EVALUATING DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS (DISH) AS LIFESTYLE INDICATORS IN THE TEXAS STATE UNIVERSITY DONATED SKELETAL COLLECTION

by

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DEDICATION

To my grandmother, Ruth Crocker,

28 February 1954 – 4 October 2018.

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LIST OF ABBREVIATIONS

Abbreviation	Description
DISH	Diffuse idiopathic skeletal hyperostosis
SES	Socioeconomic status
W	American White
B	American Black
H	Hispanic
BMI	Body mass index
SUA	Serum Urate Acid

1. INTRODUCTION

This project will evaluate diffuse idiopathic skeletal hyperostosis (DISH) in the Texas State Donated Skeletal Collection (TXSTDSC) to establish whether or not there are correlations between the condition and lifestyle indicators, such as socioeconomic status and medical histories. This research will contribute to the broader discourse on DISH especially in regards to the comorbidities of the condition. Also, this research adds to the discourse of donated skeletal collections as reference samples to draw parallels to the larger population.

Background

DISH is a non-inflammatory condition that affects individuals typically above the age of 50, and has been observed in a host of species including but not limited to dinosaurs and dogs (Forestier and Rotes-Querol, 1950; Rothschild, 1987; Wienfeld, Olsen, Maki, & Griffiths, 1997; Kranenburg, Herman, & Björn, 2014). It is characterized by the ossification of the anterior longitudinal ligament typically on the right side (Resnick & Niwayama, 1976). The location of DISH some suggest has to do with the location of the descending aorta, whose pulsating may keep the ossification confined to the right side (Kacki et al., 2018; Mori et al., 2019). The lower thoracic vertebrae are most affected, followed by the upper thoracic and the lumbar vertebrae (Tsukamoto, Onitsuka, & Lee, 1977; Resnick et al., 1978; Utsinger, 1985; Suzuki, Oshida, & Ohmori, 1991; Mader, 2002; Verlaan et al., 2011; Toyoda et al., 2017). It can also occur in the cervical vertebrae, but this is less common (Utsinger, 1985; Seidler, Pèrez Àlvarez, Wonneberger, Hacki, 2008). Possible causes and risk factors will be discussed later, but there seems to be a predictable progression (Yaniv et al. 2013; Kuperus et al. 2018).

Yaniv et al. (2013) used CT scans taken over 10 years to describe two ways in which the osteophytes grow: one growth pattern is more vertical, and the other is more horizontal. While the horizontal growth is more common in DISH patients, vertical growth is common and indicates possible inflammatory pathogenesis (Yaniv et al. 2013). In addition to vertebral fusion, extraspinal manifestations of DISH often occur at entheseal sites, such as the hips, elbows, shoulders, knees, and ankles (Resnick et al., 1975; Utsinger, 1985; Mader, & Lavi, 2009; Holgate, & Steyn, 2016).

DISH is largely asymptomatic, with most people only being diagnosed with DISH when receiving a chest radiograph for another condition (Kortyna, 2017). However, some complications can arise with the condition. If symptoms arise, they typically are stiffness that lessens throughout the day, pain in the lumbar region, and reduced range of motion in the thoracic and lumbar regions (Kortyna, 2017). As mentioned previously, DISH rarely progresses into the cervical vertebrae; but if it does, the conditions can cause dysphagia, or difficulty swallowing, laryngeal edema, dysphonia, and immobilization of the vocal cord (Suzuki, Ishida, Ohmori, 1991; Seidler et al., 2008; Diederichs et al., 2011; Alsaadawi, 2017; Bakker et al., 2017). Dysphagia has the potential to be fatal as well (Alsaadawi, 2017). If DISH becomes this serious, surgical intervention could be necessary (Alsaadawi, 2017). Other treatments include medication, change in diet, and physical therapy (Nascimento et al. 2014).

The condition has been recognized since the late 19th century and has undergone a few name changes (Ortner 2003, 558). In 1938, Meyer and Forster were the first to describe an overgrowth of bone on the right side of thoracic vertebrae of a patient, and they called it "moniliform hyperostosis" (Utsinger, 1985; Weinfeld et al., 1997). In 1942, Oppenheimer conducted a larger study with 282 senior citizens with the aforementioned condition (Utsinger, 1985). Oppenheimer began calling it "spondylitis ossificans ligementosa" due to the ossification of the anterior longitudinal ligament (Utsinger, 1985). Then in a 1950 article, authors Forestier and Rotes-Querol described a flowing ossification present on the anterior or right lateral aspect of the vertebral bodies of nine older individuals and two cadavers that differed from ankylosing spondylitis (AS) (Forestier, & Rotes-Querol, 1950; Resnick, Shaul, & Robins, 1975; Utsinger, 1985). The authors then suggested renaming the condition to senile ankylosing hyperostosis. They described the condition as being relatively painless and that it had to consist of a continuous osteophytic bridge between at least two vertebrae that kept the integrity of the intervertebral discs for a definite diagnosis (Forestier, & Rotes-Querol, 1950; Mazières, 2013). Senile ankylosing hyperostosis also became known as Forestier's disease (Resnick et al., 1975). In 1975, Drs. Resnick, Shaul, and Robins conducted a study on 21 individuals and suggested the name be changed to diffuse idiopathic skeletal hyperostosis (DISH) to encapsulate the manifestations outside the vertebral column (Resnick et al., 1975). Those authors also set the standard for diagnosing DISH in radiographs by the following characteristics: the flowing ossification of at least four vertebrae, the preservation of disc height, and the absence of apophyseal joint bony ankylosis and sacroiliac erosion (Resnick et al., 1975; Resnick, & Niwayama, 1976). While these criteria were originally for radiographs, some authors use these same criteria in diagnosing it in skeletal remains (Kortyna, 2017). Others argue that in skeletal remains the number of continuous vertebrae can be reduced from four, but the number is not agreed upon (Kuperus et al., 2017). This has created a discrepancy in how DISH is defined between fields and has come under scrutiny in recent years.

Since the Resnick and Niwayama (1976) paper, there have been other attempts to redefine the classification criteria of DISH. Kuperus et al. (2017) compiled articles from multiple online databases that proposed new classifications for DISH and included only those where two or more researchers agreed on the proposed definitions. In total, 24 articles fit this definition. They found that most of the diagnostic discrepancies lie in the minimum number of contiguous vertebral bodies affected and that many authors did not include DISH's progressive nature. Kuperus et al. (2017) found that the most commonly used criteria for modern populations were Resnick and Niwayama (1976). However, in many archaeological studies involving DISH and a few studies with modern remains, researchers lower the minimum number of fused vertebrae from four to three continuous (i.e., Julkunen, 1971; Harris, 1974; Marcelli et al. 1995; Rodgers and Waldron, 1995; Rodgers and Waldron, 2001; Guiffra et al., 2009). Also, in many papers, the reasoning for why the three versus four continuous vertebrae definition is used is not clear and the lack of standardization is likely the reason rates differ between studies.

Another issue with the Resnick and Niwayama (1976) criteria is that it does not prove a measure to assess how progressive or severe the DISH is (Mata et al., 1998; Kortyna, 2017). Mata et al. (1998) recognized this problem and attempted to correct it. The authors developed a scoring system which included: no ossification present, ossification present without bridging, ossification present with incomplete bridging of the disc space, and complete bridging of the disc space by ossification (Mata et al., 1998). This scoring system is used in conjunction with the Resnick et al. (1975) criteria and provides an easily reproducible measure.

Risk Factors

The etiology of DISH is not fully understood, and some wonder if DISH is a disease or a syndrome (Weinfeld et al., 1995; Yaniv et al., 2014; Pappone, Ambrosino, Di Minno, & Iervolino, 2017). The difference between these lies in the causation of the symptoms, whereas disease has a clear etiology (American Psychiatric Association, 2013). Since the exact etiology of DISH is not fully understood, more research is needed to determine this. Even with this, researchers have noticed that the condition most frequently occurs in the thoracic spine (Nascimento et al. 2014) and has been associated with a number of factors. These factors, or lifestyle indicators, include obesity, diabetes, gout, ancestry, sex, and age. Obesity is one of the most studied co-occurring conditions (Coaccioli et al., 2000). Utsinger (1985) found that 40% of the 200 individuals examined with DISH were obese. Kiss et al. (2017) found that individuals who were obese at a younger age were more likely to develop DISH later in life.

Along the same line as obesity, there are metabolic factors that are comorbidities with DISH. These include diabetes, hyperinsulinemia, and hyperlipidemia, among others (Terzi, 2014). Diabetes mellitus is often cited with having a co-occurrence with DISH (Sencan et al., 2005). Diabetes is a group of diseases related to glucose intolerance, which includes the following three types: type 1, type 2, and gestational diabetes (CDCP, 2017). Currently, researchers believe that type 1 diabetes is caused by an autoimmune reaction, while type 2 is due to the body's inability to use insulin properly (CDCP, 2017). Sencan, Elden, Nacitarhan, Sencan, and Kaptanoglu (2005) found that the percentage of individuals with both DISH and diabetes mellitus was greater than those with only DISH in their sample, but there was no statistically significant difference between the two. This study was repeated in the Texas State Donated Skeletal Collection, and no correlation was found (Lewman, Veltri, Cunningham, & Wescott, 2016).

Another disease of metabolic origin that has a high occurrence in individuals with DISH is gout (Littlejohn and Hall, 1982). There is a high correlation to an abundance of serum urate acid (SUA) in the body that crystallizes into sodium urate in joints and causes an inflammatory response, which is called the tophus. Studies also show that gout can occur at normal levels of SUA (Littlejohn and Hall, 1982; Ortner, 2003; Sibson, 2013; Lockyer and Stanner, 2016). These tophi can grow in and around bones and joints painlessly until an "attack" occurs (Falasca, 2006). When it grows in this way, typically an arthritic response is seen in the bones, and this typically seen in lower joints, especially the metatarsophalangeal, metacarpophalangeal, and interphalangeal joints of the hands and feet (Littlejohn and Hall, 1982; Ortner, 2003; Falasca, 2006). Littlejohn and Hall (1982) found that 43% of the individuals in their sample who had DISH also had gout.

Researchers have also looked into genetic factors. DKK-1, or Dickkopf-related protein 1, and OSC, or osteocalcin, are Wnt inhibitors that likely play an important role in bone turnover (Mader and Verlaan, 2012; Nui et al., 2017). Lower levels of DKK-1 and OSC have been associated in patients with DISH (Mader and Varlaan, 2012; Senolt et al., 2012; Nui et al., 2017). It has also been suggested that DISH can be familial. An example of this is the Medici family in Italy (Giuffa et al., 2010). However, the authors also suggest that this case could be associated with social class (Giuffa et al., 2010).

Ancestry has also been assessed as a possible factor in who develops DISH. Those studied include African Blacks, Whites from the Midwest, Blacks from the

Midwest, Native Americans, Hispanics, Koreans, Japanese, and Pacific Islanders (Cassim et al., 1990; Weinfeld et al., 1997; Kim et al., 2004; Kagotani et al., 2015; Bateman, Hapuarachchi, Pinto, & Doyle, 2018). These studies were all conducted on living patients using radiographs or CT scans and the Resnick and Niwayama (1976) criteria. Five hundred people were evaluated in Cassim et al.'s (1990) sample of Black individuals. Within this sample, the overall rate of DISH was 3.9%, with the largest portion of the sample being over 70 years old. Some 2,364 individuals of American Black, American White, Native American, Asian, and Hispanic ancestry were examined through radiographs from two large hospitals in Minnesota using the Resnick and Niwayama (1976) criteria (Weinfeld et al., 1997). Weinfeld et al. (1997) found that DISH was less common in the Black, Native American, and Asian populations, though they admit their sample was small. The authors also found that DISH occurred in higher than expected levels in the White population (Weinfeld et al., 1997). According to Kim et al. (2004), the participants for their study of DISH in Korea had significantly lower rates as compared to American Whites or Japanese (Kim et al., 2004; Kagotani et al., 2014). Bateman et al. (2018) found that there is a statistically significant difference between the prevalence of DISH in Pacific Islanders and Europeans, with Pacific Islanders having higher rates.

Sex is also a possible correlation with the development of DISH. Earlier studies, however, were heavily skewed towards males (Harris, Carter, Glick, & Storey, 1974; Resnick et al., 1975; Tsukamoto et al., 1977; Utsinger, 1985). Some have questioned these results; however, in more recent large-scale studies males are slightly more affected (Utsinger, 1985; Bombak, 2012). Other possible correlations include trauma, occupational stress, osteoarthritis, environmental factors, medication or medical intervention, and infectious disease (Weinfeld et al., 1997; Kiss et al., 2002; Ohishi et al., 2003; Diederichs et al., 2011; Mazières, 2013; Yaniv et al., 2013; Mader et al., 2017).

In archaeological contexts, DISH has also been associated with obesity and metabolic conditions, as well as being of higher social status (Rogers and Waldron, 1995; Weisz, Matucci-Cerinic, Lippi, & Albury, 2011; Bombak 2012; Smith et al. 2013). Rodgers and Waldron (1995) found a highly significant difference in the prevalence of DISH at historic monastic sites as compared to lay locations. In this case, the authors hypothesized that the higher rates were due to the diet (Rodgers and Waldron 2001). In Italy, members of the Medici family in Florence suffered a number of diseases, including but not limited to DISH (Giuffra et al., 2009; Weisz et al., 2011). Giuffra et al. (2009) also suggested that diet caused the higher rates, while Weisz et al. (2011) indicated that it could be hereditary. While these are European examples, probable cases from pre-Columbian North America have also been discovered (Smith, Dorsz, & Betsinger, 2013). Using the criteria of four or more continuous vertebral bodies affected or three continuous vertebral bodies with extra-spinal manifestations, Smith et al. (2013) found two probable cases from two Late-Mississippian Native Americans in the Tennessee River Valley.

In both the modern and archaeological discussions of DISH, social status was mentioned. Social status refers to an individual's rank within society; in combination with economic status, it refers to an individual's socioeconomic status (SES) (Baker, 2014). In previous studies, SES has been tied to education, occupation, and income (Baker, 2014). Education is a marker of social status, especially in that it can illustrate the mobility of an individual through the different social classes (Baker, 2014). Also, people who are more educated tend to be healthier because they have been educated on how to shape their lifestyles (Baker, 2014). Occupation is related to education in that your education level can influence the jobs you are able to have. Occupations can change throughout an individual's lifetime, which makes it a difficult predictor (Baker, 2014). Closely related to occupation is income. Income is the wages, normally pre-taxed, from an individual or household (Baker, 2014). There is a positive correlation between income and health because those with more disposable income can allot more money towards health expenditures (Baker, 2014). While on the other end of the spectrum, lower income typically means an individual does not have resources available to purchase health insurance, or other health expenditures (Baker, 2014; Fritz, 2014). While SES can be difficult to use in research because there is no universal measure, and typically relies on self-reported data, it is still a potential factor for which to account. However, the greatest risk factor for DISH remains age in both the modern and archaeological contexts (Resnick et al., 1975; Kim et al., 2012; Fornaciari, & Giuffra, 2013; Smith et al., 2013; Toyoda et al. 2017; Kuperus et al. 2018).

Research Questions

This research project is a pilot study to examine the presence of DISH in a contemporary documented skeletal sample and will build off studies of co-occurrences. There are three main questions on which this research will focus.

1. Is there a correlation between socioeconomic status and DISH? Since diets and lifestyles have changed through time, I predict that modern individuals of low or low-middle SES classes will have higher rates of DISH expression, essentially the inverse of the work put forth by Rodgers and Waldron (2001). I assume this because the kinds of

dietary factors implicated, as well as other factors, such as socioeconomic status, mentioned by Rodgers and Waldron (2001), have shifted from higher status individuals in historical periods to lower status individuals in the modern era.

2. What relationships among lifestyle indicators (including BMI, medical documentation of diabetes, etc.) can be learned about DISH in the Texas State Donated Skeletal Collection? This builds off the previously mentioned research to provide more information about the individuals affected in this collection.

3. Finally, what are the differences in DISH expression between sex and age categories in the Texas State Donated Skeletal Collection?

In the following pages, I will present the research that arose from these questions. Chapter 2 will discuss how I conducted the research, stored my observations, and analyzed this data. In Chapter 3, I will present my results. Chapter 4 will be a discussion of these results and limitations of this project, and Chapter 5 will consist of concluding thoughts and future directions.

2. MATERIALS AND METHODS

Sample

This study utilizes data from individuals who willed their bodies as a part of Texas State's Willed Body Donation program. Living-donors or next-of-kin donations will remains to the Forensic Anthropology Center at Texas State (FACTS) for use in decomposition and osteological research in the Texas State University Donated Skeletal Collection (TXSTDSC) at the Grady Early Forensic Anthropology Laboratory (GEFARL) located in the Grady Early Building (GEB) off the Texas State University in San Marcos, Texas. This collection began in 2008, and currently holds 257 individuals available for study, and is well documented due to the medical and historical questionnaire donors or the next-of-kin complete prior to donation. While individuals are constantly being added to the collection, ages for the individuals currently span from neonatal to 102 years old, with most donors at the older adult ranges. Most of the donors are of American White, American Black, or Hispanic ancestry. Other self-reported data such as medical issues or procedures, socio-economic statuses, height, weight, occupation, and habits are also documented for each individual donor.

Definitions

For the purposes of this study on skeletal remains, DISH will be defined as the presence of two or more continuous fused vertebral bodies, the retention of intervertebral disc space, and the absence of bony ankylosis. The decision to include those who had only two or more continuous vertebral bodies fused instead of four was due to the fact that the Resnick and Niwayama (1976) definition was formulated for use when diagnosing via radiographs. Lowering the threshold to two fused vertebral bodies allows for the inclusion of individuals with a less progressed condition (Utsinger, 1985; Yaniv et al., 2013). Two was also chosen because it is the precursor, a stage that all patients must go through, to four. Rates of DISH will also be examined to see how it varies with change in definition, which includes the current definition of two or more continuous vertebrae for this project, as compared to three or more and four or more continuous vertebrae.

Figure 1. This photo illustrates the three defining characteristics of DISH: at least two vertebral bodies fused by a flowing ossification, retention of intervertebral disc space, and absence of bony ankylosis.

While there are many definitions of socioeconomic status, the childhood socioeconomic status utilized in this project is self-reported by the donor or the donor's next-of-kin. Therefore there is no exact meaning that is tied to a particular monetary value, only to the TXSTDSC donor's decision to check off a box that best represented their perceived childhood and adult SES levels, given the five options: low, low-middle, middle, middle-high, and high. Childhood SES was chosen for use in this research based on data available and because of its affiliation with health and behaviors (Baker, 2014). The highest level of education will be used in conjunction with childhood SES because education can be an indicator of adult SES (Baker, 2014). In the TXSTDSC the highest level of education is also self-reported; however, this is more easily quantifiable than childhood SES.

As previously mentioned, diabetes is a group of diseases related to glucose intolerance, which includes the following three types: type 1, type 2, and gestational diabetes (CDCP, 2017). However, for the purposes of this research there were no differentiations between the three types in this study because other studies have not done so (CDCP, 2017; Feeser and Ratliff, 2018). Information for diabetes was found in both the donor's paperwork or listed as a mechanism in the cause of death.

Figure 2. Gouty response as seen in the metatarsophalangeal joint of the first metatarsal.

Gout is a build up of sodium urate in joints (Littlejohn and Hall, 1982; Ortner, 2003; Sibson, 2013; Lockyer and Stanner, 2016). Gout, as mentioned earlier, manifests as tophi in the bones of the hands and feet among others, and sometimes it can appear as lytic lesions occurring in multiple areas in the same region (Ortner, 2003; Falasca, 2006). While the information for gout in the TXSTDSC was found in the aforementioned areas of the skeleton, it was also found in the available medical histories.

The term “race” is used throughout the paper instead of ancestry because this is the phrasing used in the donor questionnaire the donor’s and next-of-kin’s identification of themselves (Forensic Anthropology Center at Texas State, 2018). New documents for those who wish to donate themselves were made in 2018, and this questionnaire also requests information on ancestry.

Data Collection

This study is composed of a sample of 246 skeletons from the TXSTDSC (infants and individuals who were cremated were excluded) (see Appendix 1). For each individual, the vertebral column was laid on a table in order. Each vertebra was examined to determine if there was fusion, where this fusion occurred if present, and if the fusion was diffuse idiopathic skeletal hyperostosis (DISH). To determine whether or not DISH was present the following questions were answered: 1. Are two or more continuous vertebrae fused? 2. Is intervertebral disc height retained? 3. Is there an absence of apophyseal joint ankylosis. If all three of these requirements were met, a diagnosis of DISH was made. However, all fusion was recorded regardless of whether or not it was DISH. Finally, those with DISH were examined for the presence or absence of gout. This was done in two stages. The first stage was examining the skeletal remains for the presence or absence of gout, and the second was examining the available medical histories for the presence of gout in the donation questionnaire. The second was performed following skeletal data collection.

After skeletal data was collected, individuals who had DISH were cross-referenced with self-reported donor information on their donation. Data compiled included the age, sex, race, height, weight, medical conditions or procedures, occupation, and socioeconomic status of the individual. Childhood SES was condensed from five categories into three categories in order to be more concise and was amended as follows: low/low-middle, middle, and middle-high/high. Education was also compiled into three categories, which included: less than a high school education, high school or the equivalent to a high school education, and more than a high school education. Diabetes was taken as present or absent. BMI was calculated by mass/((stature/100)^2). This data was collected at the end of the data collection to ensure the author collected skeletal data in an unbiased manner. All data was collected and stored on Microsoft Excel 2008® for Mac.

Using the statistical programs JMP PRO® and RStudio®, logistic regressions were run with a significance level of .05. This type of statistic measures the relationship between a dependent variable and one or more independent variables (Baker and Pearson, 2006; SAS Institute, 2012). This method, according to Baker and Pearson (2006), is more powerful than other techniques, like chi-squared tests, in studies that examine population risk. It allows the researcher to create outcomes that can allow for concurrent evaluation of variables (Baker and Pearson, 2006). This type of analysis was used to test DISH against the factors of age and BMI. Contingency analyses were used to analyze DISH against race, sex, childhood SES, highest level of education, diabetes, and gout. This type of analysis also allows a user to examine the relationship between an X variable and a Y variable (SAS Institute, 2012). These were conducted in JMP PRO®, and if the table was a 2x2, JMP PRO® automatically conducts a Fisher's Exact Test (SAS Institute, 2012). Rates of DISH were also examined. This was done to examine at how changing the diagnostic criteria changes rates within a sample.

Because of the nature of this project, neither the Institutional Review Board (IRB) or the Institutional Animal Care and Use Committee's (IACUC) approval was needed. While IRB pertains to use of human subjects in research, the Texas Anatomical Gift Act covers the use of donated bodies for research purposes (D. Wescott, personal communication, November 11, 2017).

3. RESULTS

Table 1. Rates of DISH in the TXSTDSC with two or more fused vertebrae.

	Male	Female	Total
DISH present	36	9	45
DISH not present	114	88	202
Total	150	97	247

The goal of this project was to determine if DISH could be used as an indicator of socioeconomic status, lifestyle, or medical history. To determine this, statistical analyses in the form of logistic regressions and contingency analyses were performed in the program JMP to determine if correlations existed, and where these correlations lay. The significance level was set to $p<0.05$ for all analyses. Out of 247 individuals examined, 45 individuals, or 18.2% had elements consistent with a diagnosis of DISH (Table 1). 9 of these, or 20%, are women, while the remaining 36, or 80%, of people with DISH, are men. Of the 247 individuals analyzed in this study, 221, or 89.5%, self-identified as White. 40 of these individuals had DISH, which makes up 88.9% of the sample of DISH individuals and gives a rate of 18.2% in White individuals. 10 individuals self-identified as Hispanic, and of these 2 individuals had DISH, or a rate of 20% in Hispanic individuals. 12 individuals identified as Black, and only one person of this sample had DISH, which puts the rate at 8%. Finally, there are 4 individuals who wrote "other," and 2 of these have DISH.

Continuing on with other lifestyle indicators, 102 individuals, or 44.2%, of 231 individuals marked that they had low to low-middle childhood SES. 94 individuals or 40.6% marked they were of middle childhood SES, and 35individuals, or 15.2%, indicated that they had upper-middle to upper childhood SES. 14 individuals were removed from this assessment for lack of data. Along similar lines, 99 individuals had less than a high school education, which make up 41.1% of the sample. 42.7%, or 103 individuals, marked that they received equivalent to a high school education or GED. Finally, 39 individuals indicated that they received more than a high school degree, which is 16.2% of the sample. 5 people were left out of this assessment due to insufficient data.

BMIs ranged from 13 to 64, with 28 being the average. This places most of the TXSTDSC as overweight or obese. Seventy-seven individuals, or 31.1%, indicated in the donor paperwork that they had diabetes, and 13 individuals, or 5.28%, either indicated in the donor paperwork or had skeletal markers that were consistent with gout.

The final indicator examined was age. The average age of the TXSTDSC is 65.54 years old. The mean age of those with DISH in this sample is 72.13 years old, and the average age of people without DISH in this collection is 64.07 years old.

Table 2. A summary of statistics ran to check correlations with DISH. Significant values are highlighted.

Lifestyle indicators	Test conducted	P-value
Age	Logistic Fit	**0.0014**
Sex	Contingency Analysis	**0.0034**
Race	Contingency Analysis	0.3179
Childhood SES	Contingency Analysis	0.3568
Highest Level of Education	Contingency Analysis	0.1817
BMI	Logistic Fit	0.4306
Diabetes	Contingency Analysis	0.0768
Gout	Contingency Analysis	**<0.0001**

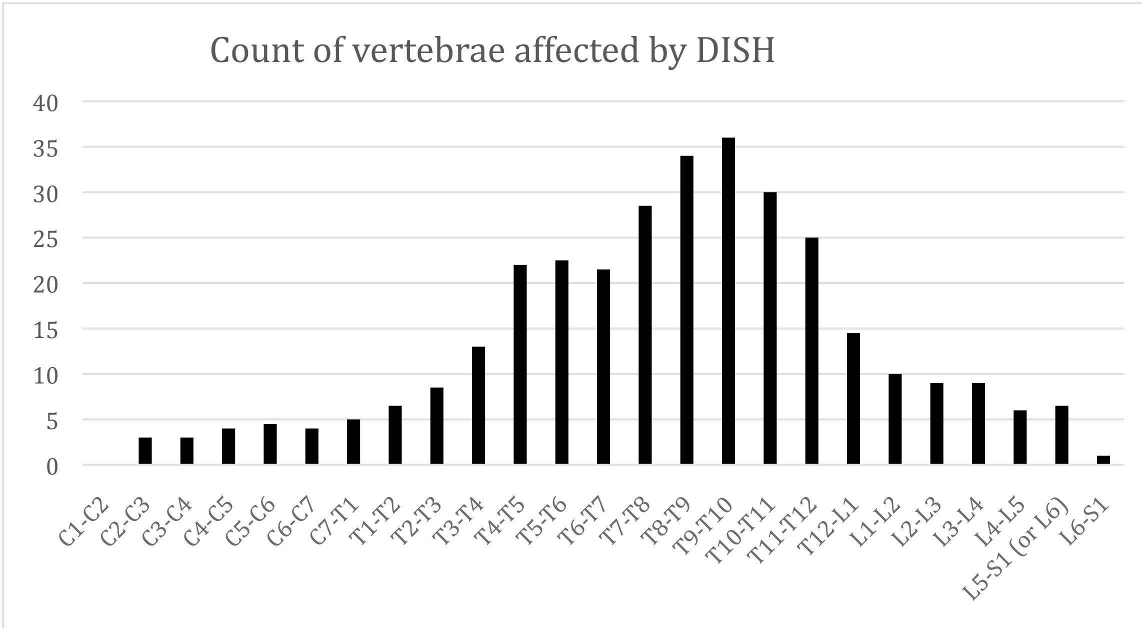


Figure 3. This graph illustrates which vertebrae are most affected by DISH.

Table 2 includes a break down of all the lifestyle indicators that were used in this study, the p-value, and which test was conducted. Charts of individual tests can be found in Appendices 3-10. In Figure 3, data was compiled as to which vertebrae were most affected by DISH. It was scored as 1 for complete fusion, 0.5 for areas that were ossifying before death, and a score of 0 was given for open disc space with no DISH-like fusion or fusion not consistent with DISH. Table 3 illustrates how varying definitions of DISH can affect the overall rate.

Table 3. This table illustrates how rates change within the TXSTDSC with the different required minimum number of vertebrae.

Number of continuous vertebrae	Number of individuals	Rate within the TXSTDSC
2 or more	45	18.2%
3 or more	29	11.7%
4 or more	19	7.7%

4. DISCUSSION

This project addressed the following questions: Is there a correlation between socioeconomic status and DISH? Do relationships exist among lifestyle indicators (such as BMI, diabetes, etc.)? Finally, what are the differences in DISH expression between sex and age categories in the Texas State Donated Skeletal Collection? The answers to these questions will now be discussed.

As illustrated in the results, race, childhood SES, highest level of education, BMI, and diabetes did not have significant correlations with DISH. Each of these, as discussed in the introduction have shown significance in previous studies on different populations. Race, for example, has shown higher rates in American White populations, though the authors admit that their other samples were small, much like this study (Weinfeld et al., 1997). Childhood SES was not as surprising as race for being non-significant. In previous studies in the historical remains, adult SES was the lifestyle indicator being tested; however, in this sample that information was not readily available (Rodgers and Waldron, 2001). Therefore, these results are unable to comment on the use in historical studies. The results presented also here suggest that there are forces outside the realm of this study that may buffer the effect of childhood SES or that it is not a factor at all. Along these same lines, highest level of education not being significant was also not unexpected, especially since childhood SES was not significant. As stated earlier, highest level of education is sometimes used as a proxy for SES, so it was important also to see if there was a correlation between the two. However, within the TXSTDSC, they are not correlated. They do however plot similarly when it comes to DISH susceptibility.

As stated above, both BMI and diabetes were not significant. With the average

BMI of the TXSTDSC being overweight, this is not surprising. Also, based on previous research, it was not surprising for diabetes to be insignificant; however, it was close to being significant with $p>0.0768$. This suggests that there might be a slight correlation there that more data would be able to parse out. Diabetes and BMI were also examined for correlation against each other, and it was statistically significant. However, when adding DISH into this equation, it was not statistically significant. Therefore, there may be other factors outside the scope of this research that are affecting this.

The final metabolic indicator examined in this study was gout. Unlike BMI and diabetes, the relationship between gout and DISH was statistically significant. This, like previous studies, suggests that there is some dietary factor in who develops DISH (Littlejohn and Hall, 2982; Fornaciari et al. 2009). These studies specifically suggest that this is due to higher fat diets, which suggests that there may be a correlation between gout and BMI. This was examined, and a statistically significant result was found, $p>0.0304$ (see Appendix 11). However, when this interaction was examined with DISH, no correlation was found. This suggests that there are other factors that may be causing this.

It is also important to note that gout does not always appear in the bones, as discussed previously. Modern medical intervention makes it possible to prevent the condition from worsening to where it elicits a bony response (Wood, Milner, Harpening, & Weiss, 1982). However, if this is the case, it may be possible that the same factors, like high SUA, which cause gout to have a bony response, can cause the ossification of the ligament. More research in the clinical realm is needed to determine this.

Another lifestyle indicator that illustrated significance was sex, which is in agreement with previous studies (Harris et al., 1974; Resnick et al., 1975; Tsukamoto et al., 1977; Utsinger, 1985; Bombak, 2012). One factor that may lead to these results is menopause. After menopause, the remodeling process of bones becomes unbalanced with more bone being resorbed than deposited (Bjørnerem et al., 2018). According to Weinfeld et al. (1997), individuals with diagnosed osteoporosis (unspecified sex) had low prevalence of DISH. More research is needed to see this relationship. However, the result presented here should be viewed with caution since, much like the previous studies, more males, 150 in total, than females, 97 individuals, were included in this study.

The final indicator examined in this study that showed significance was age. Age is the number 1 cited correlation with DISH, so this result was not surprising (Resnick et al., 1975; Kim et al., 2012; Fornaciari & Giuffra, 2013; Smith et al., 2013; Toyoda et al., 2017; Kuperus et al., 2018). This correlation is a positive one, meaning as a population increases in age, prevalence and, severity of DISH increases. This can be seen within this sample. As stated in the results, the average age of the TXSTDSC is 65.54 years old, the mean age of those with DISH in this sample is 72.13 years old, and the average age of people without DISH in this collection is 64.07 years old. As shown in this, the overall average of people with DISH is higher than both the overall sample as well as the sample without DISH. While this sample is skewed towards older individuals, it appears that there are factors that are allowing individuals with DISH to live longer than others within this sample. However, it also comes down to who chooses to donate their body.

Another aspect of this study was to examine which area of the spine was most affected by DISH. As table 3 illustrates, the most affected vertebral joint was thoracic (T) 9 and T10, with the joint above and below closely following in frequency. This finding is in

Figure 4. Illustrated in this photo is a cervical manifestation of DISH and medical hardware. A bony growth can be observed on the dens process of C2.

agreement with previous studies that say the lower thoracic are most affected, followed by upper thoracic and lumbar, and cervical vertebrae are least affected (Tsukamoto et al., 1977; Resnick et al., 1978; Utsinger, 1985; Suzuki et al., 1991; Madar, 2008; Verlaan et al., 2011; Smith et al., 2013; Toyoda et al., 2017). It should be noted that no fusion of cervical (C) 1 and C2 were observed; however, abnormalities were observed on the dens process. More research needs to be conducted to determine if this is a manifestation of DISH.

A final aspect of this study was to examine how changing the minimum number of vertebrae required in a DISH diagnosis can affect the overall rate of DISH in a population or sample. With the least strict definition of 2 or more continuous vertebrae, the rate within the TXSTDSC was 18.2%, or 45 individuals. This is the largest of the samples. When the parameters are increased to 3 or more, the prevalence is 11.7%, or 29 individuals. Finally, following the Resnick and Niwayama (1976) criteria, the overall prevalence of DISH is 7.7%, or 19 individuals. All ranges fall within ranges of clinical studies that place the overall prevalence from nearly 0 to 44% in an overall population depending on parameters (Bateman et al., 2018). However, there is a large decrease in prevalence among these definitions. While it may be beneficial in clinical contexts to use the more conservative definition for better diagnosis, there may be consequences, such as not providing treatments, for individuals who have a less severe condition. Also, as mentioned previously in skeletal remains it is not uncommon for researchers to use the Resnick and Niwayama (1976) criteria; however, this may be too conservative. With soft tissue removed, it is relatively easy to perform differential diagnosis for DISH with the 2 or more definition. Therefore, in forensic, historic, and bioarchaeological remains, the threshold should be lowered to 2 or more.

Limitations

One of the major limitations of this study is the quality or quantity of antemortem information available. While donor data is collected for all TXSTDSC individual, many times it is incomplete. This could be due to the phrasing of the questions, or in the case of legal next-of-kin who are donating the body of a loved one, there may be a lack of comprehensive knowledge. Another issue with self-reported data is that it cannot be verified, or, as in the case of childhood SES, there is no exact measure on the donor data sheets. Much like the information provided by next-of-kin, this does not imply that this information is false, just that it a factor to consider.

Continuing on the limitations of childhood SES, it may not be the best indicator for this study; however, it was the only data available to test. While stressors and lifestyle of childhood have been found to affect adult life, it is more likely that adult SES affects the rate of DISH. This makes sense when compared with the historical studies of monks and such since the researchers are examining adult SES.

Along the same lines as limitations in antemortem data is the fact that this sample was overwhelmingly white, with 221 of the 247 individuals self-identifying as such. Being such a homogenous sample, this study cannot accurately make claims on whether this factor truly affects DISH presence or rate. A larger, more diverse sample is needed to assess such claims.

Diet was also inferred from SES; however, it would be interesting for future studies to include the analysis of stable isotopes (Fornaciari et al., 2009). This could assess how diet differs between SESes, which could more clearly examine whether there is a correlation between diet and DISH.

5. CONCLUSION

Diffuse idiopathic skeletal hyperostosis (DISH), a condition with unknown etiology, causes a candle-wax fusion of the vertebral column along the anterolateral aspect of the vertebral bodies (Forestier, & Rotes-Querol, 1950; Resnick et al., 1975; Resnick, & Niwayama, 1976; Utsinger, 1985). DISH can affect extraspinal areas, such as entheseal sites (Resnick et al., 1975; Suzuki et al., 1991; Seidler et al., 2008; Diederichs et al., 2011; Alsaadawi, 2017; Bakker et al., 2017; Kortyna, 2017). This study examined DISH in the Texas State Donated Skeletal Collection to see if there were correlations between lifestyle and those who had the condition. The lifestyle indicators tested for correlation with DISH in this study include age, BMI, childhood socioeconomic status, highest level of education, presence of diabetes, presence of gout, race, and sex. This information was recorded from paperwork completed by each donor or their next-of-kin. This study illustrated that within the TXSTDSC the only significant correlations seen are between DISH and age, DISH and gout, as well as DISH and sex. These results are in agreement with previous studies. Also like previous studies, the most commonly affected to the least commonly affected vertebrae were as follows: lower thoracic, upper thoracic, lumbar, and cervical. No observations of DISH were observed at the C1-C2 joint; however, more research needs to be conducted. Rates of DISH differed greatly depending on which definition was used, and I suggest that in situations where there are dry, skeletal remains, the minimum required number of continuously fused vertebrae should be 2. The importance of this research lies in that this research adds to the literature of DISH and interactions with different aspects of lifestyle.

This study could be strengthened with a larger sample size. Though this thesis made use of all available individuals of the TXSTDSC at the time of this writing, this amounted to 246 people, only 26 of whom had DISH. Larger sample sizes and more diversity could be accomplished using other modern skeletal collects, or with using larger numbers of CT scans from clinical settings (Resnick et al., 1975; Cassim et al., 1990; Weinfeld et al., 1997; Kim et al. 2004; Hirasawa et al., 2015; Kangotani et al., 2015; Bateman et al., 2018). With the latter, information about diet could be directly collected via interviews, and with the former, stable isotope analysis could assist with determining diet (Fornaciari et al. 2009). A final note, future research into the field of work, such as manual versus non-manual occupations, could be assessed. This work could provide more information into how DISH affects entheseal sites, which in turn could add to the larger literature on ossification at these locations. It could also provide more insight into how DISH affects those who did certain jobs because there has been some association with manual labor.

Finally, this study is representative of the entire US population in regards to DISH and the lifestyle indicators examined here. Much like a cemetery sample in an archaeological site, interpretations of these results should air on the side of caution. Donated skeletal collections are still under the pressure of the Osteological Paradox (Wood et al. 1992).

APPENDIX SECTION

Appendix 1. Vertebral fusion datasheet

Donation #

Vertebral Joint	Fusion?	Is there preservation(s) of intervertebral disc height?	Is there the absence of apophyseal joint ankylosis?
C1-C2			
C2-C3			
C3-C4			
C4-C5			
C5-C6			
C6-C7			
C7-T1			
T1-T2			
T2-T3			
T3-T4			
T4-T5			
T5-T6			
T6-T7			
T7-T8			
T8-T9			
T9-T10			
T10-T11			
T11-T12			
T12-L1			
L1-L2			
L2-L3			
L3-L4			
L4-L5			
L5-S1			

Appendix 2. Donor demographic data.

#	Age	Sex	Race	Childhood SES	Education	BMI	DISH	Diabetes	Gout
D01-2008	81	M	H			22	No	No	No
D02-2008	65	F	W	1	2	64	No	Yes	No
D03-2008	77	M	W	2	2	43	Yes	Yes	Yes
D01-2009	49	M	W	2	1	21	No	No	No
D02-2009	91	M	W	3	1	19	No	No	No
D03-2009	32	M	W	2	2	34	No	No	No
D04-2009	87	F	W	3	2	18	Yes	Yes	No
D05-2009	61	M	W	3	1	19	No	No	No
D06-2009	77	F	W	2	2	27	No	No	No
D07-2009	65	F	W	1	2	20	No	No	No
D08-2009	53	F	W	2	2	47	No	No	No
D09-2009	58	F	W	1	1	31	No	No	No
D10-2009	76	F	W	3	2	24	No	No	No
D11-2009	79	F	W	2	2	47	No	No	No
D01-2010	75	M	B	1	2	27	No	Yes	No
D02-2010	71	M	W	1	3	20	No	No	No
D04-2010	53	F	W	2	2	21	No	No	No
D05-2010	67	M	W	1	2	49	No	Yes	No
D06-2010	57	M	B	1	1	24	No	No	No
D07-2010	46	M	W	2	2	26	No	No	No
D08-2010	67	M	H	1	1	24	No	Yes	No
D09-2010	63	M	W	2	3	21	Yes	No	No
D10-2010	32	M	W	2	1	26	No	No	No
D11-2010	91	M	W	1	3	18	No	No	No
D12-2010	54	M	W	1	1	17	No	No	No
D13-2010	70	M	W		1	52	No	Yes	No
D14-2010	63	F	B	2	1	37	No	No	No
D15-2010	64	M	H	2	1	27	No	No	No
D01-2011	40	M	W	1	1	50	No	No	No
D03-2011	66	M	W	1	2	38	Yes	Yes	Yes
D04-2011	68	F	W	2	2	41	No	Yes	No
D05-2011	80	M	W	2	2	23	No	No	No
D06-2011	53	F	W	1	1	42	No	Yes	No
D07-2011	87	M	W		1	39	Yes	No	Yes
D08-2011	53	M	W	3	2	26	No	No	No
D09-2011	54	F	W	2	3	27	No	No	No
D10-2011	63	M	W	2	1	22	No	No	No
D11-2011	75	M	W	2	2	30	No	No	No
D12-2011	53	F	W	1	2	35	No	No	No
D13-2011	65	M	W	2	2	22	Yes	No	No
D14-2011	51	M	W				No	No	No
D15-2011	49	M	W	1	1	24	No	No	No
D16-2011	84	M	B	1	1	13	No	No	No
D17-2011	75	F	W	3	2	21	No	Yes	No
D19-2011	56	M	W	1	1	29	No	Yes	No

Appendix 2 (cont.). Donor demographic data.

#	Age	Sex	Race	Childhood SES	Education	BMI	DISH	Diabetes	Gout
D20-2011	73	F	W	1	2	59	No	Yes	No
D21-2011	56	F	W	2	2	31	No	No	No
D22-2011	56	M	W	1	2	27	No	No	No
D23-2011	66	F	W	1	2	23	No	Yes	No
D01-2012	57	F	W	2	1	17	No	No	No
D02-2012	68	F	W	1	1	24	Yes	Yes	No
D03-2012	78	F	W	2	1	21	No	No	No
D04-2012	63	F	W	2	2	25	No	No	No
D05-2012	79	M	W	1	1	26	Yes	No	No
D06-2012	58	M	W	2	1	23	No	Yes	No
D07-2012	53	F	W	2	2	44	No	No	No
D08-2012	77	F	W	2	2	44	No	No	No
D09-2012	88	M	B	1	2	23	No	No	No
D10-2012	59	F	B	2	2	44	No	Yes	No
D11-2012	76	M	H	2	1	31	No	Yes	No
D12-2012	64	F	W	1	2	21	No	No	No
D13-2012	48	M	W	2	1	30	Yes	No	Yes
D14-2012	85	M	H	1	1	22	No	Yes	No
D15-2012	62	M	W	2	2	22	No	No	No
D16-2012	47	M	W	2	1	37	No	No	No
D17-2012	90	F	W	2	3	22	No	No	No
D18-2012	59	M	W	2	3	48	No	Yes	No
D19-2012	18	M	W	1	2	26	No	No	No
D20-2012	34	M	W	3	2		No	No	No
D21-2012	42	M	W	3	2	21	No	No	No
D22-2012	78	M	W	1	1	43	Yes	Yes	Yes
D23-2012	56	M	W	1	1	31	Yes	Yes	Yes
D24-2012	83	F	W		3	34	Yes	Yes	No
D26-2012	102	F	W	1	2	35	No	No	No
D27-2012	58	F	W	3	2	26	No	No	No
D28-2012	75	M	W	1	1	25	No	No	No
D29-2012	68	M	W	1	2	27	No	Yes	No
D30-2012	74	M	W	1	2	31	No	No	No
D31-2012	65	F	W	2	1	20	No	No	No
D32-2012	47	F	W	1	1	14	No	No	No
D33-2012	72	M	W	1	1	31	Yes	No	Yes
D34-2012	72	M	O	2	1	23	No	No	No
D35-2012	63	F	W	2	1	41	No	No	No
D36-2012	42	F	W	1	1	48	No	Yes	No
D37-2012	49	M	B		2	33	No	No	No
D38-2012	50	M	W	1	1	21	No	No	No

Appendix 2 (cont.). Donor demographic data.

#	Age	Sex	Race	Childhood SES	Education	BMI	DISH	Diabetes	Gout
D38-2012	50	M	W	1	1	21	No	No	No
D39-2012	57	M	W	2	3	16	No	Yes	No
D40-2012	67	F	H	1	2	23	No	Yes	No
D41-2012	60	M	W	1	2	35	No	No	No
D42-2012	68	M	W	1	1	38	No	Yes	No
D43-2012	71	M	W	3	2	29	No	No	No
D44-2012	79	M	W	3	1	27	Yes	No	No
D45-2012	65	M	W	1	1	20	No	No	No
D46-2012	60	M	W	2	1	40	No	No	No
D47-2012	68	M	W	2	2	33	No	Yes	No
D48-2012	64	F	W	2	3	30	No	Yes	No
D49-2012	43	F	W	2	1	31	No	No	No
D50-2012	64	M	W	1	1	38	Yes	Yes	No
D02-2013	53	M	W	2	3	24	Yes	No	No
D03-2013	89	F	W	3	1	16	No	No	No
D04-2013	79	M	W	2	1	21	No	No	No
D05-2013	54	M	W	2	1	36	No	Yes	No
D06-2013	68	M	W	1	3	44	No	Yes	No
D07-2013	76	M	W	2	3	45	Yes	Yes	No
D08-2013	68	F	W	1	1	21	No	No	No
D09-2013	45	F	W	2	3	34	No	No	No
D10-2013	83	F	W	1	1	19	Yes	No	No
D11-2013	64	M	W	2	1	23	No	Yes	No
D12-2013	89	F	O	3	3	23	Yes	Yes	No
D13-2013	69	M	W	1	2	44	No	No	No
D14-2013	58	M	W	2	1	19	No	Yes	No
D15-2013	55	F	W	3	2	24	No	No	No
D16-2013	53	M	W	2	3	46	No	Yes	No
D17-2013	47	F	W	2	2	20	No	No	No
D18-2013	91	F	W	1	1	19	Yes	No	Yes
D19-2013	60	F	W				No	No	No
D20-2013	67	M	W	2	2	25	Yes	Yes	No
D21-2013	66	M	W			35	Yes	No	No
D22-2013	54	M	W	2	2	26	No	No	No
D23-2013	63	M	W	1	2	22	Yes	Yes	Yes
D24-2013	53	F	W		2	29	No	Yes	No
D25-2013	62	M	W	3	2	32	No	No	No
D26-2013	69	M	W	1	1	22	Yes	No	No
D27-2013	69	M	W	3	3	28	No	No	No
D28-2013	85	M	W	1	1	27	No	No	No
D29-2013	71	F	W	1	1	26	No	No	No
D30-2013	86	M	W	2	2	25	Yes	No	No

Appendix 2 (cont.). Donor demographic data.

#	Age	Sex	Race	Childhood SES	Education	BMI	DISH	Diabetes	Gout
D31-2013	64	M	W	3	1	32	No	No	No
D32-2013	87	F	W	3	2	19	No	No	No
D33-2013	52	M	W	3	1	22	No	No	No
D34-2013	79	F	W			36	No	No	No
D35-2013	77	M	W	1	2	26	Yes	Yes	No
D36-2013	88	M	W	2	3	20	No	Yes	No
D37-2013	64	M	W	3	2	15	Yes	No	No
D38-2013	89	F	H		1		No	Yes	No
D39-2013	90	F	W	1	1	21	No	No	No
D41-2013	76	F	W	1	1	15	No	No	No
D42-2013	74	F	W	1	2	23	No	No	No
D43-2013	70	M	W	2	1	18	No	No	No
D44-2013	64	M	W	2	3	21	No	Yes	No
D45-2013	52	M	W	3	1	20	No	No	No
D46-2013	55	M	W	2	1	34	No	No	No
D47-2013	56	F	W	2	2	35	No	Yes	No
D49-2013	61	M	W	2	2	21	No	Yes	No
D50-2013	71	M	W	2	2	22	Yes	No	No
D51-2013	75	M	W	1	1	28	Yes	No	Yes
D52-2013	52	M	W	2	1	24	No	No	No
D53-2013	65	M	W	1	2	21	No	No	No
D54-2013	94	M	W	1	1	22	Yes	No	No
D55-2013	57	M	W	1	2	32	No	No	No
D56-2013	63	F	W	1	2	24	No	No	No
D57-2013	54	M	W	1	1	18	No	No	No
D59-2014	58	M	W	1	3	19	No	No	No
D61-2013	61	M	W	3	2	21	No	No	No
D65-2013	61	M	W	1	2	26	No	No	No
D66-2013	72	M	W	3	2	36	No	Yes	No
D01-2014	72	F	H	1	1	24	No	No	No
D02-2014	64	F	W	2	2	41	No	No	No
D03-2014	64	F	W	3	1	20	No	No	No
D04-2014	63	M	W	1	2		Yes	Yes	No
D05-2014	88	F	W	1	1	22	No	Yes	No
D06-2014	74	M	W		2	30	No	No	No
D07-2014	79	F	W	3	1	27	Yes	Yes	No
D08-2014	57	M	B	3	1	40	Yes	Yes	No
D09-2014	70	M	W	3	2	15	No	No	No
D10-2014	64	F	W	2	2	23	No	Yes	No
D11-2014	46	F	W	1	1	33	No	No	No
D12-2014	64	F	W	2	3	36	No	No	No
D13-2014	29	M	B	1	1	22	No	Yes	No

Appendix 2 (cont.). Donor demographic data.

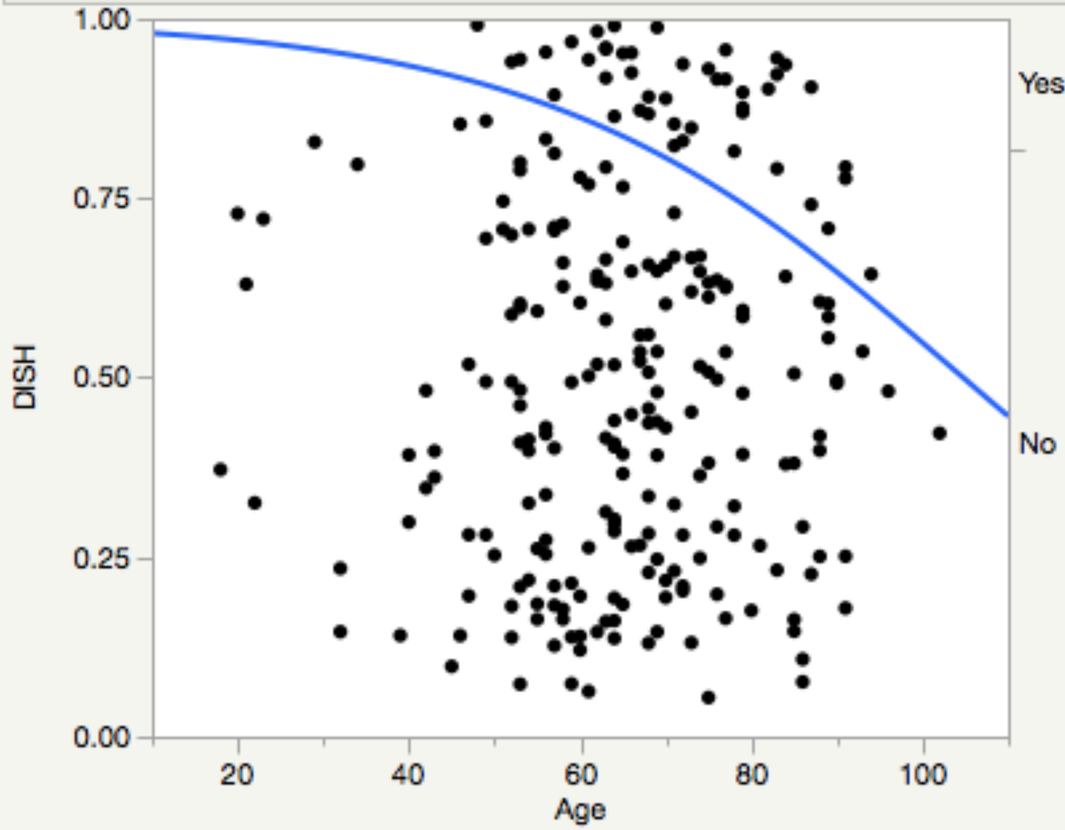
#	Age	Sex	Race	Childhood SES	Education	BMI	DISH	Diabetes	Gout
D14-2014	78	M	W	1	1	24	No	No	No
D15-2014	52	M	W	1	2	24	No	Yes	No
D16-2014	59	F	W	1	2	26	No	Yes	No
D17-2014	68	M	W	2	1	34	No	Yes	No
D19-2014	77	F	W	1	2	22	No	No	No
D20-2014	83	M	W	1	3	22	Yes	Yes	No
D21-2014	23	F	W	3	2	50	No	No	No
D22-2014	57	M	B		2	30	No	No	No
D23-2014	57	F	W	2	2	27	No	No	No
D24-2014	70	M	W	2	1	28	No	No	No
D25-2014	61	M	O	1		35	Yes	No	No
D26-2014	72	M	W	2	3	21	Yes	No	No
D27-2014	56	M	W	1	2	26	No	No	No
D28-2014	68	F	H	1	2	27	Yes	Yes	Yes
D29-2014	72	M	W	1	1	22	No	No	No
D30-2014	66	F	W		1	29	No	No	No
D32-2014	69	F	W	2	3	59	No	No	No
D33-2014	20	M	W	2	2	35	No	No	No
D35-2014	62	M	W	2	2	21	No	No	No
D36-2014	83	F	W	2	1		No	No	No
D37-2014	73	F	W	1	3	22	No	Yes	No
D38-2014	79	M	W	1	1	30	No	No	No
D39-2014	70	F	W	1	1	30	Yes	No	No
D40-2014	84	M	W	1	1	20	No	No	No
D41-2014	69	F	W		1	27	No	Yes	No
D42-2014	67	F	W	2	1	39	No	No	No
D43-2014	73	M	W	1	1	37	Yes	No	No
D44-2014	73	M	W	1	3	21	No	No	No
D47-2014	69	F	W	2	2	41	No	Yes	No
D48-2014	52	M	W	2	1	30	No	No	No
D49-2014	56	M	W	2	2	28	No	No	No
D50-2014	75	M	W	2	2	18	No	No	No
D51-2014	74	M	W		1	25	No	No	No
D52-2014	63	M	B	2	2	33	No	Yes	No
D53-2014	60	M	O	1	2	29	No	No	No
D54-2014	52	M	H	1	1	39	Yes	No	Yes
D55-2014	62	M	W	2	3	30	Yes	No	No
D56-2014	69	F	W	1	1	25	No	No	No
D57-2014	59	M	W	2	2	46	Yes	Yes	No
D59-2014	60	M	W	3	3	22	No	No	No
D60-2014	59	M	W	1	3	25	No	No	No
D62-2014	53	M	W	1	1	28	No	Yes	No

Appendix 2 (cont.). Donor demographic data.

#	Age	Sex	Race	Childhood SES	Education	BMI	DISH	Diabetes	Gout
D64-2014	89	F	W	2	2	16	No	No	No
D65-2014	43	M	W	3	2	23	No	Yes	No
D68-2014	84	M	W	1	3	28	Yes	No	No
D02-2015	82	M	W	2	2	42	Yes	No	No
D03-2015	85	M	W	2	1	27	No	No	No
D05-2015	39	F	W	3	1	17	No	No	No
D06-2015	93	M	W	1	1	37	No	Yes	No
D08-2015	51	M	W	1	1	40	No	Yes	No
D10-2015	66	M	W	1	2	44	No	Yes	Yes
D12-2015	40	F	W	2	2	27	No	Yes	No
D14-2015	70	M	W	2	2	26	No	Yes	No
D15-2015	71	M	W	2	1	28	Yes	No	No
D16-2015	96	M	W	3	3	23	No	Yes	No
D18-2015	91	F	W	2	3	15	No	No	No
D20-2015	74	M	W	2	1	22	No	No	No
D21-2015	63	F	W	3	1	23	No	No	No
D24-2015	67	F	W	1	2	30	No	No	No
D25-2015	68	F	W	1	3	16	No	No	No
D26-2015	21	F	W	2	2	26	No	Yes	No
D28-2015	76	F	W	1	1	48	No	Yes	No
D30-2015	86	M	W	2	2	23	No	No	No
D31-2015	55	F	W	1	3	28	No	No	No
D32-2015	73	F	W	1	2	30	No	No	No
D35-2015	69	F	W	2	3	23	No	No	No
D37-2015	55	F	W	2	2	18	No	No	No
D38-2015	77	F	W	1	1	33	No	Yes	No
D39-2015	85	M	W	1	3	21	No	No	No
D41-2015	57	F	W	2	2	19	No	No	No
D52-2015	22	M	W	2	2	22	No	No	No
D60-2015	49	F	W	2	3	29	No	No	No
D68-2015	62	M	W	3	3	18	No	No	No
D01-2016	79	F	W	1	2	17	No	No	No
D12-2016	88	M	W	3	3	22	No	No	No
D16-2016	71	M	W	1	2	26	No	No	No
D22-2016	68	F	B	1	2	26	No	Yes	No
D26-2016	86	F	W	1	3	19	No	Yes	No

Appendix 3. Logistic fit of DISH and age.

Logistic Fit of DISH By Age



Iterations

Whole Model Test

Fit Details

Parameter Estimates

Term	Estimate	Std Error	ChiSquare	Prob>ChiSq
Intercept	4.29762376	0.9233058	21.67	<.0001*
Age	-0.0410254	0.0128772	10.15	0.0014*

For log odds of No/Yes

Covariance of Estimates

Appendix 4. Contingency analysis of sex and DISH.

Contingency Table

Sex	Count / Total % / Col % / Row %	DISH: No	DISH: Yes	Total
F	Count	88	9	97
	Total %	35.63	3.64	39.27
	Col %	43.56	20.00	
	Row %	90.72	9.28	
M	Count	114	36	150
	Total %	46.15	14.57	60.73
	Col %	56.44	80.00	
	Row %	76.00	24.00	
Total	Count	202	45	247
	Total %	81.78	18.22	

Tests

N	DF	-LogLike	RSquare (U)
247	1	4.6207390	0.0394

Test	ChiSquare	Prob>ChiSq
Likelihood Ratio	9.241	0.0024*
Pearson	8.569	0.0034*

Fisher's Exact Test	Prob	Alternative Hypothesis
Left	0.9993	Prob(DISH=Yes) is greater for Sex=F than M
Right	0.0022*	Prob(DISH=Yes) is greater for Sex=M than F
2-Tail	0.0038*	Prob(DISH=Yes) is different across Sex

Appendix 5. Contingency analysis of DISH and race.

Contingency Table

Race	Count Total % Col % Row %	DISH: No	DISH: Yes	Total
B	Count	11	1	12
	Total %	4.45	0.40	4.86
	Col %	5.45	2.22	
	Row %	91.67	8.33	
H	Count	8	2	10
	Total %	3.24	0.81	4.05
	Col %	3.96	4.44	
	Row %	80.00	20.00	
O	Count	2	2	4
	Total %	0.81	0.81	1.62
	Col %	0.99	4.44	
	Row %	50.00	50.00	
W	Count	181	40	221
	Total %	73.28	16.19	89.47
	Col %	89.60	88.89	
	Row %	81.90	18.10	
Total	Count	202	45	247
	Total %	81.78	18.22	

Tests

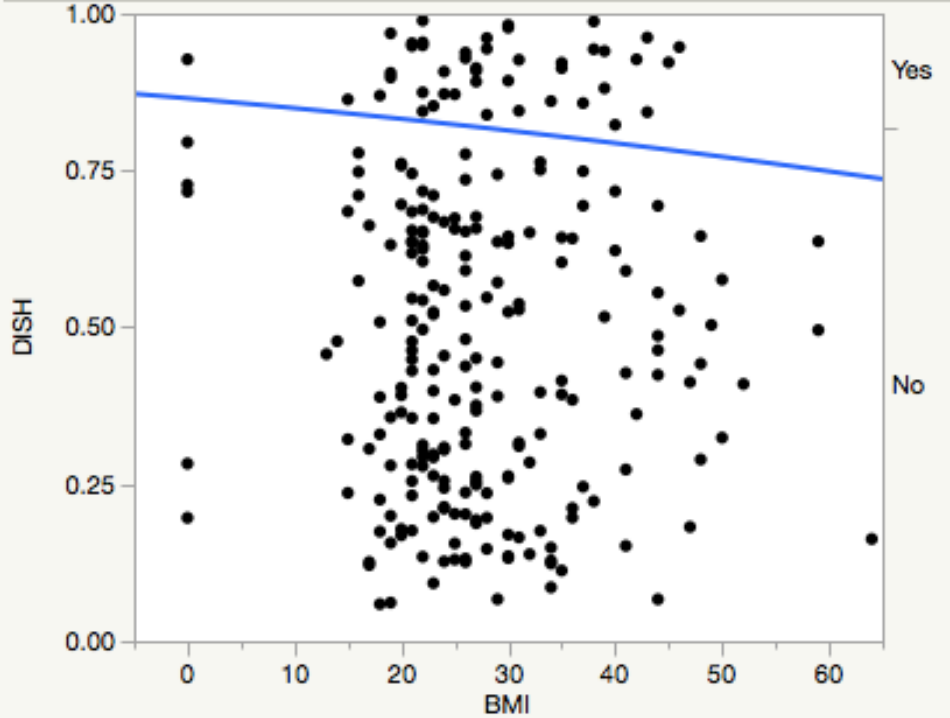
N	DF	-LogLike	RSquare (U)
247	3	1.5195713	0.0130

Test	ChiSquare	Prob>ChiSq
Likelihood Ratio	3.039	0.3856
Pearson	3.522	0.3179

Warning: 20% of cells have expected count less than 5, ChiSquare suspect.

Appendix 6. Logistic regression of DISH by BMI.

Logistic Fit of DISH By BMI



Whole Model Test

Model	-LogLikelihood	DF	ChiSquare	Prob>ChiSq
Difference	0.30765	1	0.615295	0.4328
Full	116.94138			
Reduced	117.24903			

RSquare (U)	0.0026
AICc	237.932
BIC	244.902
Observations (or Sum Wgts)	247

Fit Details

Parameter Estimates

Term	Estimate	Std Error	ChiSquare	Prob>ChiSq
Intercept	1.85699697	0.4863306	14.58	0.0001*
BMI	-0.01276	0.0161895	0.62	0.4306

For log odds of No/Yes

Appendix 7. Contingency analysis of DISH and childhood SES.

Contingency Table

DISH

Child SES	Count / Total % / Col % / Row %	No	Yes	Total
1	Count	80	22	102
	Total %	34.63	9.52	44.16
	Col %	42.33	52.38	
	Row %	78.43	21.57	
2	Count	81	13	94
	Total %	35.06	5.63	40.69
	Col %	42.86	30.95	
	Row %	86.17	13.83	
3	Count	28	7	35
	Total %	12.12	3.03	15.15
	Col %	14.81	16.67	
	Row %	80.00	20.00	
Total	Count	189	42	231
	Total %	81.82	18.18	

Tests

N	DF	-LogLike	RSquare (U)
231	2	1.0549479	0.0096

Test	ChiSquare	Prob>ChiSq
Likelihood Ratio	2.110	0.3482
Pearson	2.061	0.3568

Appendix 8. Contingency analysis of highest level of education and DISH.

Contingency Table

DISH

School	Count / Total % / Col % / Row %	No	Yes	Total
1	Count	78	21	99
	Total %	32.37	8.71	41.08
	Col %	39.39	48.84	
	Row %	78.79	21.21	
2	Count	90	13	103
	Total %	37.34	5.39	42.74
	Col %	45.45	30.23	
	Row %	87.38	12.62	
3	Count	30	9	39
	Total %	12.45	3.73	16.18
	Col %	15.15	20.93	
	Row %	76.92	23.08	
Total	Count	198	43	241
	Total %	82.16	17.84	

Tests

N	DF	-LogLike	RSquare (U)
241	2	1.7511431	0.0155

Test	ChiSquare	Prob>ChiSq
Likelihood Ratio	3.502	0.1736
Pearson	3.411	0.1817

Appendix 9. Contingency analysis of DISH and diabetes.

Contingency Table

Diabetes \ DISH	Count / Total % / Col % / Row %	No	Yes	Total
No	Count	144	26	170
	Total %	58.30	10.53	68.83
	Col %	71.29	57.78	
	Row %	84.71	15.29	
Yes	Count	58	19	77
	Total %	23.48	7.69	31.17
	Col %	28.71	42.22	
	Row %	75.32	24.68	
Total	Count	202	45	247
	Total %	81.78	18.22	

Tests

N	DF	-LogLike	RSquare (U)
247	1	1.5039408	0.0128

Test	ChiSquare	Prob>ChiSq
Likelihood Ratio	3.008	0.0829
Pearson	3.130	0.0768

Fisher's Exact Test	Prob	Alternative Hypothesis
Left	0.9724	Prob(DISH=Yes) is greater for Diabetes=No than Yes
Right	0.0577	Prob(DISH=Yes) is greater for Diabetes=Yes than No
2-Tail	0.1082	Prob(DISH=Yes) is different across Diabetes

Appendix 10. Contingency analysis of gout and DISH.

Contingency Table

Gout	Count / Total % / Col % / Row %	DISH: No	DISH: Yes	Total
No	Count	201	33	234
	Total %	81.38	13.36	94.74
	Col %	99.50	73.33	
	Row %	85.90	14.10	
Yes	Count	1	12	13
	Total %	0.40	4.86	5.26
	Col %	0.50	26.67	
	Row %	7.69	92.31	
Total	Count	202	45	247
	Total %	81.78	18.22	

Tests

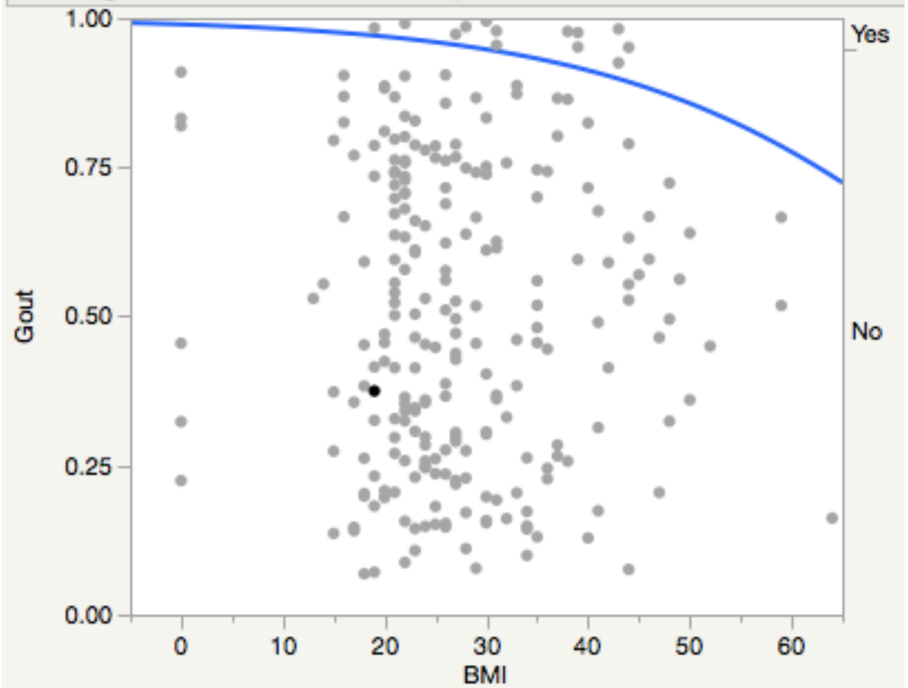
N	DF	-LogLike	RSquare (U)
247	1	18.527465	0.1580

Test	ChiSquare	Prob>ChiSq
Likelihood Ratio	37.055	<.0001*
Pearson	50.555	<.0001*

Fisher's Exact Test	Prob	Alternative Hypothesis
Left	1.0000	Prob(DISH=Yes) is greater for Gout=No than Yes
Right	<.0001*	Prob(DISH=Yes) is greater for Gout=Yes than No
2-Tail	<.0001*	Prob(DISH=Yes) is different across Gout

Appendix 11. Logistic regression of BMI and gout.

Logistic Fit of Gout By BMI



Iterations

Whole Model Test

Model	-LogLikelihood	DF	ChiSquare	Prob>ChiSq
Difference	2.208939	1	4.417878	0.0356*
Full	48.720498			
Reduced	50.929437			

RSquare (U)	0.0434
AICc	101.49
BIC	108.46
Observations (or Sum Wgts)	247

Fit Details

Parameter Estimates

Term	Estimate	Std Error	ChiSquare	Prob>ChiSq
Intercept	4.54650668	0.8822581	26.56	<.0001*
BMI	-0.0550817	0.0254378	4.69	0.0304*

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