leading to these chronic diseases are a relatively small list of significant risk factors: tobacco and alcohol use, poor nutrition, and lack of physical activity. Individuals with inactive lifestyles or lifestyles that do not meet the guidelines of physical activity per week are at risk of obesity can be a factor for the chronic diseases mentioned on the CDC list (Salis et al. 2012).

Socioeconomic Status (SES)

Studies on socioeconomic status imbalance have shown that individuals in a lower socioeconomic status have a higher risk of chronic disease (Shaw et al. 2013). The study by Shaw et al. (2013) concluded that neighborhoods with higher chronic disease cases reside in deprived counties. In contrast, communities that have lower chances of chronic diseases live in more prosperous counties. Ancestral disparities have been linked to the increase of chronic diseases (Horowitz et al. 2017).

In Howoritz et al. (2017) genomic study, African Americans have been linked to increased genetic variants of chronic cardiovascular disease, kidney disease, and hypertension due to socioeconomic factors such as residing in poorer residential neighborhoods and lacking access to health insurance and lack of quality healthcare. Studies have linked chronic diseases to environmental stresses during fetal development. (CDC 2019, Gowland 2015). The rise of Covid-19 in 2020 has shown that minority groups suffering the effects of long-lasting social inequalities have an increased risk of

getting sick and dying from Covid (CDC 2020). This exemplifies studies that have linked chronic diseases to environmental stressors, explaining why minority groups are more at risk for Covid.

Comorbidity and Multimorbidity

There is a high risk of an individual with one chronic disease developing another chronic disease in aging populations (N'Goran et al. 2016). The two terms that discuss the presence of multiple conditions coinciding are comorbidity and multimorbidity. Comorbidity is the manifestation of one or more chronic conditions. There is no consensus on defining multimorbidity, how to define it, or how many chronic diseases equate to multimorbidity (N'Goran et al. 2016 and McPhail 2016). However, this research will define comorbidity as an individual with one to two chronic disease diagnoses; and multimorbidity as an individual diagnosed with three or more other chronic diseases.

Literature Review

The research conducted by Marklein et al. (2016) looked for trends between stress and chronic and acute skeletal lesions within past populations (medieval monastic and non-monastic). The authors proposed a Skeletal Frailty Index (SFI) based on frailty and stress models among living populations. Their goal was to use those models to assess frailty in past populations. SFI can help us better understand stress, frailty, and health among individuals and the variation between populations. The authors came up with 13 biomarkers to assess stress, frailty, and activity among individuals and categorized them into four stress categories: 1) growth, 2) nutrition and infection, 3) activity, and 4) trauma. They measured the 13 biomarkers on a presence or absence scale and took measurements on limb length for growth patterns. They concluded that the SFI is useful

in a bioarchaeological context when applied to assess skeletal biomarkers of stress. Their finding showed that there was variation in medieval monastic and nonmonastic heath. This SFI appears to work well for bioarchaeological cases in terms of understanding environmental stress among individuals. Environmental stress is negative stimuli in that cause stress. However, using SFI in contemporary populations is not appropriate, since SFI uses biomarkers that are not commonly present in contemporary humans. This current research retained some biomarkers from the SFI that were appropriate for modern populations, but then replaced some of the non appropriate biomarkers (e.g., syphilis) with those that were more fitting for contemporary populations.

Research on environmental stressors focuses on the way we look at and interpret health and growth among past human remains and requires a re-evaluation of looking at the long life of an individual (Gowland 2015). Gowland argues that environmental stress and socioeconomic status can have a generational effect that can cause diseases and affect growth development. Gowland bases her research on the Developmental Origins of Health and Disease (DoHaD) hypothesis. DOHaD provides an analysis of children growing up in environmental stress can develop chronic diseases as they grow into adults. Gowland discusses epigenetic changes and the generational link that can affect fetal development *in utero*. Gowland concludes that by combining DOHaD and the understanding of epigenetic changes, we can start looking at skeletal lesions on bone and better understand the bone and how environmental stress affects it. Knowledge of epigenetic changes and environmental stressors is useful in biological anthropology because it can assist in understanding stress and chronic disease as well as piece together what occurred in the past.

Chronic Diseases

The CDC has declared that chronic disease is one of the leading causes of disability and death in the United States (CDC 2019). This current research focuses on chronic disease; and as such it is important to discuss and define the chronic diseases used in this research. The chronic diseases examined in this research are observable on the skeleton using a mix of indicators from Marklein et al. (2016) and new indicators that I have chosen.

Raghupathi and Raghupathi (2018) conducted research on the prevention of chronic diseases using data from the Centers for Disease Control and Prevention to create a statistical analysis of correlations between chronic diseases (Raghupathi and Raghupathi 2018). The correlations can bring insight for creating preventive measures, minimizing costs and risks. The authors studied five categories: chronic conditions, demographics, mental health, behavioral health (physical activity, tobacco use, and physical activity), and overarching conditions. The authors continue by saying that individuals with chronic diseases suffer from multiple chronic conditions as individuals age. According to the authors, about two-thirds of deaths are caused by one or more chronic diseases: cancer, stroke, heart disease, diabetes, and chronic obstructive pulmonary disease. They looked at chronic disease characteristics within the United States and compared behavioral habits, chronic disease, demographics, and other health conditions. In their statistical analysis, the authors looked at these characteristics by age, gender, and race. Results showed that men with chronic diseases have a higher mortality rates than women with chronic diseases. They also found that non-white individuals have a higher chronic disease mortality rate than white individuals.

The article is beneficial in anthropology because it gives a statistical analysis of different chronic diseases and how it affects different individuals. It gives us a better understanding of different ethnic groups and raises the question of why non-white individuals have more chronic diseases than white individuals. The authors assessed the many aspects of chronic disease to create preventive measures.

The American Dental Association defines periodontal disease as a chronic gum inflammation that can become severe and lead to tissue loss in the alveolar process that surrounds the teeth. Research in clinical and medical studies has shown that there is a correlation between periodontal disease and chronic diseases such as cardiovascular disease (CVD), diabetes, and hypertension (Belstrøm et al., 2012; Aschner et al., 2014). Additionally, periodontal disease is associated with socioeconomic status and with behavioral habits like smoking (CDC; Bergström, 2004). Biological anthropologists have studied periodontal disease in bioarchaeological research in correlating sex and age (DeWitte, 2012). However, because the cases are bioarchaeological, there is no known medical background information on the individuals, especially in terms of their behavioral habits and socioeconomic status.

Cardiovascular disease (CVD) is a chronic disease that is highly prevalent and is one of the leading causes of death (Pollard 1997). Family history and parental behavioral health (i.e., tobacco use and alcohol consumption) have been used to assess CVD development risk in childhood, which has found a link between family history and maternal tobacco use to increased risk of CVD in adolescents (Silva et al. 2017). Anthropologists have studied CVD risks among hunter-gatherers by analyzing the CVD biomarkers of contemporary hunter-gathers and activity patterns (Raiclen et al. 2016).

These studies are crucial in understanding CVD from an anthropologic perspective; however, these studies work with living individuals and are not looking for biomarkers on the skeleton.

According to the CDC, cancer is the second leading cause of death in the United States. Cancer metastasizing to the bone is a leading cause of morbidity and has been linked to prostate and breast cancer (Macedo et al. 2017). Skeletal-related incidents can occur due to bone metastases such as fractures, vertebral collapse, hypercalcemia, mobility impairment, and bone marrow aplasia (Biehler-Gomez et al. 2019 and Macedo et al. 2017). Skeletal pathology has been researched to help understand or reconstruct an individual's lifestyle or help narrow the search for a missing individual (Biehler-Gomez et al. 2019). The Biehler-Gomez et al. (2019) article discusses skeletal pathologies caused by cancer and that not all forensic anthropologists know what bone metastases look like. However, the article does not discuss comorbidity or individual frailty.

Patients with diabetes have an increased risk of fractures and sweet bones, which alters the bone's strength, structure, and metabolism (Al-Hariri 2016). Diabetic research has shown how medication can affect an individual. Medication for diabetic individuals can cause negative effects to the osteoblastic factors and can decrease osteoblastic activity (Meier et al. 2016). Additionally, research has shown that diabetic individuals that developed sarcopenia have a higher mortality rate after undergoing leg amputations (Kim et al. 2018). The importance of the research that is being done is beneficial to forensic anthropology because there is not a lot of research discussing how diabetes affects the bone (Al-Hariri 2016). However, the research does not look at the frailty, comorbidity, or even socioeconomic status of individuals.

Anthropologists have looked at autoimmune arthritis such as rheumatoid arthritis and psoriatic arthritis (Rothschild et al. 1999 and Zias and Mitchell 1996). Additionally, anthropologists have researched degenerative joint disease (DJD), such as osteoarthritis, and the cause and effects of DJD (Klaus et al. 2009). However, researchers have not looked at both autoimmune arthritis and degenerative arthritis. Some individuals do suffer from both types of arthritis, and it is important to understand how that can affect the skeleton.

Body Mass Index (BMI) has been heavily researched with association to obesity. BMI associated with frailty has shown an increased risk of mortality in male individuals between the ages of 50 – 65 years of age than in females (Jayanama et al., 2019). The research has brought up interesting information regarding BMI and frailty; however, it only associates it with being obese and does not look at other possible contributing factors. Furthermore, there have been studies that have looked at the relationship between childhood SES and BMI; though they were only able to see overweight/obesity among minorities but were unable to correlate SES as a factor (Rogers et al., 2015). A focus towards childhood SES is important better to understand chronic disease among individuals in low economic status.

A study conducted by Maddaloni et al. (2017) looked to understand the effects of diabetes and bone health (Maddaloni et al., 2017). The focus of the article is to understand and describe bone fragility and identify factors that associate Type 1 diabetes and low bone density. According to the authors, past research has focused on individuals <40 years of age, not an accurate account. Type 1 diabetes longevity increases and older individuals can provide more insight into bone fragility, biomarkers,

and other factors of skeletal health.

The authors examined non-vertebral fractures (hip and wrists) and measured for bone density at the femoral neck, lumbar spine, and radius using a dual-energy x-ray absorptiometry (DXA). They also took urine and blood samples after an 8-hour fast. They selected individuals from the Joslin 50-Year Medalists, a group of people who had insulin-dependent diabetes since the time of diagnosis for 50 years or longer, and non-diabetic individuals.

The authors concluded that there was a low prevalence of fractures among the Joslin 50-Year Medalists. The results also showed that there was a low prevalence of osteoporosis compared to non-diabetic individuals. The authors suggest that a factor for their outcome could be that these individuals have consistently cared for their diabetes and being diligent in their diet, exercise and other health factors.
This article is important because it shows that taking care of diabetes could have different effects on bone than individuals who do not take care of their diabetes. If an individual is diligent in their diabetic care, will there be any indicators on the bone?

Foot amputations can be a result of infection or ulcers among individuals with diabetes (Lavery et al., 1996). The research conducted by Lavery et al. (1996) discusses the ideologies accepted by researchers about the influencing factors of high-risk amputations among diabetic patients. The elements are peripheral neuropathy, ulceration, infection, and peripheral vascular disease. According to the researchers, ulceration is the most common reason, and about 85% of the time, ulceration is the single component for amputation. The goal of the authors is to create a system that can aid in identifying and categorizing wounds to prevent amputations.

The authors use a classification system to identify diabetic wounds and base them on a severity scale. The authors used the standard classification criteria based on past laboratory and clinical data that studied diabetic wounds. The stages divide into four grades, and then within those four grades, then divided further into four stages of the development of the ulcers and infected wounds.

This article is crucial because it categorizes diabetic wounds. Ulcers and infections can sometimes show up on bone. It is essential to see if these diabetic wounds also show up on bone before amputation occurs and if so, they will be an important biomarker to look for. This type of research can help understand diabetes as a chronic disease and frailty among individuals, especially in a forensic context.

Goals and Research Questions

This research aims to identify additional markers of skeletal frailty that might correlate with frailty, chronic disease, and environmental stressors.

1. Will frailty indicators on the bone differ from individuals with chronic diseases compared to individuals without chronic disease in a contemporary skeletal sample?
2. Will age increase the chance of having multiple chronic diseases, and if so, will they have more frailty indicators?
3. Is there a difference in frailty and chronic disease among males and females?

II. MATERIALS AND METHODS

Sample

This study examined the entire skeleton of 72 individuals ages 65 and older from the Texas State Donated Skeletal Collection (TXSTDSC). 60 individuals were in the group with one or more documented chronic diseases, whereas 12 individuals were in the control group with no documented chronic disease. The TXSTDSC at Texas State University is composed of contemporary American individuals who donated their bodies to the willed-body donation program. Documentation of medical, lifestyle, and demographic information is provided by the donor themselves, or their legal next of kin. The data provided within this information included behavioral health (i.e. tobacco use), demographic (i.e. childhood socioeconomic status (SES) and race/ethnicity), and medical such as chronic diseases (i.e. cardiovascular disease (CVD), diabetes, fractures, cancer, arthritis, osteoporosis), surgeries (i.e. open heart and trauma), and trauma (fractures). The medical, lifestyle and demographic information from the donor documentation is the first indicator used to assess frailty indicators on bone.

The samples for the chronic disease group were chosen based on criteria of age and if their medical records listed the presence of chronic diseases (Table 1). The non-chronic disease group samples were chosen based on age and if their medical records did not list chronic diseases. However, due to individuals' ages, it was difficult to find any skeletal remains that were completely disease or trauma-free. Adjustments were made to allow individuals without chronic diseases to have fractures listed in their medical history. Fractures are not a chronic disease but one of the biomarkers in this study. This adjustment was necessary to get a non-chronic disease group. Demographic information

and behavioral health was utilized in this research to see if there were are any patterns. Tables 2-5 show the distribution of ancestry, sex, and smoking for both sample groups. Studies have shown that females are at a higher risk of frailty than males, whereas males are at a higher risk of chronic disease than females (Lee et al. 2018, Gavarkovs 2015). Based on the studies, I expect to see a difference between males and females when it comes to frailty and chronic disease. I anticipate males having a higher risk of chronic disease than females, and I expect to see females having a higher risk of frailty than males based on previous research.

Table 1. *Distribution of the TXSTDSC sample by listed chronic diseases and sex*

Chronic Disease Group		
Listed Chronic Diseases	**Sex**	
	Female	Male
Diabetes	10	9
Hypertension	5	7
CVD	11	17
Osteoporosis	4	0
Arthritis	6	3
Cancer	13	19
Total	49	55

Table 2. *Distribution of the TXSTDSC sample groups by ancestry*

Ancestry	Chronic Disease Group	Non-Chronic Disease Group
Black	1	0
Hispanic	2	1
Other	1	0
White	56	11
Total	60	12

Table 3. *Distribution of the TXSTDSC sample groups by sex*

Sex	Chronic Disease Group	Non-Chronic Disease Group
Female	27	8
Male	33	4
Total	60	12

Table 4. *Distribution of the TXSTDSC sample groups by smoking*

Smoking	Chronic Disease Group	Non-Chronic Disease Group
Smoker	15	8
Non-Smoker	45	4
Total	60	12

Table 5. *Distribution of the TXSTDSC sample groups by sex and smoking*

	Chronic Disease Group		**Non-Chronic Disease Group**	
Smoking	Sex			
	Female	Male	Female	Male
Smoker	20	25	5	3
Non-Smoker	7	8	3	1
Total	27	33	8	4

The Skeletal Frailty Index (SFI) indicators that are applicable to contemporary populations include: 1) periodontal disease, 2) degenerative joint disease (DJD), 3) fractures, and 4) osteoporosis. A series of additional skeletal frailty markers added by this researcher include: 5) cancer (should it reach the bone), 6) diabetes (e.g., amputations), 7) diffuse idiopathic skeletal hyperostosis (DISH), 8) open-heart surgery, 9) fractures related to DJD, and 10) surgeries that are related to traumatic injuries or to chronic conditions as additional indicators to examine (Table 6).

Table 6. *SFI Indicators and this researcher's additional frailty markers*

Added Indicators	**SFI Indicators (Marklein et al. 2016)**
Open Heart Surgery	Periodontal disease
Diabetic Amputations	Cancer
Dental Caries	Osteoporosis
Disease Related Fractures	Osteoarthritis
Amputation (traumatic)	Fractures
Diffuse Idiopathic Skeletal Hyperostosis (DISH	
Surgery for DJD related fractures	
Surgery for traumatic fractures	
Diabetes (Amputations)	

Procedure

This research modifies the Marklein et al. (2016) Skeletal Frailty Index (SFI) and proposes a method that is applicable to contemporary remains. This study looked at biomarkers of stressors and frailty indicators within individuals with chronic disease and individuals without chronic disease from the Texas State Donated Skeletal Collection (TXSTDSC) to compare the number of indicators present or absent within the different samples (Appendix 1).

The visual assessment consisted of taking each bone element out of the box and examining each bone individually for evidence of any of the chosen 10 frailty indicators as listed above. I will define the presence or absence of chronic disease by the medical records from donated individuals in the TXSTDSC. I expect to see a difference between these two populations with chronic disease with more frailty indicators on the bone and individuals without chronic disease having fewer frailty indicators on the bone. If there is no difference between the two populations, it might mean that frailty indicators are only visible on certain bone elements or do not translate to bones.

Periodontal Disease and Dental Caries

Periodontal disease and dental caries can be an indicator of chronic smoking or personal hygiene (sometimes because of socioeconomic status, but also as a function of age). A CP-12 color-coded periodontal probe was used to measure the presence or absence of periodontal disease. This study used the standard clinical method of assessing periodontal disease by measuring the distance between the alveolar crest and the cementoenamel junction (Gargiulo et al., 1961; Papapanou et al., 2018; Page & Eke, 2007). I scored periodontal disease as being present if there were 3 millimeters (mm) or

greater of alveolar resorption or if the individual was edentulous (Figure 2). Scoring the presence or absence of dental caries was determined if caries were visible or dental fillings were present (Figure 1) (Pitts et al. 2017; American Dental Association).

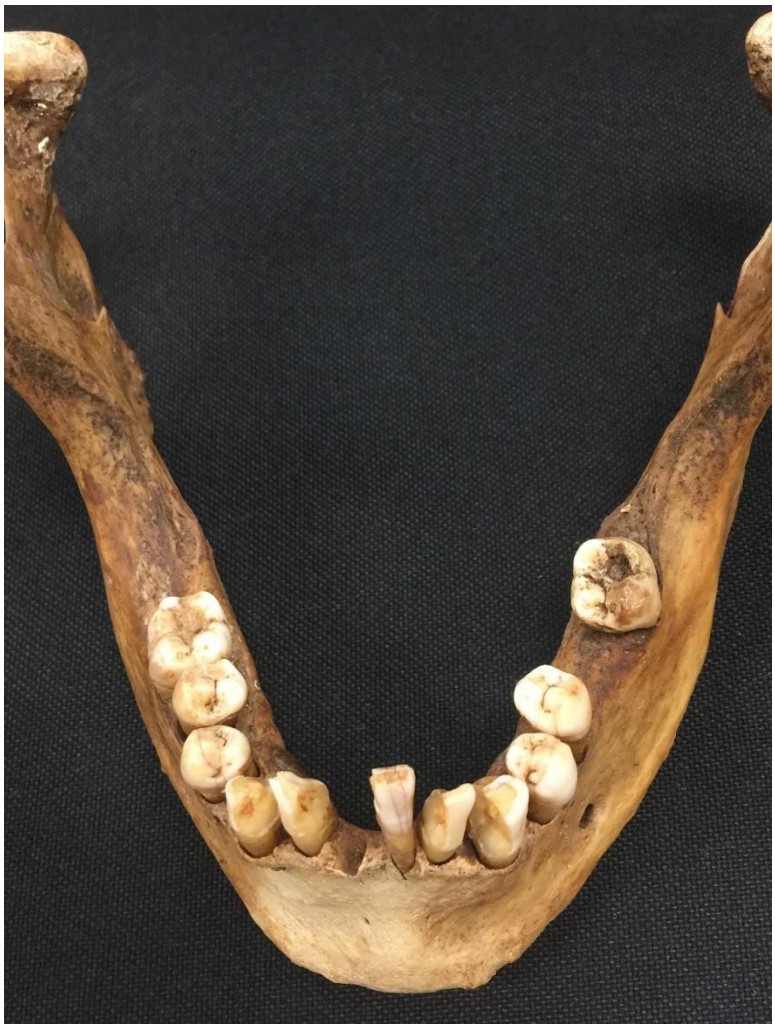


Figure 1. *Donor 2008.002: large cavity present on the left mandibular molar*

Figure 2. *Donor 2015.023: edentulous maxilla (top) and mandible (bottom).*

Fractures

Fractures can be an indicator of a chronic health condition or trauma. This research did take note of fractures initially listed on the medical histories of individuals. However, each skeletal element was examined for additional fractures for indicators of chronic health or trauma. There are four different scoring sections for fractures. The first scoring section is traumatic fractures and is scored as 0 for absent and 1 for present (Marklein et al. 2016). Fractures are scored by examining the bone for any antemortem

fractures by looking for signs of healing and then scoring the antemortem fractures as present or absent (Figure 3).

Figure 3. *Donor 2016.029: healed fractured on distal end of right rib.*

Surgery

Surgery on frail individuals can have complications with long-term adverse outcomes (Lin et al. 2018). To score surgery, a score of present or absent will consist of a visual assessment of surgery related to trauma and surgery related to chronic diseases. (Figure 4 and Figure 5).

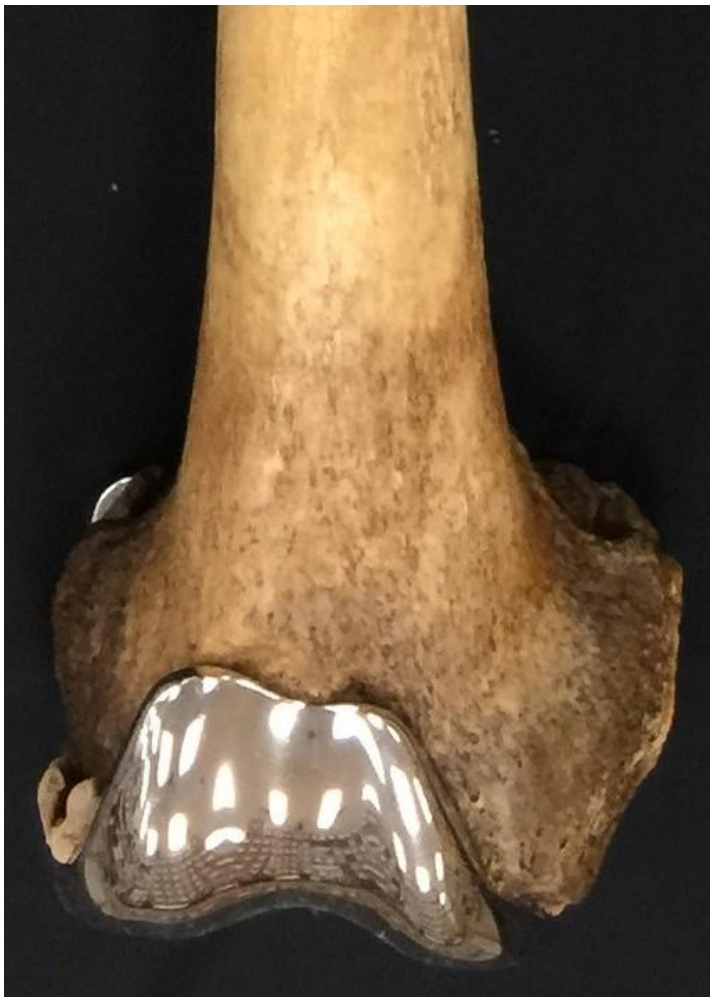


Figure 4. *Donor 2015.055: right femur hip (not depicted) and knee replacement.*

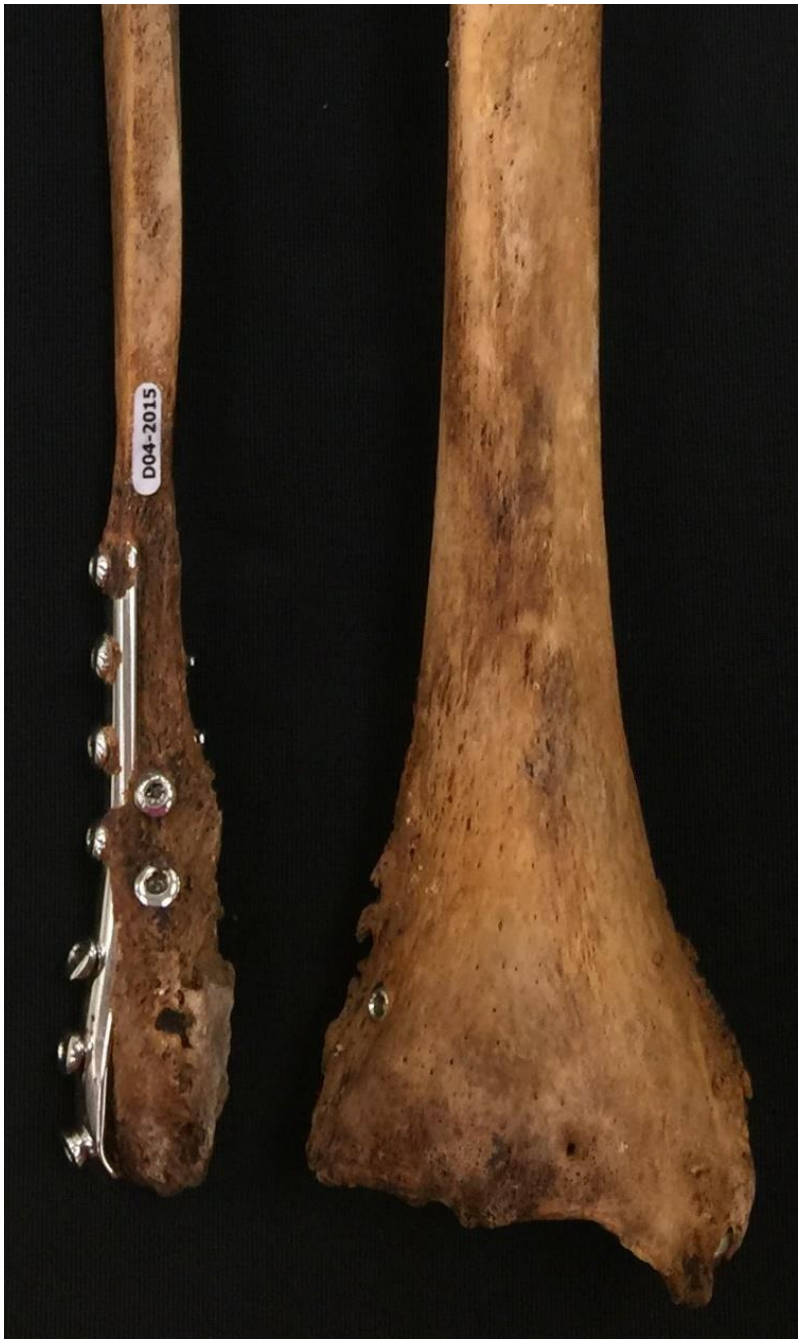


Figure 5. *Donor 2015.004: healed fracture with surgical appliances at distal end of right fibula and tibia.*

Cancer

Cancer can metastasize to the bone if the cancer cells have aggressively spread. Scoring cancer as present or absent will consist of examining the bones for metastatic lesions (e.g., osteoclastic and osteoblastic activity) (Figure 6).

Figure 6. *Donor 2009.007: lytic lesions from neoplastic bone metastases*

Diffuse idiopathic skeletal hyperostosis (DISH)

DISH is the calcification and ossification of bone and is most apparent in the spine; however, it can occur on other bones. The spine will be the focus for this indicator because that is the better indicator, and DISH will be scored as present or absent. To score as present, four or more vertebral elements need to be fused. (Figure 7).

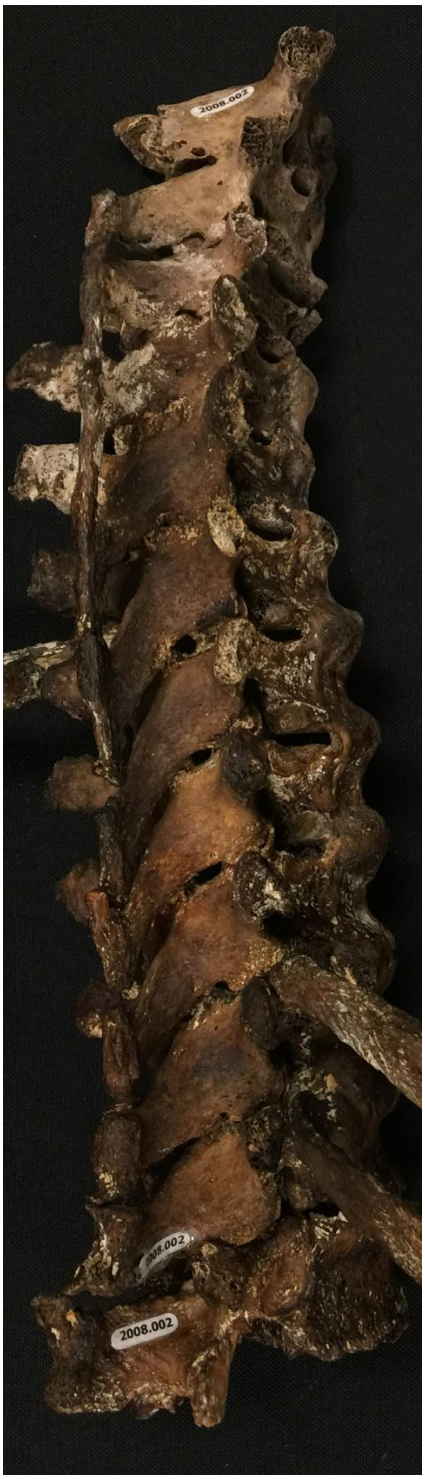


Figure 7. *Donor 2008.002: DISH in the thoracic vertebrae*

Amputations

Amputations can be an indicator of diabetes or trauma; a visual assessment of the lower limbs and feet will be conducted for signs of amputation (Carlson and Reed 2003). Medical records were viewed to see which category the amputation belongs to. Additionally, an assessment of the skeletal inventory to see if feet were present during the intake process were also reviewed.

Open-heart surgery

Open-heart surgery can be an indicator of cardiovascular disease, which is a chronic health condition with risk factors that include diabetes, smoking, and obesity. Viewing the medical records for cardiovascular disease will allow for cardiovascular disease to be scored as present or absent. Additionally, a score of present will be given if there are skeletal indicators showing that the individual had open-heart surgery (e.g. sternal wires) (Figure 8).

Figure 8. *Donor 2015.055: sternal wires indicative of open-heart surgery*

Degenerative joint disease (DJD)

DJD is seen in the joint surface. A visual assessment was conducted of all of the skeleton for eburnation, marginal lipping, and changes to the head of ball-and-socket joints. DJD was scored as present or absent if it occurred on 3 or more of the joints (Figure 9).

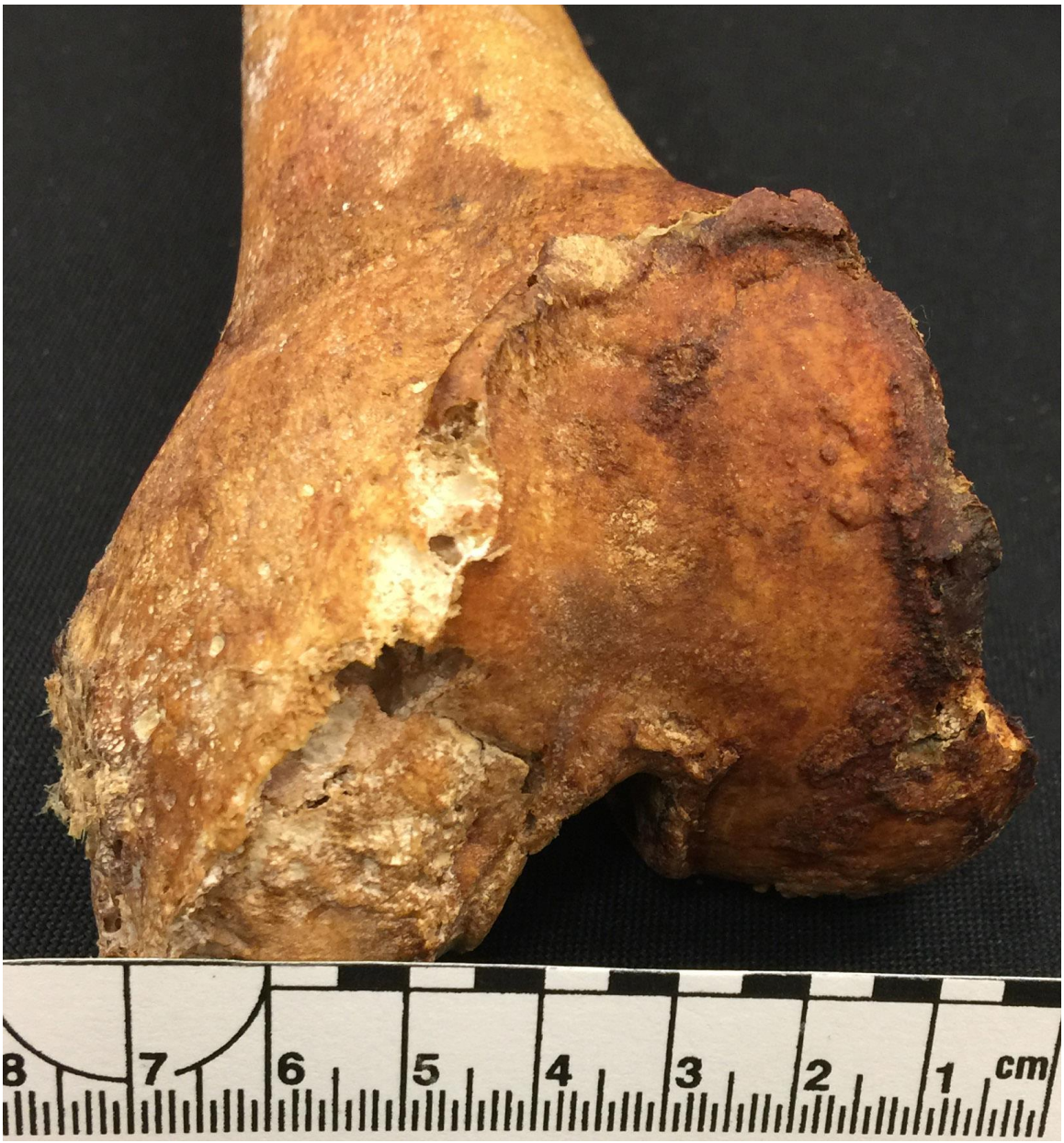


Figure 9. *Donor 2008.002: distal left femur marginal lipping*

Data Analysis

The raw scores for both groups were collected on a hard copy sheet and then inputted into an Excel spreadsheet. The biomarkers are multiple data points that are combined for each individual into a single composite score. The composite scores and demographic information (i.e., race/ethnicity, sex, age, childhood socioeconomic status), behavioral health (smoking), and listed chronic diseases were then inputted into an Excel worksheet. Then the information was transferred to SPSS statistics 27 for analysis.

The data was tested for normality by a series of histograms and Q-Q plots. Nonparametric statistical tests were run on the experimental group to address the relationship due to non-normal distributions for ancestry and the number of composites. A Kruskal-Wallis test was run to recognize the differences that occurred between ancestry (IV) and composite score (DV).

An ANOVA test for the chronic disease group was run to assess the variation between all of the variables (e.g. age, sex, ancestry, SES, etc.) and the composite score. The first ANOVA test consisted of running an ANOVA that assessed the variation among the groups and between the groups. Chronic diseases, demographic information, and behavioral health were dummy coded to get predictor variables. A post hoc Tukey comparison test was run to see the difference of biomarkers between the different variables.

A second ANOVA test was run for the non-chronic disease group. The test assessed the variation between the composite score and all of the variables (e.g. age, sex, ancestry, SES, etc.). Similar to the chronic disease group, demographic information, and behavioral health were dummy coded to get predictor variables. The only information

that was not added was chronic disease due to this being the non-chronic disease group. Additionally, a post hoc Tukey test was was run to see the difference of biomarkers between the different variables.

Two tests were run to explore the relationship between the chronic disease group and the non-chronic disease group and the composite score variable for both groups. A descriptive statistic test was run to find the mean of both groups; this test included the median as well as an ANOVA table and eta, which is effect size. An Independent Samples T-Test was run to see if there is a significant difference between the chronic disease group and the non-chronic disease group with the composite score variable for both groups.

Two statistical correlation tests were run with the data for each sample group. The first correlation evaluated the relationships between smoking, BMI, and socioeconomic status (SES) in the chronic disease group. The second correlation evaluated the same relationships within the non-chronic disease group.

All of the tests that were run in a two-tailed test with a significant level of p-values ≤ 0.05 which means the p-values need a score of 0.05 or less to be considered significant. For the purpose of this research, all p-values that are ≤ 0.30 are considered trending for this research. Trending means that a p-value does not meet the requirements of being significant; however, it leans towards significance.

III. RESULTS

There is not an even distribution between ancestry and chronic diseases. A Kurskal-Wallis test was performed and showed there is no significance between ancestry (mean rank= 3.87, n=60), U= .536, p=.483 and composite score (mean rank= 4.7, n=60), U= 1.25, p=.483. In both groups, there is a lack of representation for non-white individuals.

In the chronic disease group, the ANOVA test showed no significance between any variables and the composite score F (25) = 1.2, p =.298. However, even though the relationship is not significant, the relationship between the composite and BMI (mean rank= 2.29, n=60), p=.255, is closer to being significant if there was a larger sample size (Figure 10). Additionally, the trend occurs between smoking and SES (mean rank= 2.01, n=60), p=.255 (Figure 11). There is still no significance; however, there is trending towards significance.

The non-chronic disease group ANOVA test showed no sign of significance F (8) =.638, p= .728), nor did any of the variables trend. The reason for this is likely the small number of individuals in the 65+ age range without chronic diseases. Still, the non-chronic disease group did show some differences between males and females.

The correlation test showed similar trends that were found in the ANOVA test for the chronic disease sample group. The relationship between BMI and smoking is not significant in the chronic disease group, but it is still trending. A small strength association occurs and shows a negative correlation between these two variables, r = -.184, n = 60, p = .160. This negative correlation occurs when the value of one variable increases and the other decreases. At the same time, smoking and SES are more

significant and not considered trending based on this research. There is no correlation between SES and BMI, but a graph was created to see the distribution between SES and BMI (Figure 12). Also, there is a trending pattern between composite scores and SES. A small strength association occurs and shows a positive correlation between these two variables, r = -.142, n = 60, p = .278 (Figure 13).

The descriptive statistic test that was run to explore the relationship between the chronic disease group and the non-chronic disease group was not significant (mean = 4.7, n=72), sd = 1.25 median = 5). The ANOVA table conducted within the descriptive statistic test also showed no significance between the two groups (mean = 4.7, n = 72, df =1, p=.771). The Independent Sample T-Test also showed there was not a significant difference in the scores for the chronic disease group (m= 4.7, SD= 1.3) and the non-chronic disease group (m= 4.6 SD=1.3) conditions; t(70)= .292, p = .771"

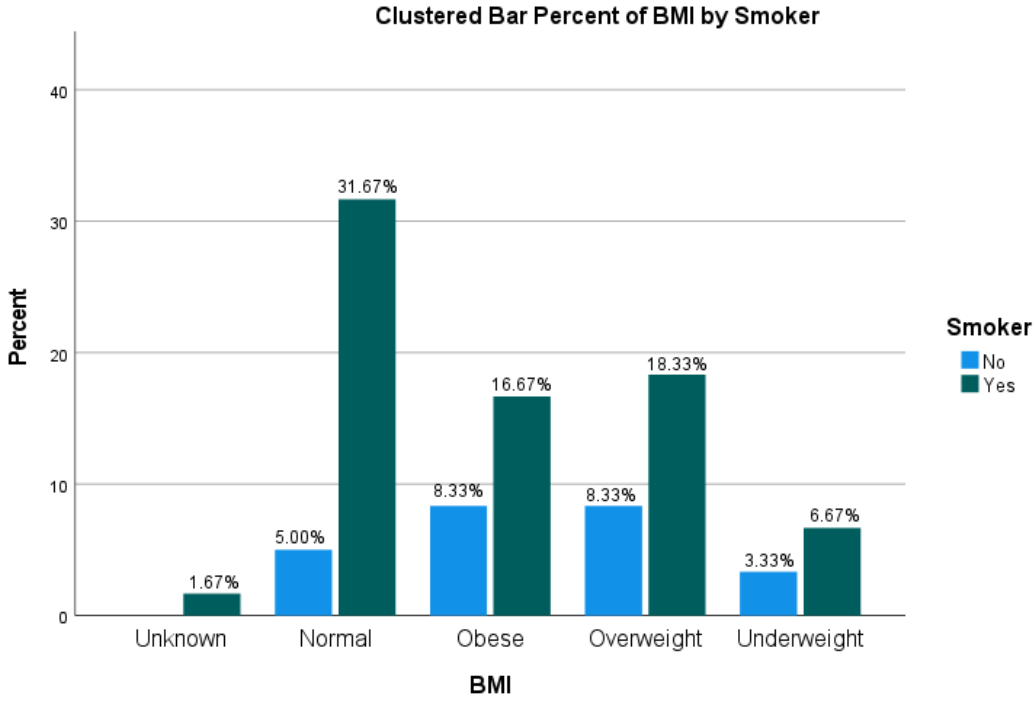


Figure 10. *Graph showing the relationship between smoking and BMI in the chronic disease group*

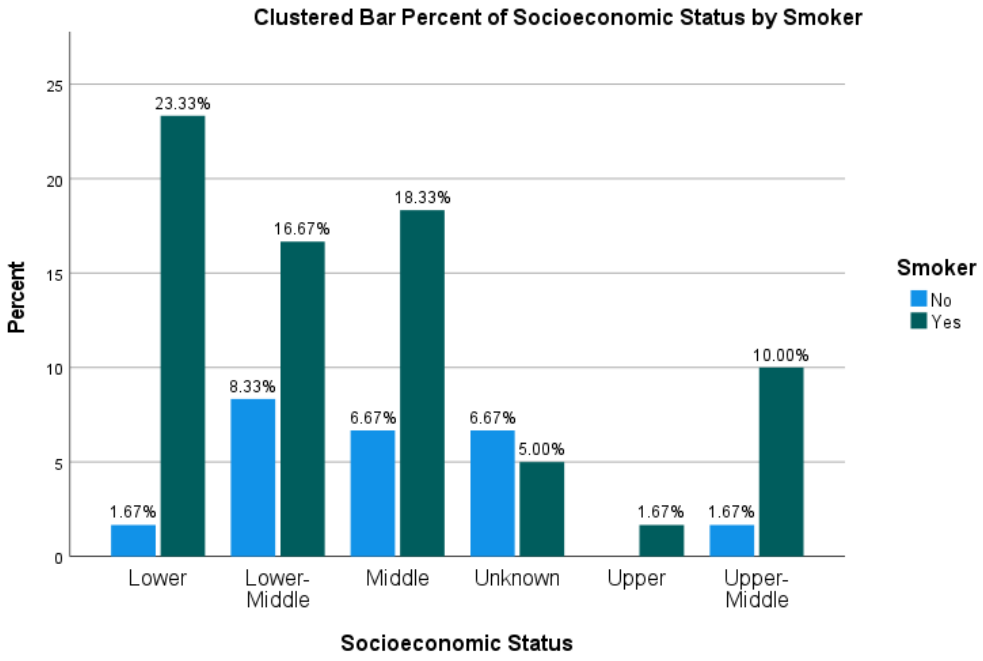


Figure 11. *Graph showing the relationship between smoking and SES in the chronic disease group*

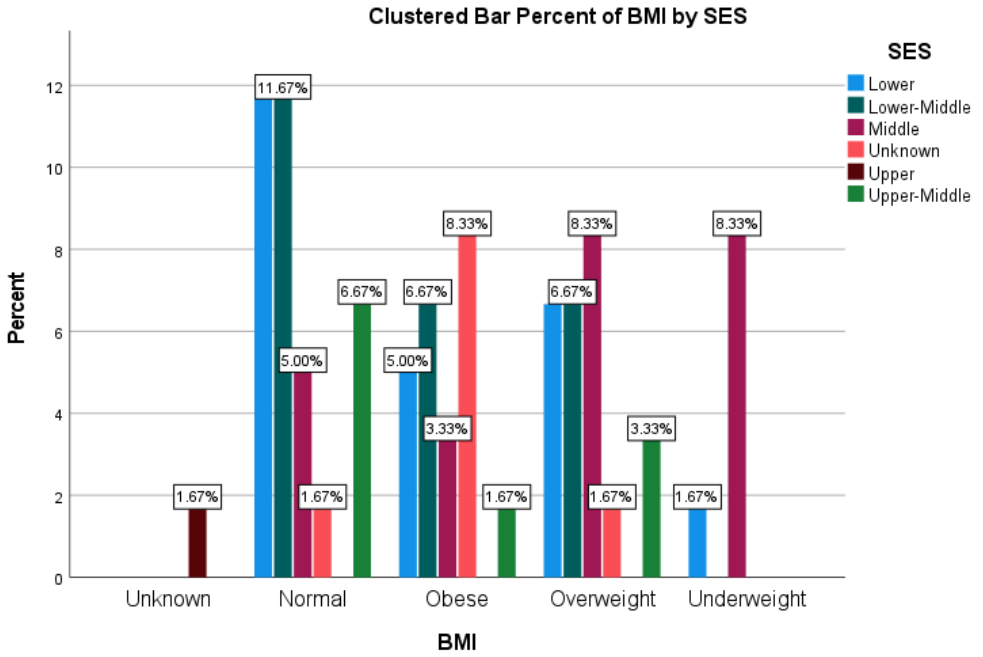


Figure 12. *Graph showing the distribution between BMI and SES in the chronic disease group*

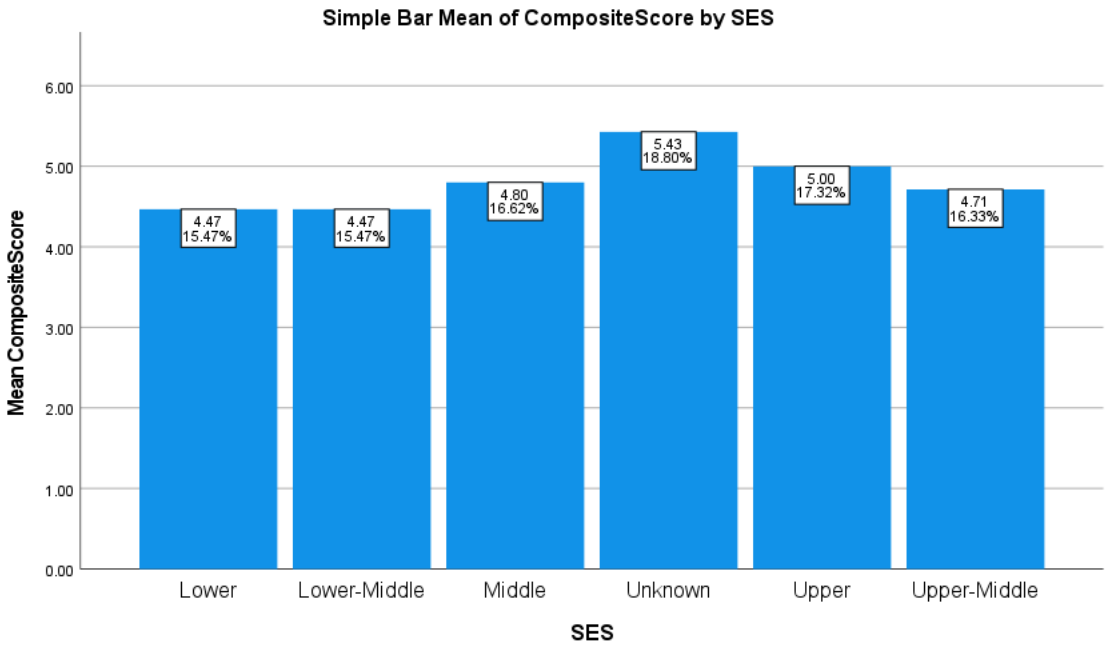


Figure 13. *Graph showing the mean between composite score and SES in the chronic disease group*

In addition, several graphs were created to see the distribution between sex and composite score and sex and the various chronic diseases. The clustered bar graph shows the mode of the composite score and sex within the chronic disease group, which shows females have more variety of scores than males (Figure 14). A graph was created showing the mean between sex and composite score in the chronic disease group, showing the percentage of females having a higher composite score (biomarkers) than males (Figure 15). Figure 16 is a graph showing the cancer occurrence between males and females. More males in this study had cancer compared to females. Another graph was created to show the occurrence of CVD between males and females (Figure 17). The graph indicates that more males in this study had CVD compared to females. Figure 18 is a graph that focuses on the non-chronic disease group and the mean distribution between sex and composite score. This graph reveals females have a higher composite score

(biomarkers) than males (Figure 18). The final graph is the mode of the composite score and sex within the non-chronic disease group. This graph shows that females have a more variety of the composite score than males (Figures 19).

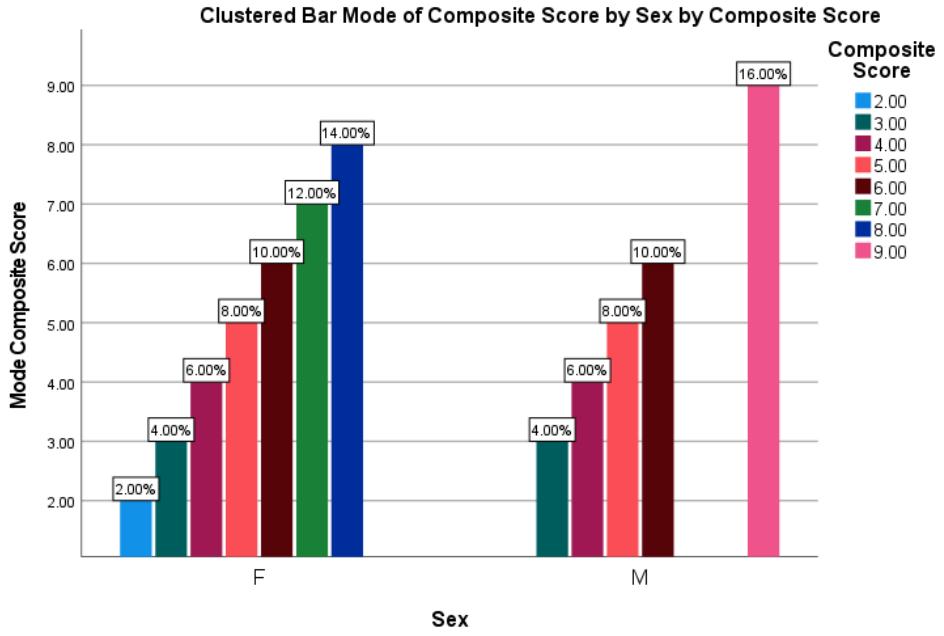


Figure 14. *Graph showing the mode of composite score and sex in the chronic disease group*

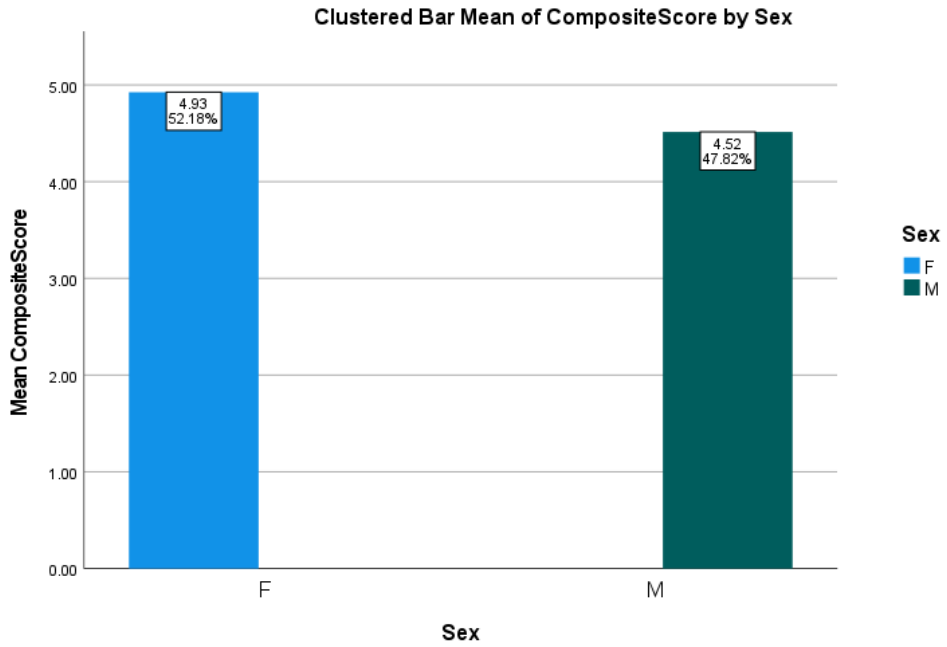


Figure 15. *Graph showing the mean between composite score and sex in the chronic disease group*

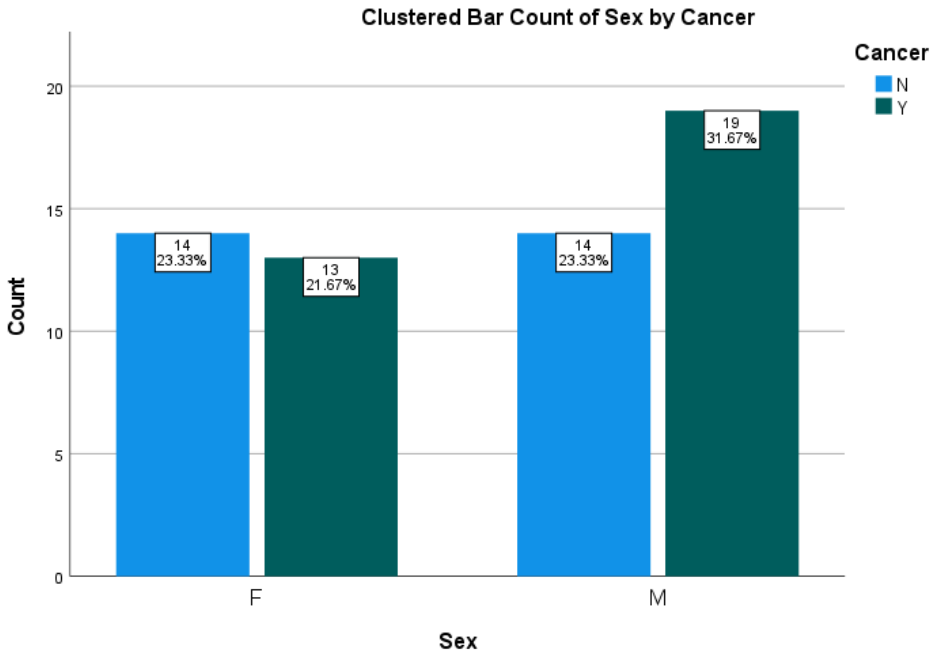


Figure 16. *Graph showing the distribution between sex and cancer in the chronic disease group*

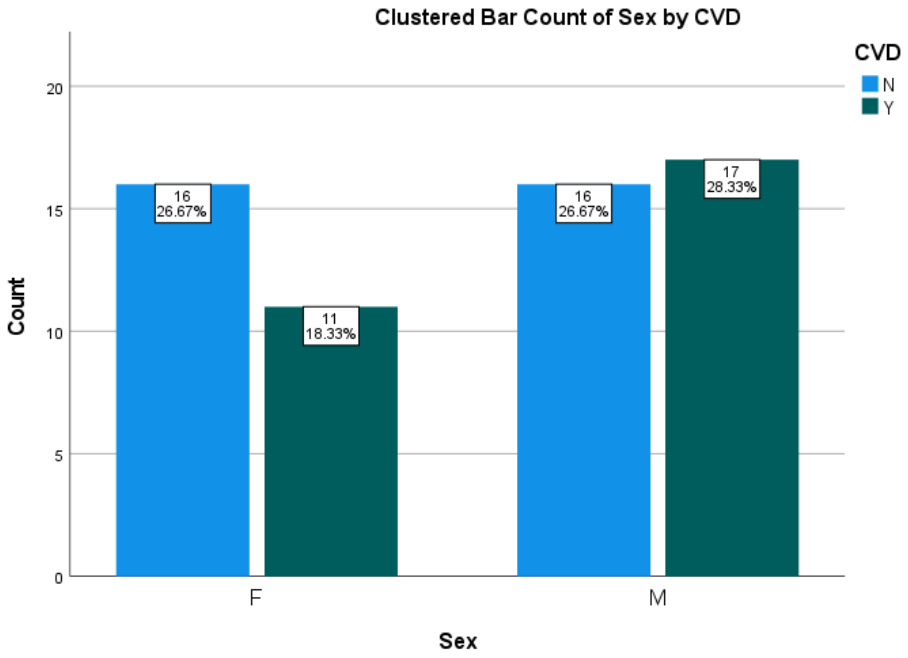


Figure 17. *Graph showing the distribution between sex and CVD in the chronic disease group*

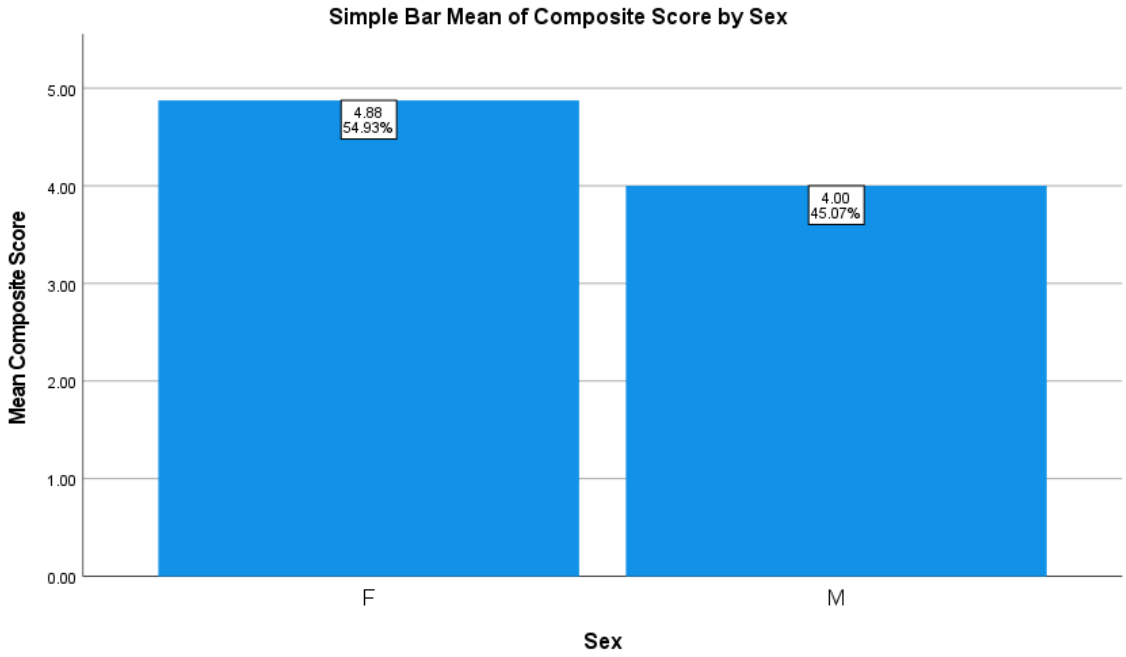


Figure 18. *Graph showing the mean distribution between sex and composite score in the non-chronic disease group*

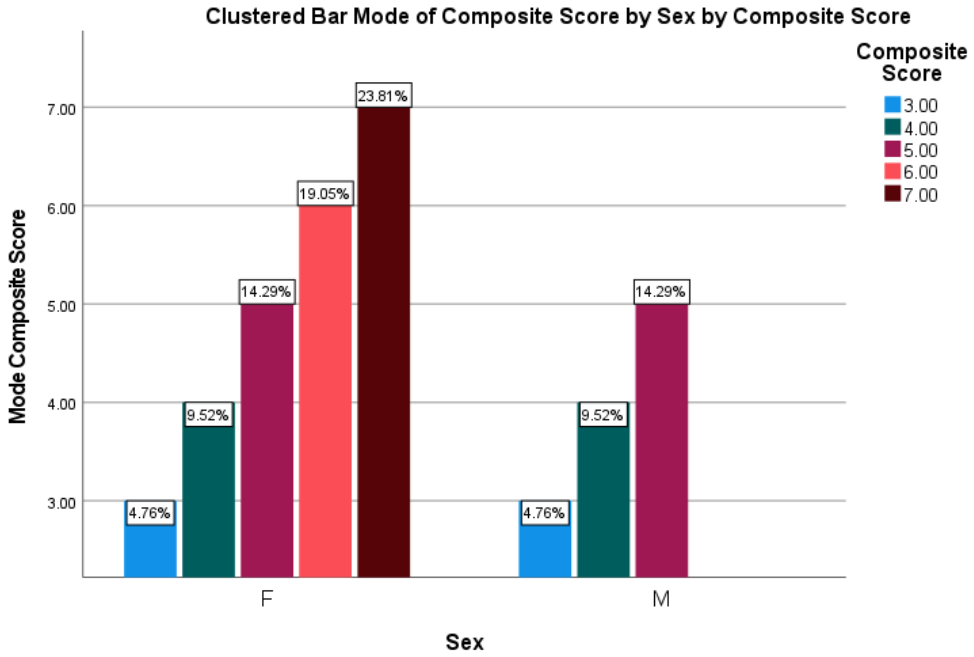


Figure 19. *Graph showing the mode of composite score and sex in the non-chronic disease group*

IV. DISCUSSION

This study aimed to assess relationships between skeletal biomarkers that might correlate with frailty, chronic disease, and stress in contemporary humans based on the skeletal frailty index (SFI) (Marklein et al. 2016). Since there is no consensus on defining frailty, this research used a simplistic definition to describe frailty as "...a loss of ability to adapt to stress because of diminished functional reserves" (Weiss 2011:1). The current researcher modified the SFI and utilized other frailty variables that included demographic information and behavioral health to understand the effect those indicators have on frailty, chronic disease, and stress. This approach was tested on two skeletal sample groups, one group with documented chronic diseases and one group with no documented chronic diseases.

The data indicate that there is no significant effect between frailty markers and chronic diseases for both sample groups. There is a trending pattern that is occurring within the chronic disease group. Self-identified childhood socioeconomic status (SES) shows a trending pattern with smoking. Also, smoking is showing a trending pattern with the body mass index (BMI) of an individual.

Study Interpretations

The results in this study were not completely in line with what was expected. There is no difference between the chronic disease group and the non-chronic disease group in terms of the presence of chronic disease and the 10 skeletal frailty indicators. There were some trending factors within the chronic disease group, but there was not much difference. One of the possibilities could be the small sample size or lack of indicators (e.g., an individual died of cancer, but it was not expressed on the bone).

Regarding chronic diseases, it was expected to see more males having a higher risk of chronic disease than females; additionally, females were expected to have a higher risk of frailty. Males did have a slightly higher risk of chronic disease than females in the chronic disease group. In both the chronic disease and non-chronic disease groups, females had a higher risk of frailty or at least had more indicators than males. This seems to be aligned with previous research that males have a higher risk of chronic disease than females, and females have a higher risk of frailty than males.

There was an expectation that as age increased, so did the chance of having multiple chronic diseases. 7 out of 16 individuals in the 65 to 70 age range group had two or more chronic diseases. This result seems to be as expected since comorbidity and multimorbidity increase with age. 18 out of 42 individuals that were in their 70s or 80s had two or more chronic diseases. This was not expected because it was expected to see more older individuals have two or more chronic diseases. In the end, 27 out of the 60 individuals in the chronic disease group that is 65 years old or older had two or more chronic diseases. An issue with these expectations is the small sample size; only a few individuals in the 65 to 70 age range were collected in the data. A larger sample size could help give a better view of these potential relationships.

One of the main possibilities for the results in this research could be due to the osteological paradox. The osteological paradox infers the health of an individual and the presence or absence of bony lesions. Bony lesions present on the skeleton means that the individual was unhealthy at the time of death. On the contrary, individuals who do not show any lesions on the bone are deemed healthy at the time of death. However, the osteological paradox theorizes that individuals that have bony lesions that manifest to the

bone must have lived longer with the disease (Wood et al. 1992). Wood et al. (1992) argue that the lack of bony lesions presence on the bone does not necessarily mean that the individual was healthy; it could mean that the individual died before the disease could reach the bone.

Furthermore, The Skeletal Frailty Index (Marklein et al. 2016) had an age range of individuals from 18 to 45 years old. The age variable needs to be taken into account because research has shown that age is significantly correlated with frailty (Bergman et al. 2006). SFI model used in this research is representing more age distributions rather than frailty distributions. Possibly lowering the age to individuals that are 40 years old and older could assist with this problem.

Study Limitations

One of the significant limitations of this study is the small sample size for both the chronic disease and non-chronic disease groups. Because this research examined only older individuals, not many individuals in the collection had no listed chronic diseases in their medical history, which made the non-chronic disease group sample especially small. A larger non-chronic disease group would have given a better idea of how many indicators are visible and the relationship between these indicators, environmental stressors, and behavioral lifestyles affecting chronic disease and frailty.

Another potential limitation is that there are more White individuals than minority individuals such as Blacks and Hispanics that have donated their bodies to the TXSTDSC for research, and given the disparities in health and health access by minorities, this is likely underestimating frailty in elderly minority skeletons.

It is important to note that no individual is the same, and everyone differs in the way the

diseases or injuries may affect the bones. For instance, for the 32 individuals that had cancer in this study, only 2 showed bone metastases, whereas the other 30 showed none. This was a challenge when figuring out which are the best indicators to use in this research. The osteological paradox plays a part when looking at this variable. Some individuals die before cancer can metastasize to the bone. The cancer variable might not be a good indicator because of this and should possibly be removed.

Future Recommendations

Continued research should be conducted with larger sample sizes for both the chronic disease and non-chronic disease groups. A larger sample size could include a more diverse population for both groups and have a larger variety of individuals in the demographic variables within the study. Additionally, a larger sample size would be ideal to have a variety of individuals with various chronic diseases.

Due to the lack of diversity within the sample, future research should be conducted with expanded minority groups in the chronic disease group. The chronic disease group in this research was made up of mostly White individuals. It is important to have that diversity to understand better how socioeconomic status plays a part in chronic health. Adding more individuals in the 65-year-old and older range or even opening it up to younger individuals to see any differences or correlations could also be explored.

The osteological paradox is routinely seen in many research articles regarding health and frailty, but it is looked at on a surface level, and not much research focuses on the cause and effect of frailty (DeWitt and Stojanowski., 2015). DeWitte and Stojanowski (2015) argue that it is crucial to have a multidisciplinary approach when conducting research on frailty. As technology and epigenetic studies advance, so should researchers

when it come to frailty.

DeWitte and Stojanowski suggest three ways to understand frailty: the first being multidisplicnary by using cultural context and understanding what is occurring within the culture at the time. The second, understanding biological variation among a family and a community and how health varies from each. Lastly, that researchers need to start by assessing diverse frailty and discriminatory mortality at the beginning of their research before data collection. Utilizing these advances could better understand frailty its cause and effect and the added suggestions by DeWitte and Stojanowski are crucial to understanding frailty in both a bioarchaeological and forensic context.

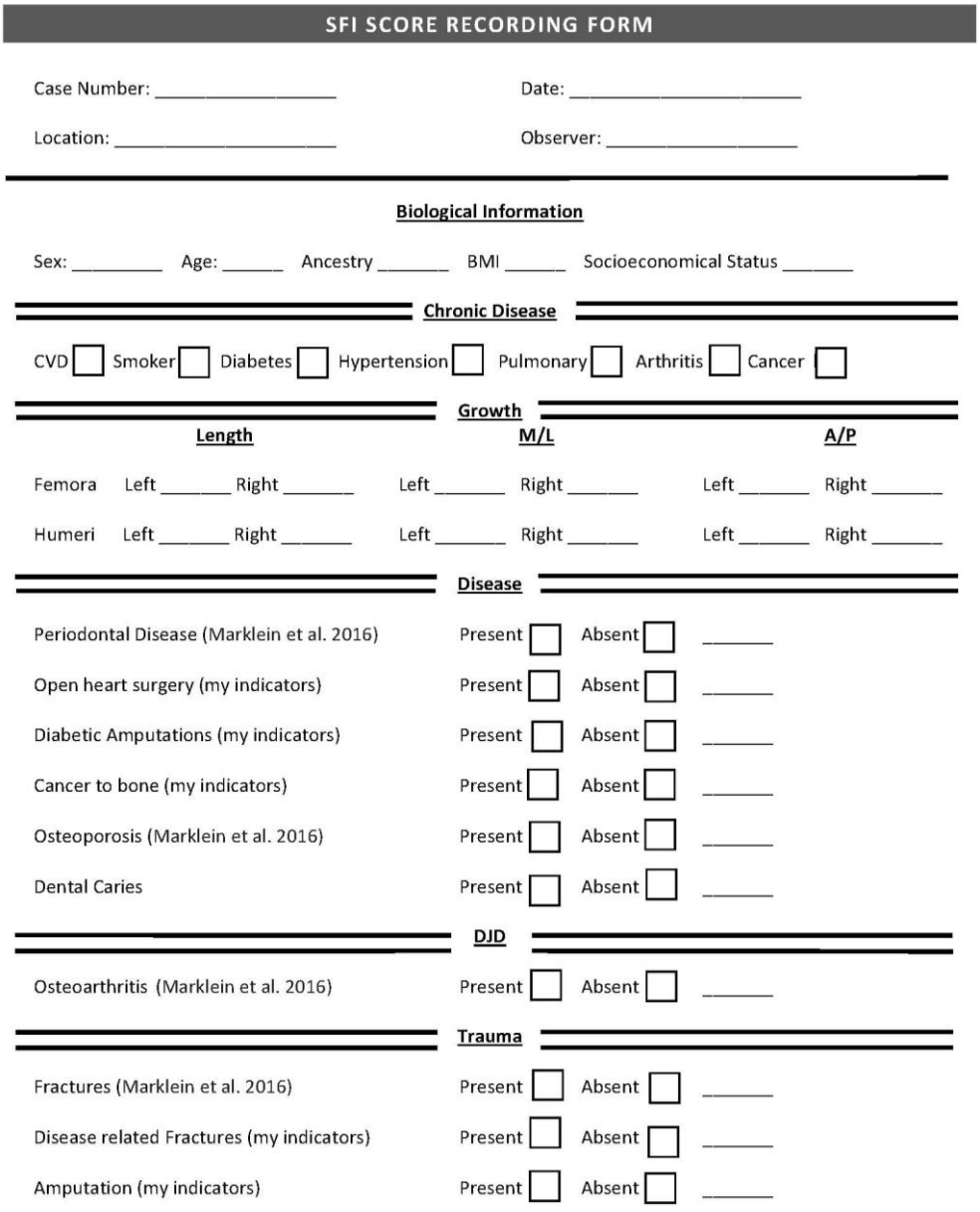
V. CONCLUSION

Studying chronic disease, frailty, stress, and bone pathology has potential for several areas of study. Having a better understanding of frailty and health, and the cause and effect that can occur among individuals is crucial. The Covid-19 epidemic is an example of how these factors may relate to an individual's health and the likelihood of getting and dying from Covid.

Pathological conditions on bone can be important indicators in forensic anthropological casework. Understanding an individual's condition and lifestyle can be used to construct a biological profile for missing individuals. It could possibly aid in narrowing down possible matches by looking for biomarkers on the bone that are indicators of certain diseases, and a better understanding and correlation between SES and chronic diseases might be useful to narrow down positive identification in unknown human remains.

There is the potential to assess stress and frailty among older contemporary populations that creates opportunities for collaboration between anthropologists and researchers in other fields, which can add to the ongoing research of stress and frailty, and their link with chronic diseases. In a forensic and historical context, the ability to measure frailty and stress may lead to identifying populations and geographic locations. It may give insight into the economic, political, and social factors of a population as well as resource availability. Skeletal frailty may help understand epidemic events like the Black Death or the ongoing Covid19 pandemic, diseases known to target individuals who were already in poor health or were predisposed to differential health outcomes by examining other indicators of morbidity and mortality on the bone.

APPENDIX SECTION



SFI SCORE RECORDING FORM

Case Number: _____ Date: _____

Location: _____ Observer: _____

Biological Information

Sex: _____ Age: _____ Ancestry _____ BMI _____ Socioeconomical Status _____

Chronic Disease

CVD ☐ Smoker ☐ Diabetes ☐ Hypertension ☐ Pulmonary ☐ Arthritis ☐ Cancer ☐

Growth

	Length		M/L		A/P	
Femora	Left _____	Right _____	Left _____	Right _____	Left _____	Right _____
Humeri	Left _____	Right _____	Left _____	Right _____	Left _____	Right _____

Disease

Periodontal Disease (Marklein et al. 2016)	Present ☐	Absent ☐	_____
Open heart surgery (my indicators)	Present ☐	Absent ☐	_____
Diabetic Amputations (my indicators)	Present ☐	Absent ☐	_____
Cancer to bone (my indicators)	Present ☐	Absent ☐	_____
Osteoporosis (Marklein et al. 2016)	Present ☐	Absent ☐	_____
Dental Caries	Present ☐	Absent ☐	_____

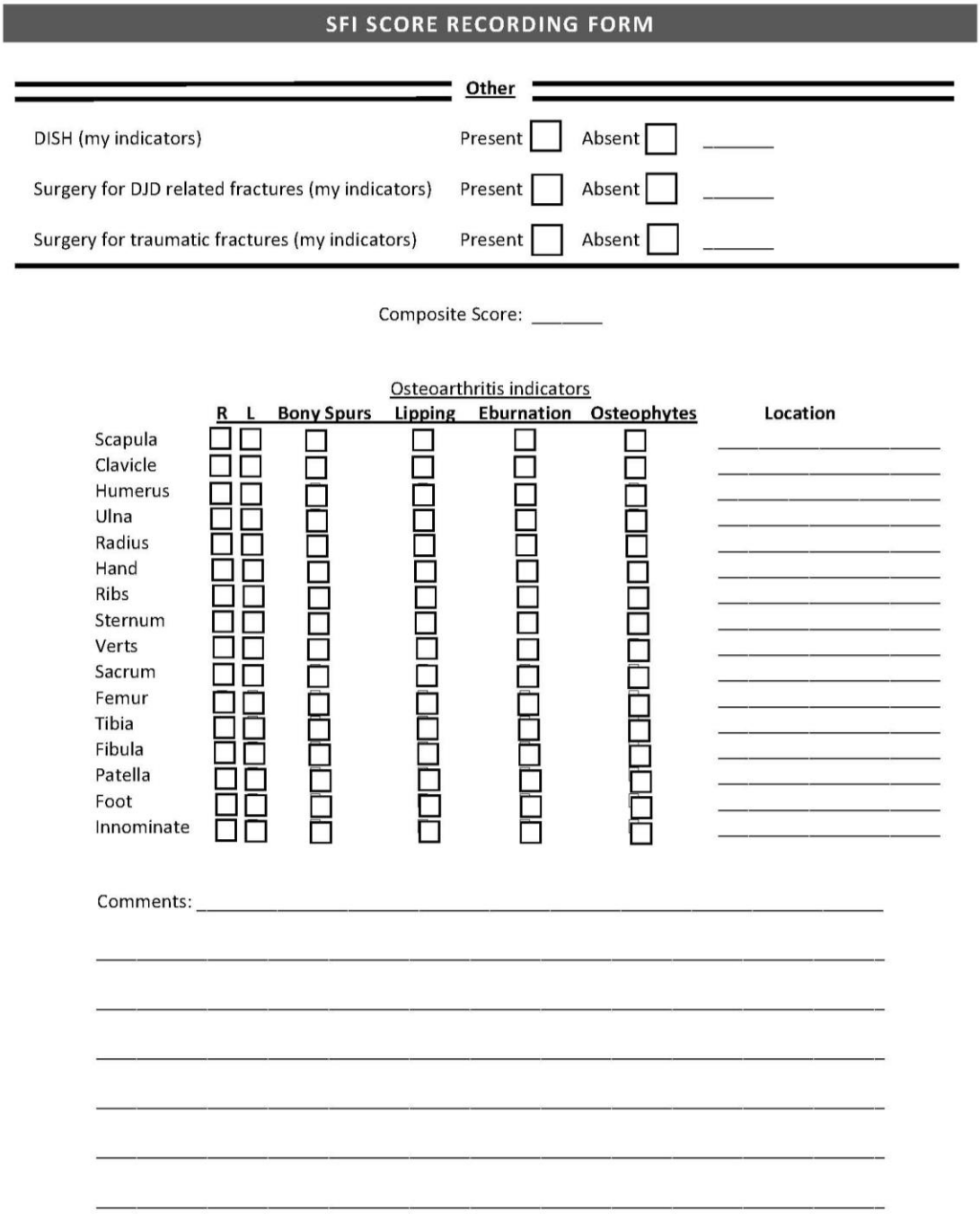
DJD

Osteoarthritis (Marklein et al. 2016)	Present ☐	Absent ☐	_____

Trauma

Fractures (Marklein et al. 2016)	Present ☐	Absent ☐	_____
Disease related Fractures (my indicators)	Present ☐	Absent ☐	_____
Amputation (my indicators)	Present ☐	Absent ☐	_____

Figure 1*. Data collection sheet used to collect data*



SFI SCORE RECORDING FORM

Other

DISH (my indicators)	Present ☐	Absent ☐	_____
Surgery for DJD related fractures (my indicators)	Present ☐	Absent ☐	_____
Surgery for traumatic fractures (my indicators)	Present ☐	Absent ☐	_____

Composite Score: _____

Osteoarthritis indicators

	R	L	Bony Spurs	Lipping	Eburnation	Osteophytes	Location
Scapula	☐	☐	☐	☐	☐	☐	_____
Clavicle	☐	☐	☐	☐	☐	☐	_____
Humerus	☐	☐	☐	☐	☐	☐	_____
Ulna	☐	☐	☐	☐	☐	☐	_____
Radius	☐	☐	☐	☐	☐	☐	_____
Hand	☐	☐	☐	☐	☐	☐	_____
Ribs	☐	☐	☐	☐	☐	☐	_____
Sternum	☐	☐	☐	☐	☐	☐	_____
Verts	☐	☐	☐	☐	☐	☐	_____
Sacrum	☐	☐	☐	☐	☐	☐	_____
Femur	☐	☐	☐	☐	☐	☐	_____
Tibia	☐	☐	☐	☐	☐	☐	_____
Fibula	☐	☐	☐	☐	☐	☐	_____
Patella	☐	☐	☐	☐	☐	☐	_____
Foot	☐	☐	☐	☐	☐	☐	_____
Innominate	☐	☐	☐	☐	☐	☐	_____

Comments: _____

_____

_____

_____

_____

_____

_____

Figure 2*. The second page of the data collection sheet*

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