Comparative Analysis of Clinical and Behavioral Factors in Diabetic and Non-Diabetic Inflammatory Disease Population

By

Hetu Gadhia

A Dissertation Submitted to

Rutgers – School of Health Professions

in partial fulfillment of the Requirements for the Degree of

Doctor of Philosophy in Biomedical Informatics

Department of Health Informatics

School of Health Professions

Rutgers, the State University of New Jersey

October 2017

RUTGERS
School of Health Professions

Final Dissertation Defense Approval Form

Comparative Analysis of Clinical and Behavioral Factors in Diabetic and Non-Diabetic Inflammatory Disease Population

BY

Hetu Gadhia

Dissertation Committee:

Shankar Srinivasan PhD

Frederick Coffman PhD

Hetal Joshi MD

Approved by the Dissertation Committee:

_____ Date: _____

_____ Date: _____

_____ Date: _____

_____ Date: _____

_____ Date: _____

TABLE OF CONTENTS

Page

ABSTRACT

Inflammation is characterized as the response of vascularized tissues to injury or infection. Inflammation usually occurs as a protective response to an injury or destruction of tissue, which intends to destroy the injured tissue. Arthritis and ulcerative colitis are two of the highly prevalent inflammatory diseases amongst US population. In addition, type-2 diabetes is one of the highly prevalent comorbidities in current US population, however very few studies have investigated the relationship between the highly prevalent inflammatory disease and the type-2 diabetes. In the current study, we aim to identify the factors that influence the prevalence of these inflammatory diseases in type-2 diabetic population. These factors that affect the prevalence of inflammatory disease patients with diabetes are characterized in two categories, clinical factors and behavioral factors. Clinical factors are defined as biological factors that cannot be easily modified and can be quantified clinically or for which a clinical diagnosis exist. Clinical factors that are analyzed in this study are BMI and the effects of sleep on the prevalence of the inflammatory diseases amongst diabetic patients. On the other hand, behavioral factors are characterized by factors that are controlled externally and can be modified and rectified very quickly. Behavioral factors investigated in this study are smoking status, alcohol consumption status and presence of physical activity. The goal of this study is to assess the risk associated with the prevalence of these behavioral and clinical factors in association with prevalence of the two inflammatory diseases in diabetic populations. The odds ratio between the prevalence of these factors and the prevalence of arthritis, ulcerative colitis or both combined amongst diabetic patients are analyzed using logistic regression. Significant observations indicated that clinical factors play a more effective

role amongst patients with arthritis who have diabetes compared to arthritis patients without diabetes. The odds of arthritis in diabetic patients increases by 2.39 folds amongst patients who are obese compared to the arthritis patients who are obese but do not have diabetes. In addition, arthritis patients with diabetes show significantly higher mean BMI of 31.04 kg/m^2 compared to arthritis patient without diabetes with a mean BMI of 27.68 kg/m^2. On the contrary, exercise decreases odds of arthritis by 1.587 folds in non-diabetic population compared to diabetic population. Amongst patients with ulcerative colitis and diabetes, increased BMI results in higher odds of prevalence of ulcerative colitis by 2.697 folds compared to patients without diabetes. Additionally, ulcerative colitis patients with diabetes have significantly higher BMI compared to patients without diabetes. We also investigated the effects and prevalence of these inflammatory diseases on healthcare cost and treatment cost.

The study indicated diabetes as one of the major risk factors for arthritis and/or ulcerative colitis. We also identified significantly increased prevalence of negative factors such as obesity, smoking and alcohol consumption in the inflammatory disease group compared to the healthy group. On the contrary, positive factors such as regular exercise was more prevalent in patient group without diabetes compared to patient group with diabetes. Additionally, research with a much-balanced sample is needed to further understand the factors that may influence the prevalence of the two diseases.

ACKNOWLEDGMENT

This dissertation would be incomplete without acknowledging all those who have contributed and supported me throughout the dissertation. I would like to acknowledge my committee chair Dr. Shankar Srinivasan for his continuous guidance, inspiration and valuable insight though out my research. I would also like to thank my advisory committee member Dr. Fredrick Coffman for his guidance through the progression of the research and providing me with such insightful questions to lead me to an innovative research goals. Dr. Hetal Joshi, my advisory committee member has played a crucial part in my research progress and has supported me with his guidance and exuberant clinical expertise. Lastly, I would like to acknowledge and thank Dr. Sudha Kamath, for her valuable feedback and comments on my dissertation. This research was only possible with the guidance and support of these essential team members who have held my hand throughout the entire process.

I would like to thank my parents Rita Gadhia and Dinesh Gadhia and my littler brother Rajan Gadhia for believing in me and supporting me throughout this journey. Their continuous support has led me to achieve what I could not have achieved alone. I would also like to thank my grand parents Dilsukhbhai and Kanchanben Chitalia and Kamlaben and Jagjivanbhai Gadhia for their blessings throughout this journey.

DEDICATION

I would like to dedicate this journey of my doctorate degree to my parents Dinesh Gadhia and Rita Gadhia. Their continued support and inspiration has driven me to pursue my dreams. I would also like to thank my little brother (not so little anymore) Rajan Gadhia for always competing with me and teaching me to always work harder.

My father has always told me:

> "It doesn't matter what you do, but be the best at what you do"

LIST OF FIGURES

Page

LIST OF TABLES

CHAPTER I

INTRODUCTION

1.1 Statement of the problem

Inflammatory diseases are on a rise but there is no clear understanding of the prevalence or prevention of these diseases. CDC in 2008 reported almost 20% of the US population is diagnosed with inflammatory diseases. In recent years, prevalence of type II diabetes has also been on the rise. Based on a recent estimate there are 29 million people in US with diabetes, which is approximately 10% of the entire population as reported in CDC 2016. However very few studies have investigated inflammatory disease population that is effected with diabetes as well as other factors that may contribute to it. In this paper, we will review the factors that may have been associated with increased prevalence of arthritis and ulcerative colitis amongst diabetic patients. In addition, arthritis and ulcerative colitis are both inflammatory diseases but there have been no studies performed to understand the prevalence of the combination of these diseases and the factors that affect diabetic patients who have both of the diseases.

Diabetes status is highly associated with obesity and may have increased prevalence in arthritis and ulcerative colitis. Women with upper body fat and obesity have 10.3 times the risk of having diabetes compared to non-obese women with lower body fat[1]. Clinical factors such as BMI and disrupted sleeping patterns are highly prevalent in this population. One of the biggest causes of the inflammatory diseases can be due to people migrating from one region to another and constantly evolving changes in one's life style that has resulted in a bigger issue of obesity epidemic[2]. Studies have indicated that higher BMI can

affect the prevalence of arthritis and ulcerative colitis in diabetic patients negatively. On the other hand, healthy body weight and BMI can also help and will be beneficial to patients with arthritis and ulcerative colitis. Additionally, the presence of ulcerative colitis and arthritis can cause disruption in patients' sleeping pattern and may be further detrimental to quality of living in this population.

On the contrary to clinical factors, studies that show effects of behavioral factors do not provide a consensus results. Several studies have shown increased prevalence of arthritis and ulcerative colitis with the presence of behavioral factors while others have reported no effects. For example, smoking status is shown to have deleterious effects on patients with arthritis and ulcerative colitis, however many studies have indicated that the quantity and duration of smoking is also important to address the prevalence of these inflammatory diseases amongst smokers[3]. Another controversial behavioral factor is alcohol consumption. Studies have indicated worsening effects of alcohol consumption amongst patients with arthritis or ulcerative colitis, however there are other studies which have indicated that moderate consumption of alcohol can help patients with these inflammatory diseases[4]. Lastly one of the behavioral factors that can trigger and effect other factors as well as other diseases is physical activity. Studies have indicated that physical activity and staying fit has beneficial effects on patients with arthritis or ulcerative colitis [5]. The purpose of this study is to assess the effects of these behavioral and clinical factors on the prevalence of arthritis and ulcerative colitis. In this study, we will also be assessing the effects of combination of multiple factors as well.

Relationship between the clinical factors and inflammatory diseases have been established, however effects of clinical and behavioral factors amongst diabetic patients

with inflammatory diseases has not yet been established. The goal of this research will be to identify the effects of the clinical as well as behavioral factors on diabetic patients with inflammatory diseases.

1.2 Background of the problem

Inflammation is defined as the response of vascularized tissues to injury or infection. The principle hallmarks of inflammation are vasodilation and increased vascular permeability, which act to facilitate the delivery of immune system cells and proteins to the site of damage. Inflammation is mediated by cells and by molecules from a variety of sources. These sources range from those immune system cells, the damaged tissues themselves, the circulation, and from reactionary molecules which accompany the damage response and repair processes[6]. Okin and colleagues have shown in recent review that inflammatory diseases have been seen for centuries; however, with the growing trends in lifestyle changes and living habits, there have been even higher number of subjects with inflammatory diseases [7]. In the same study they identified alzheimer's, asthma, dermatitis, ulcerative colitis, and arthritis as more prevalent inflammatory diseases compared to others. Specifically, ulcerative colitis and arthritis are two of the many growing inflammatory diseases with the evolving society and the environment [8]. These diseases although occurs due to inflammation in a certain part of the body, there exists several factors that may have triggered this inflammation. There also exist several other factors that prolong this inflammation throughout the lifetime, resulting in decreased life expectancy and decreased standard of living in these patients. Inflammatory diseases rarely have a permanent cure, and they occur due to an inflammation in a certain part of the body, this inflammation can be temporary or permanent based on the condition and severity. However, there is no one

direct cause that is indicated as the major factor for any of these inflammatory diseases. Several studies have shown that inflammatory diseases are triggered due to clinical, genetic and behavioral factors [9]. Studies have also indicated increased prevalence of arthritis and ulcerative colitis in relation to these factors, however no studies have investigated the effects of clinical and behavioral factors combined as well as compared them directly with diabetic patients with inflammatory diseases, and the prevalence of such diseases in patients who may have many of these clinical and/or behavioral factors.

For the purpose of this study, the factors that trigger arthritis and ulcerative colitis are broken down in two categories: clinical factors and behavioral factors. Clinical factors are defined as factors that are associated with a clinical condition or quantified with clinical condition. On the other hand, there are other factors, which are quantified as voluntary factors and can be avoided by the user, these are defined as behavioral factors. The two clinical factors assessed in this study are chosen due to increasing number of research that have indicated the effects of BMI status and sleeping pattern on prevalence of arthritis and ulcerative colitis as well as the effects on the patients with both of these diseases. One of the major clinical factor that can trigger or affect such inflammatory diseases is obesity of the subject, which is assessed by measuring the BMI of the subject. Several studies have shown that obesity is highly prevalent amongst patients with inflammatory diseases [10]. With increasing obesity and rising numbers in inflammatory diseases, more analysis and studies are focused on other comorbidities that are associated with obesity. Type- 2 diabetes is highly prevalent in obese population and hence is an important factor associated with the prevalence of the disease. The second clinical factor investigated is sleeping patterns. Although sleeping patterns may have little effect on the prevalence of

inflammatory diseases, the presence of inflammatory diseases can affect the sleeping patterns in the patients which can have significant effects on the quality of life amongst these participants.

Behavioral factors are defined as the factors that are associated with the environment around us. Participants have control over the exposure to these factors. These factors may or may not be responsible for triggering the inflammatory disease; however, they are quite important to healthy lifestyle associated with decreased prevalence of the inflammatory diseases. Some of the behavioral factors are alcohol consumption, smoking habits, and involvement in regular physical exercise. These significant lifestyle changes are highly prevalent in today's population. These changes may not have been prevalent many years ago but may have associations with increased prevalence of inflammatory diseases today. One such factor is smoking; studies have shown increased prevalence of smoking in general population. Several studies have shown deleterious effects of tobacco consumption on healthy living. These harmful effects include lung diseases, cancer, cardio vascular diseases and many more. Similar to smoking, alcohol consumption has also been shown to have diminishing effects on healthy living and excessive alcohol consumption may also cause liver damage. In addition to the smoking status and alcohol consumption which may have negative effect on healthy living; regular exercise is an additional behavioral factor which may have positive effect on reducing the prevalence of these inflammatory diseases. These are some of the behavioral factors, which are studied and have indicated significant effects on prevalence or prevention of arthritis and ulcerative colitis. In current study, we aim to investigate these factors.

As indicated in many studies it is important to understand that there may be involvement of more than one of these factors to trigger and prolong the inflammatory disease [11]. Clinical factors such as BMI and sleeping patterns, and behavioral factors such as smoking status, drinking status and physical activity are all studied individually in previous research, however they have not been analyzed in combinations especially in diabetic patients with inflammatory diseases. Additionally, previous studies have focused on investigating these factors individually within only one type of inflammatory disease population. There are many patients who are effected by more than one of these behavioral factors and clinical factors as well as have more than one inflammatory disease. The goal of this research is to identify which factors out of the two clinical and three behavioral factors are more prevalent as well which factors in combination cause higher prevalence of the diseases in diabetic patients. The goal of this study is to understand and asses the combination of various factors and its prevalence on arthritis and/or ulcerative colitis amongst diabetic patients.

1.3 Hypothesis

Central Hypothesis:

Based on previous studies we hypothesize that diabetic patients with inflammatory diseases are effected more by clinical factors such as BMI and sleep status and behavioral factors such as smoking status, alcohol consumption and physical activity compared to non-diabetic patients with inflammatory diseases.

The Central hypothesis will be answered using following research questions:

1. **Do clinical factors such as BMI and sleep patterns status have significant effect on inflammatory disease patients with and without diabetes?**

A. Is BMI significantly different between diabetic and non-diabetic patients with inflammatory diseases.

(HA0): There is no statistically significant difference between the BMI of inflammatory disease patients with and without diabetes.

(HA1): There is statistically significant difference between the BMI of inflammatory disease patients with and without diabetes.

B. Is sleeping status significantly different between diabetic and non-diabetic patients with inflammatory diseases?

(HB0): There is no statistically significant difference between the sleep patterns of inflammatory patients with and without diabetes

(HB1): There is statistically significant difference between the BMI of inflammatory disease patients with and without diabetes.

2. **Do behavioral factors such as alcohol consumption, smoking status and physical exercise have significant effect on inflammatory disease patients with and without diabetes?**

C. Is alcohol consumption status significantly different between diabetic and non-diabetic patients with inflammatory diseases.

(HC0): There is no statistically significant difference between the alcohol consumption status of inflammatory disease patients with and without diabetes.

(HC1): There is statistically significant difference between the alcohol consumption status of inflammatory disease patients with and without diabetes.

D. Is smoking status significantly different between diabetic and non-diabetic patients with inflammatory diseases?

(HD0): There is no statistically significant difference between the smoking status of inflammatory patients with and without diabetes

(HD1): There is statistically significant difference between the smoking status of inflammatory disease patients with and without diabetes.

E. Is physical exercise significantly different between diabetic and non-diabetic patients with inflammatory diseases?

(HE0): There is no statistically significant difference between the physical exercise of inflammatory patients with and without diabetes

(HE1): There is statistically significant difference between the physical exercise of inflammatory disease patients with and without diabetes.

3. Does behavioral or clinical factors have significant effect on inflammatory diseases conditions in diabetic patients?

(H30): Behavioral or clinical factors do not have significant effect on inflammatory diseases conditions in diabetic patients.

(H31): Behavioral or clinical factors have significant effect on inflammatory diseases conditions in diabetic patients.

1.4 Need for the study

The study is being performed to analyze and assess effects of behavioral and clinical factors on prevalence of inflammatory diseases amongst diabetic patients. The two inflammatory diseases investigated in this study are arthritis and ulcerative colitis. Arthritis and ulcerative colitis are two of many inflammatory diseases that are on the rise[12], however these diseases can have significant effects on quality of life especially when combined with diabetes and other factors. Earlier studies have investigated effects of these behavioral and clinical factors on only one of the inflammatory diseases, however no studies have investigated patient population having both arthritis and ulcerative colitis. In addition, there are no studies that have focused on diabetic patients amongst the diseases population and have studied the effects of various factors on this population. There are many factors that react similarly amongst patients with ulcerative colitis or arthritis such as BMI. However, there may be some of the factors such as physical exercise or sleeping pattern that may have differential effects on prevalence of arthritis and ulcerative colitis amongst diabetic patients. By studying patients with arthritis and ulcerative colitis, we will be able to assess the similarities and differences amongst patients with diabetes with just arthritis or ulcerative colitis and patients with both arthritis and ulcerative colitis.

Several studies have investigated the prevalence of the behavioral and clinical factors in arthritis and ulcerative colitis population [13]. These studies in general focus on only one or two of the factors investigated in the current population and are not quantifiable. These studies also do not take into account presence of diabetes amongst the disease population and the effects that various factors may have on this patient population. For example, Tedeschi and colleagues have investigated prevalence of BMI on arthritis

population, and showed that odds of being diagnosed with arthritis increases with higher BMI [14], however they did not investigate presence of other comorbid condition such as diabetes status or beneficial effects of exercise frequency in this population. Similarly, in ulcerative colitis population, studies have shown increased prevalence of alcohol consumption [15] however, these studies have not been able to quantify the effects and has failed to account for other addictions such as tobacco use and its effects on prevalence of ulcerative colitis. Investigating these factors in combination with each other may help understand interdependencies between these factors and may help decrease the prevalence of arthritis and ulcerative colitis. Most importantly, when diabetic patients are diagnosed with either ulcertaive colitis or arhtritis or both, it is very important to understand which factors between clinical and behavioral factors are the most prevalant and needs to be controlled and which factors are more effective versus the ones that are not.

In addition to analyzing the patients with ulcerative colitis and arthritis, we plan to study the clinical factors (BMI and sleeping pattern) and behavioral factor (smoking status, alcohol consumption status and exercise). Many studies have shown the effects of each of these behavioral or clinical factors. The goal for this study is to analyze the combination effects of these factors in diabetic patients with inflammatory diseases. In addition, we will also be identifying factors that are more prevalent than others. This study is performed in order to understand how behavioral factors and clinical factors effect the prevalance of inflmmatory dieases, such as arthritis and ulcerative colitis in diabetic patients. The need for this study is present because there are no studies performed that have conducted analysis of both clinical factors such as BMI and sleeping patterns and enviornmental

factors such as alcohol consumption status, smoking status and excercise status and its effects in diabetic patients with inflamamtory dieases.

In addition to the behavioral factors and clinical factors that affect arthritis and ulcerative colitis, the rise in these diseases have dramatically effected the healthcare economy. Due to the rise in inflammatory diseases and diabetes, consequently there is also a rise in doctors' visits, ER visits and the patients' involvement with healthcare. With the growing society, there are also better ways and options to improve healthcare and provide much better accessibility to physicians as well as other healthcare professionals. Economical as well as the healthcare involvement with these patients becomes very important to study and can give a lot more details about how these diseases will be progressing in the next few years as well as how involved healthcare professionals are in finding treatments and a cure for these diseases. The rise in the prevlance of arthritis and ulcerative colitis in diabetic patients has effected the healthcare industry dramatically. Patients who have arthritis and ulcertaive colitis will have increased number of doctors' visits, ER visitis and preventative care visits. This paper reviws the rise in healthcare due to the increased number of patients which lead to increased numbers of medical vitis and treatments.

All in all, the purpose for this study is to analyze the factors that have cuased the rise in arthritis and ulcertaive colitis in diabetic patients as well as identifying the changes this rise has cuased in the helathcare industry.

CHAPTER II

LITERATURE REVIEW

2.1 Inflammatory diseases

Inflammatory diseases include a vast array of disorders and conditions that are characterized by inflammation, which is hosts defense against other infectious agents and injury. Inflammatory diseases are chronic diseases which may have large scale implications on patients' quality of life and may also trigger several other chronic diseases [16]. Inflammatory diseases and diabetes are more prevalent than before, arthritis and ulcerative colitis are the two inflammatory diseases rising amongst the U.S population. Diabetes has also been increasing over the years, in 2016 there are 29 million people in United States with diabetes, which entails about 10% of the US population as reported by CDC in 2016. In addition to exhibiting increased prevalence in US population for these inflammatory diseases and diabetes independently, interrelation between these two inflammatory disease populations have also been established. Studies have also indicated that having arthritis can increase the prevalence of ulcerative colitis and vice versa [13]. A study performed indicated that a drug created to treat arthritis could cause ulcerative colitis [17]. In addition to the presence of one of the inflammatory diseases that may trigger other inflammatory diseases, there exists several other factors that may independently trigger, affect and prolong these inflammatory diseases.

Combinations of clinical, behavioral and genetic factors are associated with the rise in prevalence of inflammatory diseases. Some of these factors such as obesity, smoking

and drinking are highly prevalent in US population and are associated with several other chronic diseases and comorbidities such as type-2 diabetes. Recent studies have shown increased prevalence of type-2 diabetes in adult US population and also within the inflammatory disease population [18]. Prevalence of these conditions also results in decline of quality of life. This decline in quality of life is quite evident from studies based on the sleeping pattern in diabetic inflammatory disease population. Several studies have shown decreased sleep hours amongst inflammatory disease population which can result in increased anxiety, stress and hormonal imbalance which may further cause decline in quality of life and trigger further comorbid conditions. Studies have also investigated remedies for several of these factors. One such method is to encourage healthy living and life style by exercising and reducing smoking as well as drinking [19]. In one of the vital studies, Mehrotra and colleagues have shown importance of medical advice on losing weight and further advantages of these efforts on improving patient's quality of life amongst arthritic patients[1]. Considering the importance of BMI and obesity in arthritis populations identified in current study, these results also imply the importance of medical visit and the medical advice to lost weight. Although many previous studies have focused on various behavioral and clinical factors individually to understand their influence on inflammatory diseases; in the current study we aim to analyze these factors in combination and understand differences between them.

As discussed formerly, studies have indicated that ulcerative colitis may be the leading cause of arthritis and vice-versa [20]. The rise in prevalence of the diseases across United States have significant effects on healthcare in general. Inflammatory diseases such as ulcerative colitis and arthritis do not result in frequent hospitalization and hence very

few studies have investigated the specifics of healthcare cost associated with it [21]. However, there has been a major rise in doctors' visits, ER visits and just the overall healthcare costs due to the rise in inflammatory diseases. Based on one estimate cost associated with arthritis and other rheumatic conditions grew by 24% from the period of 1993 to 2003 as reported by CDC. Similarly, the percentage of total population with ulcerative colitis and crohn's disease also grew significantly from 1999 to 2015 as reported by CDC. On the other hand several of the behavioral and clinical factors mentioned earlier have 10-50% increase in health care cost related to medication and services [22]. For example obesity seems to be a much bigger factor in reference to chronic medical conditions, quality of life and healthcare costs compared to the issues that may be on a rise due to smoking and drinking [19].

Other studies have also gone further and have indicated one major factor that has increased the prevalence of the diseases and as a result has increased the healthcare cost. The rise in healthcare cost has not just been seen in United States but all across the world. Studies conducted in Europe have also indicated a rise in healthcare cost due to the rise in inflammatory diseases. In a similar study, it has been shown that increase in age causes a significant increase in the healthcare cost per capita as well as total cost. Although conducted in Europe, similar results also applies to the US populations. These results also imply importance of studying the older population and inflammatory diseases affecting these populations [21]. Due to these intricacies between the clinical and behavioral factors there is a rise in healthcare cost, and understanding the effects of these factors on inflammatory diseases will help us minimize the healthcare cost through modification in lifestyle as well as decreasing the prevalence of these conditions. The goal for this study

will also be to analyze the rise in healthcare cost due to the increased prevalence of arthritis and ulcerative colitis.

2.2 Prevalence of arthritis in diabetic patients

One of the inflammatory diseases investigated in the current study is arthritis. Arthritis is defined as chronic inflammation of joints accompanied by pain. Censuses of the US population have shown that more than 21% of the US population has reported to having arthritis [17]. Arthritis is not only on a rise in United States, but also all across the world, studies have indicated that in 2011 there are approximately 4 million Canadians living with arthritis [23]. Although there is no cure for arthritis, it can be treated or the onset can be prolonged with the corrective actions. Arthritis has also shown to reduce life expectancy and can cause harmful effects, which can lead to death [24]. Several studies have shown effects on presence of multiple comorbidity factors on quality of life in patients with arthritis [25].

Arthritis prevalence rate is shown to be different across various age groups and some age groups are more susceptible to arthritis compared to other age groups. The older age (around 60 years) where there has been more exhaustion and higher obesity rate is where the rise in arthritis is usually seen [26]. It has been further shown that the prevalence rate of arthritis is high in adult populations ages 55 and even higher for subjects with BMI higher than 25 [27]. In addition to the BMI and age group division, there have also been indications of arthritis being more specific to certain ethnicities. Studies have indicated that arthritis is more prevalent amongst White and non-Hispanic populations compared to other

races implying the significance of race in the prevalence rates of arthritis in obese population. [1].

Due to biological as well as hormonal differences, prevalence and location of arthritis has also been shown to differ between men and women. Studies have indicated that arthritis is more prevalent in obese female (29.8%) compared to obese male (18%) [23]. This may be due to various life changes that occur in women and where they may accumulate fat, versus men and where they accumulate fat. The accumulation of fat can be an important factor for indication in location of arthritis in the body. Women may have higher chances of arthritis at different times in their lives compared to men. For example, during pregnancy and puberty, there are many hormonal changes that may trigger more weight gain and obesity. This can also result in an increased risk to the life of the mother as well as the child. A study performed on pregnant women has also shown that patients with arthritis have a much higher number of miscarriages compared to patients without arthritis [28]. With the increasing weight gain in certain parts of the body, arthritis may be triggered in areas where there is more pressure due to that weight. These results point to differential prevalence and effects of arthritis between genders, which needs to be studied in detail.

In addition to age and gender related differences in prevalence of arthritis, there also exists several other clinical and behavioral factors that may have associations with prevalence of arthritis. In order to understand these relationships, we will study the presence of both behavioral and clinical factors on prevalence of arthritis as a whole and not related age, gender or the specific types of arthritis. Prevalence of arthritis is not just

indicated by one factor but multiple factors combined, some of which are analyzed in this study.

2.2.1 Effects of clinical factors on arthritis

As mentioned previously, there is no one major factor that can be associated with the causation of arthritis, however, there may be multiple factors which trigger or effect the prevalence of the disease. In this study, we have incorporated many clinical factors that are associated with and can increase the prevalence of arthritis. These factors are defined as clinical factors because of the biological conditions they are derived from. One important characteristic of these factors is that they cannot be controlled in a short time frame and large-scale changes in lifestyle are required to modify or alter these factors. The clinical factors that are investigated in the current study are BMI and sleep status.

Diabetes is a one of the major comorbidities associated with arthritis and is highly prevalent in the US population. In recent years, US population has seen growing trend in percentage of population with diabetes compared to without diabetes where 1 in every 3 of US adult has type-2 diabetes. Sugar levels for diabetics as per the American Diabetes Association is between the ranges of 5.0–7.2 mmol/l (90–130 mg/dL) before meals, and less than 10 mmol/L (180 mg/dL) after meals. These patients with diabetes are usually obese, have a higher BMI and have reduced physical activity. It can be argued that having arthritis can lead to diabetes due to patients' inability to perform physical activity. On the other hand, having diabetes can also be an indicator of patients' unhealthy lifestyle, which can cause arthritis as well as obesity. There are very few studies that have investigated prevalence of diabetes and its association with prevalence of arthritis. In one of these

studies, Symmons and colleagues have shown that patients with diabetes are at a higher risk of arthritis compared to patients without diabetes [28], however this studies are sparse in nature.

Due to this intrinsic relationship between the BMI of the patients, prevalence of arthritis as well as between obesity and prevalence of diabetes, it is of utmost important to investigate the relationship between the prevalence of arthritis and type-2 diabetes.

Diabetes can also be correlated with the patients' BMI because subjects with higher BMI have a higher probability of diabetes. A study performed on patients with age 65 or higher that there is a risk in higher BMI patients to develop diabetes, arthritis and lead to physical disability [29]. BMI and diabetes status of a patient goes hand in hand when studying the prevalence of arthritis because of the interrelationship both obesity and BMI have in the entire patient population.

2.2.1.1 Effects of BMI

Body Mass Index (BMI) of an individual is defined as the ratio of weight to the squared height of individual. BMI is one of the widely used measures to characterize the weight of any individual with respect to their height. An individual can be characterized in to being underweight, normal weight, overweight, obese and morbidly obese based on their BMI. Obesity in normal population is defined by the BMI range of 30 kg/m² or higher. Based on BMI, studies have shown growing trends of obesity across the world [30], but also has been increasing across United States. A study that was conducted, reported that in 2001 about 60% of the adults were overweight with the BMI between 25 and 30 and 20% of the adults were obese with a BMI higher than 30 [1]. This can be largely associated with

increased dependence on fast-food as well as the sedentary life style. As a result, obesity has increased across US and has been on the rise since 2001, which is correlated with a rise in patients with arthritis.

Figure 1 Arthritis Prevalence amongst obese individuals across United States.

As indicated in Figure 1, arthritis prevalence is highest amongst obese individuals in the region circled. These regions such as Alabama, Kentucky, Michigan, Ohio, Pennsylvania, and West Virginia, showed almost 50% of patients with arthritis prevalence amongst obese adults.

Across several studies, it has been addressed that obesity is a major factor for prevalence of arthritis. It is also indicated that an increase in obesity will not only increase prevalence of arthritis but it will also increase the progression of the disease [23]. Studies

have shown that higher BMI has been associated with higher risk of arthritis and there are significantly higher number of individuals with arthritis with the BMI between 25-29.9 kg/m² [29]. Specifically, arthritis effected 36.5% of adults with obesity [31]. In addition to the overall obesity, fat distributed in certain areas can also be more harmful to patients. Studies have shown that the outer abdominal weight shows an inverse U-shaped curve when it is distributed across the age range between 20-80 years [26]. With the increased visceral fat in certain parts of the body, there is a high probability of arthritis in areas of the body where there is more weight than a body can normally take. Some of the body parts such as knees and ankles are thus more prone to arthritis in obese individuals due to the increased amount of weight in abdominal areas and due to excessive amount of weight distribution on those body parts [31].

In addition, the inverse is also possible where there is a large number of patients with arthritis who cannot be as physically active, hence developing obesity and weight gain. Because arthritis limits the patients' ability to perform physical activity, it is hard to decipher whether arthritis causes obesity or does the increase in obesity cause arthritis. Janssen and colleagues have shown that older individuals with arthritis and between the ages of 65 to 74 are more prone to morbid obesity compared to normal population between the same age range [29].

On the contrary, there are also very few studies that have shown some contradictory results that, there is no relationship between the increased BMI of the patients and prevalence of arthritis [32]. In this paper we plan to decipher these studies and understand if there is a positive or a negative relationship with the prevalence of arthritis and high BMI.

In the current study we aim to understand the relationship between prevalence of obesity and prevalence of arthritis, however understanding the causation between them is out of the scope of current study. Studies indicated that higher BMI and obesity is a trigger for arthritis and other studies indicating arthritis as a cause for obesity, shows the bidirectional relationship between arthritis and obesity, which is caused due to high BMI.

2.2.1.2 Effects of sleep

One of the important clinical factors that is indicative of the quality of life and shown to be affected amongst inflammatory disease population is the sleeping pattern. Healthy sleep is defined by multiple factors such as being able to sleep within 15-20 minutes of lying down and sleeping for 7 to 9 hours within a 24-hr period. Decreased or disrupted sleep pattern in individuals has been associated with several physical and mental deficits, where irregular sleep patterns has been shown to cause hallucinations, anxiety and stress. Several studies have indicated adverse effects of arthritis on sleep patterns in patients. This has been associated with respect to the constant pain experienced by these individuals. Studies have indicated that hours of sleep and prevalence of arthritis can be easily correlated to assess how much pain patients with arthritis can be in. Due to this, arthritis has also been associated with various symptoms of insomnia. The lack of sleep during long term also causes depression amongst these patients. [33]. With the studies performed on patients with arthritis and their sleep patterns it is clear that when patients are in severe pain they are not able to sleep. Hence reducing the pain in patients with arthritis will help them lead a healthier life and sleep better. Medical experts have also recommended that better pain management would have a major impact on sleep improvements amongst patients with arthritis [34].

In this study we will be analyzing the sleep patterns amongst patients with arthritis to assess how many hours they sleep and how arthritis pain effects their sleep patterns.

2.2.2 Effects of behavioral factors on arthritis

In addition to the clinical factors that influence the prevalence of arthritis, there are also several behavioral factors that play a crucial role in prevalence of arthritis. Behavioral factors are defined as factors that patients are involved in by choice and/or are available in that specific environment. These factors also have one of the important distinction from clinical factors as individuals have a control over these factors and they can be started or stopped at any time. There are many behavioral factors that play an important role in patients with arthritis and other behavioral factors which may indicate a cure or a relief amongst arthritis patients. In the current study, we investigated prevalence of smoking, alcohol consumption and physical activity in arthritis.

2.2.2.1 Effects of smoking

One of the behavioral factors that have been studied in depth to understand the prevalence and the cause of arthritis is smoking status. Smoking status is a behavioral factor because it is an external factor that can be started or stopped at any time. In addition, smoking can cause many clinical factors through prolong use but the goal for this study is to assess the prevalence of smoking in arthritis population and to understanding its relationship to prevalence of arthritis.

Relationship between smoking status and prevalence of types of arthritis is studied in detail throughout this literature. Studies have indicated that there are higher number of arthritis patients who smoke in higher amounts compared to individuals without arthritis.

One of the important aspects of smoking and arthritis has been the gender differences observed in arthritis population who smoke regularly. Specifically, rheumatoid arthritis is shown to be increasing more with female subjects as well as obese female smokers. There have also been indications of higher risk of arthritis amongst women who smoke 15 or more cigarettes per day [35]. It has also been shown that there is a 40% increase of arthritis amongst women when they did not smoke, however amongst women smokers that risk rose up to 140% among patients who smoke 15 cigarettes or more per day [32]. As mentioned earlier, arthritis is highly prevalent in female population compared male population and smoking status might have significant interactions with this prevalence.

In addition to smoking status, studies were further conducted to understand how the length, frequency and the duration of smoking effects patients with arthritis. The gender of the smoker also plays an important role in the prevalence of arthritis. Quantity of smoking is as equally important as the duration of smoking. In a study performed, increased relative risk of rheumatoid arthritis was observed with estimated smoking amount during the day. Increased smoking frequency was associated with increased risk of arthritis [36]. In another study, Klareskog and colleagues indicated that subjects who smoke five cigarettes a day for a year have a 63% chance of arthritis, however when subjects smoke twenty cigarettes per day for a year their risk of arthritis increases to 76% [37].

Finally, several studies have shown lasting effects of smoking on human anatomy even after the participants have quit smoking. Additionally, it has been shown that amongst arthritis population that the disease is more prevalent amongst former smokers then current smokers. [23].

On the contrary, some of the studies have shown beneficial and therapeutic effect of smoking on patients with arthritis and prevalence of arthritis amongst healthy subjects[36]. Although smoking can cause other comorbidities it may have therapeutic advantages with respect to pain management. In this study, we aim to identify prevalence of smoking in arthritis population along with several other factors such as quantity of smoking and duration of smoking.

2.2.2.2 Effects of alcohol consumption

In addition to smoking status, alcohol consumption is another behavioral factor that has been associated with arthritis in several studies. Alcohol consumption is defined as an behavioral factor because it is similar to other behavioral factors, in that alcohol consumption occurs voluntarily and the quantity may vary based on the region as well as the surrounding environment [38].

Earlier studies have shown that there is a higher risk of arthritis with current drinkers, compared to former drinkers or individuals who have never drank alcohol. In the same study, it is also indicated that more than three drinks of alcohol per day was associated with increased relative risk of arthritis [36]. Recently several studies have showed negative role of alcohol consumption in the prevalence of arthritis. Similar to smoking status, studies have also shown gender specific differences in risk of RA, associated with alcohol consumption and smoking. Studies identified significant differences in the distribution of arthritis between gender, which was associated with the regular alcohol consumption status, and corresponding risk of arthritis [39]. Studies have also indicated that there is a reduced risk of arthritis amongst patients who drink amongst postmenopausal women.

Further investigating the prevalence of alcohol consumption in arthritis population can help understand these effects in detail.

In addition to understanding the alcohol consumption status, studies have also assessed the quantity of alcohol consumption. It has been shown that individuals who drank more had a lower risk for arthritis, compared to patients who drank less [40] which is contradictory to the results obtained in previous alcohol consumption studies. Similarly studies have indicated preventative effects of alcohol consumption on prevalence of arthritis [41], though it has been shown to beneficial effects, they are highly dependent on the quantity of alcohol consumed [39]. We aim to assess alcohol consumption as a behavioral factor in this study to decipher if alcohol consumption is more prevalent in arthritis population and to understand the frequency/quantity of consumption.

On the contrary, to the deleterious effects of alcohol consumption on arthritis, other studies have also shown beneficial effects of alcohol consumption on patients with arthritis. Studies have also indicated preventative effects of alcohol on prevalence of arthritis [41]. Other studies have also indicated that although alcohol consumption may have beneficial effects it is also dependent on the quantity of the amount of alcohol consumed [39].

2.2.2.3 Effects of exercise

Lastly, one of the behavioral factors that is proven to have more beneficial effects on the prevalence of arthritis is physical activity. In many cases, individuals with arthritis tend to have limited or no physical activity. The lack of physical activity for a longer time period causes obesity because of the reduced energy expenditure with similar or increased energy consumption. Pain associated with arthritis also hinders patients from performing

day-to-day physical activities and it is quite possible for recreational physical activities as well. A study indicated that there is high prevalence of physical inactivity amongst patients with arthritis who are also obese, compared to just obese patients [31]. The lack of exercise may also cause an increase in obesity, increase in arthritis and other comorbid conditions such as diabetes status. Arthritis is shown to be most prevalent in individuals who are not physically active compared to people who are more physically active [23]. However, this can be vice versa as well, since having arthritis can reduce the amount of physical activity an individual is able to perform, hence it causes obesity. In general arthritis is shown to be most prevalent in individuals who are not physically active compared to people who are more physically active. [23].

Hence, it is important to be physically active and exercise in order to prevent or reduce the effects of arthritis. Several studies have shown that one most efficient ways to reduce or prevent arthritis is to have a healthy combination of exercise and moderate amount of exercise which can help reduce the knee pain [42]. Studies have indicated that even a small weight reduction (10%) can help patients with arthritis in alleviating pain and improving their life style [43]. In this study, we aim to investigate the prevalence of physical activity in arthritis population as well as quantify effects of exercise on decreased odds of having arthritis.

2.2.3 Treatment and oversight cost

With the increase in prevalence of Arthritis, the cost of treatment, as well as prevention have also gotten expensive and creates a major burden on healthcare costs. In

addition to the cost of treatment and prevention, the cost of patients' lifestyle that have arthritis is even higher due to their inability to function normally [44].

In general, studies have shown that there is significantly higher rate of ankle replacement in obese patients with arthritis compared to non-obese patients with arthritis [45]. In comparison to other counties such as Japan, large scale differences are observed in the healthcare costs covered in patients with arthritis where 80% of healthcare cost of patients with arthritis is covered compared to US [46]. As the three main components for arthritis that are costly are drugs, hospitalization and outpatient procedures [47] and the amount of healthcare cost covered for arthritis are low and patients are forced to pay these costs through of pocked expenses. This may also lead them to either not be able to keep up with the cost or patients who may stop treatment due to the excessive costs [47].

Studies have indicated that the best way to reduce the prevalence of arthritis is by encouraging physicians to promote weight loss, which can also reduce healthcare costs[1] associated with other comorbid conditions. Encouraging a healthy lifestyle and the reduction of obesity and such inflammatory diseases will evolve the healthcare industries in reassessing the healthcare costs of such inflammatory diseases. In this study, we will be looking at healthcare visits of patients with arthritis to understand if the healthcare visits and healthcare costs are higher for patients with arthritis compared to healthy population.

2.3 Prevalence of ulcerative colitis in diabetic patients

Ulcerative colitis is characterized by chronic ulceration in the large intestine, which is accompanied with abdominal cramps and diarrhea containing pus, blood and mucus. Ulcertaive colitis is highly prevelant across United States and effects 1-2 million people in

Unite states. Studies have indicated that ulcerative colitis has wide variety of commonly prevalent symptoms including diarrhea, fatigue, and weight loss and lost appetite. These symptoms also make self-detection of ulcerative colitis difficult [20]. Ulcerative colitis has also has been associated with several other factors such as behavioral, clinical and genetic factors investigated in current study. The prevelance of ulcerative colitis and crohan's dieases are at a greater increase in North Europe and North America, and specifically amongst Jewish population [48]. Since ulcerative colitis is an inflmmatory dieases of a gut, it is very important to assess effects of dietary consumption on the prevalence. In addition, since dietary intake varies by the region as well as ethnic background, it is very clear to say that certain ethnicities are at a higher risk of having ulcerative colitis, compared to others. Studies are also performed with a breakdown of various races and ethnic groups to see the prevalnce of ulcerative colitis in various groups[49]. A recent study investigating prevelance of ulcertaive colitis amongst various ethnicities in North America, that white individuals have the highest risk of ulcertaive colitis when compared to hispanics, asian and african american individuals. Similarly, in one of excellent reviews of ulcerative colitis, authors have showed significantly higher number of studies investigating ulcerative colitis in Asian populations and have shown significantly higher prevalence rate of ulcerative colitis in Asian population compared to Hispanic or African American populations [50]. Biologically, ulcertaive colitis is caused due to inappropriate immune repsonse to microbial antigens of commensal microorganisms that are genetically succeptable in subjects [48]. This is controlled by various factors such as diatry intake, as well as their genetic background.

Although ulcertaive colitis can occur anytime in the lifetime, it is usually diagnosed prior to age 30 [20]. However there has been reports of gender differenecs in prevalence and

severity of ulcerative colitils. In one such study, Valentini and colleauges have significant gender differences in serum CRP (c-Reactive Protein) values in patients with ulcerative colitis, where female population showed decreased percentage body cell mass compared to male population, implying differential gender effects of ulcerative colitis [51]. Alternatively, ulcerative colitis has been associated with prevalence of several comorbid conditions such as colorectal cancer [52]. Specifically studies have shown signficant relation between age of onset of ulcerative colitis and age of onset of cancer [53].

Finally, although ulcerative colitis is a disease with no cure, it can be preveanted and treated with correct measures thoughout life. Lifestyle and dieatry consumption plays a crucial role in the treatment of this disease. In this study we will aim to identify and focus on various factors that increase the prevelance of ulcerative coltis.

Diabetes is highly prevalent in today's population. Hence we will be identifying diabetic patients amongst ulcerative colitis patients to identify which clinical and behavioral factors play a crucial role. Diabetes for healthy individuals is identified as blood glucose levels higher than 100mg/dL in fasting state. Diabetes can be triggered because of various factors such as weight, age and dietary intake. Based on several studies, diabetes plays a crucial role in the prevalence of ulcerative colitis. There are several studies that have shown relationships between prevalence of type-2 diabetes in ulcerative colitis population [54]. Additionally, studies have indicated that it becomes crucial to monitor diabetic patients with ulcerative colitis because their recovery is very slow compared to healthy patients with ulcerative colitis [55].

On the contrary, there have also been studies that have indicated that diabetes has no direct relationship with the prevalence of ulcerative colitis. In this study, we will be assessing the diabetes patients in combination with ulcerative colitis and understanding the effects of diabetes status on the prevalence of ulcerative colitis.

2.3.1 Effects of clinical factors on ulcerative colitis

Ulcerative colitis is one of the inflammatory diseases which has been on the rise along with arthritis [56]. Similar to arthritis, there is no one identified cause of this disease, but several studies have indicated that certain factors can prolong the prevalence and onset of the disease. In order to understand various factors that may affect the prevalence of ulcerative colitis, we have broken down these factors in two groups, clinical factors and behavioral factors.

2.3.1.1 Effects of BMI

As described earlier, BMI is calculated by dividing the weight of the person in kilograms by the height in centimeters squared and BMI of 30 kg/m2 or higher is identified as obese individuals. In a study of obesity in US, it was found that about 68.8% of people in United States are obese [57]. This ratio was specially skewed in the ulcerative population, where only 1% of total population with ulcerative colitis was underweight and ~70% of population was in overweight or obese categories. This describes one of the important issues about roll of obesity amongst ulcerative colitis population [57].

Studies have indicated that obesity can be caused due to several internal factors as well as many external factors of people, such as their life style, dietary intake and the location as well as their physical activity [58]. These changes directly lead to the increased

BMI of the patients and are identified in patients with ulcerative colitis. Despite of majority of the studies indicating a negative relationship between higher BMI and the prevalence of ulcerative colitis, some studies have indicated that there is no relationship between higher BMI and prevalence of the ulcerative colitis. Specifically, Chan and colleagues have shown no indication or effect on prevalence of ulcerative colitis amongst obese patients. [59]. In this study our goal will be to identify and assess if BMI can affect the prevalence of ulcerative colitis. We will also be studying the patient population with ulcerative colitis to identify their BMI ranges.

2.3.1.2 Effects of sleep

One of the important indicators of a patients' quality of life is the sleeping pattern of an individual. In the current study, we will identify sleep as a clinical factor as it is based on a biological clock and can be affected by physical or biological changes. Healthy sleeping habits are identified as 7-9 hours of sleep in a 24-hour period.

Studies have shown bidirectional effects between sleeping patterns and ulcerative colitis. Specifically, some studies have shown that reduced sleeping hours and poor sleeping patterns may also trigger ulcerative colitis. A recent study has identified that poor sleeping patterns can increase the prevalence of ulcerative colitis. [60]. This can be associated to stress factors, its effects on patients' immune system [60] and reduction in response to inflammatory diseases such as ulcerative colitis. Ulcerative colitis on the other hand can also results in reduction in sleeping pattern due the pain and discomfort associated with the disease.

On the contrary, studies have also indicated that sleep does not have any effects on prevalence of ulcerative colitis. In the current study we aim to answer questions regarding the possible impact of sleep on ulcerative colitis and vice-versa.

2.3.2 Effects of behavioral factors on ulcerative colitis

As defined earlier, behavioral factors are defined as factors that can be changed or modified externally. These factors are effected or are present due to the surrounding environment. The most prevalent factors affecting the prevalence of ulcerative colitis have been identified as smoking status, alcohol consumption and physical exercise.

2.3.2.1 Effects of smoking

In the current study, we specifically focus on smoking as a behavioral variable due to the deleterious effects it has on the individuals' health and because the patients have control over whether to smoke or not. Studies have shown that Smoking is one of the leading causes of death across United States along with poor diet and physical inactivity [61]. In general, smoking has shown to have deleterious effects on healthy subjects in general, however studies have indicated some effects of smoking on patients with ulcerative colitis. It has been observed that a percentage of patients who smoke are higher in ulcerative colitis group, though these differences were not statistically significant [59]. On the other hand, studies have also showed that the length of smoking also has an effect on the prevalence of the ulcerative colitis because patients who previously smoked may react differently to presence of other factors such as obesity then patients who smoke currently. For example, some studies have also shown that former smokers may be at a greater risk of ulcerative colitis [46]. One of the important aspect to smoking is the age a patient starts smoking and its

effects on prevalence of ulcerative colitis, however very few studies have investigated this relationship.

Contradictory studies have supported that ulcerative colitis is a disease of non-smokers and it is not a common disease amongst smokers[62]. Some studies have also indicated beneficial effects of nicotine on patients with ulcerative colitis. Some of these effects are also described to be therapeutic in nature. [63,20].

In general, the literature on effects of smoking on ulcerative colitis is quite heterogeneous in nature. In the current study, we will investigate multiple facets of smoking such as age first started smoking, number of cigarettes smoked as well as duration of smoking to quantify these factors and its effects on prevalence of ulcerative colitis.

2.3.2.2 Effects of alcohol consumption

In conjunction with smoking, alcohol consumption is an extremely important factor in understanding the prevalence of ulcerative colitis due to its effect on human gastrointestinal system. Studies conducted in international population such as Japan have shown increased odds of ulcerative colitis in older patients who are former smoker [46]. Although, there are wide-scale differences in US and Japanese populations these results shade important light on role of alcohol consumption on prevalence of ulcerative colitis. Drinking effects are correlational and are studied simultaneously as behavioral effects. Studies performed in other parts of the world have also indicated negative effects of drinking and smoking on patients with this inflammatory disease. One of the reasons for investigating alcohol consumption with the prevalence of ulcerative colitis has been the effect increased alcohol consumption on presence of ulcer in liver and overall health. It has

been shown that increased alcohol consumption may affect the hormonal system which may also be related to presence of ulcerative colitis [50].

On the contrary, very few studies have also indicated no effects or beneficial effects of alcohol consumption on prevalence of ulcerative colitis [49]. In this study, we will aim to understand the role of alcohol consumption on the prevalence of ulcerative colitis. In addition, we will also try to identify if the quantity and the duration of alcohol consumption also plays a role on the prevalence of ulcerative colitis.

2.3.2.3 Effects of exercise

In addition to the alcohol consumption and smoking status one of the additional behavioral factor that is correlated with multiple clinical factors such as BMI and diabetes status is exercise and the patients' ability to perform physical activity. Majority of the studies that have indicated high BMI as the major cause of ulcerative colitis has also indicated the benefits of exercise and using exercise as even a treatment for patient with this inflammatory disease [64]. Specifically studies have also indicated the deleterious effect of not exercising and this increasing the prevalence of ulcerative colitis [65,66]. Additionally, increased energy intake was associated with increased risk of ulcerative colitis Albeit in a small sample size (n=100). Similarly, decreased physical activity has been shown to be associated with increased risk of developing ulcerative colitis. In addition, the same study showed significant interaction between increased in energy intake and risk of developing UC [59]. The clinical and behavioral factors discussed in this study are interdependent in the sense that individuals with a higher BMI or higher blood glucose levels usually do not

perform sufficient physical activity and the combination of these factors increase the prevalence of ulcerative colitis.

Although studies have shown different risk factor for ulcerative colitis such as difference in dietary risk factors across world population, in the current study we focused on US population and some specific behavioral and clinical factors. Future studies should investigate these dietary factors across the US population and across the world population. In addition to using exercise as a treatment it is also equally important to monitor the dietary intake and healthy habits overall to establish and continue a healthy lifestyle and prolong the prevalence of such inflammatory diseases.

2.3.3 Treatment and oversight cost

Ulcerative colitis is one of many inflammatory diseases that has been on the rise with the current lifestyle and various factors that has increased the prevalence of this disease. A study indicated that there is a rise in patients with ulcerative colitis in that there are nearly 20,000 children and adults who have ulcerative colitis per 1 million residents [22]. Each of these individuals spend about 5,000-6,000 dollar per year on treatment and healthcare visits [67]. The cost of treatment has been increasing for ulcerative colitis but more importantly, the costs also vary based on inpatient and outpatient treatment as well as preventative care and general doctor's visits. studies have indicated that the mean total inpatient cost is $1906 per year. However, since this is a long-term inflammatory disease, the outpatient cost is as high as 5066 per year [22]. One of the important factor to consider is that the aforementioned study was performed in 2003-2004 time frame, which also indicates that the cost has increased since then due to the rise in ulcerative colitis amongst

patients but also due to the increasing healthcare cost and the lack of insurance support for certain health conditions. In a recent detailed study, it is has been further shown that this costs are even higher amongst these patients when who are obese or if they smoke or drink[45,51].

Patients with ulcerative colitis and healthy subjects who are at a risk of having ulcerative colitis are recommended to lead a healthy lifestyle and reduce habits that may trigger this inflammation however very few studies have investigated this factors in conjunction with each other. Healthy lifestyle does not cure these diseases but it promotes a healthy lifestyle which prolongs the onset of the disease and may help patients with the disease. Although dietary intake may not change, the patients' health but it can affect them dramatically [20,68]. Overall, in order to address and minimize the healthcare costs it is crucial to reduce the prevalence of this disease by addressing clinical and behavioral factors in detail.

CHAPTER III

METHODS

3.1 Overall research study and source of data

We obtained data for this analysis from CDC, specifically from National Center for Health Statistics. Although, the data was available for a period (since 2012), we extracted data for the year 2015 in order to investigate the most recent data for the analysis.

We obtained seven different data sets from the 2015 dataset. These datasets included various types of patient's data for a particular year. Abundance of patient's information are collected through hospitals and eventually categorized in to seven different files. These files are Family file, Household file, Injury file, Person file, Sample child file, Sample Adult file and Sample Adult Cancer file. These files as the names suggest include various patients' information categorized in to multiple categories. Amongst these files, family file contains patients' family demographics and family lifestyle data, Household file entails of number of individuals in the household, the injury file covers the patents' injuries and the severity of injuries. In addition, Person file entails a wide range of data of the patients' personal lifestyle and their health habits, the Sample child file covers all of the children data, the Sample Adult file entails data of patients 18 and above and their personal and health habits as well as their health conditions and their lifestyle. Finally, the Sample Adult Cancer file covers the cancer types and the presence of cancer amongst the Sample Adult population.

In order to correctly analyze the data, the first step is to merge the patient's specific data from multiple category files. In order to perform this step, we first started by creating a unique identifier code based on HHX code and a number of participants from a household. Upon creating the unique identifier for each of the participants, we threshold the data at 18 years of age or higher to investigate only the adult population. This Dataset consists of 121,466 numbers of subjects. This data set also reviews 1408 variables for each of those subjects. Subject numbers are identified by patient number labeled as "HHX" called the household number (unique identified for each patient).

3.2 Major variables reviewed

-HHX: HHX is the household number, which is used as an identifier for each of the individuals. This identifier is different for each of the rows in the datasets and is individual to each patient. This identifier helped us avoid the repetition of the data and during the randomization process to identify independent samples from the population.

-Sex: The gender for participants was denoted by the variable "SEX". This categorical variable is broken down into two identifiers where male are identified as one and female are identified as two.

-Age: Within all of the datasets, the age of the subject is identified as "AGE_P". The patient group encompasses patients within the range of 1 year to 84 years and all of the patients 85 or higher are identified as 85. However, we only selected the data from adult population using Sample Adult dataset where the age range started from 18 and older since this analysis focused on the adult population.

-Arthritis: One of the inflammatory diseases investigated in this analysis is Arthritis. The variable used to specify the presence of arthritis in each of the patients is a categorical variable ARTH1. In order to create the variable, the participants were asked the question whether they were told if they have either arthritis.

Question: whether they were told if they have either arthritis.

Response:

Response	**Yes**	**No**	Refused	Not ascertained	Don't know
Code	**1**	**2**	7	8	9

For the purpose of this analysis, only the patients who either answered yes, coded as 1 or no, coded as 2 were considered for the specific arthritis analysis to avoid any data discrepancies to interfere with the analysis being performed.

-Ulcerative colitis: The second inflammatory disease investigated in this analysis is ulcerative colitis. The variable specifying presence of this condition across patients is ULCEV. This variable consists of patients who were asked the question. For the purpose of this analysis only the patients who either answered yes or no were considered for the specific ulcerative colitis analysis to avoid any data discrepancies to interfere with the analysis being performed.

Question: Whether they were told if they have ulcerative colitis.

Response	**Yes**	**No**	Refused	Not ascertained	Don't know
Code	**1**	**2**	7	8	9

In order to investigate the effects of clinical and behavioral variables on the inflammatory diseases such as Ulcerative colitis (ULC) and Arthritis (ARTH), we investigated several other variables indication patients' present health and habit conditions. The variables studied in this analysis are:

Clinical Variables:

-BMI: One of the clinical variables that was reviewed for overall population as well the patients with arthritis and ulcerative colitis. BMI is the Body Mass Index of the patient, which is calculated by

- $BMI = \frac{Weight\ (kg)}{Height(in)^2}$ Which is then rounded two decimal places. The BMI value is an indicator of the patients' health based on the weight, which is divided into healthy and unhealthy as shown in the table below.

BMI of the patients	Weight classification
BMI < 18.5	Under Weight
BMI 18.5 to 25	Healthy Weight
BMI ≥ 25 to <30	Overweight
BMI ≥ 30	Obese

The assessment of the patients' health is identified using the table with their BMI and their weight.

-DIBEV: The second clinical variable that was analyzed for the entire population is the diabetes status. This variable was identified with "DIBEV". The subjects in the entire population were asked whether the patients were ever told by a doctor or a health

professional if they have diabetes (pregnant women were excluded from this question). The patients were asked to answer.

Question: Have you ever been by a doctor or a health professional that you have diabetes (pregnant women were excluded from this question).

Response	**Yes**	**No**	Refused	Not ascertained	Don't know
Code	**1**	**2**	7	8	9

For the purpose of analysis, patients who either responded yes or no were used for further computations.

Behavioral Variables

In addition to the clinical variables that are reviewed and analyzed in this paper, other variables such as alcohol consumption, smoking status, exercise status and sleep characteristics are also studied to investigate the effects of these behavioral variables on the inflammatory diseases.

- ALCLIFE: One of the behavioral factors being studied is alcohol consumption. In order to study the alcohol consumption of the patient "ALCLIFE" is used as a variable and subjects over the age of 18 were asked if they have consumed at least 12 alcoholic beverages in their entire lifetime. This question was created just to identify the definition of alcohol consumption.

Question: Did you consume at least 12 alcoholic beverages in the entire lifetime?

Response	Yes	No	Refused	Not ascertained	Don't know
Code	1	2	7	8	9

For the purpose of analysis only the subjects who answered with the code of 1 or 2 were used.

- SMKEV: Smoking status is another behavioral variable which is very crucial to study with the two inflammatory diseases reviewed in this paper. In order to study the smoking status subjects in the population were asked the question of whether they have smoked 100 or more cigarettes in their entire lifetime. The number of 100 was used to identify the definition of a smoker from a nonsmoker.

Question: Have you ever smoked more than 100 cigarettes in your entire lifetime?

Response	Yes	No	Refused	Not ascertained	Don't know
Code	1	2	7	8	9

For the purpose of analysis only the subjects who answered coded yes or no were used.

- Number of Cigarettes: To further assess the smoking status of the subjects amongst the smokers the analysis was further broken down to see how many cigarettes current smokers smoke in a day "CIGSDAY". The data points raged from 1-94 cigarettes. Patients who answered to smoking 95 or more cigarettes a day were given 95. Subjects who refused were coded 95, not ascertained 98 and do not know as 99. For the purpose of accuracy and

analysis only patients who responded between the ranges of 1-94 cigarettes per day were used to further analyze the data.

- MODFREQW: One of the essential behavioral factors which may show a beneficial effect in either of the inflammatory diseases as well the clinical factors is the frequency of the exercise. The subjects were asked the question of how many times they perform light to moderate activity per week, which is coded as "MODFREQW. The subjects who answered less than once per week were coded as 00, patients who did respond between the range of 1-28 times per week and the patient who said never were coded as 95, unable to do light or moderate activity as 96, refused as 97, not ascertained as 98 and don't know as 99. This data point is studied for both inflammatory diseases as well for the entire population and for the accuracy of the analysis output of 1-28 times per week is used. We also converted this variable in to categorical variable in order to derive difference with respect to patients who exercise and compared to the patients who do not exercise.

3.3 Tools used for analysis

To conduct the analysis SPSS and SAS were used. The analysis was performed using various computations and analysis tools in both software. Here were briefly describing tools used for the analysis.

Compute Variable:

Computing variable allows you to make certain calculations using the variables; in addition, it also allows you to transform data in different units as well as filling in missing variables. New columns can be created with the computations and/or the conversions using

this function. This function from SPSS software is a very powerful tool and was used to modify and merge existing variables.

Compute variable is performed by following these steps:

Transform > Compute Variable

During the compute variable dialogue, one can use the already available variable /column and apply multiple operations to create a new variable/columns. It is very important to understand that if conditions need to be applied they are put into the "if" window as shown in part B of this figure. This particular function is widely useful in modifying the variables and selecting patients with certain condition.

Frequency: The frequency option gives summary and data overview for each categorical variable at a time in addition to providing frequency tables, pie charts and bar charts. This procedure is one of the most important procedures in the SPSS which allows us to clearly visualize our data distribution.

The frequency reviews are run with following steps:

Analyze >Descriptive Statistics > Frequencies

This window allows us to choose which variable we would like to review the frequency of. Addition statistical analysis can also be performed along with frequency by following this step:

Analyze >Descriptive Statistics > Frequencies > Statistics

Frequency was run during this analysis for all variables to understand the basic summary of the data (mean, median, mode, etc.) for each of the variables.

Crosstabs: To explain and visualize a single categorical variable, frequency table is used, however when two categorical variables need to be reviewed in context of each other and to understand their relationship between them crosstab (cross tabulation) is used.

Crosstab tables are created by following these steps:

Analyze > Descriptive Statistics > Crosstabs

Crosstabs can be further analyzed with various other statistics, which compare the two categorical variables.

Analyze > Descriptive Statistics > Crosstabs > Statistics

Crosstabs was performed using this analysis to understand the relationships of the inflammatory diseases (arthritis and ulcerative Colitis) with various clinical and behavioral factors (BMI, Alcohol Consumption, Smoking Status, Diabetes Status, and Physical Activity). We also used crosstab procedure to calculate a chi-square test of normality and to investigate odds ratio between variables.

T-test: Independent sample t-test is performed to compare mean of two groups across a continuous variable. It is performed to assess whether the differences observed between the groups due to chance (H0) and whether or not they are significant.

The independent t-test is performed using the following steps:

Analyze > Compare Means > Independent Sample T-test

Within this window the variables are listed under the test variables and, grouping variables are listed under the "grouping variables". For the purpose of this analysis Independent sample t-test was performed for all variables to the significant difference in means between the test variables such as (BMI, Sex, Diabetes, Alcohol Consumption, Smoking status and Light to moderate exercise) and the grouping variable is used for Arthritis (Y or N) being either 1 or 2 and ulcerative colitis (Y or N) being either 1 or 2.

ANOVA: Univariate analysis is performed to see if there is a statistically significant difference between the two means of independent variables.

Univariate analysis is done by following these steps:

Analyze > General Linear Model > Univariate

In order to perform Univariate analysis, dependent variables, fixed variables and covariates are decided and selected. In addition, one can also investigate the main effects and the interaction effects of this variables.

In this study, ANOVA is used very frequently for all of the behavioral and clinical variables (inputted as dependent variables) and inflammatory diseases (inputted in the fixed factors). Age was used as covariate for many of this analysis. In addition, we studied the main effects as well as the interaction effects of all of the variables with the variables for inflammatory diseases.

Logistic regression:

Logistic regression was performed in SPSS and SAS to produce visualizations that would display data appropriately. This test was performed to assess the risk factors and

how they may affect the prevalence of the inflammatory diseases studied. Odds ratio was derived using logistic regression for each factor.

CHAPTER IV

RESULTS

4.1 Overall data

The total numbers of subjects investigated in this study are 121,466. In the next section, we provide descriptive and inferential statistics about this data.

4.1.1 Age and sex distribution of overall data

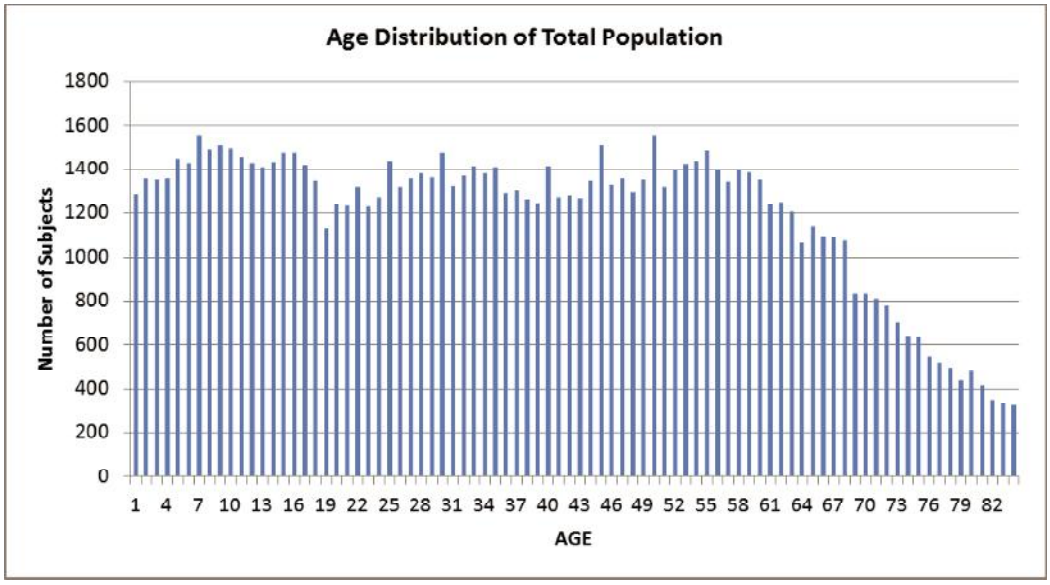


Figure 2 Age distribution for the entire population

Figure 2 shows the overall age distribution of the entire population, while table 1 shows the age data in tabular form. The entire population of 121,466 subjects was distributed across a wide age range of 1 to 85 years. A large of number of individuals were present between the ages of 1 to 18 years, due to this being a community sample. Additionally, upon closer approximation, we observed that this data has household

information, implying that it included information about children in the family. As shown in the figure the age distribution is equally distributed across all age, however the highest number of patients are in their 50s and very few subjects are in their late 80s. In order to avoid the age related bias in prevalence of inflammatory diseases, we performed the analysis on only adult population. Out of the total population of 121,466 subjects, the distribution of male and female was quite similar.

Table 1 Number of subjects across age groups

Age of the Subject	Number of the subjects		Age of the Subject	Number of the subjects		Age of the Subject	Number of the subjects		Age of the Subject	Number of the subjects
1	1286		23	1232		45	1508		67	1094
2	1355		24	1270		46	1329		68	1074
3	1350		25	1440		47	1355		69	835
4	1354		26	1320		48	1293		70	835
5	1445		27	1355		49	1352		71	809
6	1429		28	1376		50	1558		72	777
7	1557		29	1361		51	1316		73	707
8	1487		30	1477		52	1401		74	644
9	1509		31	1324		53	1424		75	641
10	1492		32	1371		54	1436		76	549
11	1455		33	1417		55	1482		77	519
12	1428		34	1380		56	1402		78	498
13	1411		35	1410		57	1343		79	440
14	1435		36	1291		58	1402		80	480
15	1476		37	1305		59	1384		81	415
16	1474		38	1263		60	1352		82	348
17	1419		39	1243		61	1241		83	330
18	1348		40	1415		62	1249		84	322
19	1134		41	1271		63	1209		85+	1764
20	1238		42	1280		64	1064		Missing	17677
21	1236		43	1266		65	1143		Total	121466
22	1319		44	1346		66	1097			

Figure 3 and table 2 describes the gender specific distribution across the population. As seen the table 2 and the figure3, the number of males and females in the are quite similar in the current population which allows us to study the differences of various

factors amongst male and female very clearly. As seen in the current population, we have higher number of females (n=53532, 51.6%) compared to male population (n=50257, 48.4%), however these differences are not significant.

Table 2 Number of males and females in entire population and percentage

Gender	Number of Subjects	Percentage
Male	50257	48.4
Female	53532	51.6
Missing	17677	14.6
Total	121466	100.0

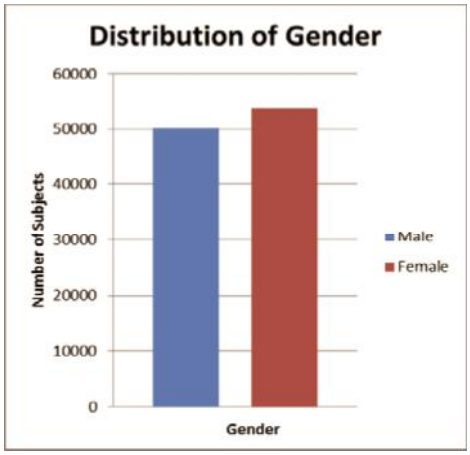


Figure 3 Distribution of Gender across entire population

4.1.2 Distribution of clinical factors for the entire population

We further segmented the data in to multiple clinical and behavioral factors to investigate its representation across the population and its prevalence in inflammatory

disease population. The clinical factors studied in these populations are BMI and the sleep pattern of individuals.

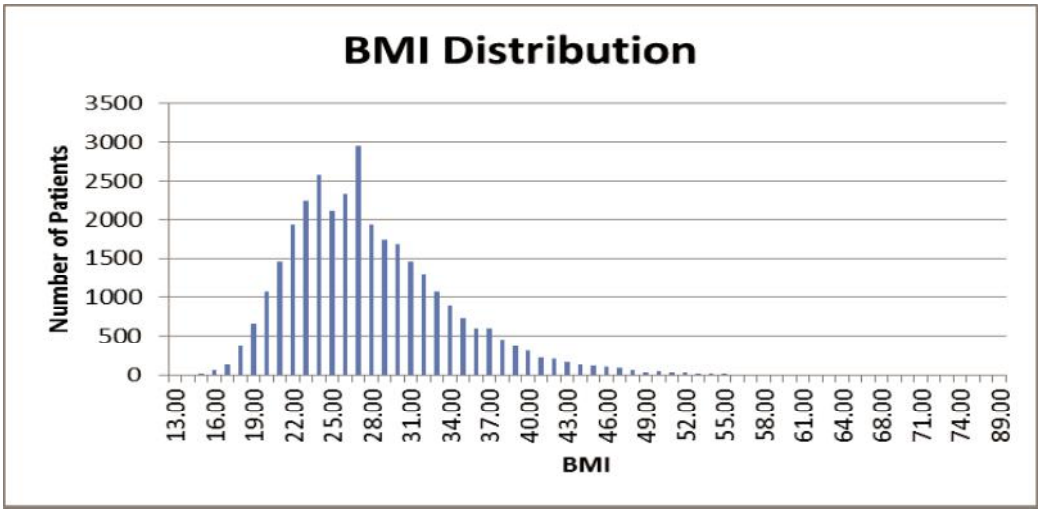


Figure 4 BMI distribution across the entire population

In order to investigate the trends of obesity across the population, we calculated the distribution of BMI for entire population (Figure 4). The distribution followed a Gaussian distribution with peak at BMI of 27. The peak at BMI of 27 implies the higher number of participants in overweight category and suggests increased BMI and obesity trend across the entire population. In addition, table 3 represents the percentage of population across various BMI. As it is evident from the table, out of the total population (26.3%) reporting BMI, 9.9% of total population is in overweight category, while 10.1% of the population is in the normal weight population. These results further solidify growing trend of obesity in adult American population.

The other clinical factor investigated in the current study is the effect of diabetes condition on inflammatory diseases. In the first step, we investigated prevalence of diabetes across the entire population. Additionally, we also investigated age first diagnosed with

diabetes. In total, we identify very little prevalence of diabetes in the entire population, where only 3% of the population responded to the question regarding age since first diagnosed with diabetes. Figure 5 shows the distribution of age first diagnosed with diabetes across the entire population.

Table 3 Number of participants with particular BMI and related percentage

BMI (kg/m2)	Number of Subjects	%		BMI (kg/m2)	Number of Subjects	%		BMI (kg/m2)	Number of Subjects	%
13.00	3	.0		35.00	732	.6		57.00	13	.0
14.00	10	.0		36.00	595	.5		58.00	6	.0
15.00	16	.0		37.00	593	.5		59.00	10	.0
16.00	62	.1		38.00	446	.4		60.00	7	.0
17.00	144	.1		39.00	365	.3		61.00	7	.0
18.00	368	.3		40.00	316	.3		62.00	6	.0
19.00	658	.5		41.00	226	.2		63.00	3	.0
20.00	1065	.9		42.00	202	.2		64.00	7	.0
21.00	1458	1.2		43.00	168	.1		65.00	3	.0
22.00	1925	1.6		44.00	133	.1		66.00	7	.0
23.00	2244	1.8		45.00	116	.1		68.00	5	.0
24.00	2583	2.1		46.00	115	.1		69.00	2	.0
25.00	2102	1.7		47.00	101	.1		70.00	2	.0
26.00	2331	1.9		48.00	67	.1		71.00	1	.0
27.00	2955	2.4		49.00	42	.0		72.00	1	.0
28.00	1935	1.6		50.00	54	.0		73.00	1	.0
29.00	1739	1.4		51.00	41	.0		74.00	2	.0
30.00	1670	1.4		52.00	41	.0		79.00	1	.0
31.00	1459	1.2		53.00	25	.0		82.00	2	.0
32.00	1301	1.1		54.00	20	.0		89.00	1	.0
33.00	1076	.9		55.00	27	.0		Missing	87794	72.7
34.00	897	.7		56.00	13	.0		Total	121466	100

As can be seen from the figure 5, the age first diagnosed with diabetes follows a Gaussian distribution, with multiple peaks observed at the ages of 35, 40, 45, 50, and 65. These represents a specific pattern of age first diagnoses with diabetes in entire population. This also marks for an important indication of age one should get checked for diabetes.

Table 4 Number of participants corresponding to age first diagnosed with diabetes

Age First Diagnosed with Diabetes	Number of Subjects	%		Age First Diagnosed with Diabetes	Number of Subjects	%		Age First Diagnosed with Diabetes	Number of Subjects	%
1.00	17	.0		31.00	27	.0		61.00	45	.0
2.00	9	.0		32.00	43	.0		62.00	80	.1
3.00	8	.0		33.00	36	.0		63.00	49	.0
4.00	6	.0		34.00	24	.0		64.00	50	.0
5.00	17	.0		35.00	80	.1		65.00	125	.1
6.00	7	.0		36.00	37	.0		66.00	50	.0
7.00	9	.0		37.00	33	.0		67.00	37	.0
8.00	13	.0		38.00	39	.0		68.00	45	.0
9.00	7	.0		39.00	24	.0		69.00	28	.0
10.00	23	.0		40.00	170	.1		70.00	60	.0
11.00	8	.0		41.00	41	.0		71.00	19	.0
12.00	16	.0		42.00	70	.1		72.00	27	.0
13.00	2	.0		43.00	28	.0		73.00	22	.0
14.00	8	.0		44.00	39	.0		74.00	15	.0
15.00	20	.0		45.00	179	.1		75.00	31	.0
16.00	9	.0		46.00	51	.0		76.00	8	.0
17.00	13	.0		47.00	70	.1		77.00	13	.0
18.00	20	.0		48.00	80	.1		78.00	20	.0
19.00	8	.0		49.00	60	.0		79.00	5	.0
20.00	37	.0		50.00	231	.2		80.00	24	.0
21.00	14	.0		51.00	59	.0		81.00	3	.0
22.00	10	.0		52.00	84	.1		82.00	2	.0
23.00	10	.0		53.00	62	.1		83.00	9	.0
24.00	10	.0		54.00	77	.1		84.00	2	.0
25.00	30	.0		55.00	172	.1		85.00	18	.0
26.00	14	.0		56.00	62	.1		Refused	5	.0
27.00	18	.0		57.00	72	.1		Not Ascertained	1	.0
28.00	27	.0		58.00	77	.1		Don't know	53	.0
29.00	22	.0		59.00	58	.0		# With Diabetes	3639	3.0
30.00	99	.1		60.00	197	.2		Missing	117827	97
								Total	121466	100

As seen in the table 4, compared to the overall population, only small percentage of participants responded to the question regarding diabetes, implying either decreased in diabetes rates across population or difficulty in understanding and responding to the particular question. Additionally, it is quite evident from the figure 5 that majority of the

patients have their onset of diabetes type 2 after age 40, with the mean of the distribution being 50 years.

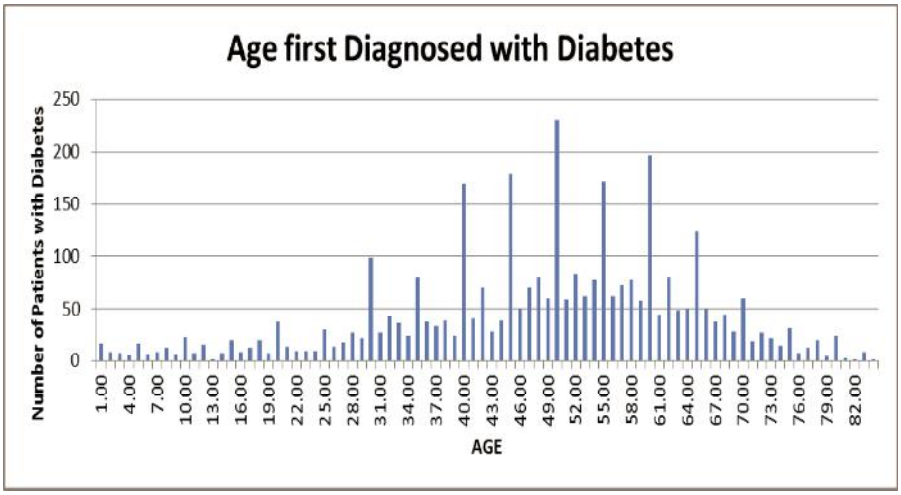


Figure 5 Distribution of Age first diagnosed with diabetes across entire population

In current study, we also investigated trends of sleep pattern in entire population. As seen in figure 6, the distribution of sleep patterns in 24 hours follows a normal distribution with peak at 8 hours. We observed that out of the 28% of the participants who responded to the question, a large number of participants (21%) sleep 6 or more hours every 24 hours. Table 5 represents the information about the sleep patterns across the populations and related percentage of total population.

In combination, these results imply large-scale changes in the clinical factors with increased BMI (trend towards obesity) and late identification of diabetes in the population (50 years). These results also imply normal sleeping pattern across the populations where a large percentage of population show normal sleeping pattern.

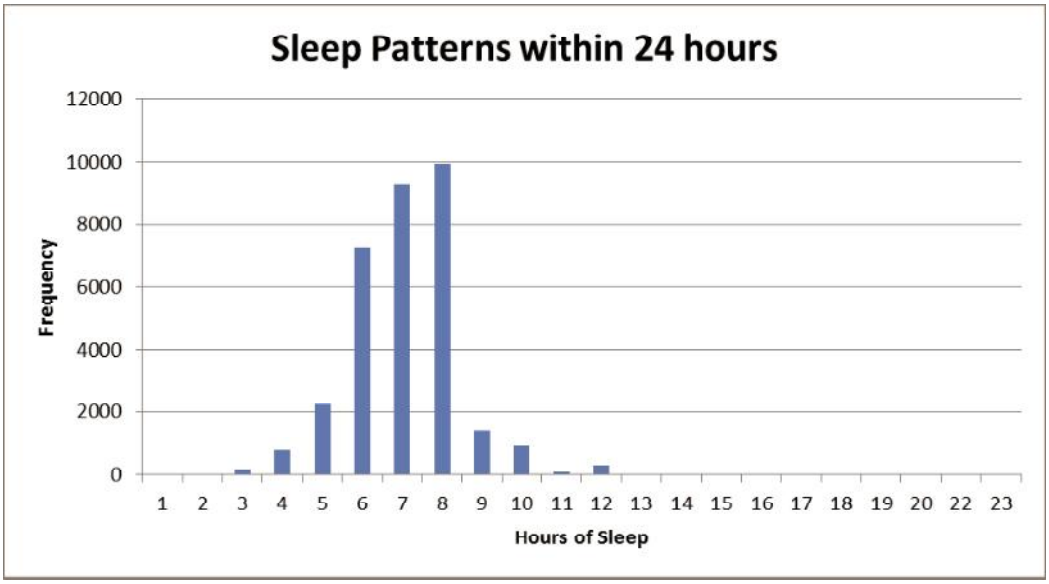


Figure 6 Distribution of sleep pattern amongst the entire population

Upon close inspection of the results, we also observed large number of missing information across the entire population. This could be due to participants not understanding the questions or refusing to answer. This also implies further attention to be given to future studies while developing questions to improve the data collection and data quality.

Table 5 Hours of sleep amongst the entire population

Hours of Sleep	Number of Subjects	%		Hours of Sleep	Number of Subjects	%		Hours of Sleep	Number of Subjects	%
1	7	.0		10	914	.8		19	2	.0
2	39	.0		11	92	.1		20	3	.0
3	150	.1		12	300	.2		22	2	.0
4	783	.6		13	14	.0		23	1	.0
5	2233	1.8		14	28	.0		Refused	39	.0
6	7241	6.0		15	12	.0		Not ascertained	1004	.8
7	9246	7.6		16	17	.0		Don't know	143	.1
8	9956	8.2		17	2	.0		Missing	87794	72.3
9	1432	1.2		18	12	.0		Total	121466	100.0

4.1.3 Distributions of behavioral factors for the entire population

In addition to the clinical factors, the behavioral factors such as alcohol consumption, smoking status and physical activity are also investigated for the entire population. One of the behavioral factors that play a crucial role in an individual's overall health is their smoking status. Out of the number of subjects who responded to the questionnaire about their smoking status 12,412 smoke regularly and 20,347 do not smoke.

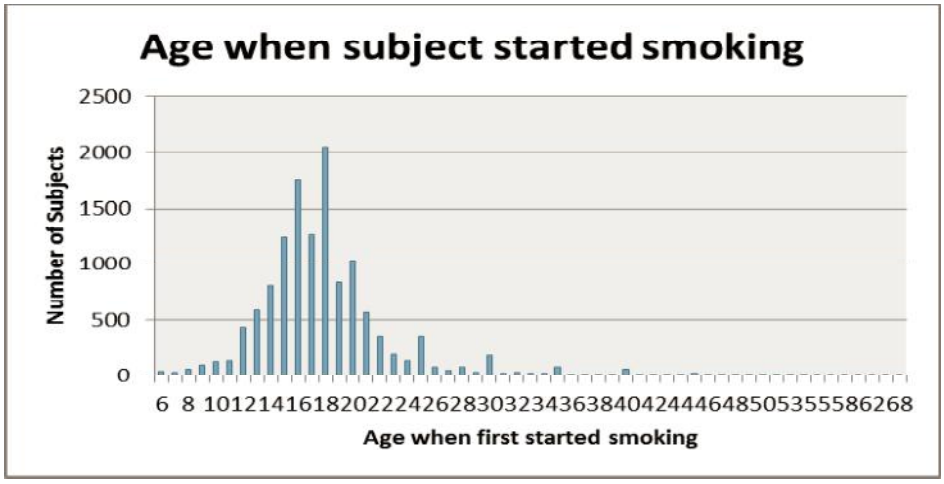


Figure 7 Distribution of age when first started smoking

Based on previous literature, we also identified an important variable associated with smoking: Age when first started smoking. As shown in figure 7, age first started smoking varies considerably across the population. The peak of the distribution is at the age of 18 years. We also observed that a large number of participants start smoking at a very early age of 10-12 years. This represents a clear shift where participants start smoking at an early age. Table 6 represents the percentage of population with respect to the age they started smoking. As shown in table almost 1.7% of total population starts smoking at the age of 18 while almost 1.4% of the studied population starts smoking at the age of 16.

Considering legal age of smoking to be 18 years, this shows a shift towards early smoking and points to important policy considerations.

Table 6 Number of participants and the age they started smoking.

Age started smoking regularly	Number of subjects	%		Age started smoking regularly	Number of subjects	%		Age started smoking regularly	Number of subjects	%
6	37	.0		25	356	.3		44	6	.0
7	34	.0		26	75	.1		45	18	.0
8	61	.1		27	45	.0		46	5	.0
9	91	.1		28	81	.1		47	3	.0
10	127	.1		29	30	.0		48	4	.0
11	133	.1		30	180	.1		49	3	.0
12	437	.4		31	17	.0		50	7	.0
13	582	.5		32	31	.0		52	1	.0
14	813	.7		33	16	.0		53	1	.0
15	1238	1.0		34	16	.0		54	2	.0
16	1761	1.4		35	76	.1		55	4	.0
17	1262	1.0		36	14	.0		57	1	.0
18	2047	1.7		37	9	.0		58	1	.0
19	835	.7		38	14	.0		60	1	.0
20	1035	.9		39	5	.0		62	1	.0
21	562	.5		40	55	.0		65	2	.0
22	354	.3		41	2	.0		68	1	.0
23	189	.2		42	7	.0		Missing	108265	89.1
24	131	.1		43	3	.0		Total	121466	100

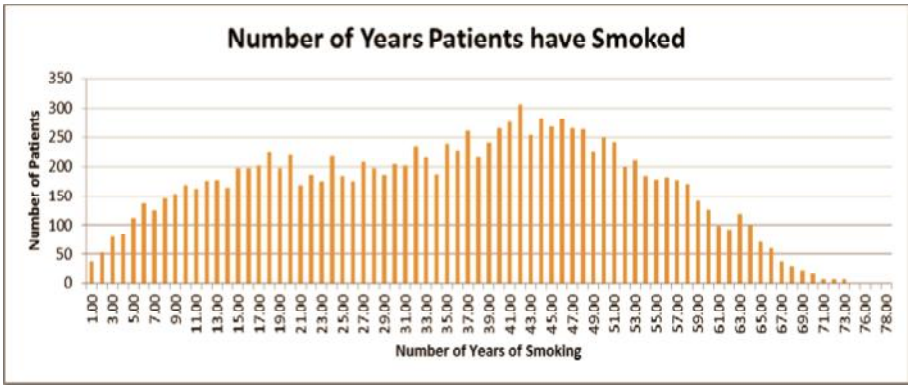


Figure 8 Distribution of subjects and the number of years they have smoked.

Table 7 Number of participants in the entire population with the number of years they have smoked.

Number of years smoked	Number of subjects	%		Number of years smoked	Number of subjects	%		Number of years smoked	Number of subjects	%
1.00	36	.0		27.00	207	.2		53.00	211	.2
2.00	53	.0		28.00	197	.2		54.00	184	.2
3.00	78	.1		29.00	186	.2		55.00	179	.1
4.00	83	.1		30.00	205	.2		56.00	181	.1
5.00	111	.1		31.00	202	.2		57.00	178	.1
6.00	137	.1		32.00	235	.2		58.00	170	.1
7.00	124	.1		33.00	216	.2		59.00	142	.1
8.00	146	.1		34.00	187	.2		60.00	125	.1
9.00	155	.1		35.00	239	.2		61.00	99	.1
10.00	168	.1		36.00	227	.2		62.00	93	.1
11.00	163	.1		37.00	260	.2		63.00	118	.1
12.00	176	.1		38.00	218	.2		64.00	100	.1
13.00	177	.1		39.00	240	.2		65.00	69	.1
14.00	165	.1		40.00	265	.2		66.00	60	.0
15.00	198	.2		41.00	277	.2		67.00	37	.0
16.00	198	.2		42.00	306	.3		68.00	30	.0
17.00	201	.2		43.00	254	.2		69.00	22	.0
18.00	224	.2		44.00	284	.2		70.00	16	.0
19.00	198	.2		45.00	268	.2		71.00	6	.0
20.00	221	.2		46.00	282	.2		72.00	6	.0
21.00	168	.1		47.00	265	.2		73.00	6	.0
22.00	186	.2		48.00	264	.2		75.00	1	.0
23.00	175	.1		49.00	226	.2		76.00	1	.0
24.00	219	.2		50.00	251	.2		77.00	1	.0
25.00	185	.2		51.00	242	.2		78.00	1	.0
26.00	174	.1		52.00	199	.2		# Smoked	12412	10
								Missing information	109054	90
								Total	121466	100

Figure 8 shows a distribution of patients who smoke and how long they have been smoking. The duration of the number of years the subjects have smoked is derived by subtracting the age of the patient and the age the patients started smoking regularly. Figure 8 shows the wide distribution between the years 37 and 57. This explains that amongst the people who do smoke, they have smoked for more than 3 decades of their lives. This may

have large-scale implications on the participants' health. The age since started smoking for individuals also correlates with results in figure 8, as they both have been derived using the same method. This also implies that many participants who start smoking at a young age are addicted to nicotine and continue to smoke throughout their lives.

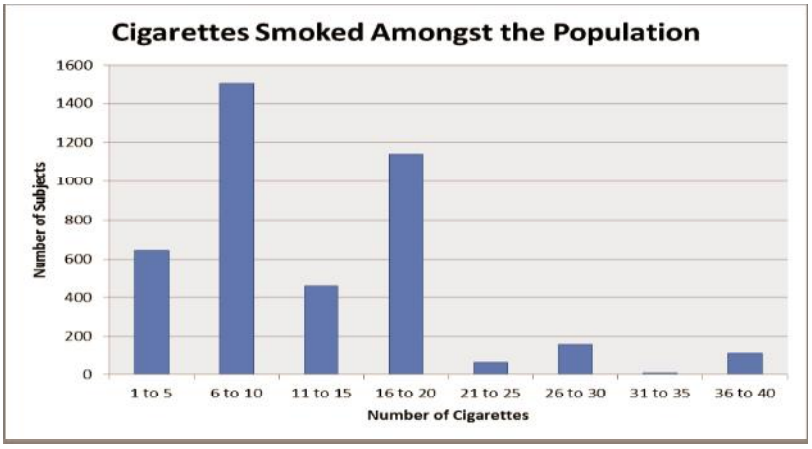


Figure 9 Distribution of subjects along with the number of cigarettes they have smoked.

One of the other important aspects for the participants who smoke regularly is the number of cigarettes smoked and the number of participants for the same. Out of the total participants who responded to the questionnaire about smoking status only a small percent responded to the questions about the number of cigarettes smoked. Figure 9 and table 8 displays this information.

Table 8 Number of cigarettes the population has smoked.

Number of Cigarettes	Number of Subjects		Number of Cigarettes	Number of Subjects
1 to 5	646		21 to 25	27
6 to 10	1510		26 to 30	0
11 to 15	457		31 to 35	0
16 to 20	1141		36 to 40	1

Figure 9 is a distribution of the number of cigarettes the smokers smoke in a day. As seen in figure 9 the highest number of patients smoke about 10 cigarettes per day, which is half a pack and the second highest number of patients smoke about 20 cigarettes a day, which is an entire pack of cigarettes. Figure 9 and table 8 indicates that in the current population, the participants who smoke, do it fairly regularly, are heavy smokers and combined with the earlier results have been smoking for more than 3 decades of their life. These combined results may explain the influence and devastating effects of smoking addiction.

In addition to smoking status, alcohol consumption status is one of the other behavioral factors investigated in the current population. Considering that smoking and alcohol can have significant effect on ulcers in liver, understanding the prevalence of these two behavioral factors can help us further our understanding of ulcerative colitis. Amongst the total population, who responded to the question of whether they drink 26197 subjects answered yes and 6930 patients answered no.

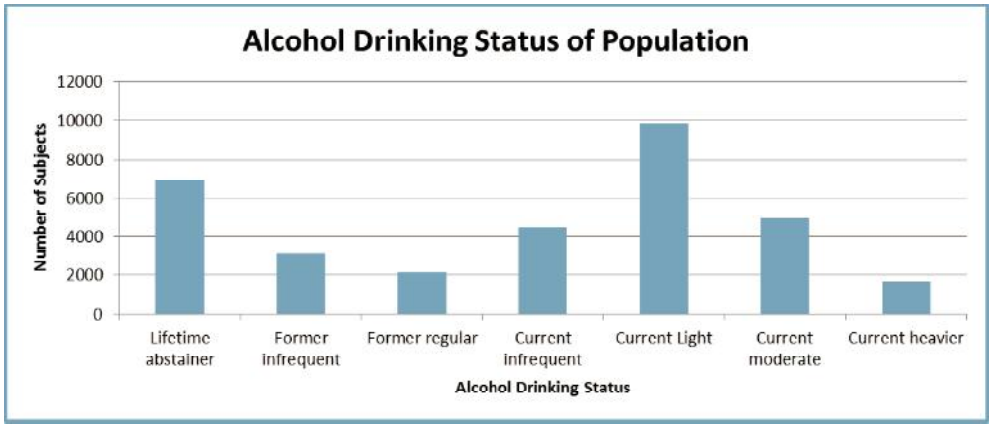


Figure 10 Distribution of drinking frequency amongst drinkers in the population.

In order to further characterize the alcohol consumption, we stratified the total population who responded yes to the Alcohol consumption question based on their consumption frequency. Figure 10 indicates this stratification in to lifetime abstainer, former infrequent drinker, former regular drinker, currently infrequent drinker, currently moderate drinker, heavy drinker and current drinker categories. Table 9 provided detailed explanation for each of this categories. As shown in figure 9 the highest number of subjects are current light drinkers. This indicates that the highest number of patients drink only few drinks on an average. The second highest numbers of population are lifetime abstainers. This may be due to other health conditions, age of the patient or just have chosen not to drink, however very little information is provided to characterize alcohol consumption.

In addition to considering the negative behavioral factors such as smoking status and alcohol consumption, we also considered a positive behavioral factor that may have positive influence in reducing the prevalence of inflammatory disease. This behavioral factor is the amount of regular physical exercise performed by these participants. This can easily be correlated with the clinical factors of the patient's BMI and their diabetes status as regular physical exercise can help reduce the risk of diabetes and help maintain healthy BMI. Considering the heterogeneity of age in current population and decrease in vigorous exercise expected with increased age, we focused on investigating light to moderate exercise performed by participants.

Table 9 Alcohol drinking status with the number of subjects

	Alcohol drinking status	Description	Number of Subjects	Percentage
1	Lifetime abstainer	<12 drinks in lifetime	6930	5.7
2	Former infrequent	12+ drinks in lifetime but never as many as 12 in 1 yr and none in past yr.	3101	2.6
3	Former regular	12+ drinks in lifetime, 12+ drinks in 1 yr, but none in past yr	2149	1.8
5	Current infrequent	12+ drinks in lifetime, 1-11 drinks in past year	4483	3.7
6	Current Light	12+ drinks in lifetime, and ≤ 3 drinks per week in past yr	9849	8.1
7	Current moderate	12+ drinks in lifetime, and (male)> 3 drinks per week up to 14 drinks per week OR (female)>3 drinks per week up to 7 drinks per week	4936	4.1
8	Current heavier	12+ drinks in lifetime, and (male) >14 drinks per week in past year OR (female) >7 drinks per week in past yr.	1679	1.4
4	Former unknown frequency	12+ drinks in lifetime, none in the past year, don't know if 12+ in any 1 yr.	2	.0
9	Current drinker, frequency/level unknown		106	.1
10	Drinking status Unknown		437	.4
	Missing		87794	72.3
	Total		121466	100.0

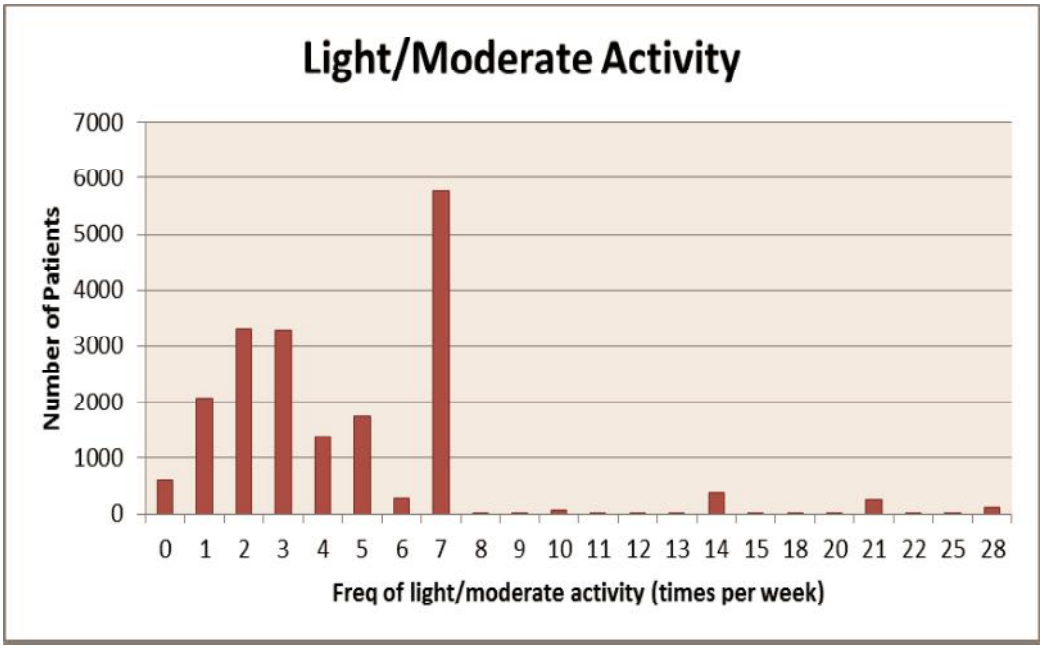


Figure 11 Distribution of number of times the population exercises with light/moderate physical activity

Out of the total population 32,110 (26%) participants responded to question about exercise, while 87794 (74%)participants did not respond to questions about exercise. Out of the participants who responded only 18764 (58% of people who responded) participants performed some type of light/moderate exercise while 13346 (42% of people who responded) did not perform any type of physical exercise. Figure 11 shows distribution of number of times these participants perform light to moderate physical activity every week outside of their daily routine work. This shows that the participants who do perform light to moderate activity perform this activity 7 times per week, implying that these participants' workout fairly regularly and presumably every day of the week.

Table 10 Frequency of light to moderate physical activity amongst the entire population.

Frequency of Light/moderate activity (times/Week)	Number of Subjects	%		Frequency of Light/moderate activity (times/Week)	Number of Subjects	%
0	611	.5		14	392	.3
1	2082	1.7		15	16	.0
2	3310	2.7		18	1	.0
3	3291	2.7		20	4	.0
4	1396	1.1		21	282	.2
5	1733	1.4		22	1	.0
6	307	.3		25	2	.0
7	5776	4.8		28	105	.1
8	6	.0		Never	13346	11.0
9	2	.0		Unable to do activity	497	.4
10	49	.0		Refused	18	.0
11	1	.0		Not ascertained	313	.3
12	6	.0		Don't Know	123	.1
13	2	.0		Missing info	87794	72.3
				Total	121466	100.0

One of the important observations from figure 11 and corresponding table 10 is the low number of participants who perform light/moderate exercise. This decreased state of exercise may help explain increased obesity and presence of related comorbid condition in US.

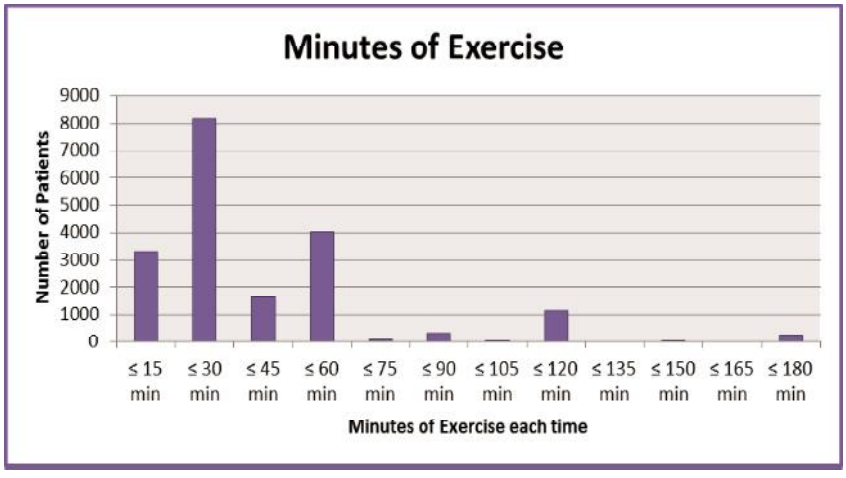


Figure 12 Distribution of number of minutes the population exercises.

In addition to the frequency of weekly exercise, we also investigated the amount of time spend performing this exercise. As seen in figure 12 and table 11, a significantly higher number of populations perform light/moderate exercise for < 30 minutes a day. The second highest numbers of patients perform physical activity for about 60 minutes of less. This average length of exercise to be less than 30 minutes may also represent an important roadblock towards healthy living. As participants perform shorter exercise routines of light/moderate activity, it may not be as beneficial as expected. This may lead to not reaching expected exercise goals and may discourage participants from further pursuing regular exercise. This time length of exercise may also represent older population which may not be able to perform longer time for exercise.

Table 11 Minutes of exercise amongst the entire population

Minutes of exercise per session	Number of subjects	%		Minutes of exercise per session	Number of subjects	%
≤ 15 min	3320	2.73		240 to 300	227	0.19
≤ 30 min	8178	6.73		300 to 360 min	40	0.03
≤ 45 min	1634	1.35		360 to 420 min	11	0.01
≤ 60 min	4019	3.31		420 to 480 min	40	0.03
≤ 75 min	50	0.04		480 to 540	2	0.00
≤ 90 min	326	0.27		540 to 600	6	0.00
≤ 105 min	1	0.00		600 to 660	1	0.00
≤ 120 min	1144	0.94		660 to 720	3	0.00
≤ 135 min	0	0.00		Refused	1	0.00
≤ 150 min	7	0.01		Not ascertained	21	0.02
≤ 165 min	0	0.00		Don't know	95	0.08
≤ 180 min	249	0.20		Missing Information	102901	84.72
				Total	121466	100

4.2 Arthritis population

One of the inflammatory diseases studied in this population is arthritis. Based on the question regarding arthritis status, we extracted id for the patients with arthritis. From the total population, a total 8689 participants responded yes to questionnaire about arthritis

and were further analyzed. Figure 13 shows the age distribution of participants with arthritis.

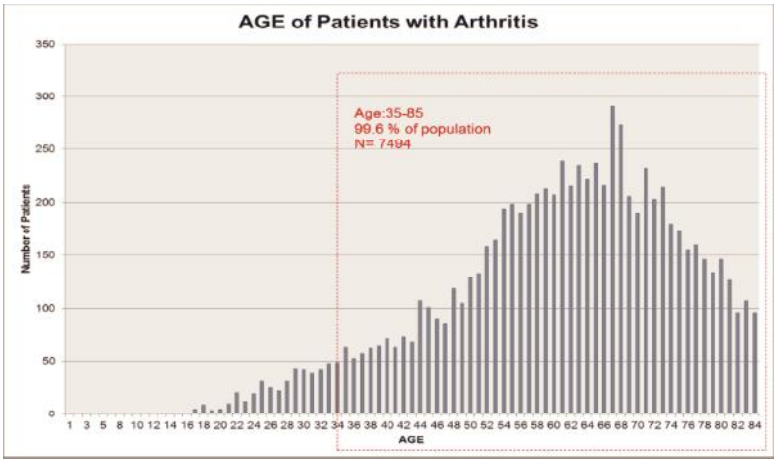


Figure 13 Age distributions amongst patients with arthritis.

Table 12 Age of number of patients with arthritis.

Age	Number of patients		Age	Number of patients		Age	Number of patients		Age	Number of patients
1	1		22	20		43	68		64	222
2	0		23	12		44	107		65	237
3	0		24	19		45	101		66	217
4	0		25	31		46	91		67	291
5	1		26	25		47	85		68	274
6	0		27	22		48	119		69	206
7	0		28	31		49	105		70	190
8	0		29	42		50	129		71	232
9	0		30	41		51	133		72	203
10	0		31	38		52	158		73	214
11	0		32	41		53	164		74	180
12	0		33	48		54	194		75	174
13	1		34	49		55	199		76	155
14	1		35	63		56	190		77	160
15	1		36	53		57	199		78	146
16	1		37	57		58	208		79	134
17	5		38	62		59	213		80	146
18	9		39	64		60	207		81	127
19	4		40	71		61	239		82	96
20	5		41	63		62	216		83	107
21	10		42	73		63	235		84	96
									85 and higher	558
									Total	8689

Figure 13 shows the age distribution of patients with Arthritis. As seen in the figure the highest numbers of patients with arthritis are between the ages of 68-70. Out of the total population the number of patients who have arthritis are 8689. It is also evident from table 12 that these patients have a wide age range with youngest participant with arthritis at age of 1. Due to this heterogeneity of the population, we focused our analysis on the arthritis patients between the ages of 35-85 years. A total of 7673 participants were selected to be between the age of 35-85 years and having positive arthritis diagnosis. On the contrary to the equal gender distribution observed in overall population, we observed difference in prevalence of arthritis between these patients. Out of 7673 subjects there are 3281 male subjects with arthritis (42.7%) and 4392 (57.2%) subjects with arthritis. This also indicates that female have higher prevalence of arthritis compared to male population.

4.2.1 Distribution of clinical factors in arthritis patients

In addition to identifying the age and gender distribution in the arthritis population, we also investigated the prevalence of clinical and behavioral factors in arthritis populations to understand their effect on arthritis prevalence. Similar to the total population the clinical factors studied included BMI, diabetes status and the sleeping pattern of the patients with arthritis.

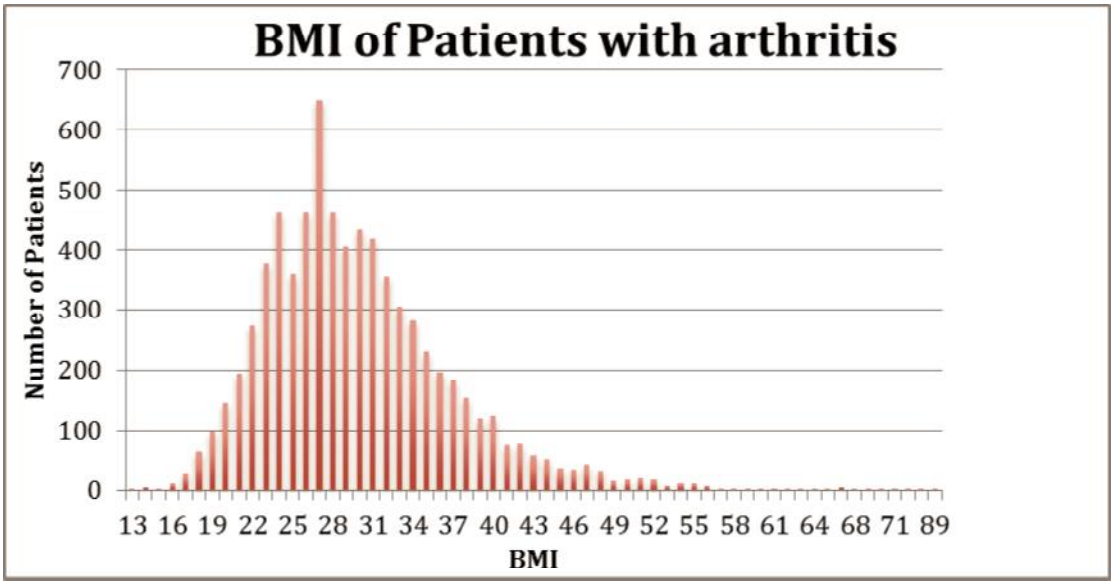


Figure 14 BMI distribution of patients with arthritis

Table 13 BMI of the number of patients with arthritis

BMI (kg/m2)	Number of Subjects	%		BMI (kg/m2)	Number of Subjects	%		BMI (kg/m2)	Number of Subjects	%
13	1	.0		34	283	3.7		55	11	.1
14	6	.1		35	232	3.0		56	7	.1
15	3	.0		36	197	2.6		57	3	.0
16	12	.2		37	185	2.4		58	1	.0
17	28	.4		38	155	2.0		59	2	.0
18	64	.8		39	121	1.6		60	2	.0
19	100	1.3		40	124	1.6		61	1	.0
20	145	1.9		41	75	1.0		62	4	.1
21	194	2.5		42	77	1.0		63	1	.0
22	274	3.6		43	58	.8		64	4	.1
23	378	4.9		44	52	.7		65	1	.0
24	464	6.0		45	37	.5		66	5	.1
25	361	4.7		46	36	.5		68	4	.1
26	462	6.0		47	43	.6		69	1	.0
27	649	8.5		48	32	.4		70	1	.0
28	463	6.0		49	16	.2		71	1	.0
29	405	5.3		50	19	.2		73	1	.0
30	434	5.7		51	20	.3		82	1	.0
31	419	5.5		52	19	.2		89	1	.0
32	356	4.6		53	7	.1		Missing	297	3.9
33	306	4.0		54	12	.2		Total	7673	100

Figure 14 shows the distribution of BMI for patients with Arthritis. This figure shows the normal distribution of BMI amongst this population. Figure 14 also displays that the highest number of patients with arthritis have a BMI of 27. The BMI of 27 is defined as overweight which is similar to the one observed in overall population. This results also imply that the growing trends of obesity in the US population is consistent within the arthritis patient population. This is an important indicator implying relationship between higher BMI of the patient and the diagnosis of arthritis. Many studies have indicated that BMI may be the cause of arthritis, however many have indicated that arthritis may cause the lack of mobility hence the increase in weight and BMI as shown in figure 14 and table 13.

One of the other important clinical factors investigated in current analysis is the diabetes status of the patient with arthritis. Amongst the patients with arthritis who responded to the questionnaire about the diabetes status, less number of patients has diabetes (n=1631) compared to the arthritic patients who do not have diabetes (n=6018). As seen in figure 15, in the arthritis patients with diabetes, age when first diagnosed with diabetes varies considerably across the patients. Peaks observed at the age of 35, 40, 45, and 55 imply higher detection rates at these age. These ages are similar to one obtained in overall population, implying importance of fairly regular diabetes testing in this population. The peak of the distribution is observed at the age of 50 years, which is quite similar to the overall population. This also specifies that this is type-2 diabetes that may also be correlated with the increased patients BMI at this age.

Table 14 Age first diagnosed with diabetes amongst patients with arthritis

Age First Diagnosed with Diabetes	Number of Subjects	%		Age First Diagnosed with Diabetes	Number of Subjects	%		Age First Diagnosed with Diabetes	Number of Subjects	%
1	6	0.08		31	5	0.07		60	97	1.26
2	4	0.05		32	11	0.14		61	22	0.29
3	4	0.05		33	16	0.21		62	40	0.52
4	3	0.04		34	7	0.09		63	26	0.34
5	7	0.09		35	36	0.47		64	24	0.31
6	3	0.04		36	14	0.18		65	65	0.85
7	2	0.03		37	11	0.14		66	27	0.35
8	4	0.05		38	14	0.18		67	19	0.25
9	4	0.05		39	4	0.05		68	24	0.31
10	9	0.12		40	80	1.04		69	13	0.17
11	3	0.04		41	10	0.13		70	33	0.43
12	5	0.07		42	34	0.44		71	12	0.16
14	1	0.01		43	16	0.21		72	16	0.21
15	10	0.13		44	15	0.20		73	16	0.21
16	2	0.03		45	89	1.16		74	9	0.12
17	5	0.07		46	22	0.29		75	13	0.17
18	3	0.04		47	29	0.38		76	6	0.08
19	2	0.03		48	32	0.42		77	7	0.09
20	18	0.23		49	30	0.39		78	11	0.14
21	6	0.08		50	121	1.58		79	1	0.01
22	3	0.04		51	28	0.36		80	7	0.09
23	1	0.01		52	46	0.60		81	1	0.01
24	2	0.03		53	28	0.36		83	1	0.01
25	13	0.17		54	39	0.51		84	1	0.01
26	4	0.05		55	83	1.08		85	4	0.05
27	6	0.08		56	35	0.46		Refused	1	0.01
28	6	0.08		57	33	0.43		Don't know	23	0.30
29	6	0.08		58	34	0.44		Missing	6018	78.43
30	46	0.60		59	26	0.34		Total	7673	100.00

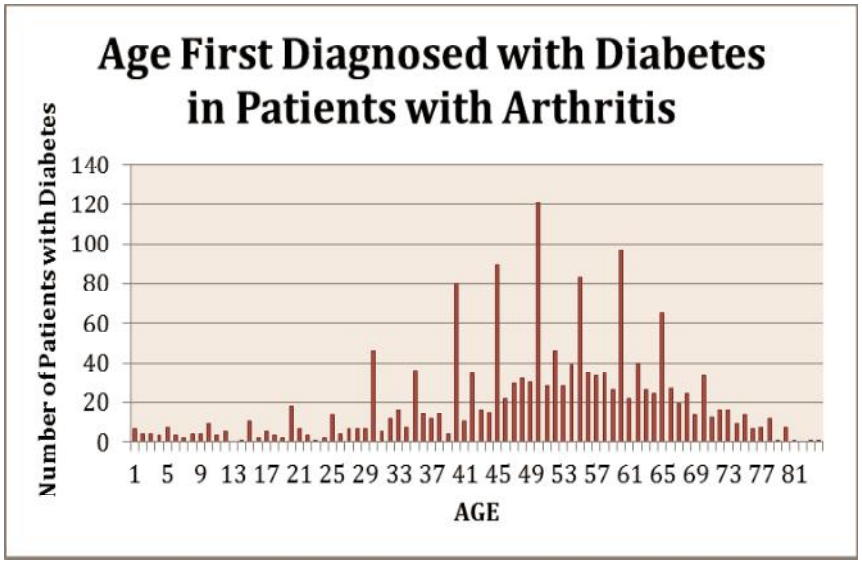


Figure 15 Distribution of patients with arthritis and the age they were first diagnosed with diabetes

One of the last clinical factors shown to be highly prevalent in arthritis population is loss of sleep amongst the patients due to continuous pain experienced by these individuals. As seen in figure 16 and table 15, sleeping patterns of patients with arthritis was divided fairly equally amongst 6, 7 and 8 hours of daily sleep pattern however this percentage were significantly higher than overall population. Higher percentage of patients with arthritis slept 6 hours for 24-hour period compared to the total population. This implies higher percentage of population sleeping less number of hours. This reduced sleep pattern highlights one of the debilitating effects of arthritis on participants, which than further cause increases prevalence of other comorbid condition. This clinical factors and their prevalence will also be compared to a control population to avoid the bias of large sample size in overall population.

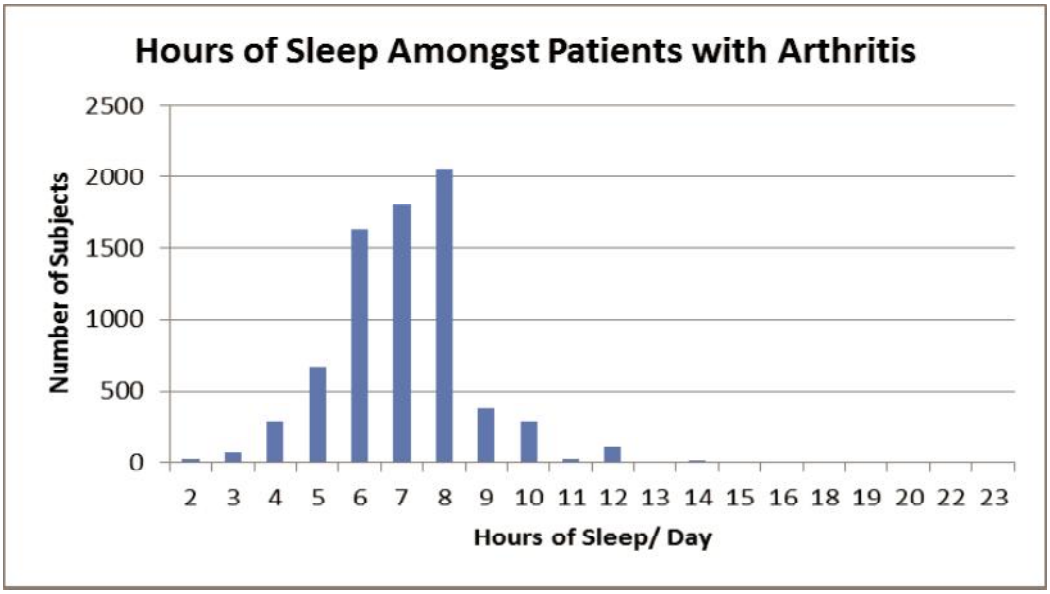


Figure 16 Distribution of frequency of hours of sleep amongst patients with arthritis

Table 15 Hours of sleep patients with arthritis have.

Hours of Sleep	Number of Subjects	%		Hours of Sleep	Number of Subjects	%		Hours of Sleep	Number of Subjects	%
2	20	.3		10	289	3.8		19	1	.0
3	67	.9		11	24	.3		20	2	.0
4	287	3.7		12	105	1.4		22	1	.0
5	679	8.8		13	5	.1		23	1	.0
6	1634	21.3		14	14	.2		Refused	9	.1
7	1808	23.6		15	6	.1		Not Ascertained	221	2.9
8	2059	26.8		16	10	.1		Don't know	50	.7
9	374	4.9		18	7	.1		Total	7673	100.0

4.2.2 Distribution of behavioral factors in arthritis patients

In addition to the clinical factors that may affect patients with arthritis or may be a cause of arthritis, there are several behavioral factors that may not be directly associated with the biology of arthritis however show significantly high prevalence in arthritis population. Some of the behavioral factors investigated in this study are smoking status,

alcohol consumption status and physical activity performed by these patients. Amongst all the behavioral factors studied in this population, smoking status of the patients was the most prevalence in arthritis patients.

Out of the number of patients who have arthritis (7673) there are almost equal numbers of patients who smoke (3895 subjects) and who do not smoke (3748). This represents a significant increase in patients who smoke compared to the overall population, where only 10% of the total population smoked compared to 51% in the arthritis population.

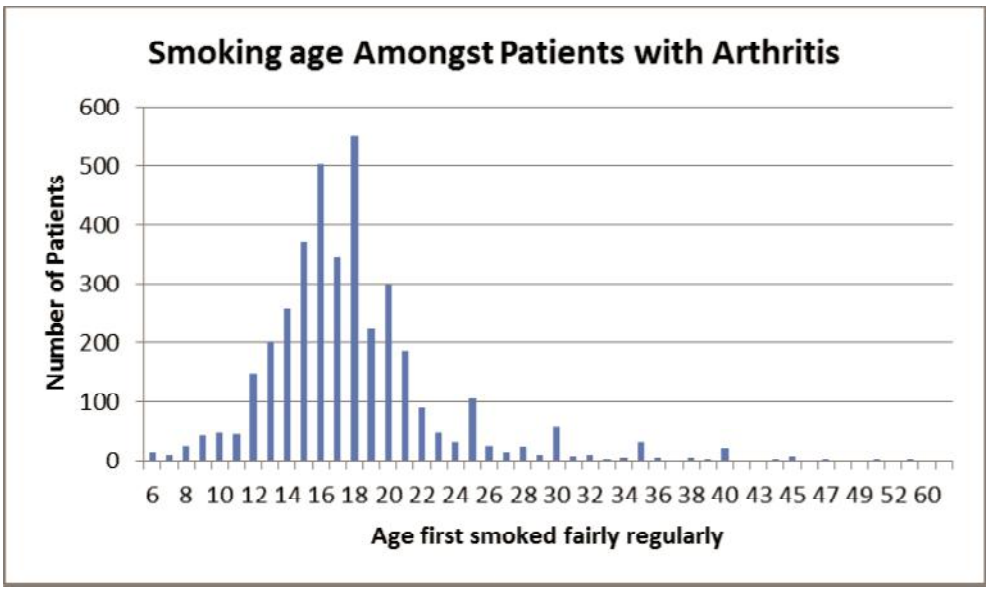


Figure 17 Distribution of age since patients with arthritis started smoking

Table 16 Age when patients with arthritis started smoking

Age first smoked fairly regularly	Number of Subjects	%		Age first smoked fairly regularly	Number of Subjects	%		Age first smoked fairly regularly	Number of Subjects	%
6	14	.2		24	32	.4		43	1	.0
7	9	.1		25	105	1.4		44	3	.0
8	26	.3		26	25	.3		45	8	.1
9	43	.6		27	15	.2		46	2	.0
10	47	.6		28	24	.3		47	3	.0
11	45	.6		29	11	.1		48	2	.0
12	147	1.9		30	58	.8		49	1	.0
13	201	2.6		31	8	.1		50	4	.1
14	257	3.3		32	9	.1		52	1	.0
15	371	4.8		33	4	.1		55	3	.0
16	504	6.6		34	6	.1		60	1	.0
17	345	4.5		35	31	.4		65	1	.0
18	551	7.2		36	5	.1		Never smoked regularly	39	.5
19	223	2.9		37	2	.0		Refused	1	.0
20	298	3.9		38	5	.1		Don't know	58	.8
21	185	2.4		39	3	.0		Missing	3778	49.2
22	90	1.2		40	21	.3		Total	7673	100.0
23	46	.6		42	1	.0				

Figure 17 indicates that amongst the population of patients with arthritis, a large number of patients started smoking at an early age of 16-18. This is quite similar to the total population where a large percentage of population started smoking at a very early age.

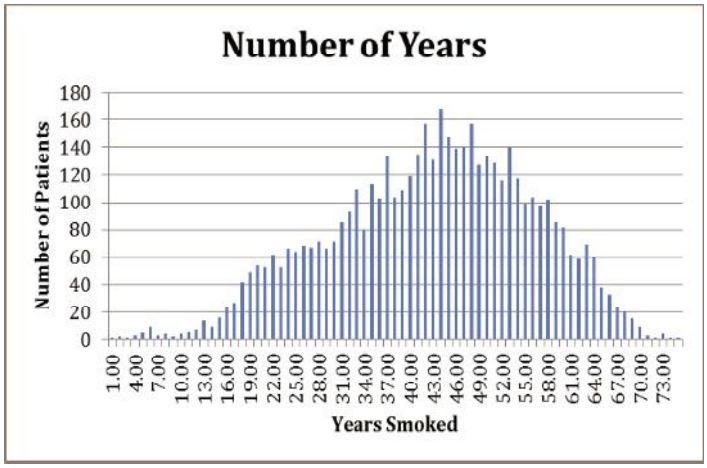


Figure 18 Distribution of number of years patients with arthritis have smoked.

Table 17 Number of years patients with arthritis have smoked.

Number of Years Smoked	Number of Subjects	%		Number of Years Smoked	Number of Subjects	%		Number of Years Smoked	Number of Subjects	%
1.00	1	.01		27.00	40	.52		53.00	113	1.47
2.00	0	.00		28.00	45	.59		54.00	105	1.37
3.00	1	.01		29.00	49	.64		55.00	88	1.15
4.00	2	.03		30.00	52	.68		56.00	91	1.19
5.00	4	.05		31.00	60	.78		57.00	89	1.16
6.00	7	.09		32.00	65	.85		58.00	88	1.15
7.00	1	.01		33.00	76	.99		59.00	74	.96
8.00	2	.03		34.00	66	.86		60.00	71	.93
9.00	1	.01		35.00	84	1.09		61.00	55	.72
10.00	1	.01		36.00	78	1.02		62.00	51	.66
11.00	4	.05		37.00	108	1.41		63.00	62	.81
12.00	3	.04		38.00	76	.99		64.00	54	.70
13.00	8	.10		39.00	80	1.04		65.00	33	.43
14.00	4	.05		40.00	95	1.24		66.00	29	.38
15.00	7	0.09		41.00	110	1.43		67.00	21	.27
16.00	13	.17		42.00	127	1.66		68.00	17	.22
17.00	11	.14		43.00	96	1.25		69.00	14	.18
18.00	20	.26		44.00	144	1.88		70.00	9	.12
19.00	31	.40		45.00	124	1.62		71.00	3	.04
20.00	34	.44		46.00	116	1.51		72.00	0	.00
21.00	32	.42		47.00	117	1.52		73.00	3	.04
22.00	33	.43		48.00	136	1.77		77.00	0	.00
23.00	28	.36		49.00	112	1.46		78.00	1	.01
24.00	31	.40		50.00	111	1.45		Missing Info	3878	50.5
25.00	33	.43		51.00	106	1.38		Total	7673	100
26.00	40	.52		52.00	99	1.29				

Using the information about the age of patients with arthritis and the age since started smoking, we calculated the number of years smoked for each of the participants. As shown in figure 18, the number of years smoked is normally distributed across the population with values ranging from 1 to 77 years. However, there are high numbers of patients with arthritis who have smoked for more than 30 years of their life (table 17). As seen in figure 17 and table 16, many of the smokers start smoking at very early age and as a large population of arthritis patients is between ages of 40 to 80 years, the results obtained in the figure 18 are expected. One of the important conclusions from figure 17 and table 17 is that arthritis patients who start smoking at an early age continue smoking for a longer period of time.

In addition to the number of years smoked, the number of cigarettes smoked can also have a higher influence on prevalence of arthritis. For example, a participant smoking 1 cigarettes per day for 20 years may have different effects on physiology compared to a participant smoking 20 cigarettes a day for 1 years. Figure 19 and table 18 display the distribution of number of cigarettes smoked in the population. As shown in figure 19 large numbers of patients smoke about 10 cigarettes a day, which is half a pack and the second highest number of subjects, smoke almost 20 cigarettes a day, which is a full pack of cigarettes. As it is evident from this results, arthritis patients who smoke, are heavy smokers and this can also be an associated factor in prevalence of arthritis. Specifically, it is possible that nicotine consumption may be a compensatory mechanism used by the patients with arthritis to cope up with the constant pain.

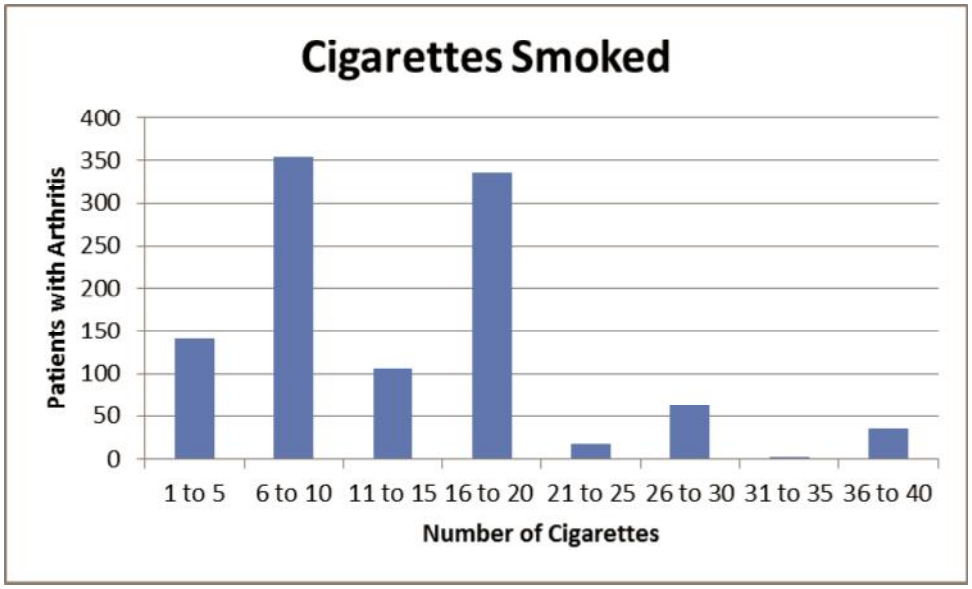


Figure 19 Distribution of number of cigarettes patients with arthritis have smoked.

Table 18 Number of cigarettes patients with arthritis have smoked.

Number of cigarettes	Number of Subjects	%		Number of cigarettes	Number of Subjects	%
1 to 5	141	1.84		41 to 50	3	0.04
6 to 10	354	4.61		51 to 60	5	0.07
11 to 15	106	1.38		95+	1	0.01
16 to 20	336	4.38		Refused	2	0.03
21 to 25	18	0.23		Not Ascertained	0	0.00
26 to 30	62	0.81		Don't Know	3	0.04
31 to 35	3	0.04		Missing	6604	86.07
36 to 40	35	0.46		Total	7673	100.00

In addition to the smoking, alcohol is one of the other factors that may show high prevalence in arthritis population compared to the overall population. Amongst the patients with arthritis, there is an equal distribution between the number of subjects who consume alcohol (4428 subjects) and the subjects who do not (3195 subjects).

Table 19 Alcohol consumption status amongst patients with arthritis.

Code	Alcohol drinking status	Description	Number of Subjects	%
1	Lifetime abstainer	<12 drinks in lifetime	1461	19.0
2	Former infrequent	12+ drinks in lifetime but never as many as 12 in 1 yr and none in past yr.	1107	14.4
3	Former regular	12+ drinks in lifetime, 12+ drinks in 1 yr, but none in past yr	806	10.5
5	Current infrequent	12+ drinks in lifetime, 1-11 drinks in past year	1161	15.1
6	Current Light	12+ drinks in lifetime, and ≤ 3 drinks per week in past yr	1736	22.6
7	Current moderate	12+ drinks in lifetime, and (male)> 3 drinks per week up to 14 drinks per week OR (female)>3 drinks per week up to 7 drinks per week	912	11.9
8	Current heavier	12+ drinks in lifetime, and (male) >14 drinks per week in past year OR (female) >7 drinks per week in past yr.	384	5.0
4	Former unknown frequency	12+ drinks in lifetime, none in the past year, don't know if 12+ in any 1 yr.	1	.0
9	Current drinker, frequency/level unknown		15	.2
10	Drinking status Unknown		90	1.2
Total			7673	100.0

As seen in figure 20 and table 19, contrary to our hypothesis, even though a large percentage of arthritis population consumes alcohol, most of these patients are in the current light (22.6%) or current abstainer (19%) categories. This indicates decreased alcohol consumption in this population compared to the overall population.

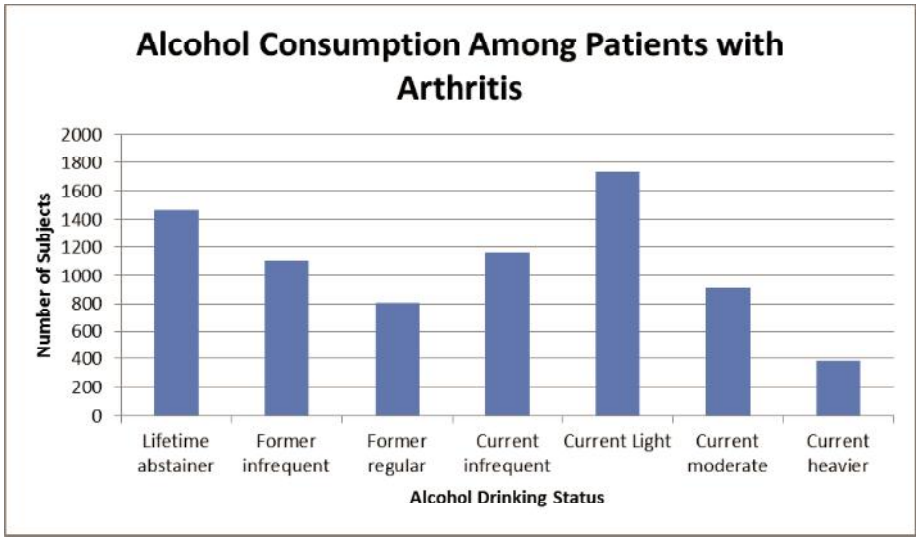


Figure 20 Distribution of alcohol consumption status of patients with arthritis.

As mentioned earlier arthritis can result in decreased mobility amongst the population and vice-versa, decreased mobility can also cause obesity which may cause arthritis. Similar to total population, we also investigated trends of physical activity performance in arthritis population. Understanding the physical activity in arthritis population may indicate and important behavioral factors due the effect it can have on clinical factors such as BMI. As seen in figure 21 and table 20, almost half of the arthritis patients (43.6%) are never involved in any type of light to moderate physical activity. This represents significant decreased compared to the overall population and may represent one of the devastating effects of arthritis. Decreased physical activity can result in increased obesity and may cause other comorbidities.

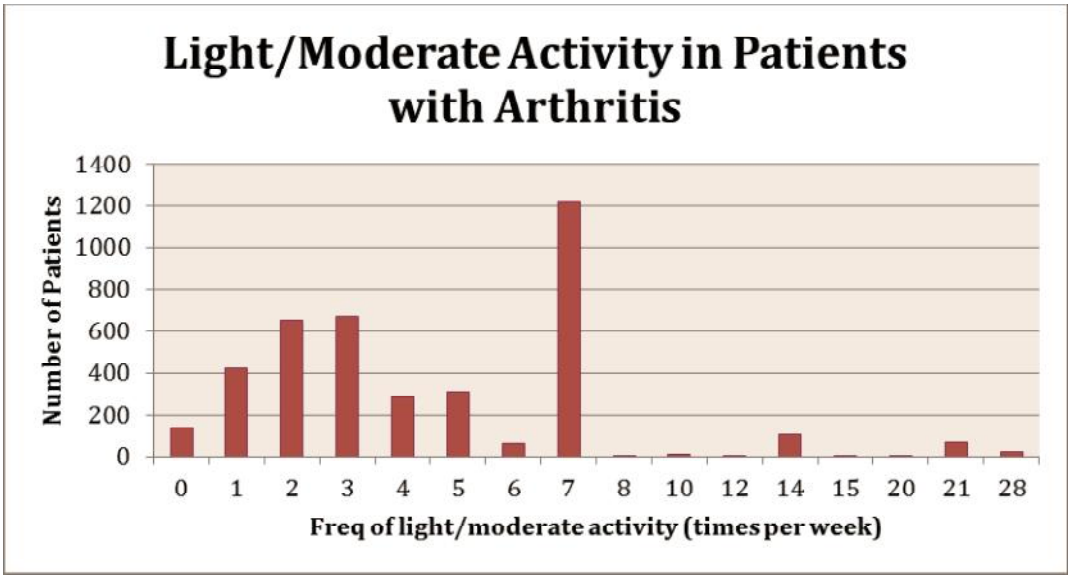


Figure 21 Distribution of frequency of light to moderate physical activity amongst patients with arthritis.

Table 20 Frequency of light to moderate activity (times/week) amongst patients with arthritis.

Frequency of Light/moderate activity (times/Week)	Number of Subjects	%		Frequency of Light/moderate activity (times/Week)	Number of Subjects	%
0	141	1.8		14	105	1.4
1	424	5.5		15	1	0
2	650	8.5		20	2	0
3	667	8.7		21	70	0.9
4	288	3.8		28	22	0.3
5	308	4		Never	3344	43.6
6	62	0.8		Unable to do activity	267	3.5
7	1218	15.9		Refused	2	0
8	2	0		Not ascertained	61	0.8
10	10	0.1		Don't Know	28	0.4
12	1	0		Total	7673	100

In addition to decreased number of patient with arthritis who performs regular light to moderate exercise, we also observed decreased trend of amount of physical activity performed in this group. Figure 22 shows that out of the patients who have arthritis and

perform light to moderate activity, the amount of time invested in such activity is less than 30 minutes. This may be due to the fatigue and pain associated with the prevalence of arthritis and needs to be investigated in detail.

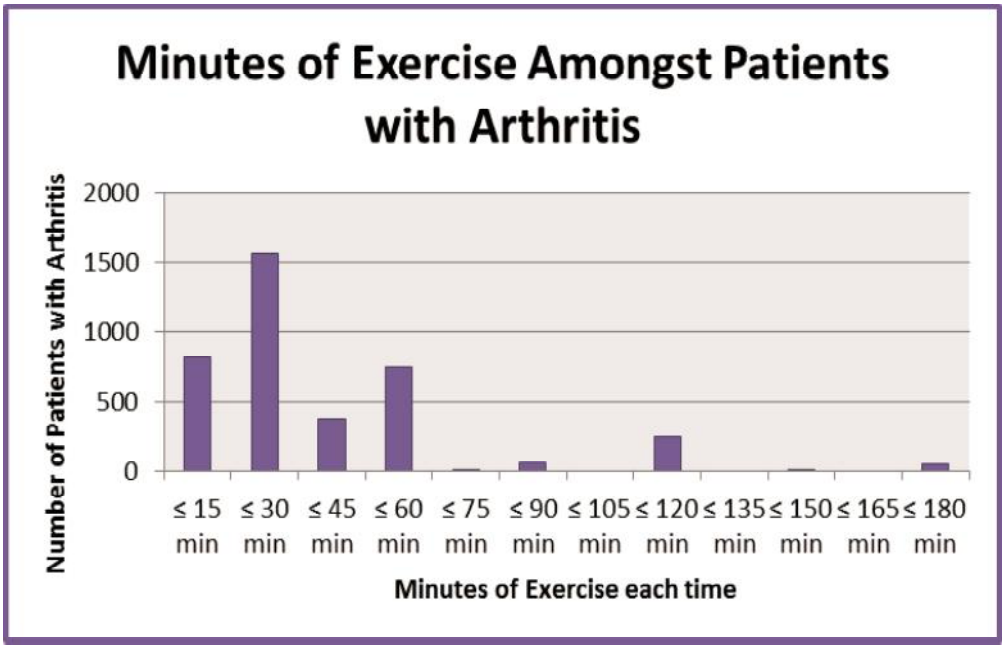


Figure 22 Distribution of minutes of exercise amongst patients with arthritis.

Table 21 Minutes of exercise per day amongst patients with arthritis

Minutes of Exercise per day	Number of subjects	%		Minutes of Exercise per day	Number of subjects	%
≤ 15 min	816	10.63		240 to 300	62	0.81
≤ 30 min	1556	20.28		300 to 360 min	7	0.09
≤ 45 min	374	4.87		360 to 420 min	3	0.04
≤ 60 min	745	9.71		420 to 480 min	8	0.10
≤ 75 min	11	0.14		480 to 540	0	0.00
≤ 90 min	61	0.79		540 to 600	0	0.00
≤ 105 min	0	0.00		600 to 660	1	0.01
≤ 120 min	243	3.17		660 to 720	0	0.00
≤ 135 min	0	0.00		Refused	0	0.00
≤ 150 min	2	0.03		Not ascertained	5	0.07
≤ 165 min	0	0.00		Don't know	25	0.33
≤ 180 min	52	0.68		Missing Information	3702	48.25
				Total	7673	100.00

4.2.3 Comparison between diabetic and non-diabetic patients with arthritis

In order to understand and identify factors that are significantly different amongst diabetic patients with arthritis, we separated the diabetic and non-diabetic groups amongst the patient population. Figure 23 presents the comparison of diabetic patients with arthritis and non-diabetic patients with arthritis.

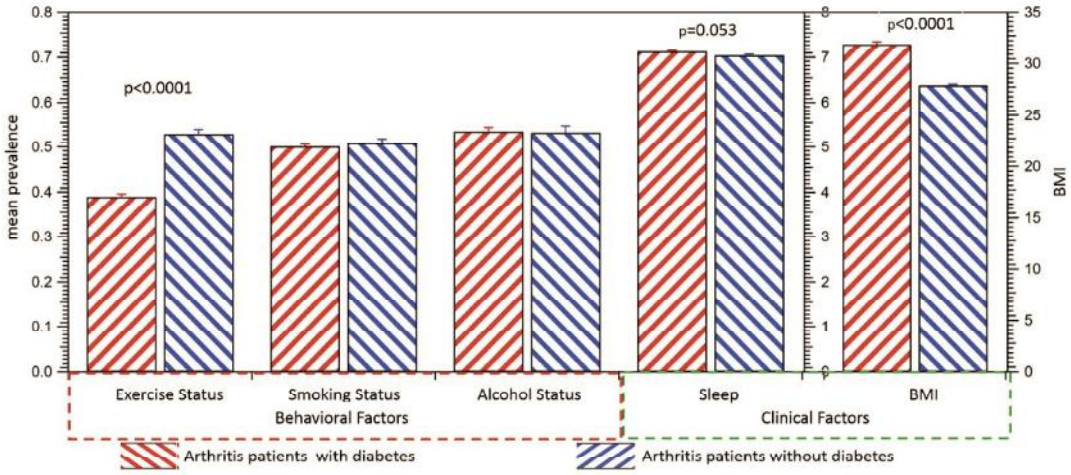


Figure 23: Prevalence of behavioral and clinical factors in arthritic patients with and without diabetes.

As shown in figure 23 the factor where mean prevalence significantly different is exercise status amongst diabetic and non-diabetic patients in arthritis. The second factor that also shows significant difference in the mean prevalence is the BMI where arthritis patients with diabetes have much higher BMI (32) compared to non-diabetic patients with BMI of 27.

In order to objectively compare the prevalence of this behavioral and clinical factors in arthritis patients, we need to compare this results with a control group. We first created an unbiased and age matched sample from the total population. We randomly

selected the same number of participants without arthritis from the same age range. All other variables were left uncontrolled to create a true random sample. Here in figure 24 we present the result from the comparison between this control group and the arthritis population. Figure 24 shows the mean prevalence of behavioral and clinical factors between the arthritis groups and the control group. This prevalence was compared using the chi-square test in SPSS and the p-values are displayed on top.

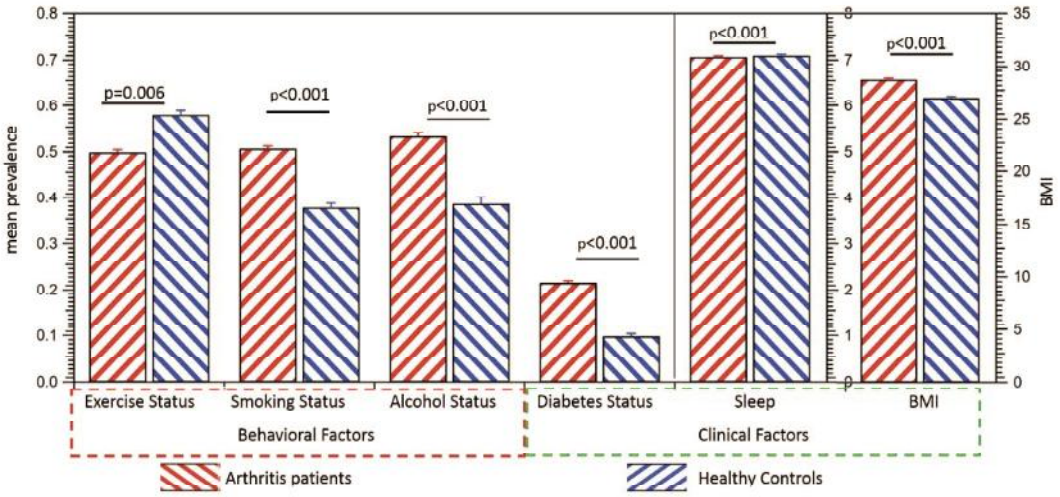


Figure 24 Prevalence of behavioral and clinical factors in arthritis and healthy control population

As shown in figure 24 the prevalence of exercise frequency is higher for control group compared to the patients with arthritis, however the prevalence of other four negative factors are higher in patients with arthritis. This indicates that the clinical factors higher BMI and diabetic status as well as the behavioral factors of smoking status and alcohol status have a negative effect on patients with arthritis. These results are further affirmed by performing a logistic regression and calculating odds ratio for the arthritis population.

4.2.4 Odds ratio for clinical and behavioral factors in diabetic and non-diabetic patients with arthritis

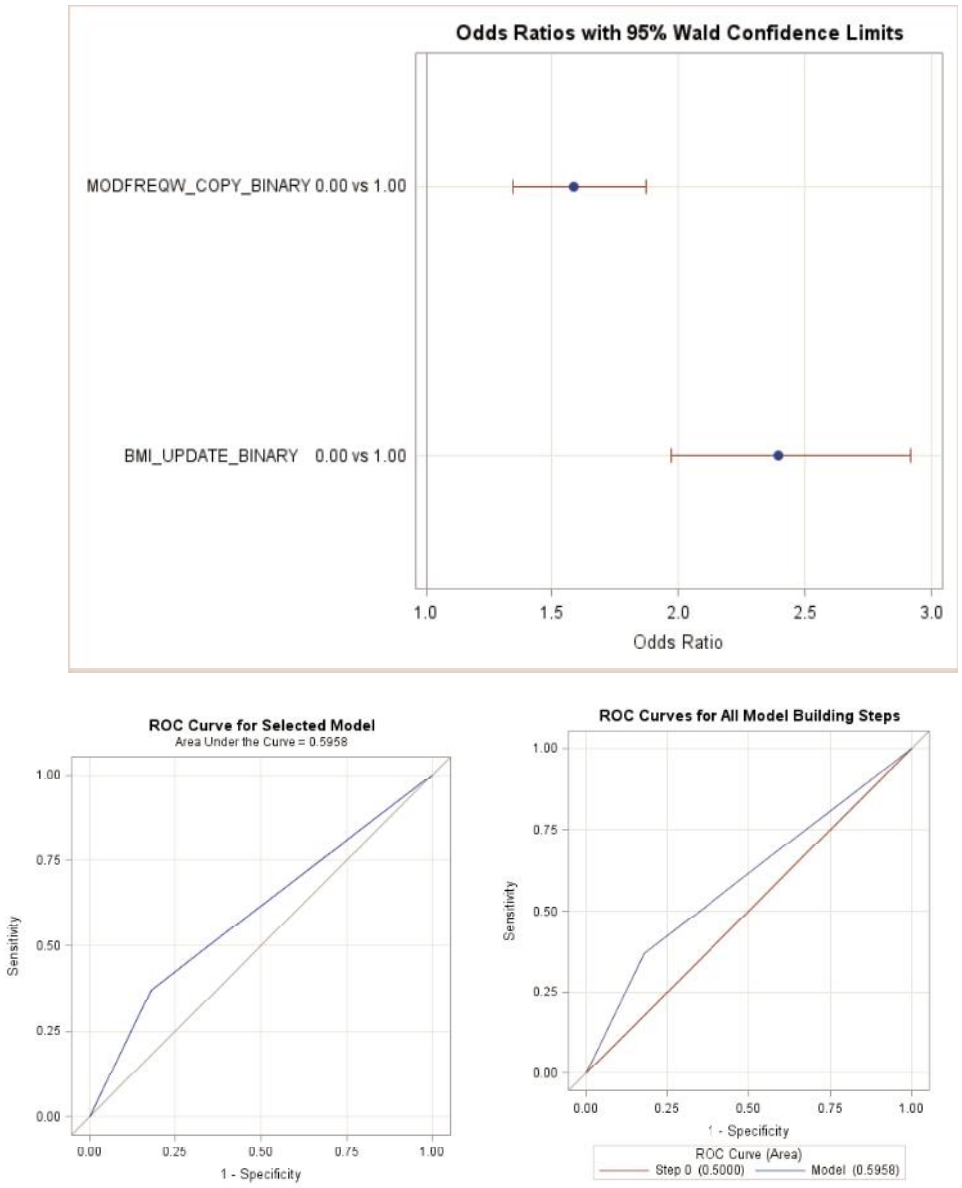


Figure 25 Logistic regression in diabetic patients with arthritis.

Table 22 Odds ratio and WALD confidence intervals for the behavioral and clinical factors on arthritis prevalence amongst diabetic patients

Effect	Unit	Estimate	95% Confidence Limits	
Exercise Status (MODFREQW_UPDATE_BINARY) (0.00 vs 1.00)	1.0000	1.587	1.346	1.871
BMI (BMI_UPDATE_BINARY) (0.00 vs 1.00)	1.0000	2.396	1.970	2.915

Figure 25 and table 22 indicate the risk of the prevalence of diabetes and arthritis with all of the clinical and behavioral factors. As indicated in figure 25 it is clear that the two major factors are BMI and exercise. Diabetic patients with higher BMI have a 2.4 folds higher risk of prevalence of arthritis. On the other hand, the beneficial effects of exercise are much higher and decreases the prevalence of arthritis in diabetic patients by1.6 folds.

Table 23 Odds ratio and WALD confidence intervals for the behavioral and clinical factors on arthritis prevalence

Odds Ratio Estimates and Wald Confidence Intervals				
Effect	Unit	Estimate	95% Confidence Limits	
Diabetes status (DIBEV_COPY) (0.00 vs 1.00)	1.0000	2.328	1.908	2.840
Alcohol consumption status (ALCLIFE_COPY) (0.00 vs 1.00)	1.0000	1.635	1.403	1.906
Smoking status (SMKEV_COPY) (0.00 vs 1.00)	1.0000	1.509	1.277	1.785
Exercise Status (MODFREQW_COPY_BINARY) (0.00 vs 1.00)	1.0000	1.419	1.228	1.640
Sleep Status (ASISLEEP_UPDATE_BINARY) (0.00 vs 1.00)	1.0000	1.317	1.129	1.535
BMI (BMI_UPDATE_BINARY) (0.00 vs 1.00)	1.0000	1.340	1.152	1.557

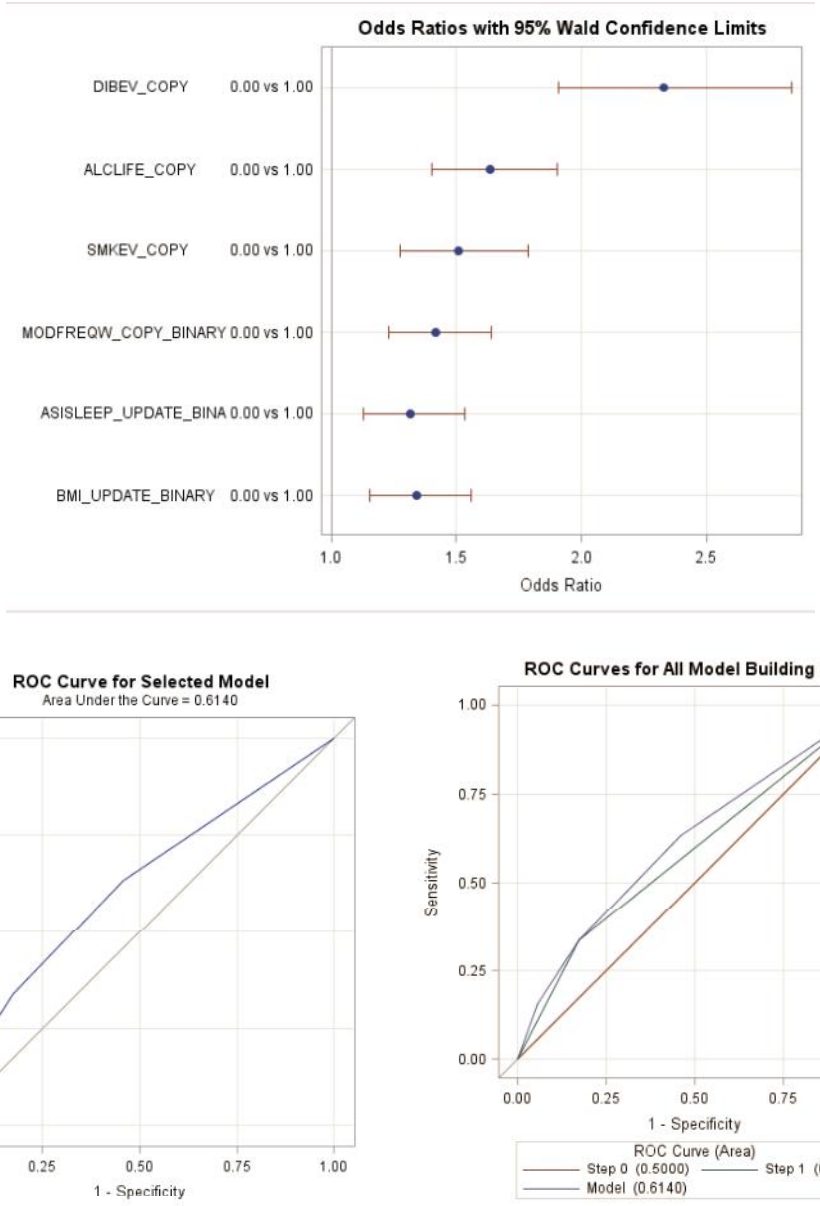


Figure 26: Logistic regression of clinical and behavioral factors in patients with arthritis

Figure 26 and table 23 represents the results of performing logistic regression between the arthritis status and the behavioral and clinical factors. We also show odds ratios of this factors on the prevalence of arthritis. As seen in figure 26 and table 23, the odds ratio is highest for diabetes followed by alcohol consumption and smoking status. In addition, the

odds ratios for diabetes status are 2.3 implying twice as much odds of having arthritis with presence of diabetes. On the contrary the BMI has odds ration very close to 1 however exercise status has odds ratios less than 1. This implies decreased odds of arthritis prevalence with increased exercise status.

4.3 Ulcerative colitis population

The other inflammatory disease investigated in this population is ulcerative colitis (ULC). Compared to the arthritis group we observed decreased prevalence of ulcerative colitis in the total population. A total of 2320 participants were identified having ulcerative colitis. Compared to the overall population this represented only a small fraction of individuals. Figure 27 represents the age distribution of the participants who responded yes to the question about ulcerative colitis.

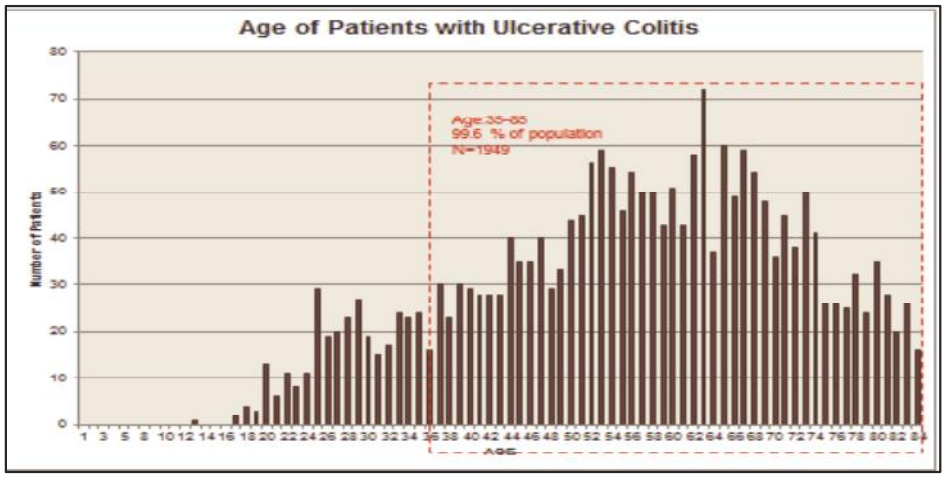


Figure 27 Age distributions of patients with ulcerative colitis

As seen in the figure 27, the highest numbers of patients with ulcerative colitis are at the age of 63 years though the differences in the number of patients at various age ranges are very minimal. Additionally, as shown in figure 27 there also exist group of patients

with age as little as 12 years with positive diagnosis of ulcerative colitis. In order to create an adult only sample of patients with ulcerative colitis and to make it comparable with the arthritis population, we only selected the patients between the age of 35 and 85 years.

Table 24 Frequency of age amongst patients with ulcerative colitis

Age	Number of Patients with ULC		Age	Number of Patients with ULC		Age	Number of Patients with ULC		Age	Number of Patients with ULC
1	0		24	11		46	35		67	59
2	0		25	29		47	40		68	54
3	0		26	19		48	29		69	48
4	0		27	20		49	33		70	36
5	0		28	23		50	44		71	45
6	0		29	27		51	45		72	38
8	0		30	19		52	56		73	50
9	0		31	15		53	59		74	41
10	0		32	17		54	55		75	26
11	0		33	24		55	46		76	26
12	0		34	23		56	54		77	25
13	1		35	24		57	50		78	32
14	0		36	16		58	50		79	24
15	0		37	30		59	43		80	35
16	0		38	23		60	51		81	28
17	2		39	30		61	43		82	20
18	4		40	29		62	58		83	26
19	3		41	28		63	72		84	16
20	13		42	28		64	37		85	96
21	6		43	28		65	60		Total	2320
22	11		44	40		66	49			
23	8		45	35						

A total of 1949 patients passed the criteria for the age range of 35 -85 years and were further included in the analysis. Out of 1949 subjects with ulcerative colitis, there are 920 male subjects and 1029 female subjects. This indicates higher prevalence of ulcerative colitis in female population compared to male population. This is also consistent with the

results of arthritis population, which had higher prevalence rates in female compared to male population.

4.3.1 Distribution of clinical factors in ulcerative colitis patients

After identifying the ulcerative colitis patients between the ages of 35- 85 years, we investigated the prevalence of various clinical and behavioral factors in the ulcerative colitis population. The first clinical factor investigated in the current population is BMI.

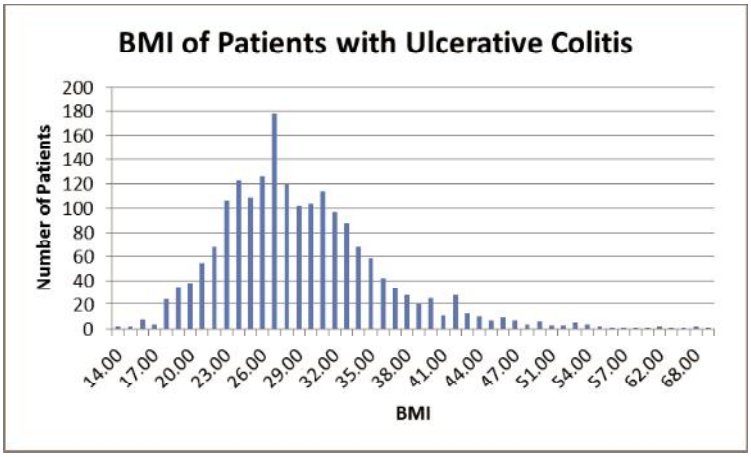


Figure 28 Distribution of frequency of patients with ulcerative colitis and their BMI.

Figure 28 and table 25 represents the distribution of BMI for patients with ulcerative colitis. As shown in figure 26 there is a normal distribution in the BMI of the patients with ulcerative colitis, with the peak observed at BMI of 27. The BMI of 27 also indicates overweight subjects as per the BMI standards. Similar to arthritis group and overall population, this implies a trend towards obesity. Considering the population investigated in current study is adult population in US, these growing trends of obesity needs to be understood and investigated in detail, specifically in context of inflammatory disease population.

Table 25 Frequency of number of patients with ulcerative colitis and their BMI.

BMI	Frequency	%		BMI	Frequency	%		BMI	Frequency	%
0.00	54	2.8		31.00	114	5.8		50.00	6	.3
14.00	2	.1		32.00	97	5.0		51.00	3	.2
15.00	2	.1		33.00	88	4.5		52.00	3	.2
16.00	8	.4		34.00	67	3.4		53.00	5	.3
17.00	4	.2		35.00	58	3.0		54.00	4	.2
18.00	24	1.2		36.00	42	2.2		55.00	2	.1
19.00	35	1.8		37.00	34	1.7		56.00	1	.1
20.00	38	1.9		38.00	27	1.4		57.00	1	.1
21.00	54	2.8		39.00	21	1.1		58.00	1	.1
22.00	67	3.4		40.00	25	1.3		61.00	1	.1
23.00	106	5.4		41.00	11	.6		62.00	2	.1
24.00	123	6.3		42.00	27	1.4		65.00	1	.1
25.00	108	5.5		43.00	13	.7		66.00	1	.1
26.00	126	6.5		44.00	10	.5		68.00	2	.1
27.00	178	9.1		45.00	7	.4		89.00	1	.1
28.00	120	6.2		46.00	9	.5		Total	1949	100
29.00	102	5.2		47.00	7	.4				
30.00	103	5.3		48.00	4	.2				

With increased BMI and the ulcerative colitis patients showing a trend towards obesity, diabetes status is another important clinical factors investigated in the current population. While investigating the prevalence of diabetes in this population, we observed a significantly low prevalence of diabetes in ulcerative colitis patients compared to arthritis patients and total population. Amongst the patients with ulcerative colitis only 384 patients had diabetes and 1565 patients did not have diabetes. This indicates that there may not be a large association between patients who have ulcerative colitis and their diabetes status. In order to further identify the factors associated with the diabetes condition, we investigated age first diagnosed with diabetes in the patient with ulcerative colitis. Figure 29 and table 26 shows distribution of age first diagnosed with diabetes in ulcerative colitis patients. As it is evident from the figure, a large number of participants had the diagnosis of diabetes at the age of 50 years. This indicates a rather late detection of diabetes

compared to total population as well as arthritis population. Additionally, similar to the arthritis group and total population, we also observed peak at the ages of 35, 40, 45, 50 and 55 years, implying a similar pattern of age when first diagnosed with diabetes across both the inflammatory diseases as well as in total population. However, in most cases, type-2 diabetes has been associated with fat inducing diet and due to the nature of the ulcerative colitis may not have significant prevalence in this population.

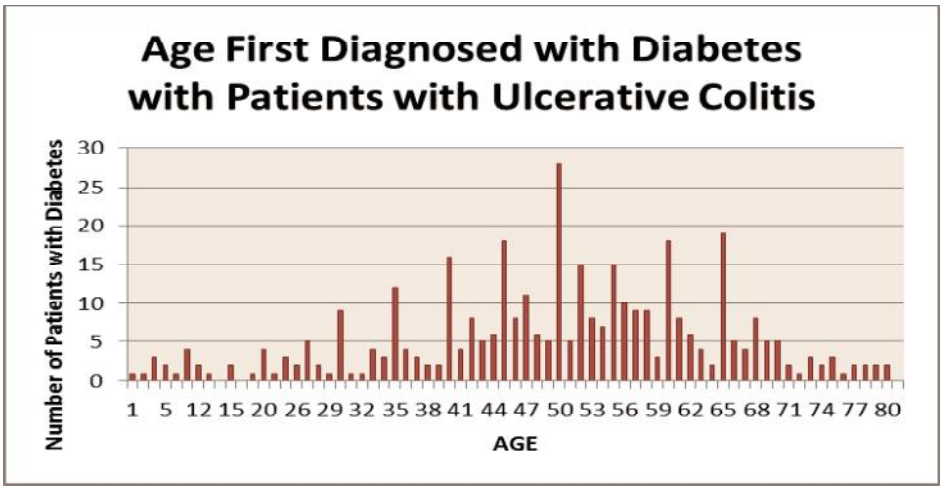


Figure 29 Distribution of number of patients with ulcerative colitis and the age when they were first diagnosed with diabetes.

One of the last factors investigated in this inflammatory disease population is the sleeping pattern in patients with ulcerative colitis. Similar to the arthritis population, we investigated hours of sleep amongst ulcerative colitis patients within a 24 hours period. As sleep has known to be associated with healthy human body function and may also be associated with digestion, understanding this clinical factor can help improve the quality of life in ulcerative colitis population. Figure 30 and table 27 represents the distribution of number of hours of sleep in ulcerative colitis patients.

Table 26 Number of patients with ulcerative colitis and the age they were first diagnosed with diabetes.

Age First Diagnosed with Diabetes	Number of Subjects	%		Age First Diagnosed with Diabetes	Number of Subjects	%		Age First Diagnosed with Diabetes	Number of Subjects	%
1	1	0.05		36	4	0.21		61	8	0.41
3	1	0.05		37	3	0.15		62	6	0.31
4	3	0.15		38	2	0.10		63	4	0.21
5	2	0.10		39	2	0.10		64	2	0.10
7	1	0.05		40	16	0.82		65	19	0.97
10	4	0.21		41	4	0.21		66	5	0.26
12	2	0.10		42	8	0.41		67	4	0.21
13	1	0.05		43	5	0.26		68	8	0.41
14	0	0.00		44	6	0.31		69	5	0.26
15	2	0.10		45	18	0.92		70	5	0.26
17	0	0.00		46	8	0.41		71	2	0.10
18	1	0.05		47	11	0.56		72	1	0.05
20	4	0.21		48	6	0.31		73	3	0.15
22	1	0.05		49	5	0.26		74	2	0.10
25	3	0.15		50	28	1.44		75	3	0.15
26	2	0.10		51	5	0.26		76	1	0.05
27	5	0.26		52	15	0.77		77	2	0.10
28	2	0.10		53	8	0.41		78	2	0.10
29	1	0.05		54	7	0.36		79	2	0.10
30	9	0.46		55	15	0.77		80	2	0.10
31	1	0.05		56	10	0.51		81	0	0.00
32	1	0.05		57	9	0.46		85	2	0.10
33	4	0.21		58	9	0.46		97	1	0.05
34	3	0.15		59	3	0.15		99	4	0.21
35	12	0.62		60	18	0.92		Missing	1565	80.3
								Total	1949	100

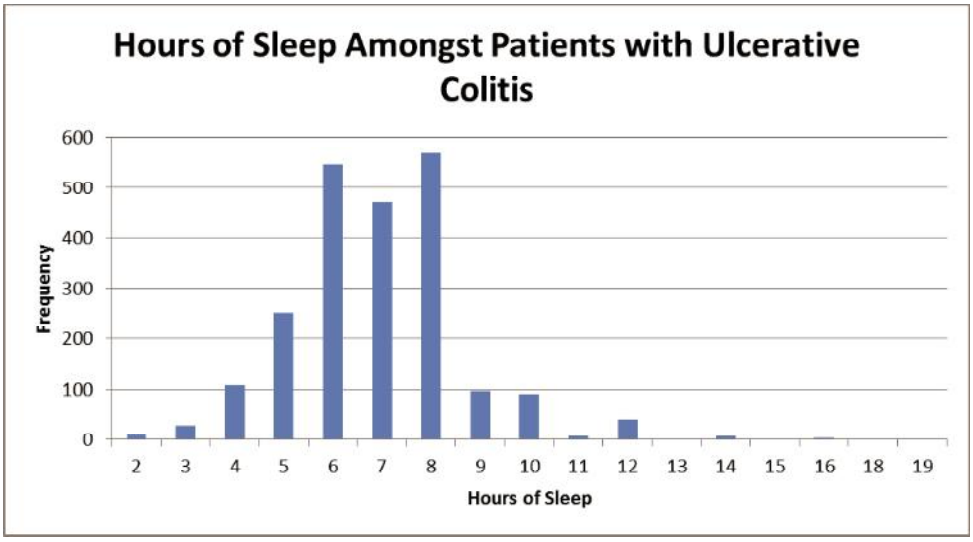


Figure 30 Distribution of hours of sleep amongst patients with ulcerative colitis.

Table 27 Frequency of hours of sleep amongst patients with ulcerative colitis.

Hours of Sleep	Number of Subjects	%		Hours of Sleep	Number of Subjects	%		Hours of Sleep	Number of Subjects	%
2	9	.5		9	85	4.4		18	1	.1
3	25	1.3		10	79	4.1		19	1	
4	102	5.2		11	7	.4		Refused	1	.1
5	210	10.8		12	33	1.7		Not Ascertained	43	2.2
6	450	23.1		14	8	.4		Don't know	17	.9
7	403	20.7		15	2	.1		Total	1949	100.0
8	471	24.2		16	2	.1				

We observed trends of decreased sleep in ulcerative colitis patients compared to arthritis patients and total population. As evident from Figure 30 and table 27, the highest number of ulcerative colitis sleep 8 hours for a 24 hours period, however we observed increased in number of participants who sleep 6 hours in this group. There are approximately 23% of the ulcerative colitis patients who sleep 6 hours a day. Decreased sleep has been associated with increase in hormonal imbalance, which may have important

implications in ulcerative colitis patients. We further compared the number of sleeping hours between these populations, which are presented in further section.

4.3.2 Distribution of behavioral factors in ulcerative colitis patients

In addition to the clinical factors such as BMI, diabetes status and sleeping patterns that may have implications in the prevalence of ulcerative colitis, we also investigated other behavioral factors and their prevalence in ulcerative colitis patients. These factors are alcohol consumption, smoking status and their physical activity.

Amongst the factors investigated smoking status is one of the first and important factors regarding prevalence of ulcerative colitis. Amongst the patients with ulcerative colitis (1949), the patient group is broken down in to two distinct groups based on the question regarding the smoking status. A total of 1100 patients who smoke and 846 patients who do not smoke. This implies higher number ulcerative colitis patients who smoke compared to the patients who do not smoke. There are many causes of ulcerative colitis and smoking may also play as one of the factors.

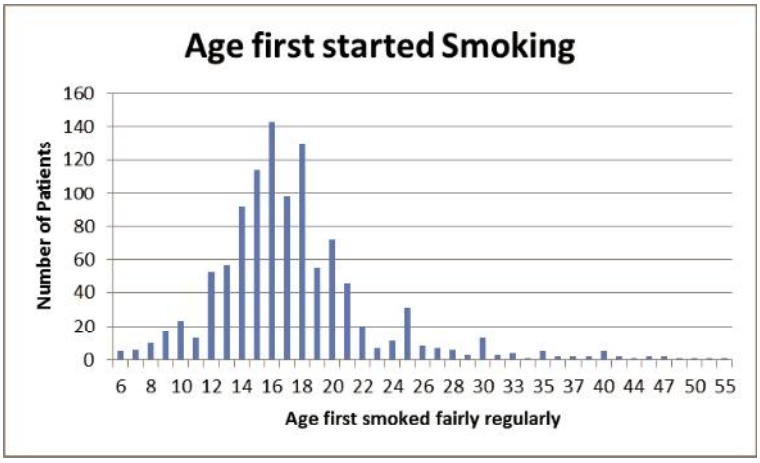


Figure 31 Distribution of number of patients with ulcerative colitis and the age they started smoking.

Table 28 Frequency of number of patients and the age they first started smoking.

Age First Smoked	Number of Patients	%		Age First Smoked	Number of Patients	%		Age First Smoked	Number of Patients	%
6	5	.3		21	46	2.4		37	2	.1
7	6	.3		22	20	1.0		38	2	.1
8	10	.5		23	7	.4		40	5	.3
9	17	.9		24	11	.6		42	2	.1
10	23	1.2		25	31	1.6		44	1	.1
11	13	.7		26	8	.4		45	2	.1
12	53	2.7		27	7	.4		47	2	.1
13	57	2.9		28	6	.3		48	1	.1
14	92	4.7		29	3	.2		50	1	.1
15	114	5.8		30	13	.7		52	1	.1
16	143	7.3		32	3	.2		55	1	.1
17	98	5.0		33	4	.2		Never smoked regularly	10	.5
18	130	6.7		34	1	.1		Don't know	15	.8
19	55	2.8		35	5	.3		Missing	849	43.6
20	72	3.7		36	2	.1		Total	1949	100.0

In addition to the overall smoking status, we also studied various characteristics for smoking. These were age first started smoking, number of years smoked and the number of cigarettes smoked regularly. As shown in figure 31, there is a normal distribution amongst patients with ulcerative colitis and the age that they started smoking. Figure 31 and corresponding table 28 displays an important trend observed in this patient population, regarding age first started smoking. As seen, the peak of the distribution is observed at the age of 16 years, which implies that significant number of patients with ulcerative colitis start smoking at a very early age, almost 2 years before the legal age of purchasing the cigarettes. This is significantly earlier than overall population as well as arthritis group, where large majority of the participants started smoking at the age of 18 years.

Table 29 Number of years smoked amongst patients with ulcerative colitis.

Number of Years Smoked	Number of Subjects	%		Number of Years Smoked	Number of Subjects	%		Number of Years Smoked	Number of Subjects	%
3	1	0.05		29	20	1.03		53	23	1.18
4	1	0.05		30	14	0.72		54	25	1.28
5	0	0.00		31	19	0.97		55	28	1.44
6	4	0.21		32	21	1.08		56	22	1.13
7	1	0.05		33	26	1.33		57	23	1.18
10	0	0.00		34	22	1.13		58	19	0.97
11	2	0.10		35	13	0.67		59	15	0.77
12	1	0.05		36	14	0.72		60	19	0.97
13	2	0.10		37	31	1.59		61	16	0.82
14	1	0.05		38	30	1.54		62	12	0.62
15	3	0.15		39	33	1.69		63	18	0.92
16	5	0.26		40	30	1.54		64	11	0.56
17	7	0.36		41	30	1.54		65	10	0.51
18	11	0.56		42	38	1.95		66	8	0.41
19	9	0.46		43	28	1.44		67	10	0.51
20	11	0.56		44	39	2.00		68	5	0.26
21	9	0.46		45	25	1.28		69	5	0.26
22	15	0.77		46	28	1.44		70	2	0.10
23	13	0.67		47	31	1.59		71	2	0.10
24	12	0.62		48	29	1.49		72	3	0.15
25	14	0.72		49	20	1.03		73	2	0.10
26	22	1.13		50	27	1.39		78	1	0.05
27	20	1.03		51	29	1.49		Missing	875	44.8
28	18	0.92		52	16	0.82		Total	1949	100

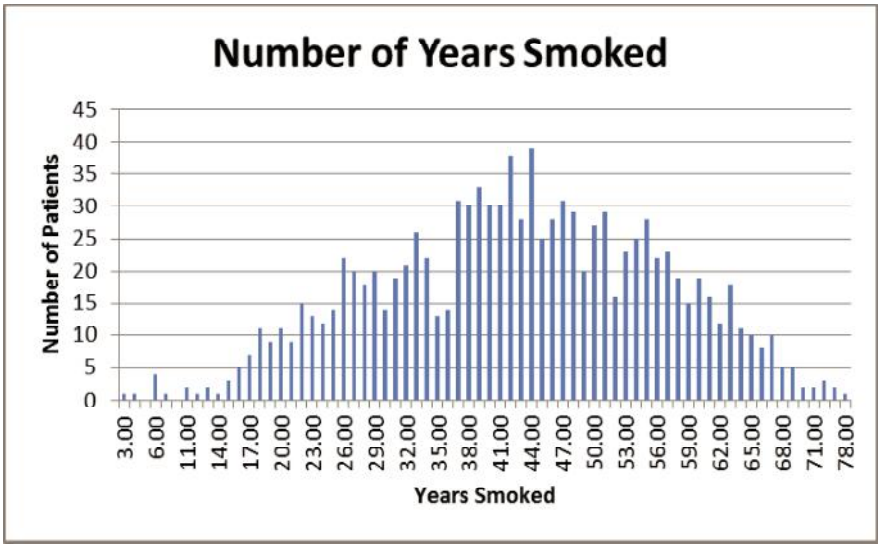


Figure 32 Distribution of number of years smoking amongst patients with ulcerative colitis.

Similar to the age first started smoking, the number of years smoked in patient with ulcerative colitis was higher than the overall population and arthritis group. As these participants started smoking at an early age, number of years these patients have smoked is between 40-60 years. As shown in figure 32, number of years patients have smoked varies between 3 to 78 years however the peak is observed at the age of 40. The number of years patients smoke may pay a huge role in patients with ulcerative colitis and when they were diagnosed with this specific inflammatory disease. This results in combination with previous results imply that the patients with ulcerative colitis start smoking at an early age and also smoke for a longer duration of time.

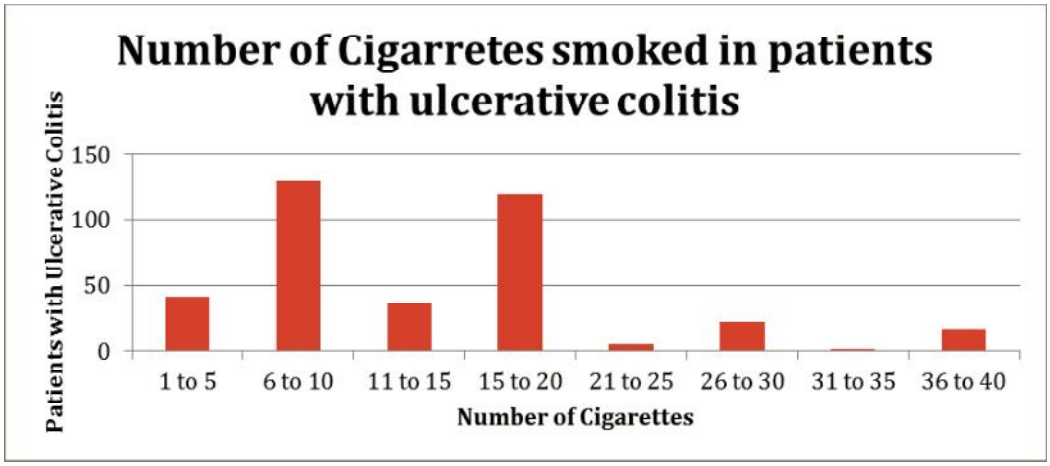


Figure 33 Distribution of number of cigarettes smoked in patients with ulcerative colitis.

Table 30 Number of cigarettes smoked amongst the ulcerative colitis patient population.

Number of Cigarettes	Number of Subjects	%		Number of Cigarettes	Number of Subjects	%
1 to 5	41	2.10		36 to 40	17	0.87
6 to 10	129	6.62		40 to 50	1	0.05
11 to 15	36	1.85		Refused	2	0.10
15 to 20	120	6.16		Not Ascertained	0	0.00
21 to 25	5	0.26		Don't know	3	0.15
26 to 30	22	1.13		Missing	1571	80.61
31 to 35	2	0.10		Total	1949	100

As shown in figure 33, a large number of patients smoke about 10 cigarettes (half a pack) a day and the second highest numbers of population smoke about 20 cigarettes a day (one entire pack). In addition to the number of years these subjects smoke, how much they smoke is also a huge factor amongst patients with ulcerative colitis and may have significant effect on the prevalence of ulcerative colitis.

In addition to smoking being a factor in patients with ulcerative colitis, alcohol consumption and how much they drink can also play crucial role in the prevalence of

ulcerative colitis. We observed significant prevalence of alcohol consumption amongst patients with ulcerative colitis. Out of 1949 patients with ulcerative colitis 1152 responded yes to the questions related alcohol consumption and 788 responded no. Similar to smoking, this shows significant increase in the number of patients who consume alcohol. Figure 34 and table 31 describes the frequency of alcohol consumption in this ulcerative colitis patients.

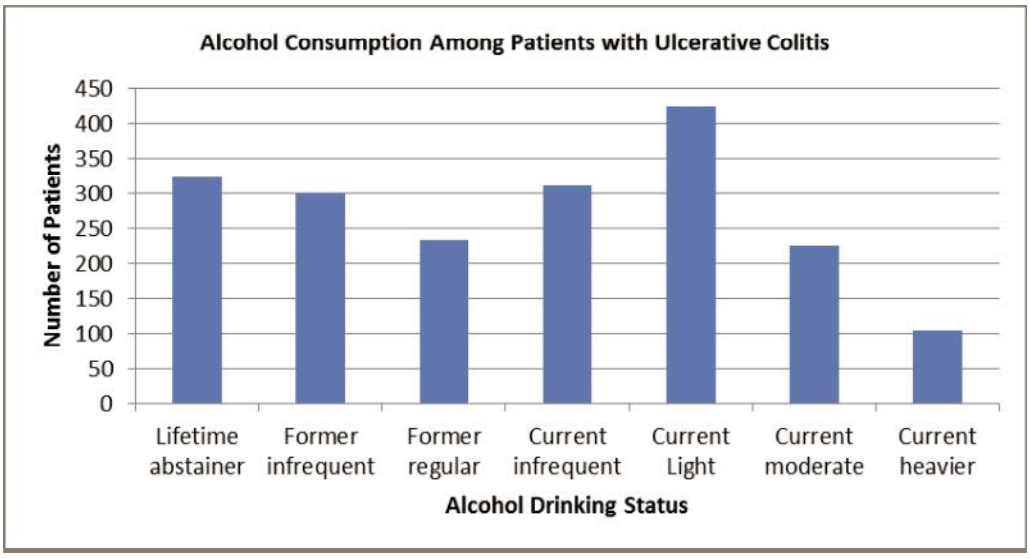


Figure 34 Distribution of drinking frequency amongst patients with ulcerative colitis.

Table 31 Alcohol consumption status in patients with ulcerative colitis.

	Alcohol drinking status	Description	Number of Subjects	Percentage
1	Lifetime abstainer	<12 drinks in lifetime	323	16.6
2	Former infrequent	12+ drinks in lifetime but never as many as 12 in 1 yr and none in past yr.	300	15.4
3	Former regular	12+ drinks in lifetime, 12+ drinks in 1 yr, but none in past yr	233	12.0
5	Current infrequent	12+ drinks in lifetime, 1-11 drinks in past year	311	16.0
6	Current Light	12+ drinks in lifetime, and ≤ 3 drinks per week in past yr	424	21.8
7	Current moderate	12+ drinks in lifetime, and (male)> 3 drinks per week up to 14 drinks per week OR (female)>3 drinks per week up to 7 drinks per week	225	11.5
8	Current heavier	12+ drinks in lifetime, and (male) >14 drinks per week in past year OR (female) >7 drinks per week in past yr.	104	5.3
4	Former unknown frequency	12+ drinks in lifetime, none in the past year, don't know if 12+ in any 1 yr.	1	.1
9	Current drinker, frequency/level unknown		11	.6
10	Drinking status unknown		17	.9
Total			1949	100.0

As seen in figure 34 and table 31, the highest numbers of patients in the group of ulcerative colitis patients are current light drinkers. These results imply that even though

higher percentages of patients with ulcerative colitis consume alcohol, these patients are not heavy drinkers currently.

One of the behavioral factors which may have positive effect on the prevalence of ulcerative colitis is the physical activity performed by these patients**.** Physical activity and energy expenditure, outside of their daily work is shown to be correlated with the BMI of the patients and their diabetes status. We investigated frequency and time-duration of light to moderate activity in ulcerative colitis patients to understand its effects on prevalence of the disease.

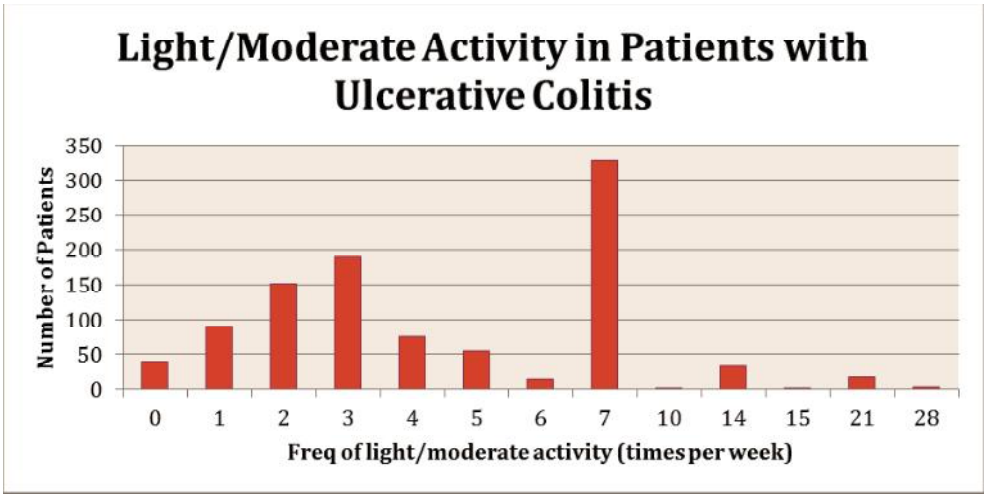


Figure 35 Distribution of light to moderate physical activity in patients with ulcerative colitis.

Table 32 Light to moderate physical activity amongst patients with ulcerative colitis.

Frequency of Light/moderate activity (times/Week)	Number of Subjects	%		Frequency of Light/moderate activity (times/Week)	Number of Subjects	%
0	39	2		14	33	1.7
1	91	4.7		15	1	0.1
2	152	7.8		21	17	0.9
3	189	9.7		28	4	0.2
4	76	3.9		Never	876	44.9
5	55	2.8		Unable to do activity	60	3.1
6	14	0.7		Refused	0	0
7	328	16.8		Not ascertained	7	0.4
10	1	0.1		Don't Know	6	0.3
				Total	1949	100

Out of the total population of 1949 ulcerative colitis patients, only 1000 patients were involved in regular physical activity while 876 patients were never involved in any physical activity. The physical activity of the patients with ulcerative colitis is further broken down to understand how frequently the subjects perfume light to moderate activity per week in figure 35 and table 32. Figure 35 shows that majority of the patients exercise 1-7 times in a week and the highest number of subjects exercises 7 times a week, which indicates that these subjects exercise almost every day of the week. In this groups of patients, we also observed that approximately 20% of the patients who perform this regular physical activity, are involved in this activity for the duration of 30 minutes or less (figure 35 and table 32).

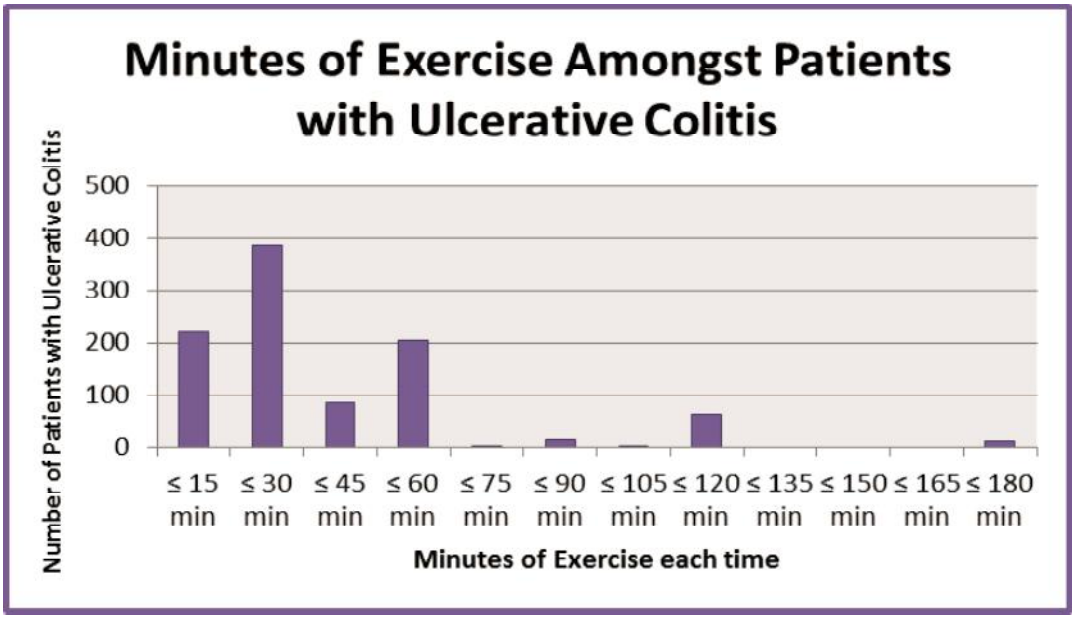


Figure 36 Distribution of minutes of exercise amongst patients with ulcerative colitis.

Table 33 Minutes of exercise amongst patients with ulcerative colitis.

Minutes of Exercise per Day	Number of subjects	%		Minutes of Exercise per Day	Number of subjects	%
≤ 15 min	221	11.34		240 to 300 min	7	0.36
≤ 30 min	388	19.91		300 to 360 min	1	0.05
≤ 45 min	86	4.41		360 to 420 min	0	0.00
≤ 60 min	204	10.47		420 to 480 min	0	0.00
≤ 75 min	2	0.10		480 to 540 min	0	0.00
≤ 90 min	14	0.72		540 to 600 min	1	0.05
≤ 105 min	1	0.05		600 to 660 min	0	0.00
≤ 120 min	63	3.23		660 to 720 min	0	0.00
≤ 135 min	0	0.00		Refused	0	0.00
≤ 150 min	0	0.00		Not ascertained	0	0.00
≤ 165 min	0	0.00		Don't know	1	0.05
≤ 180 min	11	0.56		Missing Information	949	48.69
				Total	1949	100

This results in conjunction with the results obtained in figure 36 imply that a large number of ulcerative colitis patients perform light to moderate activity 7 days a week and the duration of this activity is 30 min for each of the time.

4.3.3 Group comparison between diabetic and non-diabetic patients with ulcerative colitis

Chi-square test and t-test is performed to analyze the difference between ulcerative colitis patients with and without diabetes. Figure 35 indicates that BMI and exercise status are two of the factors with high significant difference amongst the diabetic and non-diabetic group.

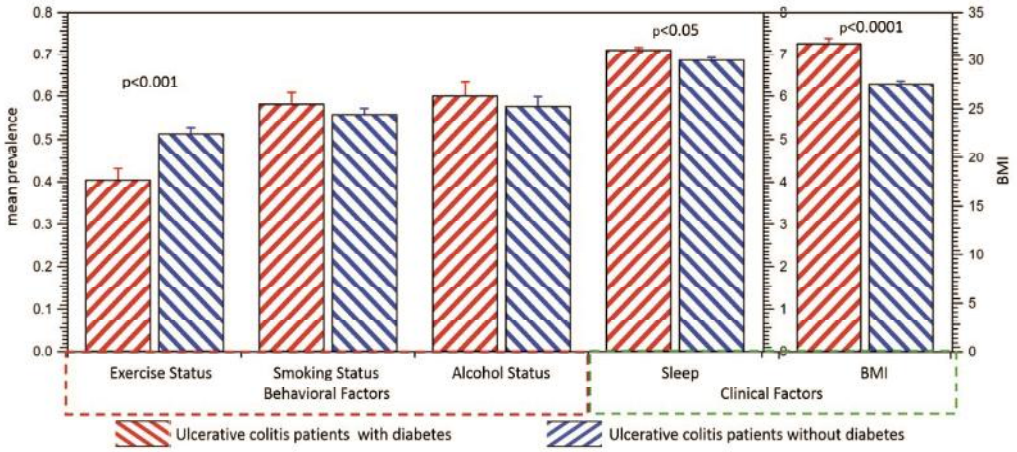


Figure 37 Mean prevalence of behavioral and clinical factors in ulcerative colitis patients with and without diabetes.

As indicated in figure 37, diabetic patients with ulcerative colitis have a significantly higher BMI of 33 compared to the non-diabetic patients with a BMI of 27.5. Similarly, we also observed that significantly higher number of ulcerative colitis patients without diabetes exercised compared to patients with diabetes. Opposite trend were observed in sleep patterns were ulcerative colitis patients with diabetes slept an average of 7 hours compared to ulcerative colitis patients without diabetes who slept for 6.5 hours.

We further compared the prevalence of this behavioral and clinical factors between the patients with ulcerative colitis and the control population. Participants in control group were derived using a similar method as implemented in arthritis groups.

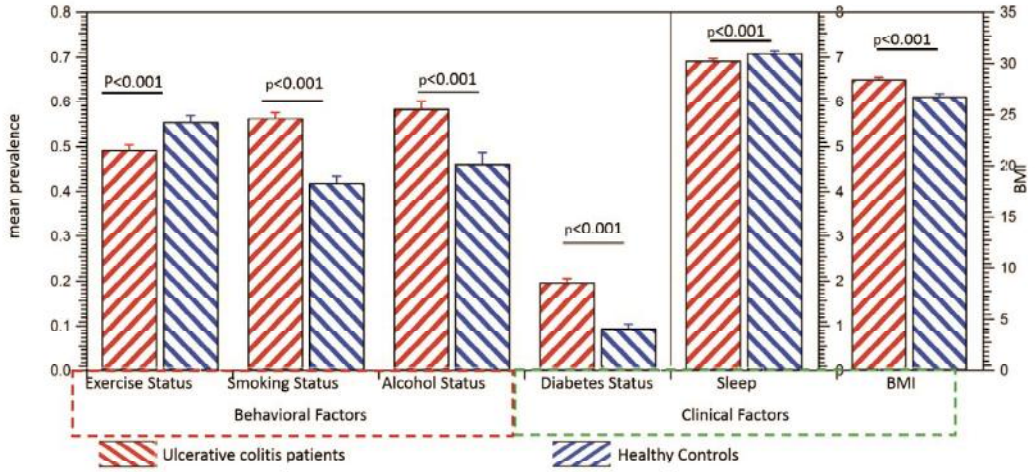
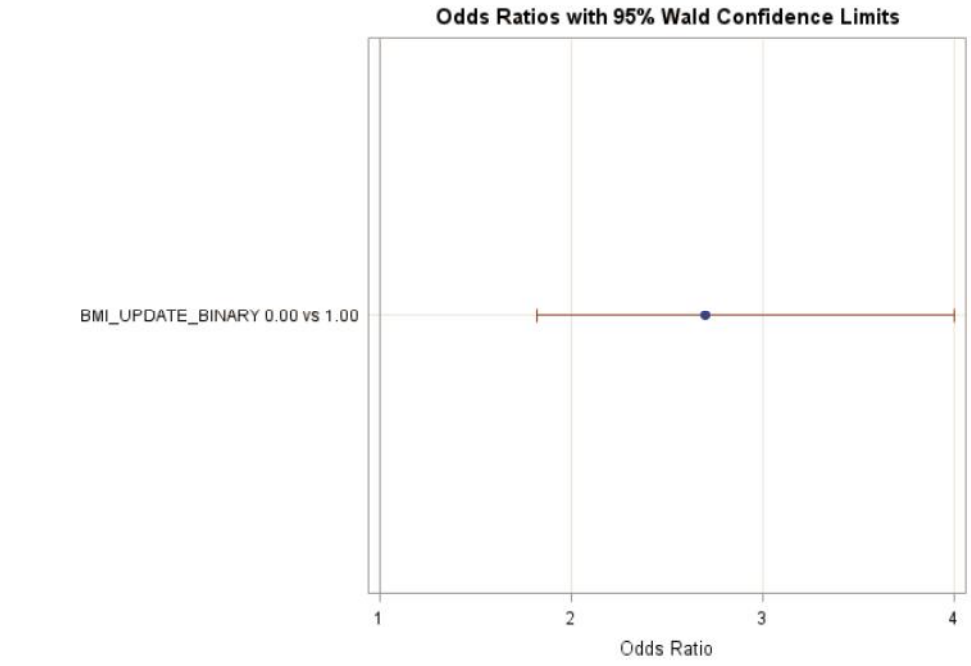


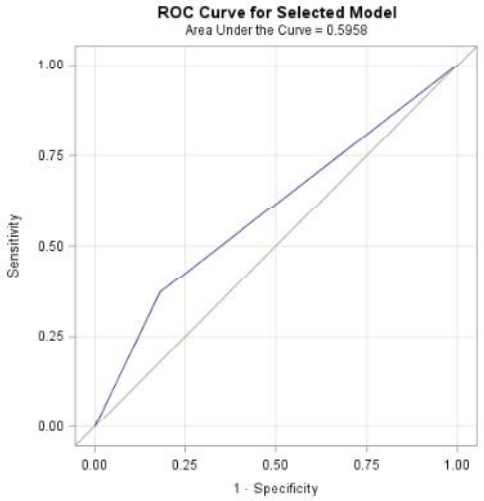
Figure 38 Mean prevalence of behavioral and clinical factors in ulcerative colitis patients and control group.

As also evident from figure 38, we observed significantly high prevalence of smoking, diabetes status, obesity and alcohol consumption in ulcerative colitis group compared to the control groups. This implies increased association between this negative factors and prevalence of ulcerative colitis. On the contrary, only exercise status had higher prevalence in control group compared to ulcerative colitis group implying that healthy population exercised more frequently compared to the patient population. As regular exercise has been associated with over all healthy living condition, this results may imply decreased in prevalence of ulcerative colitis associated with regular physical exercise.

4.3.4 Odds ratio for clinical and behavioral factors in diabetic and non-diabetic patients with ulcerative colitis

Logistic regression is performed to assess the risk of factor of ulcerative colitis and diabetes combined with each of the behavioral and clinical factors.





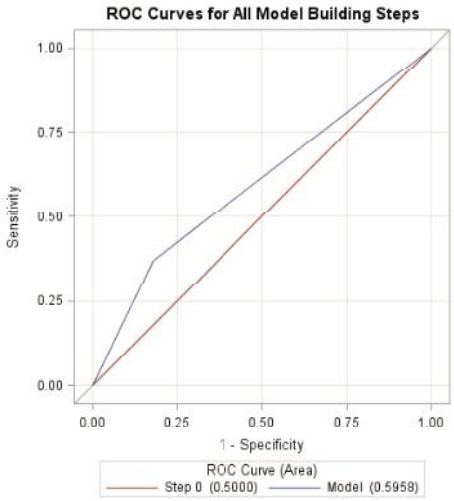


Figure 39 Logistic regression of clinical and behavioral factors in diabetic patients with ulcerative colitis

Table 34 Odds ratio estimates and Wald confidence Interval for ulcerative colitis patients with diabetes.

Effect	Unit	Estimate	95% Confidence Limits	
BMI (BMI_UPDATE_BINARY) (0.00 vs 1.00)	1.0000	2.697	1.819	4.000

As shown in figure 39 and table 34 it is clear that there is only one factor that plays a s major risk factors on prevalence of diabetes and ulcerative colitis. This indicates that BMI is the only risk factor, which increases the risk of having ulcerative colitis in diabetic population by 2.7 folds if the patient has high BMI.

Table 35 Odds Ratio Estimates and Wald Confidence Intervals for ulcerative colitis patients.

Effect	Unit	Estimate	95% Confidence Limits	
Diabetes status (DIBEV_COPY) (0.00 vs 1.00)	1.0000	2.397	1.719	3.341
Alcohol consumption status (ALCLIFE_COPY) (0.00 vs 1.00)	1.0000	1.327	1.025	1.717
Smoking status (SMKEV_COPY) (0.00 vs 1.00)	1.0000	1.620	1.235	2.126
Sleep status (ASISLEEP_UPDATE_BINARY) (0.00 vs 1.00)	1.0000	1.681	1.299	2.175

In order to further characterize the odds ratio between this behavioral and clinical factors and the prevalence of ulcerative colitis, we calculated the logistic regression on this population by using ulcerative colitis as dependent variable and the other behavioral and clinical factors as independent variables. Table 35 and Figure 40 represents the results of this logistic regression. As seen in table 35 and Figure 40, the diabetes status had the highest odds ratios for prevalence of ulcerative colitis.

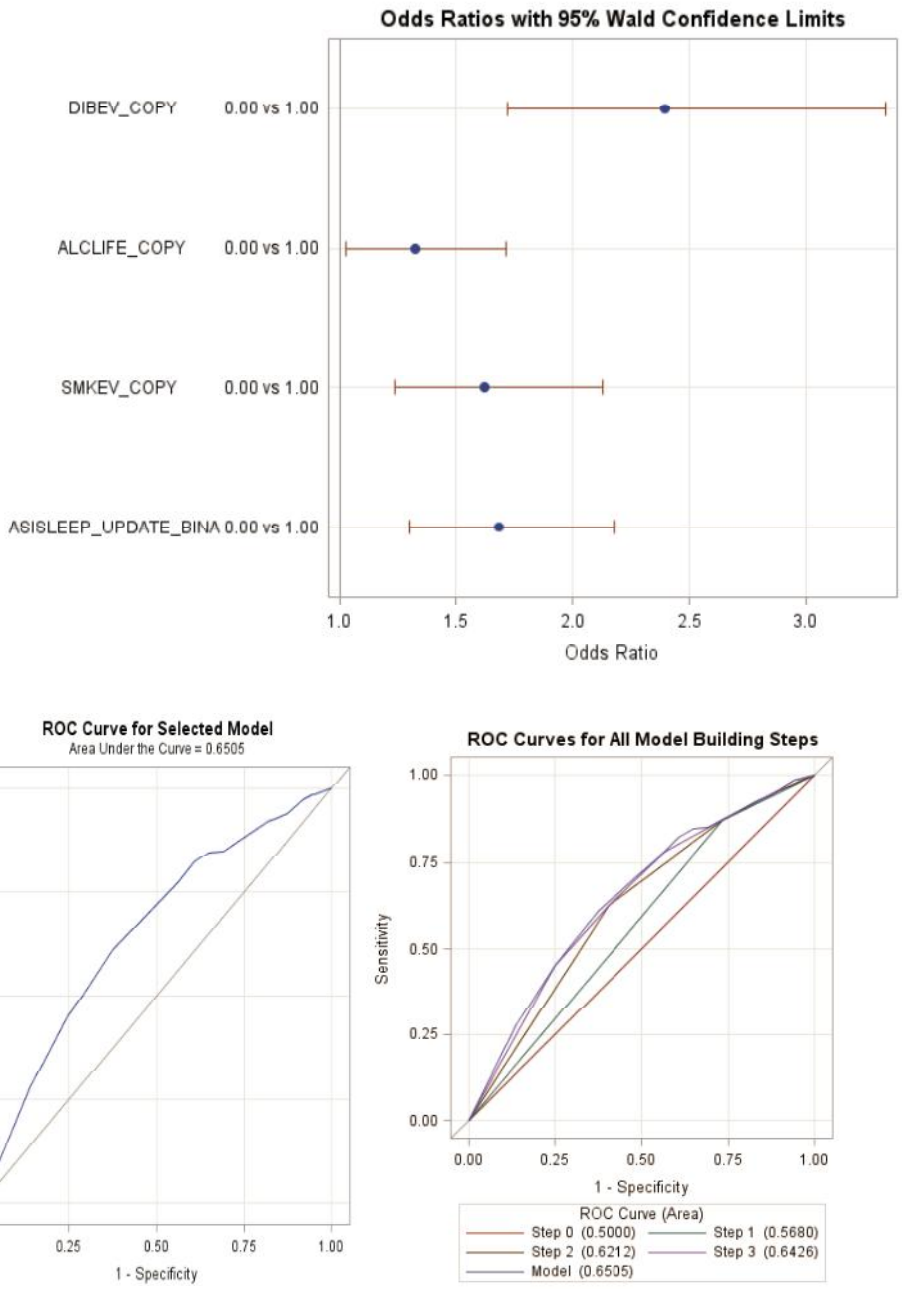


Figure 40: Logistic regression of Clinical and Behavioral factors in patients with ulcerative colitis.

Additionally, we observed that the second highest odds ratio was observed with the behavioral factor smoking status. Compared to arthritis group where the second highest odds ratio was observed for alcohol consumption status, the results obtained for ulcerative

colitis group hints at difference in inflammatory disease mechanism between the two diseases investigated. Additionally, none of the other factors including exercise status and BMI had significant odds ratios, implying little influence of this factors on prevalence of ulcerative colitis.

4.4 Combined arthritis and ulcerative colitis population

In addition to investigating the effects of behavioral and clinical factors on the arthritis and ulcerative colitis population separately, we also investigated participants with both the inflammatory diseases. We identified these participants as the patients who had answered yes to the questions about diagnosis of both arthritis and ulcerative colitis.

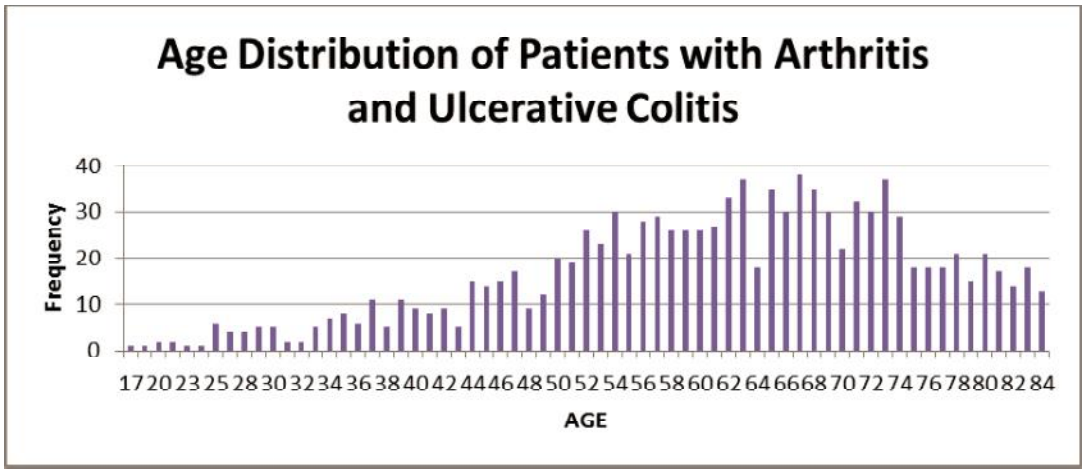


Figure 41 Distribution of age in the patients with arthritis and ulcerative colitis.

Table 36 Tabular representation of age and number of patients in specific age group for the patients with both arthritis and ulcerative colitis.

Age	Number of Patients		Age	Number of Patients		Age	Number of Patients		Age	Number of Patients
17	1		37	11		54	30		71	32
18	1		38	5		55	21		72	30
20	2		39	11		56	28		73	37
22	2		40	9		57	29		74	29
23	1		41	8		58	26		75	18
24	1		42	9		59	26		76	18
25	6		43	5		60	26		77	18
26	4		44	15		61	27		78	21
28	4		45	14		62	33		79	15
29	5		46	15		63	37		80	21
30	5		47	17		64	18		81	17
31	2		48	9		65	35		82	14
32	2		49	12		66	30		83	18
33	5		50	20		67	38		84	13
34	7		51	19		68	35		85	67
35	8		52	26		69	30		Total	1149
36	6		53	23		70	22			

Out of the total population we identified a total of 1149 individuals having diagnosis of both arthritis and ulcerative colitis. Compared to the total population investigated, this represents a very small percentage (<1%) of the population. As seen in figure 41 and table 36, this combined patients population also showed a very wide age range with youngest patient at age of 17 years while the oldest patient being at age 85. Additionally, we also observed that most of the patients in this population were between the ages of 50 to 85 years. In order to further compare this population with the arthritis and ulcerative colitis population, we only use the patients between the ages of 35 to 84 years. Only 1034 patients were between these age ranges. We now describe the prevalence of various behavioral and clinical factors in these populations. Prevalence of the behavioral and clinical factor in this combined population was quite similar to the one described for

ulcerative colitis group as this combined population is same as the ulcerative colitis patients with arthritis.

4.4.1 Distribution of clinical factors for ID patients

One of the first clinical factors investigated for this combined population is the patients BMI and their obesity level. As seen in figure 42, the BMI of this patient population showed a normal distribution with peak observed at the BMI of 27 years. This result is quite similar to the results obtained for the ulcerative colitis patients. As seen in table 37, the highest percentage of patients had BMI higher than 25, implying a trend towards obesity in this population.

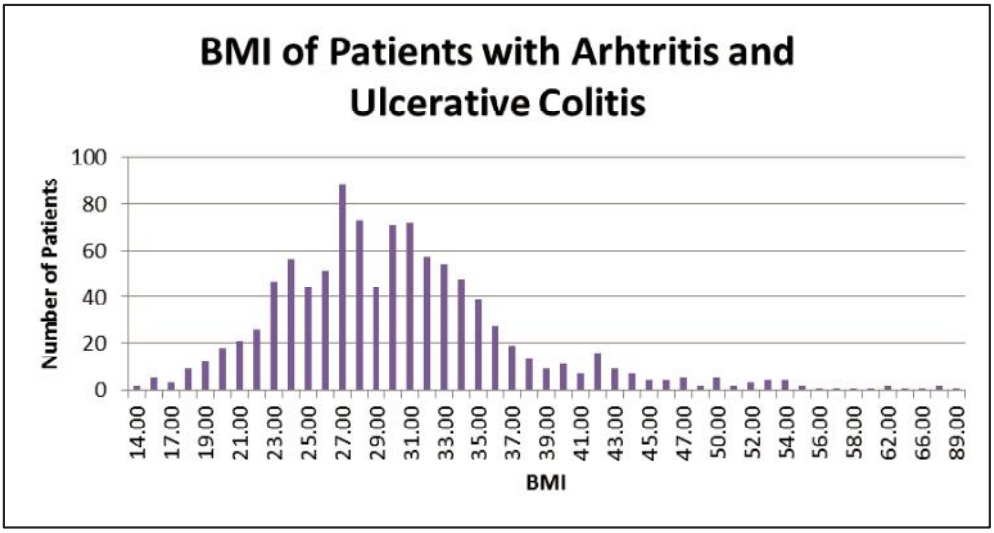


Figure 42 BMI distribution of patients with arthritis and ulcerative colitis.

Table 37 BMI of patients with arthritis and ulcerative colitis.

BMI (Kg/m^2)	Number of Subjects	%		BMI (Kg/m^2)	Number of Subjects	%		BMI (Kg/m^2)	Number of Subjects	%
.00	30	2.9		31.00	72	7.0		48.00	2	.2
14.00	2	.2		32.00	57	5.5		50.00	5	.5
16.00	5	.5		33.00	54	5.2		51.00	2	.2
17.00	3	.3		34.00	48	4.6		52.00	3	.3
18.00	9	.9		35.00	39	3.8		53.00	4	.4
19.00	12	1.2		36.00	27	2.6		54.00	4	.4
20.00	18	1.7		37.00	19	1.8		55.00	2	.2
21.00	21	2.0		38.00	13	1.3		56.00	1	.1
22.00	26	2.5		39.00	9	.9		57.00	1	.1
23.00	47	4.5		40.00	11	1.1		58.00	1	.1
24.00	56	5.4		41.00	7	.7		61.00	1	.1
25.00	44	4.3		42.00	16	1.5		62.00	2	.2
26.00	51	4.9		43.00	9	.9		65.00	1	.1
27.00	88	8.5		44.00	7	.7		66.00	1	.1
28.00	73	7.1		45.00	4	.4		68.00	2	.2
29.00	44	4.3		46.00	4	.4		89.00	1	.1
30.00	71	6.9		47.00	5	.5		Total	1034	100

There are several other comorbidities associated to increased BMI and one the clinical condition is Diabetes status amongst this population. Similar to the population with ulcerative colitis, only a small percentage of population had type-2 diabetes. In this limited sample, we observed that highest number of patients had the diabetes diagnosis at the age of 50 years (Figure 43 and table 38). However, we observed that a large percentage of combined disease population did not have diabetes.

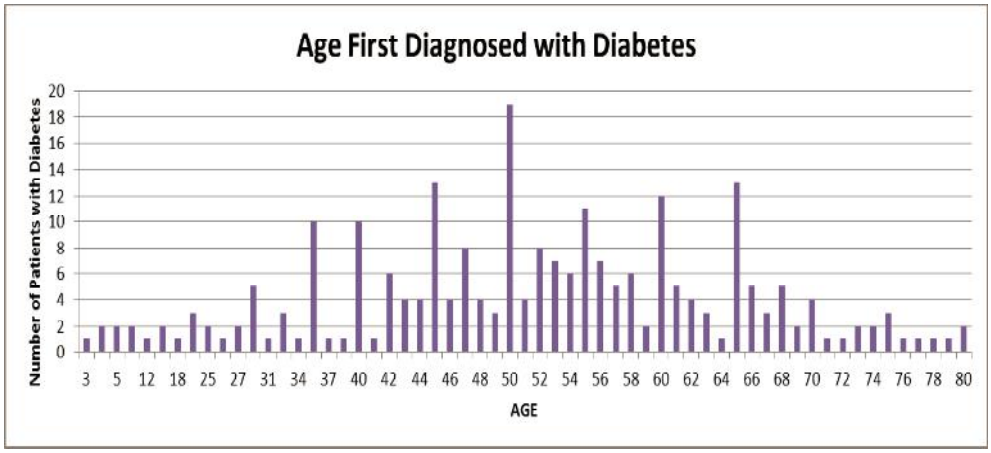


Figure 43 Distribution of age first diagnosed with diabetes.

Table 38 Age first diagnosed with diabetes amongst patients with arthritis and ulcerative colitis.

Age First Diagnosed with Diabetes	Number of Patients	%		Age First Diagnosed with Diabetes	Number of Patients	%		Age First Diagnosed with Diabetes	Number of Patients	%
3	1	.1		43	4	.4		64	1	.1
4	2	.2		44	4	.4		65	13	1.3
5	2	.2		45	13	1.3		66	5	.5
10	2	.2		46	4	.4		67	3	.3
12	1	.1		47	8	.8		68	5	.5
15	2	.2		48	4	.4		69	2	.2
18	1	.1		49	3	.3		70	4	.4
20	3	.3		50	19	1.8		71	1	.1
25	2	.2		51	4	.4		72	1	.1
26	1	.1		52	8	.8		73	2	.2
27	2	.2		53	7	.7		74	2	.2
30	5	.5		54	6	.6		75	3	.3
31	1	.1		55	11	1.1		76	1	.1
33	3	.3		56	7	.7		77	1	.1
34	1	.1		57	5	.5		78	1	.1
35	10	1.0		58	6	.6		79	1	.1
37	1	.1		59	2	.2		80	2	.2
38	1	.1		60	12	1.2		85	2	.2
40	10	1.0		61	5	.5		Refused	1	.1
41	1	.1		62	4	.4		Don't know	1	.1
42	6	.6		63	3	.3		Missing	785	75.9
								Total	1034	100

One of the last clinical factors investigated in this combined ID population is the hours of sleep within this population. As seen in figure 44 and table 39, this population similar to the ulcerative colitis population sleeps very few hours. 22.4 % of this population sleeps 6 hours for every 24 hours' period that is lower than the overall population.

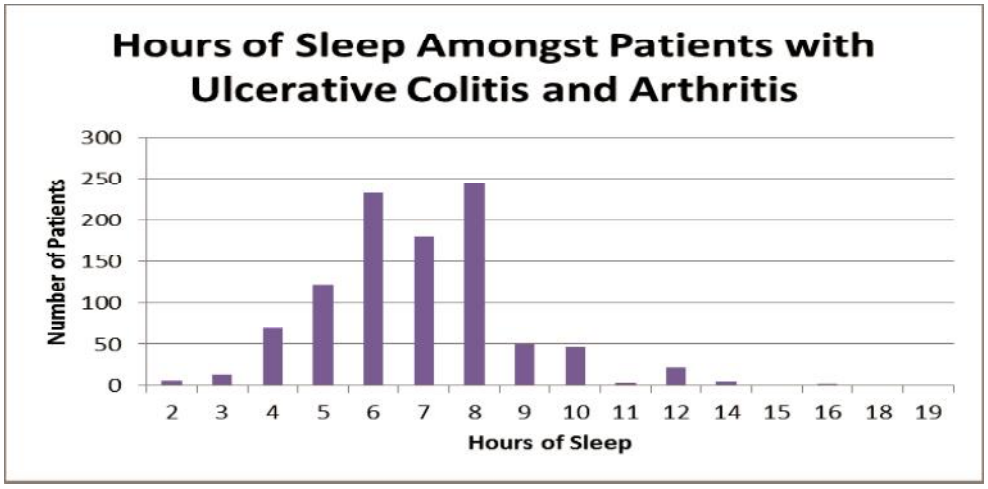


Figure 44 Distribution of hours of sleep amongst patients with ulcerative colitis and arthritis

Table 39 Hours of sleep amongst patients with arthritis and ulcerative colitis.

Hours of Sleep	Number of Patients	%		Hours of Sleep	Number of Patients	%
2	6	.6		12	21	2.0
3	13	1.3		14	5	.5
4	69	6.7		15	1	.1
5	122	11.8		16	2	.2
6	232	22.4		18	1	.1
7	180	17.4		19	1	.1
8	243	23.5		Not ascertained	30	2.9
9	50	4.8		Don't know	9	.9
10	46	4.4		Total	1034	100.0
11	3	.3				

4.3.2 Distribution of behavioral factors in ID patients

Similar to the clinical factors, behavioral factors were also found to be closely related to the ulcerative colitis population. As seen in table 37, more than 50% of the patients smoked regularly which is higher than the ulcerative colitis group as well as arthritis group separately. Additionally, as seen in figure 45 and table 40 large percentage of patients in this combined inflammatory disease population, large percentage of started smoking at a very early age of 16 years or younger.

Table 40 Frequency of number of patients with arthritis and ulcerative colitis and the age they started smoking fairly regularly.

Age smoked fairly regularly	Number of Patients	%		Age smoked fairly regularly	Number of Patients	%		Age smoked fairly regularly	Number of Patients	%
6	4	.4		21	24	2.3		37	2	.2
7	1	.1		22	13	1.3		38	2	.2
8	5	.5		23	5	.5		40	2	.2
9	10	1.0		24	6	.6		42	1	.1
10	16	1.5		25	17	1.6		44	1	.1
11	11	1.1		26	3	.3		45	2	.2
12	30	2.9		27	3	.3		47	2	.2
13	37	3.6		28	3	.3		48	1	.1
14	48	4.6		29	1	.1		50	1	.1
15	59	5.7		30	7	.7		52	1	.1
16	86	8.3		32	1	.1		55	1	.1
17	53	5.1		33	1	.1		Never smoked regularly	6	.6
18	69	6.7		34	1	.1		Don't know	8	.8
19	30	2.9		35	2	.2		Missing	421	40.7
20	35	3.4		36	2	.2		Total	1034	100.0

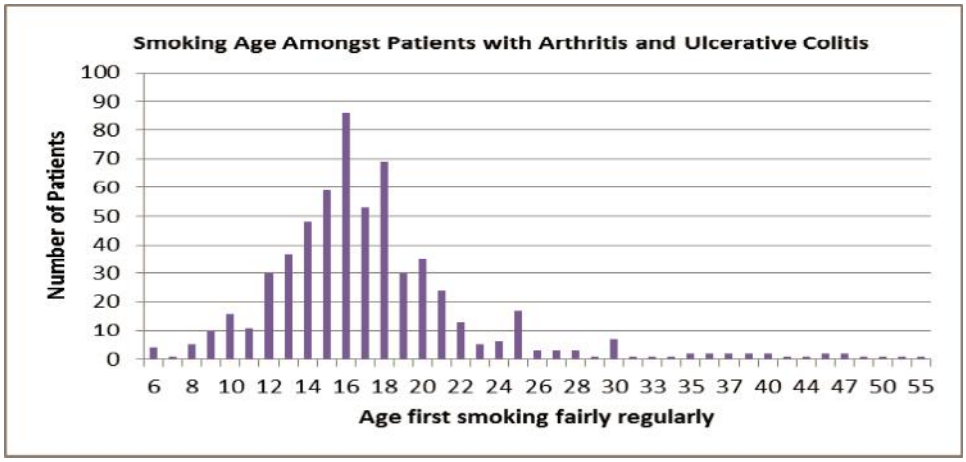


Figure 45 Smoking age distribution amongst patients with arthritis and ulcerative colitis.

In addition to this population who starts smoking at a very early age, as seen in figure 46 and table 41 large percentage of this population smoke for the remainder of their life. As seen in figure 46, the peak of the distribution is at 40 years however, there are higher numbers of people who have smoked for more than 40 years compared to 40 years.

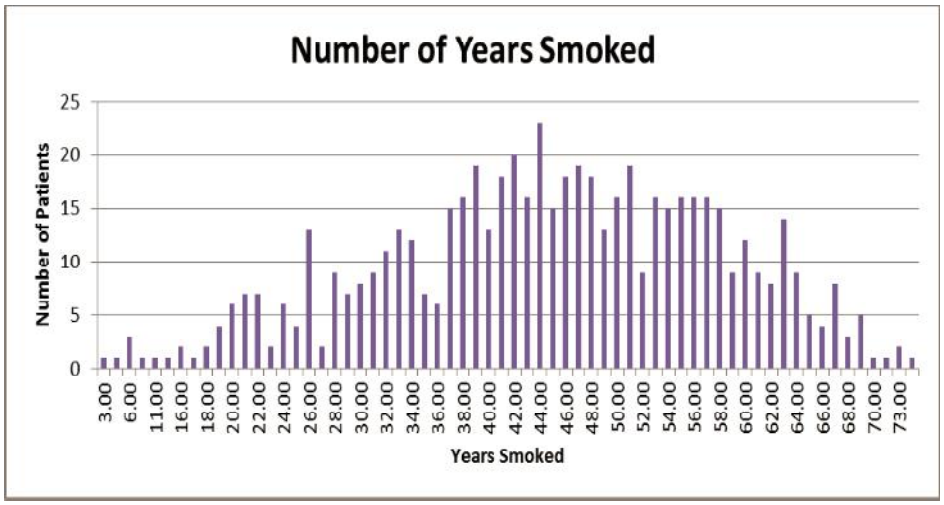


Figure 46 Distribution of number of years smoked amongst patients with arthritis and ulcerative colitis.

Table 41 Number of years patients with arthritis and ulcerative colitis who have smoked.

Number of years smoked	Number of Patients	%		Number of years smoked	Number of Patients	%		Number of years smoked	Number of Patients	%
3.00	1	.1		32.00	11	1.1		54.00	15	1.5
4.00	1	.1		33.00	13	1.3		55.00	16	1.5
6.00	3	.3		34.00	12	1.2		56.00	16	1.5
7.00	1	.1		35.00	7	.7		57.00	16	1.5
11.00	1	.1		36.00	6	.6		58.00	15	1.5
15.00	1	.1		37.00	15	1.5		59.00	9	.9
16.00	2	.2		38.00	16	1.5		60.00	12	1.2
17.00	1	.1		39.00	19	1.8		61.00	9	.9
18.00	2	.2		40.00	13	1.3		62.00	8	.8
19.00	4	.4		41.00	18	1.7		63.00	14	1.4
20.00	6	.6		42.00	20	1.9		64.00	9	.9
21.00	7	.7		43.00	16	1.5		65.00	5	.5
22.00	7	.7		44.00	23	2.2		66.00	4	.4
23.00	2	.2		45.00	15	1.5		67.00	8	.8
24.00	6	.6		46.00	18	1.7		68.00	3	.3
25.00	4	.4		47.00	19	1.8		69.00	5	.5
26.00	13	1.3		48.00	18	1.7		70.00	1	.1
27.00	2	.2		49.00	13	1.3		71.00	1	.1
28.00	9	.9		50.00	16	1.5		73.00	2	.2
29.00	7	.7		51.00	19	1.8		78.00	1	.1
30.00	8	.8		52.00	9	.9		Missing	435	42.1
31.00	9	.9		53.00	16	1.5		Total	1034	100.0

In addition to the number of years smoked, number of cigarettes smoked can also be an important factors associated with smoking. Out of the total combined population, only a few patients answered question regarding number of cigarettes. Although the sample size is much smaller for this population, we observed that significantly higher number of participants smoke half pack of cigarettes compared to the full pack of cigarettes (Figure 47 and table 42).

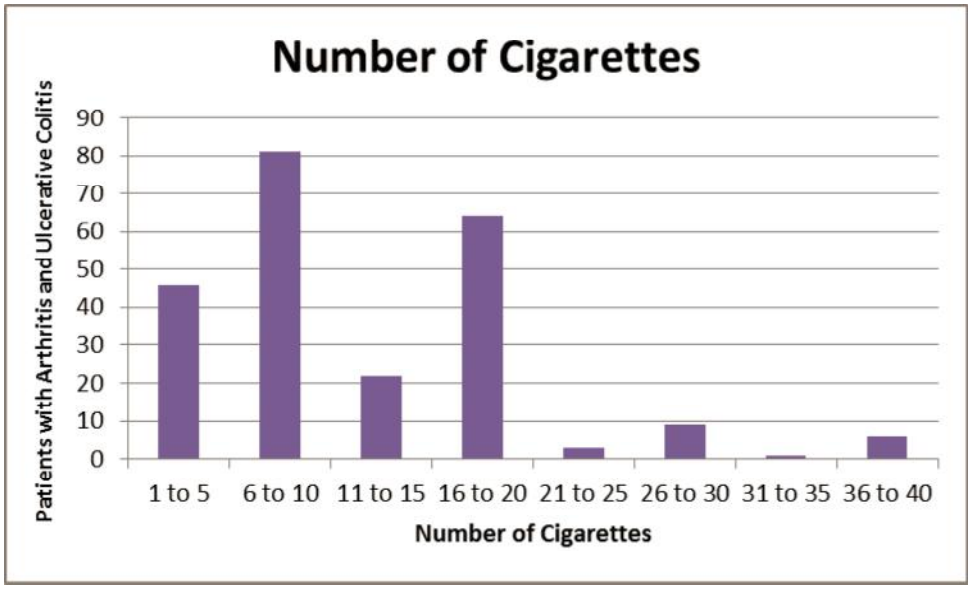


Figure 47 Number of cigarettes smoked amongst patients with arthritis and ulcerative colitis.

Table 42 Number of cigarettes smoked amongst patients with arthritis and ulcerative colitis.

Number of cigarettes	Number of Subjects	%		Number of cigarettes	Number of Subjects	%
1 to 5	46	4.45		31 to 35	1	0.10
6 to 10	81	7.83		36 to 40	6	0.58
11 to 15	22	2.13		41 to 50	1	0.10
16 to 20	64	6.19		Refused	3	0.29
21 to 25	3	0.29		Missing	798	77.18
26 to 30	9	0.87		Total	1034	100.0

In addition to smoking, alcohol consumption is one of the other behavioral factors showing increased in prevalence in arthritis and ulcerative colitis groups. In the combined patient population with both of this inflammatory disease, we observed a heterogeneous alcohol consumption status across the population. Approximately 45% of the total population does not consume alcohol currently or within last year (Table 43).

Amongst the patients who currently consume alcohol, a large percentage are infrequent or light drinkers, implying less than 3 drinks a week for the year. This results

show decreased alcohol consumption in this population compared to arthritis or ulcerative colitis participants. This may be due to the health condition in these participants as well as due to doctor's recommendation.

Table 43 Alcohol drinking status amongst patients with arthritis and ulcerative colitis.

	Alcohol drinking status	Description	Number of Subjects	Percentage
1	Lifetime abstainer	<12 drinks in lifetime	170	16.4
2	Former infrequent	12+ drinks in lifetime but never as many as 12 in 1 yr and none in past yr.	182	17.6
3	Former regular	12+ drinks in lifetime, 12+ drinks in 1 yr, but none in past yr	155	15.0
5	Current infrequent	12+ drinks in lifetime, 1-11 drinks in past year	173	16.7
6	Current Light	12+ drinks in lifetime, and ≤ 3 drinks per week in past yr	190	18.4
7	Current moderate	12+ drinks in lifetime, and (male)> 3 drinks per week up to 14 drinks per week OR (female)>3 drinks per week up to 7 drinks per week	104	10.1
8	Current heavier	12+ drinks in lifetime, and (male) >14 drinks per week in past year OR (female) >7 drinks per week in past yr.	48	4.6
4	Former unknown frequency	12+ drinks in lifetime, none in the past year, don't know if 12+ in any 1 yr.	1	.1
9	Current drinker, frequency/level unknown		4	.4
10	Drinking status Unknown		7	.7
Total			1034	100.0

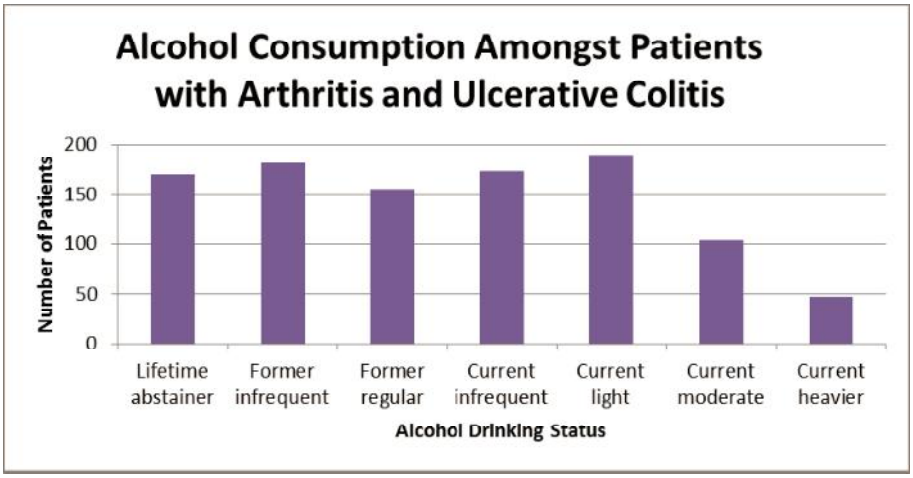


Figure 48 Distribution of alcohol consumption amongst patients with arthritis and ulcerative colitis.

One of the positive behavioral factors investigated in this population is the frequency of the exercise amongst this combined ID population. As seen in table 44, only a 50% of the combined inflammatory disease population perform regular physical exercise and within this group a large number of participants are involved in this exercise for less than 30 minutes. This implies deceased trend towards regular physical activity that may be associated with increased BMI and prevalence of diabetes condition.

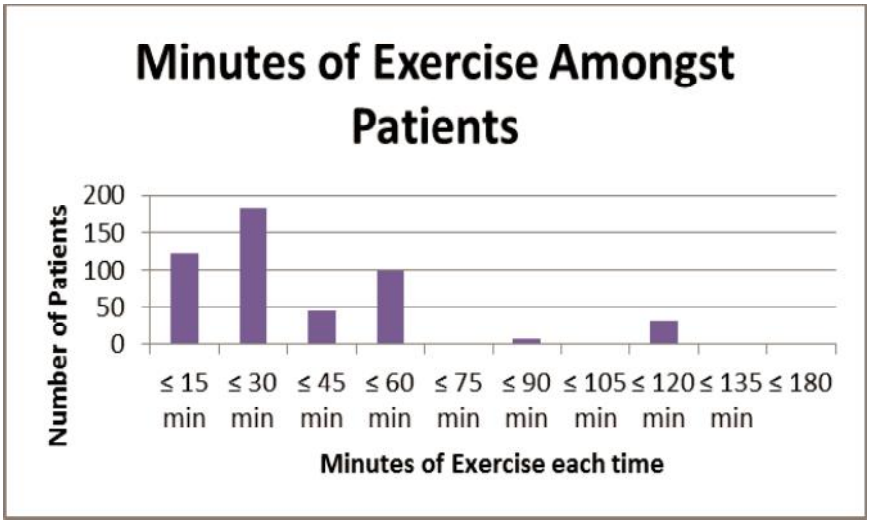


Figure 49 Minutes of exercise amongst patients with arthritis and ulcerative colitis.

Table 44 Frequency of number of patients with arthritis and ulcerative colitis and the minutes of exercise they have performed.

Minutes of Exercise per day	Number of Subjects	%		Minutes of Exercise per day	Number of Subjects	%
10	52	5.0		60	98	9.5
12	1	.1		75	1	.1
15	69	6.7		90	6	.6
18	1	.1		120	32	3.1
20	58	5.6		180	2	.2
25	5	.5		240	1	.1
30	117	11.3		300	1	.1
35	1	.1		600	1	.1
40	10	1.0		Don't know	1	.1
45	35	3.4		Missing	541	52.3
50	1	.1		Total	1034	100.0

4.4.3 Group comparison between diabetic and non-diabetic patients with inflammatory diseases

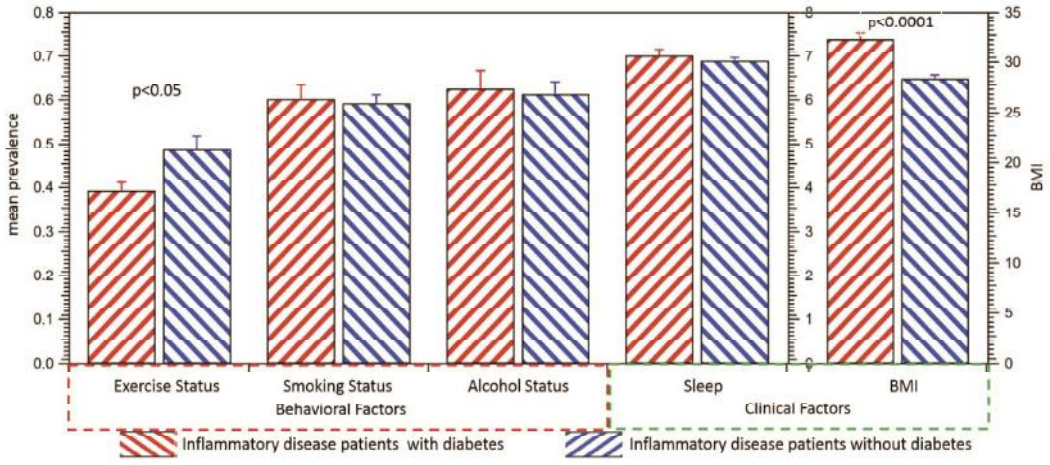


Figure 50 Mean prevalence of clinical and behavioral factors in patients with ulcerative colitis arthritis with and without diabetes

Figure 50 indicates results of chi-square test and t-test performed to compare the significant difference between diabetic and non-diabetic patients amongst ulcerative colitis patients. As shown in figure 50 the two factors that show significant difference are BMI

and Exercise status. Amongst the disease group the diabetic patients have a BMI of 32, whereas the non-diabetic group has BMI of 28. On the other hand, the exercise status is much lower with the mean prevalence of 40% amongst diabetic group versus 47% amongst non-diabetic group.

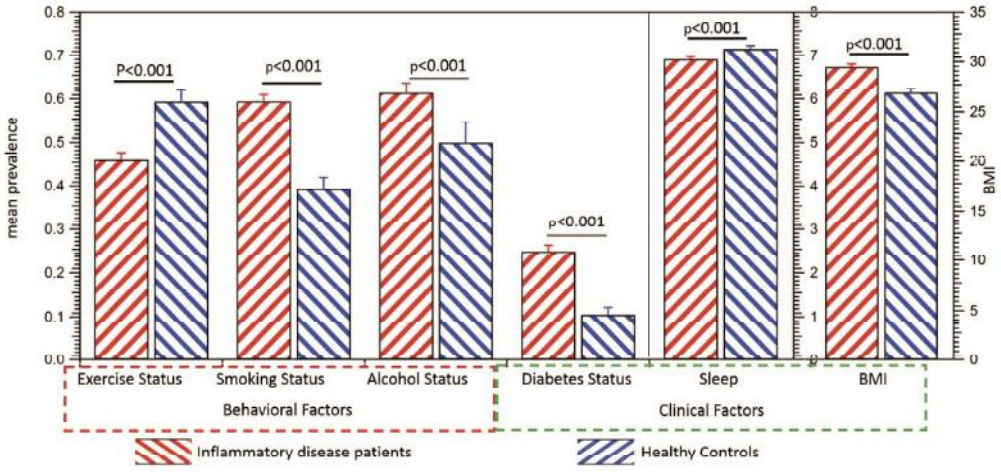


Figure 51 Mean prevalence of clinical and behavioral factors in patients with ulcerative colitis and arthritis and control group.

On the contrary when we compared the combined inflammatory disease population with the control group, we observed significant differences in multiple behavioral and clinical factors. Specifically, we observed significant increase in smoking status, alcohol status and diabetes status in inflammatory disease population compared to control group which were not observed when compared between diabetic and non-diabetic ID patients.

4.4.4 Odds ratio for clinical and behavioral factors in inflammatory disease patients

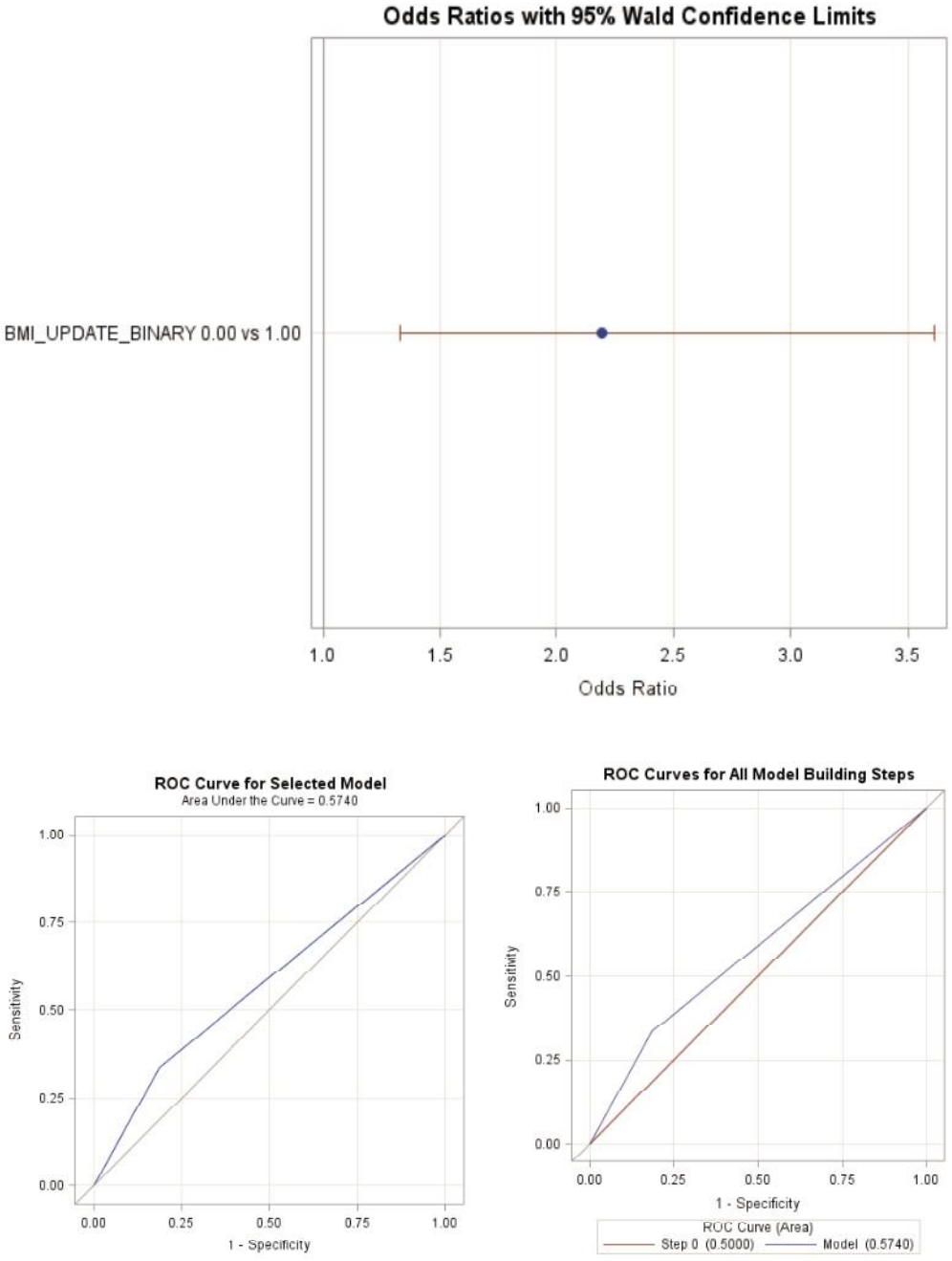


Figure 52 Logistic regression of clinical and behavioral factors in patients with arthritis and ulcerative colitis with diabetes.

Table 45 Odds ratio estimates and Wald confidence intervals for ulcerative colitis and arthritis patients with diabetes.

Effect	**Unit**	**Estimate**	**95% Confidence Limits**	
BMI (BMI_UPDATE_BINARY) (0.00 vs 1.00)	1.0000	2.192	1.329	3.615

Figure 52 and table 45 indicate the risk of prevalence of diabetes and both inflammatory disease with clinical and behavioral factors. As shown in the figure the only factor that plays a crucial role in the risk of diseases and diabetes is the BMI of the patients. Diabetic patients with both diseases who have a higher BMI, their risk of the disease increases by 2.19 folds.

Table 46 Odds Ratio Estimates and Wald Confidence Intervals for ulcerative colitis and arthritis patients

Effect	Unit	Estimate	95% Confidence Limits	
Diabetes status (DIBEV_COPY) (0.00 vs 1.00)	1.0000	2.748	1.535	4.921
Smoking status (SMKEV_COPY) (0.00 vs 1.00)	1.0000	2.223	1.375	3.593
Exercise Status (MODFREQW_COPY_BINARY) (0.00 vs 1.00)	1.0000	1.992	1.282	3.094
Sleep status (ASISLEEP_UPDATE_BINARY) (0.00 vs 1.00)	1.0000	2.261	1.406	3.638

In addition, two factors, alcohol status and BMI are not included in the odds ratio or regression because they have very little influence on the prevalence of both arthritis and ulcerative colitis combined.

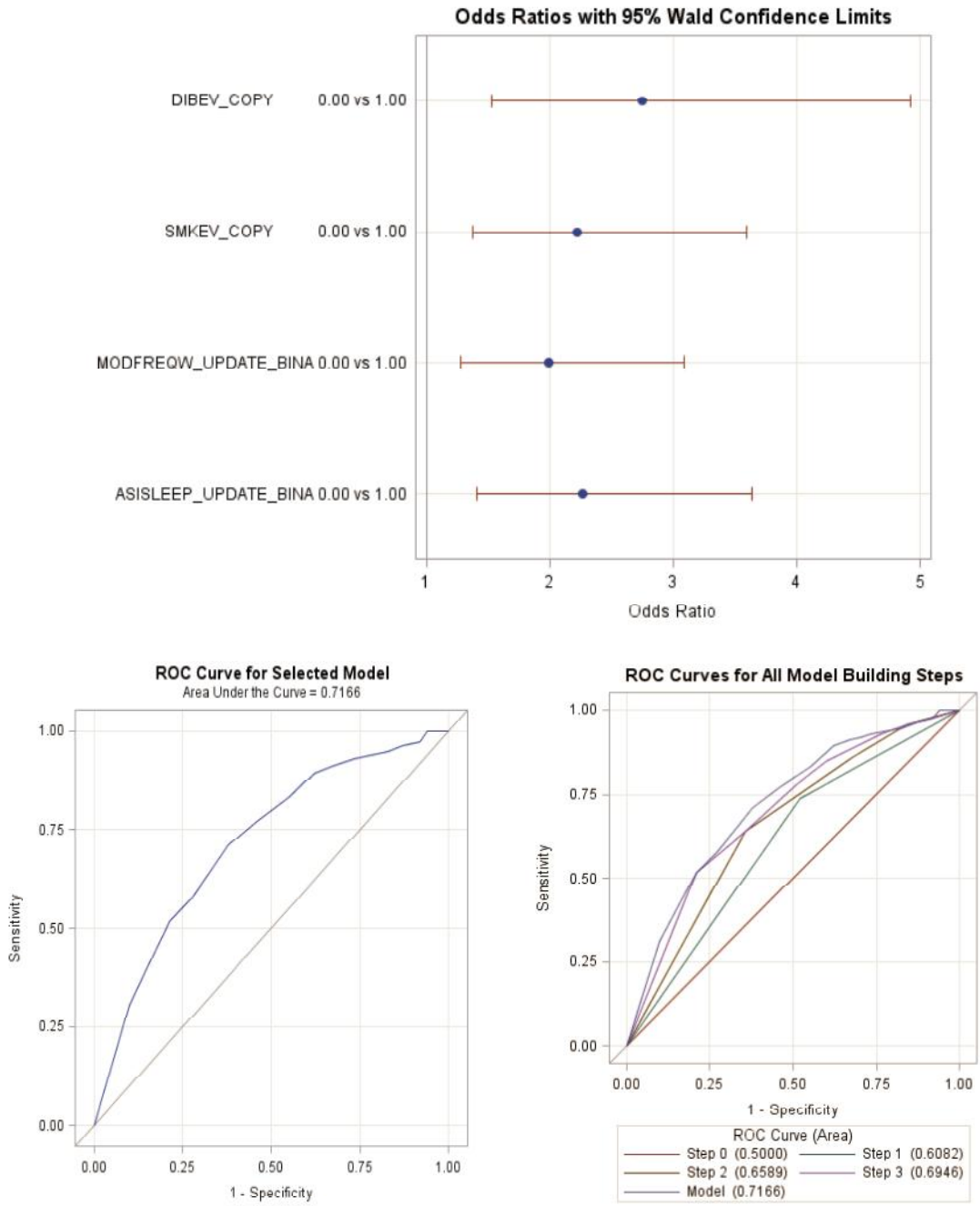


Figure 53 Logistic regression of Clinical and Behavioral factors in patients with ulcerative colitis and arthritis.

In table 46 and figure 53 logistic regression is calculated on the patients with both arthritis and ulcerative colitis. Table 43 indicates that diabetes has the highest odds ratio, similar to patients with only ulcerative colitis. However, the second highest odds ratio was

sleep pattern in patients with both diseases, which differs from both arthritis and ulcerative colitis group.

4.5 Treatment and oversight for arthritis and ulcerative colitis populations

In the last section of the results, we describe the costs associated with the inflammatory diseases, specifically with respect to doctor's visit and emergency care visits.

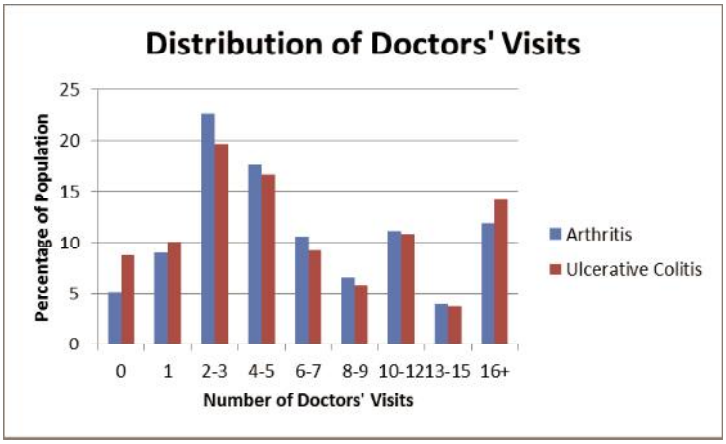


Figure 54: Distribution of number of doctor's visit between arthritis and ulcerative colitis population

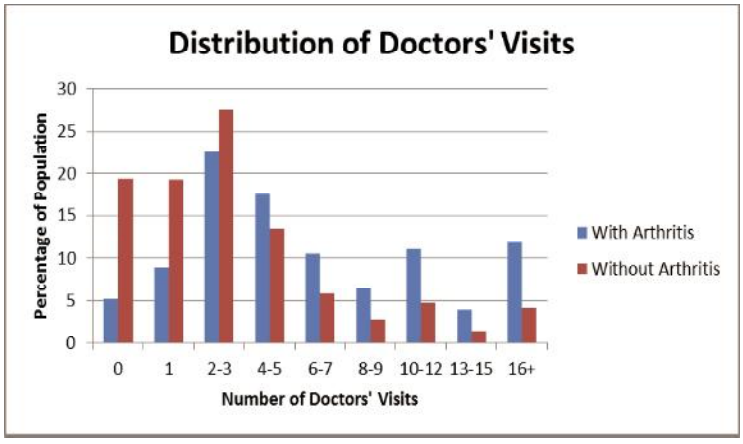


Figure 55: Distribution of number of doctor's visit between arthritis and without arthritis population

Figure 54, 55 and 56 show differences observed between the percentages of population with respect to doctors' visit over the last 12 months. We observed that higher percentage of control population visited doctor office less than 3 times over the last 12 months compared to the arthritis population. On the contrary, higher percentage of populations visited doctor's office more than 6 times over the period of last 12 months. More than 60% of arthritis population visited doctor's office more than 3 times over the last 12 months while only 32 % of the control population visited the doctor's office more than 3 times.

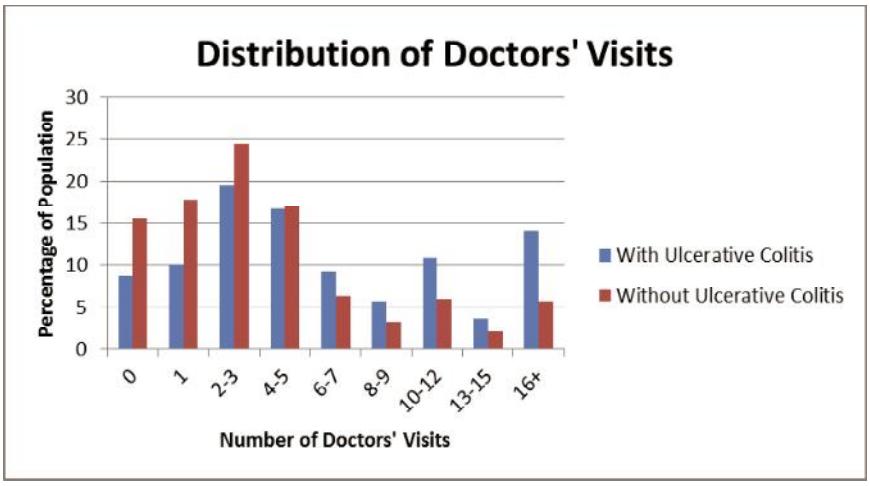


Figure 56: Distribution of number of doctor's visit between ulcerative colitis and control population

Compared to the doctor's visit, the number of ER visits was quite similar across the populations studied. A large percentage of Arthritis and ulcerative colitis population did not visit the emergency room over the last 12 months. This can be associated with the nature of this two inflammatory diseases. Both of these inflammatory disease is chronic in nature and does not require immediate attention in terms of visit to emergency room.

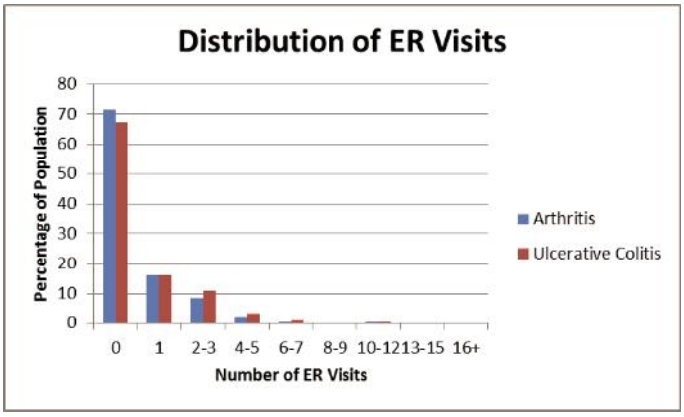


Figure 57: Distribution of number of ER visit between ulcerative colitis and arthritis population

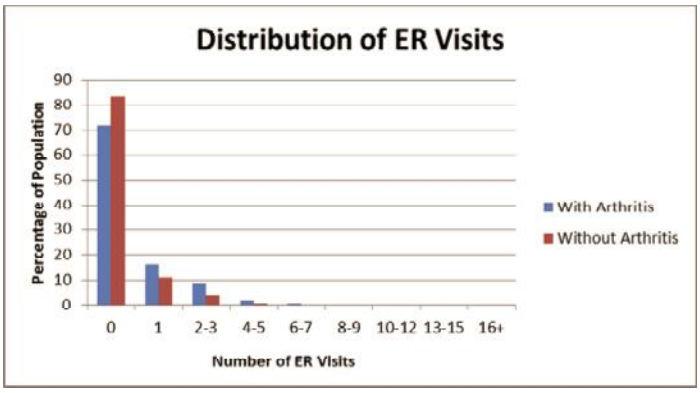


Figure 58: Distribution of number of ER visit between arthritis population and control population

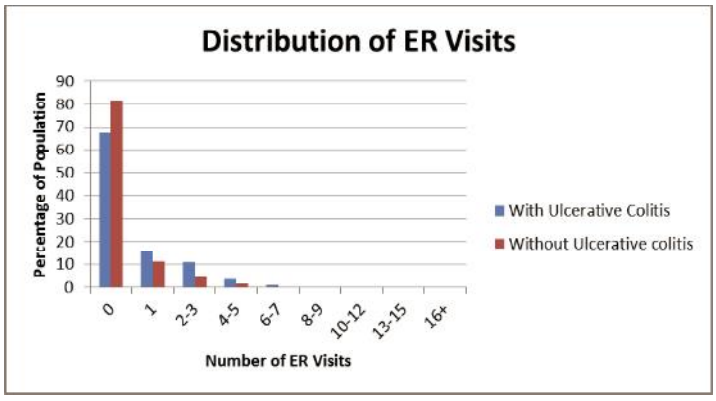


Figure 59: Distribution of number of ER visit between ulcerative colitis population and control population

On the contrary, we observed that compared to control population, both the arthritis and ulcerative colitis patients had higher number of ER visits compared to control population.

Preventative care

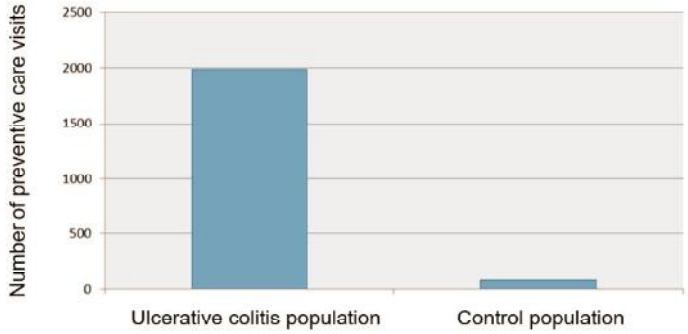


Figure 60: Distribution of number of preventive care visit between ulcerative colitis population and control population

We also observed that a large percentage of populations with ulcerative colitis had regular visit to the preventive care. The same trend was also observed for arthritis populations. These results imply easy access to the preventive care but also patients' willingness to access this preventive care.

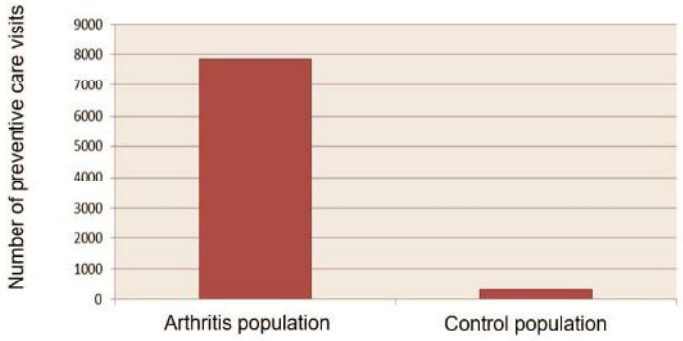


Figure 61: Distribution of number of preventive care visit between arthritis population and control population

CHAPTER V

DISCUSSION

One of the most striking findings observed in the current study is related to the age of onset of diabetes. Across the entire population and the population with inflammatory disease (arthritis and ulcerative colitis) population there were some significant similarities in age first diagnosed with diabetes, these ages were 35,45,50,55, and 60 years. Consistency of this age first detected with diabetes represents a very crucial step in detection, and creating remedies for this serious condition. These results could indicate that the ages of 35,45,50,55, and 60 are a good indication of when patients should get tested for diabetes.

In addition, we also observed significantly high prevalence of diabetes in inflammatory disease group compared to control groups. The prevalence of diabetes was higher in arthritis group compared to the ulcerative colitis group. This increased diabetes status can easily be associated with increased BMI observed in the arthritis group compared to the control group. Several studies have shown effect of increased BMI and being overweight on being detected with diabetes [1]. Studies have shown significant effect of increase energy intake on comorbidity associated with arthritis and ulcerative colitis [59]. Additionally, in the current study we obtained higher odds of having arthritis in patients who have diabetes compared to any other clinical factors such as BMI or sleep status. These results clearly specify and emphasize effect of diabetes management and dietary influence on presence of inflammatory diseases.

In the current study, we systematically investigated effect of clinical and behavioral factors on inflammatory diseases patients with diabetes. In this population we observed significant effects of both clinical and behavioral factors on the prevalence of inflammatory diseases in patients with diabetes. Specifically, we observed that clinical factors such as BMI and sleep status were more prevalent compared to behavioral factors such as smoking status and alcohol consumption status. However, exercise, a behavioral factor has significant effects on prevalence of inflammatory disease patients with diabetes. We also observed that obesity is the highest risk factor for presence of these inflammatory diseases in diabetic patients. Here we will discuss the significant findings of the study and their implications on prevalence, treatment and healthcare cost associated with inflammatory diseases.

Across the entire populations, we observed significant increase in BMI in inflammatory diseases patients with diabetes compared to non-diabetic population. There were significantly higher numbers of individuals with BMI of 27 (overweight). This is an indication of a move towards the obesity in the entire population, which has been associated with variety of diseases. Being overweight is not only an indication of the inflammatory diseases but many other life threatening conditions and chronic diseases that are triggered and caused due to obesity and being overweight. Previous studies have shown significant differences in BMI of the patients with and without ulcerative colitis [59]. However, in the current study, BMI was significantly higher in both the inflammatory disease groups compared to control groups. In addition, the difference observed in the BMI between the diabetic arthritis and non-diabetic arthritis group was significantly smaller than the difference observed between the non-diabetic and diabetic ulcerative colitis groups. It is

important to understand that due to the disease condition, patients with arthritis are not able to exercise as much as patients with ulcerative colitis which may also result in increased diabetes and BMI for patients with arthritis. Future studies should investigate these relationships in detail. In addition, several studies have shown significant effects of BMI greater than 30 as a hazard ratio for morbidity associated with arthritis [29]. BMI has been associated with increase mortality ratios across several populations. Similarly, in the current study we observed significant effect of BMI on prevalence of arthritis in diabetic patients, further affirming the effect of BMI on the healthy living. In addition, several independent studies have shown significant increase in survival rates in non-obese patients with irritable bowel disease, implying the crucial role BMI plays in recovery of inflammatory disease [57].

One of the most important methods to control the effects of increased BMI on human health is to control the dietary intake. Studies have investigated effect of alternative therapeutic effect such as diet and fiber intake and have showed improved therapeutic benefits of such approaches on clinical populations with increased BMI [20], though no studies have investigated effects of this alternative therapeutic approaches on inflammatory diseases in diabetic patients. Future studies should investigate these dietary factors across the US population as well as across the world population.

Finally, one of the least studied clinical variables is the average sleeping hours in these inflammatory disease groups with diabetes. In the current study, we investigated changes in number of sleep hours between the diabetic and non-diabetic inflammatory disease groups. We observed that higher percentage of diabetics and ulcerative colitis and combined arthritis and ulcerative colitis populations slept for an average of 6 or less hours,

compared to non-diabetic population and arthritis populations, where a large percentage of population slept for 7-8 hours. This represents a large difference in sleeping hours between the groups. Consistent with these results we observed that patients with ulcerative colitis slept ~1 hour less than control group. Reduced sleeping has been associated with clinical condition associated with digestion and gastrointestinal tract infection. These may represent one of the causal relationships between hours of sleep and prevalence of ulcerative colitis. On the contrary, patients with diabetic arthritis slept higher number of hours compared to non-diabetic populations. Most patients with arthritis are prescribed sleeping aid medicines to mitigate the constant pain, which may be associated with increased sleeping hours observed in this population. Future studies should investigate these effects of sleeping condition and medication status on quality of life in these inflammatory diseases.

In addition to investigating the clinical factors such as BMI and sleep status, we also investigated effects of behavioral factors on presence of inflammatory diseases across populations as well as effects of these factors on the disease condition. Out of the behavioral factors investigated, smoking status, number of cigarettes had the highest influence on prevalence of inflammatory disease amongst diabetic population. Specifically, we observed increased percentage of population who smoke between the ID patients with diabetes compared to ID patients without diabetes. These trends were also present when comparing the ID patients with control populations. Previous studies have investigated differences in smoking characteristics in ulcerative colitis group compared to control group, though no differences were observed due to small sample size. On the contrary, some studies have shown significantly lower number of smokers in ulcerative

colitis group compared to control group [69]. In the current study, we show significant differences in smoking characteristics between diabetics and non-diabetic in ulcerative colitis populations using a large data comprised of US populations as well as between the diabetic and non-diabetic patients in arthritis populations [59]. In addition, in the current study we also show significant interaction effect of smoking status and increased BMI on prevalence of arthritis populations with diabetes, as reported in earlier independent studies[29].

In addition to the number of diabetic patients who smoke and have inflammatory disease conditions, we also observed significant difference in the age they first started smoking between groups. Specifically, we observed that patients with just ulcerative colitis condition or with both arthritis and ulcerative colitis started smoking significantly earlier (~16 years) compared to subjects without inflammatory diseases (~18 years). On the contrary, patients with arthritis started smoking around the same age (~18 years) as patients without arthritis. These results imply possible effect of age first started smoking on developing ulcerative colitis condition and prevalence of arthritis and ulcerative colitis or both. Specifically, human body experiences significant physical development between the ages of 9 – 16 years and is undergoing large-scale hormonal changes. Smoking during this period of time, leading to nicotine consumption can results in hormonal imbalance which may be responsible for developing uncreative colitis at later ages.

On the contrary, to age first started smoking, the mean number of cigarettes smoked was significantly higher in arthritis group compared to control group as well as between the arthritis disease group with and without diabetes. This current smoking status was although higher in the arthritis group and ulcerative colitis group, but had little effect on

the odds ratio. Studies have shown that current smoking status has little effect on odd ratios in older population compared to former smoking and drinking status in variety of clinical populations [46]. Similarly, in the current study, we show that amongst ulcerative colitis patients and the patients with both ulcerative colitis and arthritis, the age they start smoking shows more prevalence and effect on presence of ulcerative colitis in diabetics compared to how much they smoke currently. These results imply significance of educating younger populations with unseen dangers of smoking. Finally, we observed that significantly higher percentage of arthritis population smoke regularly compared to non-arthritic population. This percentage was also higher than ulcerative colitis population. These results can be associated with effects of nicotine on human brain and physiology. Smoking may help patients handle the pain associated with arthritis better and may be a reason for increased current smoking status in arthritis populations.

In addition to smoking, alcohol consumption is an important behavioral factor associated with presence of inflammatory diseases. We specifically observed that higher percentage of diabetic patients with inflammatory diseases were consuming alcohol compared to non-diabetic patients. In addition, higher percentage of arthritis population was regular drinker compared to control population. These differences although present in ulcerative colitis group, were smaller compared to the arthritis group. One of the reasons why increased number of arthritis patients who drink alcohol may be associated with its effect on sleeping and in dealing with the pain associated with arthritis. Additionally, in the current study we observed significant relationship between alcohol consumption identified by more than 12 alcohol drinks per year and the presence of arthritis. These results are in accordance with previous studies that have shown significant relationship

between relative risk of RA and more than 2 alcohol consumption during the day[39,36], implying role of alcohol consumption on other arthritis conditions as well. In the same study [39], frequency of alcohol consumption was associated with severity of RA across the population including male and female populations; though in the current study we did not identify a significant relation between alcohol consumption frequency and presence of arthritis. These may be due to multiple reasons, mainly, in the current study, alcohol consumption frequency was not a specific number rather an average number of drinks over a period of a year. A more focused study on multiple parameters describing alcohol consumption characteristics and their effects on arthritis population should be performed.

We observed no significant difference in current alcohol consumption between diabetic patients and non-diabetic patients in the ulcerative colitis group. This may be due to dietary and healthy living restriction placed on the patients with ulcerative colitis by doctors. One of the most important dietary restrictions associated with ulcerative colitis is reduced/stopped consumption of alcohol, which may give rise to the results regarding alcohol consumption obtained in the current study. Surprisingly, we observed that most of the ulcerative colitis patients with diabetes and patients with both arthritis and ulcerative colitis with diabetes were former regular drinker (consuming on an average more than 2 drinks every day). These results imply the role of former regular alcohol consumption on current presence of ulcerative colitis condition and can be used to guide and develop intervention strategies for current regular drinkers.

From all of the environment factors studied, status of daily exercise was the only factor showing positive effect on prevalence of inflammatory diseases with diabetes. Specifically, we observed that non-diabetic population exercised more frequently, and also

for longer period of time compared to diabetic inflammatory disease group. Specifically, higher percentage of non-diabetic population with arthritis were involved in vigorous activity at least 3 times a week compared to patients with diabetes and arthritis. These may be due to the inability of the arthritis patients to perform regular vigorous activity and severe pain associated with it, this then also leads to obesity and diabetes. However, there is no specific reason for decreased vigorous activity in diabetic patients in ulcerative colitis population compared to non-diabetic population and studies should investigate these reductions in detail. In an earlier study Chan and colleagues have shown significant effect of energy consumption and energy expenditure (through vigorous activity) on comorbidity status associated with arthritis and ulcerative colitis. Specifically, decrease vigorous activity and increased calorie intake was associated with increased odds ratio and comorbidity status in this population. In the current study, we show that diabetic patients with inflammatory diseases have reduced amount of physical activity, which as shown by Chan and colleagues is associated with increased prevalence and comorbidity, thus representing a vicious cycle of events associated in inflammatory disease groups[59].

Daily exercise also helps the patient group with losing and maintaining weight, thus helping to control the diabetes and BMI of the patients. As we have shown > 25 BMI has significant effect on prevalence of inflammatory disease, thus exemplifying widespread role of daily exercise on these disease groups. Additionally, daily exercise has been implicated in helping patients control diabetes status as well as helping them with serious addiction. In the current study, we have shown significant effects of smoking and alcohol status has on prevalence of inflammatory diseases amongst diabetic patients and as daily

exercise is associated with helping population deal with these condition, we believe it may also be helpful in improving diabetic patients' condition with inflammatory diseases.

One of the biggest obstacles to involve patients in regular physical activity is associated with motivation and encouragement. As shown in the current results, diabetic patients with inflammatory diseases are less inclined to involve in regular exercise. One of the solution to the problem is the encouragement and advice by consulting physician to be involved in some physical activity. Studies have shown significant differences in effort to lose weight in diabetic patients with arthritis when advised by a physician compared to not advised by the physician. Diabetic patients with arthritis lost more weight when advised by the physician compared to not advised by physician. This differences reduced in the patients with high BMI (obese population), implying the self-motivation to lose weight in patient populations with higher BMI [1]. This resulted in decreased BMI and increased quality of life in these populations. As we have shown positive effect of exercise in diabetic arthritis and ulcerative colitis group, we believe that with a little more physician encouragement and involvement one can improve the exercise effort in arthritis and ulcerative colitis populations with diabetes, ultimately improving quality of life and decreased prevalence of both diabetes and inflammatory diseases[1].

One of the motivations behind the current study is to understand the healthcare cost associated with these inflammatory diseases. These populations and clinical conditions rarely result in ER visits and hence the healthcare costs are studied briefly to show the impact. More than 85% of arthritis, ulcerative colitis and control populations had 0 ER visits in the last year and ~10% of the three populations has 1 ER visits in the last 12 months, implying reduced acute and immediate cost of these diseases. On the contrary,

both arthritis and ulcerative colitis patients with diabetes visited doctor's office significantly higher number of time compared to the patients without diabetes. Specifically, we observed that approximately 62% of the total arthritis populations visited doctors' office 5 (6-12 visits per year) times of more compared to control population where only 30% of the studied population has more than 5 doctors visit over the period of 12 months. Similarly, approximately 58% of ulcerative colitis patients visited doctor's office more than 5 times in the last 12 months compared to 27% of the control population. On an average arthritis population visited doctors 4 times more compared to age matched control population, where the ulcerative colitis patients on average visited doctors 2.5 times more compared to control population.

These repeated increase in doctors' visits results in significant accumulation of healthcare cost. On an average each doctor's visit under most insurance plans results in ~$200 in healthcare costs, which implies on an average increased cost of ~$800 in arthritis population and ~$500 in ulcerative colitis population. In addition, presence of several other comorbidity conditions can significantly increase the healthcare cost across the US and have significant implications on quality of life for these patients.

Finally, in the current study we identified several behavioral and clinical factors that had significant effect on prevalence of the diabetic patients with inflammatory conditions. Some of the major negative factors were increased BMI (>25 BMI), smoking status, age first started smoking, current alcohol consumption, past alcohol consumption status and past smoking status amongst many. These negative factors were associated with increased prevalence of diabetes, arthritis and ulcerative colitis or both combined. On the contrary, we observed significant positive factors such as exercise status and number

of sleeping hours that were associated decreased prevalence inflammatory diseases in diabetic patients with inflammatory diseases. As commonly interpreted, these positive and negative factors can be changed easily and can have wide scale implications on current and future quality of life. Several studies have emphasized on educating patients with these factors in association with the symptoms of ulcerative colitis that may help improve the self-detection of ulcerative colitis [20]. We also suggest performing the same steps for arthritis to improve the self-detection and quality of life in these populations.

CHAPTER VI

LIMITATIONS AND FUTURE SCOPES

One of the limitations of this study was the dataset of the population. In this study performed, there can be more robust and more significant results with more data.

This study has analyzed the clinical and behavioral factors which effect the two inflammatory diseases, however the region of the population may also play a great impact on the prevalence of the inflammatory diseases as well as how they can be treated. For example, in the study performed there were indications that each of the inflammatory diseases may be more prevalent in one race compared to another. When further analysis is performed with considering the region of the patients, it can be very helpful in understanding how these inflammatory diseases are effected by genetics, dietary intake as well as their lifestyles.

Many of the inflammatory diseases are lifelong diseases, which can be monitored throughout the patients' life. This study can also be further performed longitudinally for patients over the years, as well as monitoring those same patients though out the years. The benefit of performing longitudinal analysis on these inflammatory diseases is that it will be able to give us more results how these diseases can effect lifestyles as well as other issues that may be caused due to these inflammatory diseases.

Another portion of the study that can further expanded is how the effect of the two inflammatory diseases (arthritis and ulcerative colitis) in pregnant women and how that

may affect the fetus as well as the unborn child. Some of the studies that were reviewed have indicated negative effects of arthritis in pregnant women. Further analysis in this area will also help physicians assess how to monitor and treat pregnant women with arthritis.

Inflammatory diseases have shown an increasing trend all over the world and studies these diseases further will provide very fruitful results.

REFRENCES

1. Mehrotra C, Naimi TS, Serdula M, Bolen J, Pearson K. Arthritis , Body Mass Index , and Professional Advice to Lose Weight Implications for Clinical Medicine and Public Health. 2004;27(1). doi:10.1016/j.amepre.2004.03.007.

2. Bosma-den Boer MM, van Wetten M-L, Pruimboom L. Chronic inflammatory diseases are stimulated by current lifestyle: how diet, stress levels and medication prevent our body from recovering. *Nutr Metab (Lond)*. 2012;9(1):32. doi:10.1186/1743-7075-9-32.

3. Alexander LEC, Shin S, Hwang JH. Infl ammatory diseases of the lung induced by conventional cigarette smoke a review. *Chest*. 2015;148(5):1307-1322. doi:10.1378/chest.15-0409.

4. Song M, Chen T, Prough RA, Cave MC, Mcclain CJ. Chronic Alcohol Consumption Causes Liver Injury in High-Fructose-Fed Male Mice Through Enhanced Hepatic Inflammatory Response. *Alcohol Clin Exp Res*. 2016;40(3):518-528. doi:10.1111/acer.12994.

5. Andersen V, Holmskov U, Bek Sørensen S, et al. A proposal for a study on treatment selection and lifestyle recommendations in chronic inflammatory diseases: A danish multidisciplinary collaboration on prognostic factors and personalised medicine. *Nutrients*. 2017;9(5). doi:10.3390/nu9050499.

6. Marieb EN, Hoehn K. *Human Anatomy & Physiology*. Pearson Education; 2007.

7. Okin D. Evolution of Inflammatory Diseases. 2012;76(October 2009):211-220. doi:10.1007/s11103-011-9767-z.Plastid.

8. Mullican KA, Francart SJ. The role of specialty pharmacy drugs in the management of inflammatory diseases. *Am J Heal Pharm*. 2016;73(11):821-830. doi:10.2146/ajhp150727.

9. Gracia MC. Inflammatory, autoimmune, chronic diseases: Bad diet and physical inactivity are causes or effects? *Med Hypotheses*. 2006;66(5):939-944. doi:10.1016/j.mehy.2005.11.033.

10. Lumeng CN, Saltiel AR. Review series Inflammatory links between obesity and metabolic disease. *Life Sci*. 2011;121(6):2111-2117. doi:10.1172/JCI57132.In.

11. Papadakis KA, Targan SR. Current theories on the causes of inflammatory bowel disease. *Gastroenterol Clin North Am*. 1999;28(2):283-296.

12. E.M. D, C. M. Bowel-associated dermatosis - arthritis syndrome in a patient with ulcerative colitis: an extraintestinal manifestation of inflammatory bowel disease. *Clin J Gastroenterol*. 2014;7(5):410-413. doi:10.1007/s12328-014-0529-8.

13. Wrightt V. The Arthritis of Ulcerative Colitis *. 1965;(September):670-675.

14. Tedeschi SK, Cui J, Arkema E V., et al. Elevated BMI and antibodies to citrullinated proteins interact to increase rheumatoid arthritis risk and shorten time to diagnosis: A nested case-control study of women in the Nurses' Health Studies. *Semin Arthritis Rheum*. 2016;46(6):692-698. doi:10.1016/j.semarthrit.2016.09.001.

15. Cannon AR, Hammer AM, Morris NL, et al. Alcohol exacerbates an ulcerative colitis flare period. *Alcohol*. 2017;59:71. doi:10.1016/j.alcohol.2016.10.018.

16. Libby P. Inflammatory Mechanisms: The Molecular Basis of Inflammation and Disease. 2007;2007(December):140-146. doi:10.1301/nr.2007.dec.S140.

17. Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the Prevalence of Arthritis and Other Rheumatic Conditions in the United States Part I. 2008;58(1):15-25. doi:10.1002/art.23177.

18. Wellen KE, Hotamisligil GS. Inflammation , stress , and diabetes. 2005;115(5):1111-1119. doi:10.1172/JCI200525102.The.

19. Sturm R. The effects of obesity, smoking, and drinking on medical problems and costs. *Health Aff*. 2002;21(2):245-253. doi:10.1377/hlthaff.21.2.245.

20. Head KA, Jurenka JS, Ascp MT. Inflammatory Bowel Disease Part I : Ulcerative Colitis – Pathophysiology and Conventional and Alternative Treatment Options. 2003;8(3).

21. Meerding WJ, Bonneux L, Polder JJ, Koopmanschap MA, Maas PJ Van Der. Demographic and epidemiological determinants of healthcare costs in Netherlands : cost of illness study. 1998;317(July).

22. Kappelman MD, Shiman SLR, Porter CQ, et al. Direct Health Care Costs of Crohn ' s Disease and Ulcerative Colitis in US Children and Adults. *YGAST*. 2008;135(6):1907-1913. doi:10.1053/j.gastro.2008.09.012.

23. De Angelis G, Chen Y. Obesity among women may increase the risk of arthritis: Observations from the Canadian Community Health Survey, 2007-2008. *Rheumatol Int*. 2013;33(9):2249-2253. doi:10.1007/s00296-013-2712-5.

24. Myllykangas-luosuj RA, Aho K, Isomiiki HA. Mortality in Rheumatoid Arthritis. 1995;3(3):193-202.

25. Michaud K, Wolfe F. Comorbidities in rheumatoid arthritis. 2007;21(5):885-906. doi:10.1016/j.berh.2007.06.002.

26. Jentzsch T, Geiger J, Slankamenac K, Werner CML. Obesity measured by outer abdominal fat may cause facet joint arthritis at the lumbar spine. *J Back Musculoskelet Rehabil*. 2015;28(1):85-91. doi:10.3233/BMR-140495.

27. Widdifield J, Paterson JM, Bernatsky S, et al. The epidemiology of rheumatoid arthritis in Ontario, Canada. *Arthritis Rheumatol*. 2014;66(4):786-793. doi:10.1002/art.38306.

28. Symmons DP, Bankhead CR, Harrison BJ, et al. Blood transfusion, smoking, and obesity as risk factors for the development of rheumatoid arthritis: results from a primary care-based incident case-control study in Norfolk, England. *Arthritis Rheum*. 1997;40(11):1955-1961. doi:10.1002/1529-0131(199711)40:11<1955::AID-ART6>3.0.CO;2-A.

29. Janssen I. Morbidity and Mortality Risk Associated With an Overweight BMI in Older Men and Women. 2007.

30. Wang Y, Zhang Q. Are American children and adolescents of low socioeconomic status at increased risk of obesity? Changes in the association between overweight and family income between 1971 and 2002 Wang and Zhang 84 (4): 707 American Journal of Clinical Nutrition. *Am J Clin Nutr*. 2006;84(4):707-716. doi:10.1080/01459740.1991.9966050.

31. Hootman JM, Murphy LB HC. Arthritis as a potential barrier to physical activity among adults with obesity – United States, 2007 and 2009. *MMWR Morb Mortal Wkly Rep*. 2011;60(19):614–8.

32. Voigt LF, Koepsell TD, Nelson JL, Dugowson CE, Daling JR. Smoking, obesity, alcohol consumption, and the risk of rheumatoid arthritis. *Epidemiology*. 1994;5(5):525-532.

33. ALBAYRAK GEZER ?lknur, BALKARLI A, CAN B, BA??ACI S, K???K?EN S, K???K A. Pain, depression levels, fatigue, sleep quality, and quality of life inelderly patients with rheumatoid arthritis. *Turkish J Med Sci*. 2017;47:847-853. doi:10.3906/sag-1603-147.

34. Power JD, Perruccio A V., Badley EM. Pain as a mediator of sleep problems in arthritis and other chronic conditions. *Arthritis Care Res*. 2005;53(6):911-919. doi:10.1002/art.21584.

35. Silman AJ, Newman J, Macgkegor AJ. CIGARETTE SMOKING INCREASES THE RISK OF RHEUMATOID ARTHRITIS Results from a Nationwide Study of Disease-Discordant Twins. 1996;39(5):732-735.

36. Hazes W, Dijkmans AC, Vandenbroucke P. Lifestyle and the risk of rheumatoid arthritis : cigarette smoking and alcohol consumption. 1990:980-982.

37. Klareskog L, Stolt P, Lundberg K, et al. A new model for an etiology of rheumatoid arthritis: Smoking may trigger HLA-DR (shared epitope)-restricted immune reactions to autoantigens modified by citrullination. *Arthritis Rheum*. 2006;54(1):38-46. doi:10.1002/art.21575.

38. Thiele TE, Koh MT, Pedrazzini T. Voluntary alcohol consumption is controlled via the neuropeptide Y Y1 receptor. *J Neurosci*. 2002;22:RC208. doi:20026073 [pii].

39. Maxwell JR, Gowers IR, Moore DJ, Wilson AG. Original article Alcohol

consumption is inversely associated with risk and severity of rheumatoid arthritis. 2010;(July):2140-2146. doi:10.1093/rheumatology/keq202.

40. Voigt L. Smoking, Obesity, Alcohol Consumption, and the Risk of Rheumatoid Arthritis.pdf.

41. Jacobsen S, Bengtsson C, Pedersen M, et al. Alcohol consumption is associated with decreased risk of rheumatoid arthritis : results from two Scandinavian case – control studies. doi:10.1136/ard.2007.086314.

42. Jeffery RW, Baxter J, McGuire M, Linde J. Are fast food restaurants an environmental risk factor for obesity? *Int J Behav Nutr Phys Act*. 2006;3:2. doi:10.1186/1479-5868-3-2.

43. Arranz LI, Rafecas M, Alegre C. Effects of obesity on function and quality of life in chronic pain conditions. *Curr Rheumatol Rep*. 2014;16(1). doi:10.1007/s11926-013-0390-7.

44. Katz JN, Wright EA, Guadagnoli E, Liang MH, Karlson EW, Cleary PD. DIFFERENCES BETWEEN MEN AND WOMEN UNDERGOING MAJOR ORTHOPEDIC SURGERY FOR DEGENERATIVE ARTHRITIS. 1994;37(5):687-694.

45. Bouchard M, Amin A, Pinsker E, Khan R, Deda E, Daniels TR. The impact of obesity on the outcome of total ankle replacement. *J Bone Jt Surg Am*. 2015;97(11):904-910. doi:10.2106/jbjs.n.00837.

46. Nakamura Y, Labarthe DR. A Case-Control Study of Ulcerative Colitis with Relation to Smoking Habits and Alcohol Consumption in Japan. 1994;140(10):902-911.

47. Study AT, Michaud K, Messer J, Choi HK, Wolfe F. Direct Medical Costs and Their Predictors in Patients With Rheumatoid Arthritis. 2003;48(10):2750-2762. doi:10.1002/art.11439.

48. Gisondi P, Del Giglio M, Cozzi A, Girolomoni G. Psoriasis, the liver, and the gastrointestinal tract. *Dermatol Ther*. 2010;23(2):155-159. doi:10.1111/j.1529-8019.2010.01310.x.

49. Probert CS, Jayanthi V, Hughes AO, Thompson JR, Wicks AC, Mayberry JF. Prevalence and family risk of ulcerative colitis and Crohn's disease: an epidemiological study among Europeans and south Asians in Leicestershire. *Gut*. 1993;34(11):1547-1551. doi:10.1136/gut.34.11.1547.

50. Hou JK, El-serag H, Th S. Distribution and Manifestations of Infl ammatory Bowel Disease in Asians , Hispanics , and African Americans : A Systematic Review. 2009;104(November 2008):2100-2109. doi:10.1038/ajg.2009.190.

51. Valentini L, Ph D, Schaper L, et al. Malnutrition and impaired muscle strength in patients with Crohn ' s disease and ulcerative colitis in remission. 2008;24:694-

702. doi:10.1016/j.nut.2008.03.018.

52. Giovannucci E, Stampfer MJ, Colditz GA, et al. Folate, methionine, and alcohol intake and risk of colorectal adenoma [see comments]. *JNatlCancer Inst*. 1993;85(0027-8874 SB-M SB-X):875-884.

53. Bodian C. Colorectal cancer in ulcerative colitis . Influence of anatomical extent and age at onset on colitis-cancer interval. 1991:167-169.

54. Shaw LJ, Merz CNB, Pepine CJ, et al. The economic burden of angina in women with suspected ischemic heart disease: Results from the National Institutes of Health-National Heart, Lung, and Blood Institute-sponsored Women's Ischemia Syndrome Evaluation. *Circulation*. 2006;114(9):894-904. doi:10.1161/CIRCULATIONAHA.105.609990.

55. Maconi G, Furfaro F, Sciurti R, Bezzio C, Ardizzone S, de Franchis R. Glucose intolerance and diabetes mellitus in ulcerative colitis: Pathogenetic and therapeutic implications. *World J Gastroenterol*. 2014;20(13):3507-3515. doi:10.3748/wjg.v20.i13.3507.

56. Shivashankar R, Tremaine W, Harmsen S, Zinsmeister A, Loftus E. Updated Incidence and Prevalence of Crohn's Disease and Ulcerative Colitis in Olmsted County, Minnesota (1970-2011). *Am J Gastroenterol*. 2014;109(6):s499. doi:10.1016/j.cgh.2016.10.039.

57. Seminerio JL, Koutroubakis IE, Ramos-Rivers C, et al. Impact of Obesity on the Management and Clinical Course of Patients with Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2015;21(12):2857-2863. doi:10.1097/MIB.0000000000000560.

58. Caruso C, Balistreri CR, Candore G. The role of adipose tissue and adipokines in obesity-related inflammatory diseases. *Mediators Inflamm*. 2010;2010. doi:10.1155/2010/802078.

59. Chan SSM, Luben R, Olsen A, et al. Body mass index and the risk for Crohn's disease and ulcerative colitis: data from a European Prospective Cohort Study (The IBD in EPIC Study). *Am J Gastroenterol*. 2013;108(4):575-582. doi:10.1038/ajg.2012.453.

60. Ananthakrishnan AN, Long MD, Martin CF, Sandler RS, Kappelman MD. Sleep disturbance and risk of active disease in patients with crohn's disease and ulcerative colitis. *Clin Gastroenterol Hepatol*. 2013;11(8):965-971. doi:10.1016/j.cgh.2013.01.021.

61. Herron MD, Hinckley M, Hoffman MS, et al. Impact of obesity and smoking on psoriasis presentation and management. *Arch Dermatol*. 2005;141(12):1527-1534. doi:10.1001/archderm.141.12.1527.

62. Baron J a. Beneficial effects of nicotine and cigarette smoking: the real, the

possible and the spurious. *Br Med Bull*. 1996;52(1):58-73. doi:10.1093/oxfordjournals.bmb.a011533.

63. Lakhan SE, Kirchgessner A. Anti-inflammatory effects of nicotine in obesity and ulcerative colitis. *J Transl Med*. 2011;9(1):129. doi:10.1186/1479-5876-9-129.

64. Stange EF, Travis SPL, Vermeire S, et al. European evidence-based Consensus on the diagnosis and management of ulcerative colitis: Definitions and diagnosis. *J Crohn's Colitis*. 2008;2(1):1-23. doi:10.1016/j.crohns.2007.11.001.

65. Cannon CP, Greenberg BH. Risk Stratification and Prognostic Factors in the Post-Myocardial Infarction Patient. *Am J Cardiol*. 2008;102(5 SUPPL.). doi:10.1016/j.amjcard.2008.06.006.

66. Mehta SJ, Silver AR, Lindsay JO. Review article: Strategies for the management of chronic unremitting ulcerative colitis. *Aliment Pharmacol Ther*. 2013;38(2):77-97. doi:10.1111/apt.12345.

67. Gottlieb S, Behar S, Hod H, et al. Trends in Management, Hospital and Long-Term Outcomes of Elderly Patients with Acute Myocardial Infarction. *Am J Med*. 2007;120(1):90-97. doi:10.1016/j.amjmed.2006.09.018.

68. Disease IB. Influence of dietary factors on the clinical course of ulcerative colitis: a prospective cohort study. 2004. doi:10.1136/gut.2003.024828.

69. Non-smoking : a feature of ulcerative colitis. 1982;284(MARCH):1982.