2005

A comparative study of prevalence rates of rheumatoid arthritis

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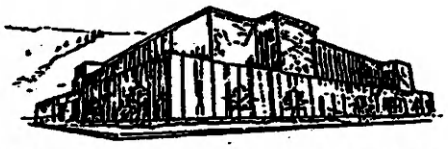

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A Comparative Study of Prevalence Rates of Rheumatoid Arthritis

by

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B.A. University of Montana, 2001

presented in partial fulfillment of the requirements

for the degree of

Master of Arts

The University of Montana

August 2005

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7-22-05
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Bennett, Rochelle K. Master of Arts, August 2005 Anthropology

A Comparative Study of Prevalence Rates of Rheumatoid Arthritis

Chairperson: Randall R. Skelton RS

The advancements in medicine and medical technology have greatly improved the lives of millions of people in both developed and developing countries. With this improvement in health has come an increase in life expectancy and subsequently an increase in chronic diseases such as rheumatoid arthritis. Several studies conducted worldwide have shown that rheumatoid arthritis has a higher average prevalence in all three ancestral groups (Caucasoid, Mongoloid, Negroid) in countries in North America when compared to ancestral groups living in other countries.

To attempt to explain this disparity, four economic and demographic variables thought to be indicative of the health of the population were applied to the prevalence of rheumatoid arthritis for each country included in the present study. The four variables consisted of gross domestic product-per capita, life expectancy of the total population, percentage of the population 65 years and older, and percentage of the population below the poverty line. Unfortunately none of the variables were found to be significant when using the Pearson Correlation and Linear Regression tests. Although, they were all found to have significant relationships when compared with each other, with the exclusion of the prevalence of rheumatoid arthritis.

Other factors were also explored in an effort to account for the difference in prevalence of rheumatoid arthritis between North American and non-North American ancestral groups, which included accessibility of health care, cultural values, problems with communication, attitudes and expectations towards modern medicine, and antiquity and etiology of rheumatoid arthritis. Of these, only cultural values and problems with communications were found to have any impact on the outcome of the prevalence studies.

ACKNOWLEDGEMENTS

I am happy to acknowledge the support of many individuals throughout the completion of this thesis. Several people of diverse backgrounds assisted me with my research and the editorial process. Thanks to Dr. Randall Skelton and Dr. Gregory Campbell of the University of Montana, and Dr. Herbert Swick of St. Patrick's Hospital for helping me bring the focus of my research into place and providing valuable editorial comments. Thanks to Dr. Kimber McKay for helping with ideas for my research and to David C. Smith for reviewing my work from an outsider's perspective. Thanks to Dr. Thomas Foor of the University of Montana for assisting with the statistical analysis and who will forever be my mentor, and to Dr. Mark Jacobson of Montana State University – Billings for helping me interpret some last minute data analysis. The University of Montana's Mansfield Library also needs to be acknowledged for making my research inexpensive and trouble-free. And finally a big thanks to my parents for giving me endless support regardless of whatever path I choose.

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CHAPTER I
INTRODUCTION

With the rise in life expectancy throughout the world and the advancements that have been made in modern medicine and medical technology, attention has been diverted from infectious diseases (communicable) to chronic diseases (non-communicable). No longer are chronic diseases affecting only individuals in developed countries. Their impact and burden is widespread and felt in many developing countries as well. The present study focuses on the group of chronic diseases known as musculoskeletal conditions, and more specifically on rheumatoid arthritis.

"Although the diseases that kill attract much of the public's attention, musculoskeletal conditions are the major cause of morbidity throughout the world, having a substantial influence on health and quality of life, and inflicting an enormous burden of cost on health systems" (World Health Organization 2003:1). Their importance is undervalued most likely because they are rarely fatal, are considered irreversible, and are usually associated with advanced age. According to the World Health Organization, "rheumatic diseases cause more pain and disability than any other group of conditions in developed countries, and the same pattern of morbidity is now being seen in the developing world" (WHO 2003:2). In the United States in 1997, "an estimated 16% of the population, or 43 million people, had some form of arthritis" (Reginster 2002:3) and as the age of the population increases so will the impact of arthritis on society. Rheumatoid arthritis affects between 2.1 and 2.5 million people in the United States (National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, American Medical Women's Association). Rheumatoid

arthritis has been shown to restrict "work capacity in a third of people within the first year" (Woolf and Akesson 2001:1080), with an average number of workdays lost between 2.7 and 30 annually (Reginster 2002:5). Within a decade of onset, rheumatoid arthritis may lead to a total cessation of employment in at least 51 percent of patients, and perhaps as many as 59 percent (WHO 2003). This decrease in work capacity is represented in the indirect costs of arthritis estimated at $47.8 billion by adding up the amount of pay lost due to absence from work. This is only part of the economic burden of arthritis, which is estimated to be $82.4 billion in the United States alone. The other $34.6 billion is spent on medical expenditures of the patient and health insurance companies, part of the direct costs of arthritis. These numbers are represented in the total economic burden of a disease, which consists of *direct costs*, such as the costs associated with medications, physician visits, hospital stays, and surgical procedures, *indirect costs*, such as loss of work productivity and chronic and short-term disability, and*intangible costs*, such as increased pain and reduced quality of life (Reginster 2002; Lubeck 2001).

Research and Goals

The goal of the present study is to locate a pattern among rheumatoid arthritis prevalence rates in three ancestral populations (Caucasoid, Negroid, Mongoloid) dependent upon their geographic location (North America, non-North America). Assessing geographic and racial/ethnic variation in disease occurrence is one way to find clues to the cause(s) of disease. This is important because rheumatoid arthritis has an unknown etiology or cause, and is becoming more and more of a burden to society. In addition to racial and ethnic differences, economic, demographic, socioeconomic and cultural factors will be considered in an attempt to explain the similarities and differences

in the prevalence of rheumatoid arthritis found between geographic regions. Racial and ethnic differences in health status are often linked to these factors in ways that are not always straightforward and are difficult to separate (Jordan 1999). This will be examined to determine ways in which the results of the prevalence studies included here may have been affected by this complexity.

Involvement

Musculoskeletal conditions affect hundreds of millions of people around the world and comprise about 150 diseases and syndromes. According to the World Health Organization, the conditions that have "the greatest impact on society include rheumatoid arthritis, osteoarthritis, osteoporosis, low back pain, and limb trauma" (WHO 2003). "Musculoskeletal impairments ranked number one in chronic impairments in the United States" (Woolf and Akesson 2001:1079) and on average they consume about three percent of total gross domestic product (GDP) in developed countries (WHO 2003). The economic impact these conditions have on society is also expected to rise in developed countries due to an ever increasing life expectancy and "to the predicted doubling of the number of people over 50 by the year 2020" (www.usbjd.org 2004). It is evident that some action needs to be taken to reduce this large burden.

Several organizations have gotten involved with this global dilemma and were created to help find answers to the questions scientists are asking about many musculoskeletal conditions. One of the largest initiatives recently created, in partnership with the World Health Organization, is the Bone and Joint Decade. "The Bone and Joint Decade is a global, multi-disciplinary initiative targeting the care of people with musculoskeletal conditions—bone and joint disorders. Its focus is on improving your

quality of life as well as advancing the understanding and treatment of those conditions through research, prevention and education" (www.usbjd.org 2004). The goals for the United States, initiated in part by the estimated $254 billion annual cost of musculoskeletal conditions in the United States, include (www.usbjd.org 2004):

- Raise awareness about the growing burden of musculoskeletal conditions
- Promote prevention and empowerment through educational programs
- Advance research in prevention, diagnosis and treatment
- Improve diagnosis and treatment

In 1981, the World Health Organization-International League of Associations for Rheumatology (WHO-ILAR) launched the Community Oriented Program for Control of Rheumatic Diseases (COPCORD). The primary objective of this program was to acquire data on the prevalence of rheumatic-musculoskeletal symptoms and disorders (RMS) in developing countries that have been neglected. Unfortunately many of the studies done by the WHO-ILAR did not meet all of the criteria established for the present study (see Chapter II) and subsequently could not be included.

The World Health Organization along with many research organizations on a smaller demographic scale such as the National Institute of Arthritis and Musculoskeletal and Skin Diseases, Arthritis and Rheumatism International, the Arthritis Foundation, and the American Rheumatism Association conduct research to help improve the lives of millions of people through prevention and treatment of arthritis and other musculoskeletal diseases.

Two other organizations that are of interest include the National Databank for Rheumatic Diseases (NDB) and the American Rheumatism Association Medical Information System (ARAMIS). Both organizations act as a longitudinal research databank for both rheumatology patients and physicians for rheumatoid arthritis,

osteoarthritis, fibromyalgia and other rheumatic diseases. Both are designed to improve treatment and outcome for patients afflicted with rheumatic diseases. But unlike the other organizations mentioned above, much of the data is collected from rheumatologists and their patients over many years (www.arthritis-research.org 2004; Fries and McShane 1986). While the mission of these organizations is of great significance, they may only prove beneficial to those who are able to reap the benefits. Factors such as culture, social status, wealth and education may limit many and prove far more important than any new treatment or technological innovation.

Background

Rheumatoid arthritis is a worldwide disease. Unfortunately the disease is not very well understood by the general public and is often confused with osteoarthritis. In order to fully comprehend the present study, it is necessary to have at least a general understanding of the disease process, how it may develop and whom it affects. This is discussed briefly and separated into sections examining the clinical features and diagnosis, pathology, etiology, classification, and antiquity of rheumatoid arthritis.

Clinical Features and Diagnosis of Rheumatoid Arthritis

Since the 'natural history' of rheumatoid arthritis is not completely understood, largely because of the unknown etiology, it is often difficult if not impossible for a physician to predict the outcome and course of the disease for any patient. However, the onset of rheumatoid arthritis can be more easily described with most patients having either a gradual onset with development of symptoms over a period of several weeks, abrupt and acute onset taking place over several days, or an isolated initial presentation.

It is difficult to determine what path or pattern the disease will take, but there are some factors that give clues to the prognosis. Factors that are in a patient's favor and may predict a positive outcome include an acute onset of the disease, periods of remission within the first year, and being of the male sex. At first thought, it seems contradictory that abrupt and severe attacks of rheumatoid arthritis could have a favorable prognosis for a patient but these patients usually seek medical advice from a rheumatologist much sooner than a patient with a slow gradual onset who may delay seeking treatment. A poor prognosis is associated with a gradual onset of the disease with large joint involvement, persistence for more than one year without remission, early appearance of bone erosions and rheumatoid nodules, and a positive rheumatoid factor (Lawrence and Shulman 1984; Hochberg et al. 2003).

In the early stages of rheumatoid arthritis many patients develop systemic symptoms such as fatigue, malaise and weight loss, while a select few develop "acute systemic toxicity with high fever, weakness and anemia" (Salter 1983:194). The disease mainly involves the joints, primarily those of the hands (metacarpophalangeal and proximal interphalangeal joints) and feet (metatarsophalangeal joints), and occasionally the larger joints such as the hips, knees, and shoulders as well as the elbows, ankles and vertebrae. This is characterized by pain and stiffness and most of all inflammation, which includes redness, swelling, heat, and loss of function. As the disease progresses these symptoms become more marked and are accompanied by muscle atrophy and tendon and ligament involvement, which leads to a rapid development of deformities in the joints involved (Salter 1983:194).

As mentioned earlier, rheumatoid arthritis is a systemic disease. Though it is generally thought to be a disease of the joints exclusively, it can affect many areas of the body. Many patients will undergo extraarticular manifestations such as malaise and fatigue but a small number will also experience inflammation in other organ systems as well. Some of these other systems include skin, ocular, respiratory, cardiac, gastrointestinal, renal, neurologic, and hematological manifestations. Risk factors that appear to influence the expression of these other manifestations include a positive rheumatoid factor, presence of rheumatoid nodules, and severity of the articular process (Schumacher et al. 1993:93).

Pathology of Rheumatoid Arthritis

The pathology of rheumatoid arthritis can be broken down into three stages (Lawrence and Shulman 1984). The first stage begins with the initiation of synovitis in the joints by the primary etiologic factor, which is still unknown. The synovium, normally a thin membrane, reacts to the inflammation by becoming edematous and protrudes into the joint cavity with villous projections. The next stage involves the immunologic events that occur because of the synovitis and perpetuate the initial inflammatory reaction. "The resultant immune process within the diseased synovium produces immune complexes which, in turn, activate a multitude of chemical mediators of inflammation" (Salter 1983:193). During this process hydrolytic enzymes are released that begin to destroy the proteoglycans and collagen of the cartilage matrix. The last stage is when the inflammatory reaction in the synovium is modified into a destructive granulation tissue called pannus. At this stage the joint ligaments and tendons may become softened and stretched which can lead to muscle atrophy, subluxation of the joint

and even dislocation. Subchondral bone becomes eroded at the margins of the joint producing areas of osteolysis and osteoporosis in the remaining bone. If this process continues long enough, fibrous adhesions may form that can eventually ossify leading to bony ankylosis.

Etiology of Rheumatoid Arthritis

A majority of the literature on rheumatoid arthritis focuses on the causal factors or etiology of the disease. As of yet the etiology is still unknown, although there are a host of factors that could be responsible. This is an important issue because in order to successfully treat the symptoms and put the inflammatory reaction into remission, an understanding of what is causing the disease must be known. These causal factors can be broken down into five broad categories: genetic, environmental, hormonal, immunologic and other.

Genetic Factors

Genetic studies have gained interest with scientists due to the observation of an increased risk of rheumatoid arthritis among relatives of those afflicted with the disease. For some patients, rheumatoid arthritis is sporadic while others can identify a family history. "Twin studies indicate that genetic factors may account for up to 60% of disease susceptibility in RA" (Ollier et al. 2001:29). These results are in regards to monozygotic (identical) twins, for dizygotic (fraternal) twins the percentage is less. This difference may be due to the fact that monozygotic twins share the same environment in the womb as well as similar conditions while maturing. Two studies done by Silman and Sanders on sibling pairs found that there is no greater similarity either in age of onset or calendar year of onset among siblings. This indicates that neither genetic nor environmental

factors were more important in explaining the development of rheumatoid arthritis and supports the idea that it occurs by chance (Silman and Hochbery 1993).

A relationship between human leukocyte antigen (HLA)-DR and rheumatoid arthritis has been known for over 25 years. Several studies conducted with many populations have revealed that a number of HLA-DRB1 alleles are associated with rheumatoid arthritis (Ollier et al, 2001). Unfortunately the only association that has been found is that it is more of a marker for indicating severity and chronicity rather than susceptibility. To date, no genes have been identified that code specifically for rheumatoid arthritis susceptibility as it is likely that it is a complex disease that may include multiple genetic and other factors.

Environmental Factors

Two groups of infectious agents, bacteria and viruses, have attracted the most attention where environmental causes of rheumatoid arthritis are concerned. To date "no organisms have been consistently recovered from synovial tissue or fluid" (Ollier et al. 2001:32) from patients with recent onset rheumatoid arthritis. One reason bacteria and viruses may be likely causes is because they can enter the blood stream and become lodged in the joint or articular cavity causing inflammation and an immune response to attack the foreign body. This immune reaction may perpetuate inflammation long after the infectious agent has disappeared in those with a predisposition for rheumatoid arthritis. No clear evidence of rheumatoid arthritis clustering in space or time has been found, but that does not negate the possibility that an infectious agent may trigger rheumatoid arthritis in some individuals (Ollier et al. 2001).

Numerous pathogens have been investigated including the Epstein-Barr virus, which has been extensively researched over several decades because of its effects on the immune system. Serologic evidence has shown that more than 80 percent of adults have had a previous infection and that the virus persists in the saliva and nasopharynx of about 20 percent of individuals (Lawrence and Shulman 1984). Those with rheumatoid arthritis have been found to have a greater frequency of antibodies to the Epstein-Barr virus in their blood. "Even though they may not have had a greater exposure to the EBV than others, rheumatoid patients may be unable to contain the organism, thereby allowing it to persist and produce disease" (Lawrence and Shulman 1984:116). Other infectious agents such as human parvovirus have gained attention as well as "numerous other microorganisms, not only viruses and bacteria but also protozoa with no overall conclusion" (Silman and Hochberg 1993:47).

Hormonal Factors

Results from several studies conducted all over the world on many different populations all have in common a female preponderance of rheumatoid arthritis. Clearly there is some hormonal risk factor at work here. Some have suggested that rheumatoid arthritis is associated with a low testosterone level in men and women, which would explain why the female to male ratio tends to even out with advanced age (Ollier et al. 2001). Therefore male hormones may be protective against rheumatoid arthritis. A problem with this conclusion is that rheumatoid arthritis may suppress testosterone, so it is difficult to say whether it is a cause or an effect (Silman and Hochberg 1993).

Pregnancy has been shown to have protective effects against developing rheumatoid arthritis and many who already have the disease go into remission during

pregnancy. The postpartum period on the other hand is a time of increased susceptibility. The oral contraceptive pill has been shown in several studies not to reduce the risk of developing rheumatoid arthritis, but to modify the disease process into a milder form and delay the onset for many years (Spector 1990). This theory is reinforced by the fact that the age of onset of rheumatoid arthritis in women is becoming higher while it remains stable in men (Ollier et al. 2001). Estrogen replacement therapy has also been investigated, although not nearly as extensively as the oral contraceptive pill. To date, no conclusions have been made whether the therapy has any effect on the development or management of rheumatoid arthritis.

Immunologic Factors

The features of rheumatoid arthritis are suggestive of an abnormal immune system or one that is hypersensitive and persistent. About 70 percent of patients with rheumatoid arthritis test positive for rheumatoid factor by serological means. For some, they initially test negative for rheumatoid factor but develop it as the disease progresses. Claiming that a positive rheumatoid factor is a marker for developing rheumatoid arthritis is rather premature since it may also "occur in a variety of unrelated connective tissue diseases" (Salter 1983:192) as well as in about three percent of healthy individuals that never develop rheumatoid arthritis (Schumacher, 1993:87). From studies done on animals, elevated levels of rheumatoid factor are generated in times of chronic infection to enhance the killing of microorganisms but may also cause inflammatory cell activation and alter the immune complexes. "The available data suggest that rheumatoid factors may play a role in amplifying rheumatoid inflammation but that they are not a primary triggering or etiologic factor" (Schumacher et al. 1993:87).

Other Factors

Some other factors that have been explored that may predispose an individual to develop rheumatoid arthritis include psychological stress, trauma, diet, smoking, alcohol consumption, obesity, infection, and immunization. Some have claimed that a psychologically stressed, anxious, or depressed person is more prone to develop rheumatoid arthritis. In reality these personality traits are more likely a result of having the disease (Salter 1983). Physical trauma has also been linked to rheumatoid arthritis, but these studies have problems with interpretation. Diet is of considerable interest to rheumatoid arthritis patients but little has been done in the area of etiology. Omega-3 fatty acids have been shown to reduce inflammation and can have a favorable outcome in those with rheumatoid arthritis. The trace element selenium is low in patients with rheumatoid arthritis and "although this could be a result of disease activity it might be of aetiological importance given that selenium probably has antiviral and anti-inflammatory effects" (Silman and Hochberg 1993:44). The effects of smoking and rheumatoid arthritis have been conflicting and no conclusions have been made. Alcohol consumption was found to be protective against rheumatoid arthritis in women in two studies and several studies have found that obese individuals were at a higher risk although the "US Nurses' Health study found no association between body mass index and RA" (Ollier et al. 2001:32). Cases of individuals developing rheumatoid arthritis after having an infection such as parvovirus and rubella have been documented. Also some immunizations such as rubella, tetanus and influenza, may have triggered rheumatoid arthritis in a few patients (Ollier et al. 2001).

Classification of Rheumatoid Arthritis

Since the etiology of rheumatoid arthritis is unknown, it was necessary to create a broad description of the disease to be used for classifying patients to establish uniformity for studies conducted worldwide. It was not until the first set of criteria for the diagnosis of rheumatoid arthritis were established in 1958 by the American Rheumatism Association (formerly the American College of Rheumatology), did a firm definition of the disease become utilized and accepted worldwide.

Establishing a set of criteria proved to be a difficult task since many symptoms are non-specific to rheumatoid arthritis and the cause of the disease has not been discovered. So the criteria were designed to include a patient in one category or another rather than for making a firm diagnosis. The diagnostic criteria established in 1958 included three categories of rheumatoid arthritis: definite, probable and possible. Patients were assigned to a category based on the number of criteria they fulfilled (Ropes et al. 1957). Two years later, a revised version of the 1958 criteria were announced adding another category, classical, which required a patient to fulfill even more criteria to be considered as having 'classical rheumatoid arthritis'. The 1958 revised criteria include the following:

- Morning stiffness
- Pain in at least one joint
- Swelling in at least one joint
- Swelling in at least two joints
- Symmetrical joint swelling
- Rheumatoid nodules
- X-ray changes
- Serum rheumatoid factor
- Synovial fluid precipitate
- Histological changes in synovium
- Histological changes in nodules

In 1961, a symposium on *Population Studies in Relation to Chronic Rheumatic Diseases* was held in Rome by the American Rheumatism Association to develop another set of diagnostic criteria, commonly called the Rome Criteria. The major differences between the 1961 and 1958 criteria are that the 1961 Rome criteria include a way to diagnose those patients who have inactive rheumatoid arthritis at the time of the study and also eliminate the need to examine histologic changes and synovial fluid which are both not easily obtained from patients (Bunim et al. 1962). The 1961 Rome criteria include the following:

- Morning stiffness
- Pain in at least one joint
- Swelling in at least one joint
- Swelling in at least two joints
- Symmetrical joint swelling
- Rheumatoid nodules
- X-ray changes
- Serum rheumatoid factor

In 1966, a symposium on *Population Studies in the Rheumatic Diseases* was held in New York by the American Rheumatism Association to further refine the diagnostic criteria for rheumatoid arthritis. While trying to establish the new criteria, commonly called the New York criteria, the scientists "stressed the importance of standardization of laboratory and radiologic techniques so that subsequent individual comparisons in longitudinal studies, and group comparisons between different studies could be made with confidence" (Bennett and Burch 1967:453). Basically the New York criteria laid out all of the appropriate steps to follow for testing for rheumatoid factor as well as recommended X-rays that should be taken and the methods to follow. Unfortunately the 1966 New York criteria could not be located.

And finally, the most recently published diagnostic criteria for rheumatoid arthritis were developed by the American Rheumatism Association in 1987. Two decades had passed since the establishment of the New York criteria in 1966 and knowledge and understanding of rheumatoid arthritis had increased since that time warranting an adjustment once again. Major revisions of the criteria include eliminating the categories of 'classical', 'definite', 'probable' and 'possible' which seemed to overlap and falsely diagnose patients, removal of procedures that required invasive techniques such as synovial biopsy, and an increase in specificity by combining criteria and decreasing the need for any additional criteria (Arnett et al. 1988). The 1987 revised criteria include the following:

- Morning stiffness
- Arthritis of 3 or more joints
- Arthritis of hand joints
- Symmetric arthritis
- Rheumatoid nodules
- Serum rheumatoid factor
- Radiographic changes

Antiquity of Rheumatoid Arthritis

Rheumatoid arthritis (RA) has become a major health concern across the globe in the past few decades and has led to a profound interest regarding whether it is a relatively modern disease (seventeenth century) or whether it substantially predates this estimate. The consensus appears to be leaning towards a New World origin of some antiquity, but there is still much to be explored before this debate can be settled or confirmed. Many scientists have looked towards medical journals and writings of antiquity, paintings, and more recently paleopathological finds to help solve these questions, all of which will be explored in the following paragraphs.

Medical Journals and Writings of Antiquity

Several early published medical journals have described many symptoms that are indicative of rheumatoid arthritis. These include but are not limited to works by Sydenham in 1676, Alonso Lopez de Hinojosos in 1578, various works by classical Greek and Roman authors, Julius Caesar's chief medical officer Scribonius Largus, Hippocrates in 460 BC, Galen, and Soranus of Ephesus in the second century (Buchanan 1994; Hochberg et al. 2003; Short 1974). Debate has ensued over who was actually the first to describe the symptoms of rheumatoid arthritis but many of these early writings are more likely a description of gout rather than rheumatoid arthritis. Of the medical writings that were published from the seventeenth century until the present, there is some agreement that in 1800 Landre-Beauvais was the first to distinguish rheumatoid arthritis from gout and other rheumatic conditions (Hochberg, et al. 2003). However it did take several decades for the disease to become clearly defined and even Sir Alfred Baring Garrod who coined the term 'rheumatoid arthritis' in 1859 was still lumping together osteoarthritis and rheumatoid arthritis in the same category. It was not until the American Rheumatism Association established a set of diagnostic criteria for rheumatoid arthritis in 1958 (discussed above), did a firm definition of the disease become accepted worldwide.

Paintings

Scientists have also begun to research paintings from Europe dated prior to the nineteenth century to look for evidence of rheumatoid arthritis. Two earlier examples from the fifteenth century come from Justus van Gent who painted Federico da Montefeltro, and Botticelli of a young man, both of which depict rather disfigured or

swollen hands. A painting of Erasmus from Rotterdam in the sixteenth century portrays swelling of three metacarpophalangeal joints on his right hand. Although written records are suggestive of a different rheumatic disease, probably seronegative spondyloarthropathy. In the seventeenth century a family painting by Jacob Jordaen includes the maidservant who has swelling of the metacarpophalangeal and proximal interphalangeal joints on both hands, very typical of rheumatoid arthritis. Several other paintings from the sixteenth and seventeenth centuries that may possibly depict rheumatoid arthritis are 'Siebrandus Sixtius', 'The Temptation of St. Anthony', and 'The Donators' (Hochberg et al. 2003). It is also important to note that many of these paintings containing possible representations of rheumatoid arthritis may actually be the artists' own interpretation or the artistic styles of the period and not medically accurate.

Paleopathological Evidence

Only a short time ago it was accepted that undeniable evidence of rheumatoid arthritis had not been found to be present on any skeletal remains before the eighteenth century. Recent finds from several archaeological excavations have revealed new information on the history of this disease. Skeletal remains of archaic Indians from 6500 to 450 BC exhibited symmetrical joint erosions most commonly involving the metacarpophalangeal, metatarsophalangeal and proximal interphalangeal joints and also was found in the shoulders and other large joints. As with modern rheumatoid skeletons, similar erosions were found and women were more commonly affected than men. Because of this discovery, it has been proposed that rheumatoid arthritis originated in the West branch of the Tennessee River in northwest Alabama and Tennessee because of the concentration in this region (Hochberg et al. 2003). A late archaic Indian group from the

Green River Region in West Central Kentucky dated from 4300 to 4050 years ago was also found to have symmetrical erosions in the hand and foot joints consistent with a diagnosis of rheumatoid arthritis (Rothschild and Woods 1990). Rothschild has claimed that rheumatoid arthritis was "confined to the Tennessee River Valley area until the Woodland period and only later expands to other parts of North America, and eventually the world" (Bridges 1992: 84). Contact with European immigrants did not occur in this region until the eighteenth century, which is consistent with the time rheumatoid arthritis is to have spread to the Old World (Buchanan 1994).

Bridges argues that the rheumatoid arthritis-like "disease seen in pre-Columbian America may not have been true RA, but may instead have been caused or triggered by an infective agent. A variety of bacterial, viral, and even parasitic diseases have been known to cause rheumatoid symptoms" (Bridges 1992:84). Another problem is trying to distinguish rheumatoid arthritis from other arthritic conditions as well as the possibility that an individual may have more than one condition that may cover up or mask lesions from rheumatoid arthritis (Merbs 1992). These conjectures make the evidence produced to date of the existence of rheumatoid arthritis in the New World thousands of years earlier than it appeared in the Old World seem less convincing.

Proof of rheumatoid arthritis in Europe before the eighteenth century has been sparse and difficult to prove, but a lack of evidence cannot substantiate claims that it did not exist before that time. In two of eleven skeletons founds during an excavation of a Neolithic burial site (2500 – 1900 BC) on the island of Gotland, Sweden "multiple and remarkable peripheral articular changes were found" (Leden et al. 1988:342). The scientists concluded that the skeletons had an arthritic condition that is consistent with

rheumatoid arthritis, but cannot rule out some other arthritic conditions (Leden et al. 1988). A complete absence of rheumatoid arthritis in Old World archaeological sites during the time period corresponding to the Woodland period in North America (Valle de Petit Morin, France 8000-4000 BP; Tessa Hasar, Iran 7000 BP; Von Luschen's, Egypt 3000 BP; Negev caves, Israel 1900 BP; Meroitic Nubian, Sudan 1600-1200 BP) helps to validate the claim that rheumatoid arthritis is a New World disease (Rothschild and Woods 1992).

After reviewing the evidence from written records, works of art and skeletal remains, it appears as though rheumatoid arthritis is not a new disease and may have originated before the eighteenth century, at least in the New World. As to whether it was present in the Old World before the eighteenth century is less clear, as the evidence gathered to date is rather limited.

Conclusion

Rheumatoid arthritis is a multifaceted disease that is largely misunderstood by the public who usually confuse it with osteoarthritis or degenerative joint disease. Unfortunately much of the etiology of rheumatoid arthritis is unknown by researchers and rheumatologists as well. This lack of knowledge and the increasing number of people afflicted with the disease has initiated many studies, such as the present study, in search of clues to help us understand this complex disease.

Hypotheses

Hypothesis 1: The prevalence of rheumatoid arthritis will be lower among the ancestral groups of North American when compared to ancestral groups living on other continents due to the advanced health care available in North America, and more specifically the United States.

Hypothesis 2: The prevalence of rheumatoid arthritis can be partially explained by carefully selected economic and demographic variables for each country addressed in this study.

Hypothesis 3: Studies conducted on the prevalence of rheumatoid arthritis will be influenced by factors that are often not given adequate consideration.

Summary of Chapters

This paper is divided into five parts. Chapter I, the current chapter, provides an introduction to this study and goals of the research. Statistics on the burden of rheumatoid arthritis and the growing interest by several organizations are also included to establish the necessity of the present study. In addition, Chapter I provides a detailed literature review to provide a general understanding of what rheumatoid arthritis is, how it may develop, the disease process, and whom it affects. This is broken down into sections examining the clinical features and diagnosis, pathology, etiology, classification, and antiquity of rheumatoid arthritis. Chapter II begins with a review of the criteria established to make the comparison of data more reliable and consistent. An explanation about the placement of each population into an established ancestral group and subgroup is also given. This is necessary to provide the reader with some insight into why certain populations were grouped together. In addition, Chapter II introduces the data and

statistics used in the present study, most of which were obtained from the CIA World Factbook online. This is presented in the form of tables and figures. Chapter III applies a statistical analysis to the data introduced in Chapter II. Chapter IV discusses how the prevalence of rheumatoid arthritis varies between different parts of the world and is influenced by economics, cultural values, communication, and expectations. Chapter V presents a summary and conclusion regarding the factors discussed in Chapter IV and how the prevalence studies included here may have been affected as a result of these factors.

CHAPTER II
MATERIALS AND METHODS

Many prevalence studies have been conducted all over the world, but to date none have specifically compared the United States with other countries. This is surprising since studies on geography and prevalence of rheumatoid arthritis have been carried out for over 40 years. The present chapter begins to address this gap in information.

Prevalence versus Incidence

Before beginning the research phase, it was necessary to determine which measurement was most appropriate for the goal of the present study, prevalence or incidence. The World Health Organization has conducted many prevalence studies on rheumatoid arthritis in countries where such data was previously lacking, hoping to fill the gap in information. Many studies have also been performed on the incidence of rheumatoid arthritis, which measures "the number of *new* cases of a disease in a population over a period of time" (Mausner and Bahn 1974:126). While this is of some significance, the prevalence rate is the first factor to take into account when considering the importance of medical issues and is described as a measure of "the number of people in a population who *have* the disease at a given point in time" (Mausner and Bahn 1974:127). Prevalence is also more suited for the present study because it

> "depends on two factors: how many people have become ill in the past and the duration of their illnesses. Even if only a few people in a group become ill each year, if the disease is chronic the number will mount and the prevalence will be relatively large in relation to incidence. On the other hand, if the illness under consideration is of short duration (acute) because of either recovery or death, or if there is migration of ill persons from the area, then prevalence will be relatively low" (Mausner and Bahn 1974:127).

In summary, "prevalence is affected by factors which influence the duration of a disease as well as its development" (Mausner and Bahn 1974:128), which in the present study will be higher than incidence since rheumatoid arthritis is a chronic disease that is rarely fatal. A higher rate may also cause differences and similarities in prevalence to stand out more abruptly.

Criteria

A vast amount of published literature addresses the prevalence of rheumatoid arthritis in countries from all parts of the world. Scientists are looking at several populations because they are interested in studying how rheumatoid arthritis affects different populations living in different environments. This study addresses this issue as well. To make a comparison of the literature more reliable and consistent for this study, six criteria were established.

The first criterion is that each study must have adhered to the American Rheumatism Association (formerly American College of Rheumatology) diagnostic criteria for rheumatoid arthritis. Either the 1958, 1961, 1966 or 1987 versions can be used. All have similar criteria and overlap in many respects, each becoming more straightforward and refined for easier replication for use in population studies. The second criterion is each study must encompass a broad age range to ensure a representative sample of the entire population. If the age range is too narrow, the prevalence may be much higher than those that have a much more broad age range and may skew the results when comparing studies. The third criterion is the sample population used in each study must be random or household-to-household to ensure a representative sample of the total population of the area defined. Those studies that rely

only on medical records from local hospitals are biased towards those that seek medical attention. They neglect the portion of the population that cannot afford to seek such medical services or do not seek medical care for other reasons. In many developing countries those that do not seek medical attention could account for a majority of the population. Even in the United States this may represent a significant amount of the population. The fourth criterion to be included is each study must identify the population they are studying. If more than one population is being examined in a study then percentages of racial/ethnic groups must be presented and the prevalence of rheumatoid arthritis must be given for each. The fifth criterion is each study must include the number of individuals represented in the study and the number of individuals found to have rheumatoid arthritis. This information is crucial in order to obtain an accurate average for each subgroup and country or population with multiple prevalence rates. Finally the last criterion is each study must have utilized x-rays and serological tests to help confirm the diagnosis of rheumatoid arthritis. X-rays are needed in order to look for joint involvement or find rheumatoid nodules. Serological tests are necessary to test for rheumatoid factor on at least a portion of the individuals involved in the study to further establish the presence or absence of the disease in certain individuals. The need for x-rays and serological tests is included in the diagnostic criteria discussed later in this chapter, yet some studies fail to perform these tests because of cost or inconvenience. Once these six criteria were applied to each of the 86 studies that were discovered during the research phase, the number was reduced to 34. Each of the 34 population studies included follow similar procedures and guidelines to warrant a sound comparison between them. Those that did not meet just one of the six criteria were excluded from

this study. A majority of the prevalence studies on rheumatoid arthritis were not included because they did not meet all of the criteria established for the present study. Some of these may have actually met all of the criteria but were too vague and excluded some necessary information. For further details on the methods used in each study, the papers by the original authors should be consulted (see References Cited).

Patient Assessment

In order for a population study to be included in the present study, a clinical, radiological, and serological assessment had to have been described in the published data, as discussed above under criterion six. Not all of the participants surveyed for each study were assessed and a legitimate reason must have been provided to explain why some participants did not undergo a full clinical, radiological and serological assessment. Some studies neglected to provide such information and were therefore excluded from the present study. The following describes what is involved in each assessment.

Clinical Assessment

Every prevalence study included in the present study performed a clinical assessment of each patient to determine whether or not they have rheumatoid arthritis. This examination was usually held in a patient's home while conducting a household-to-household survey. Healthcare workers, nurses and/or rheumatologists, who attended a training course on the proper procedures to conduct consistent interviews and examinations of each patient, usually conducted the clinical assessment. The clinical assessment usually included an examination of the hands and/or feet for signs of tender or swollen joints. A personal interview with each patient was conducted as well to assess their overall condition.

Radiological Assessment

A radiological assessment needed to be performed to be included in the present study. Most of these examinations were conducted in patient's homes, although some of the studies required participants to visit a clinic or hospital for evaluation. At least half of the patients in each study or those that required further evidence of rheumatoid arthritis had x-rays taken of the hands and/or feet with some including larger joints as well. The Atlas of Standard Radiographs of Arthritis was used in many of the studies to assess the grade or severity of deformity of the joints. This also helped to establish some consistency between studies when reading radiographs.

Serological Assessment

Finally, a serological assessment needed to be performed to be included in this study. As with the radiological assessment, most of the serological tests were conducted in patient's homes, although some studies required attendance at a local clinic or hospital. At least half of the patients or those that required further evidence to demonstrate the presence of rheumatoid arthritis had serological tests in each study. Serological tests were mainly performed to test for the presence of rheumatoid factor although some studies included results of tests associated with rheumatoid arthritis but not an indicator for it. Some of the tests that indicate the presence of rheumatoid factor include the bentonite flocculation test (BFT), the human erythrocyte agglutination test (HEAT), the latex fixation test (LFT), and the sheep cell agglutination test (SCAT). The use of any one of these tests allowed a prevalence study to be included in the present study.

Table 2.1 lists each prevalence study that met all of the criteria discussed above and as a result was included in the present study. Information about each study including

the country or population, year of the American Rheumatism Association diagnostic criteria used, age of the population surveyed, how the sample population was surveyed, the prevalence of rheumatoid arthritis, and the author(s) are given.

Table 2.1 – Prevalence Studies

Country	Criteria	Age	Sample	Prevalence of RA (%)	Author(s)
South Africa	1961	15+	Random	0.87	Beighton et al
South Africa	1961	18+	Random	2.2	Meyers et al
South Africa	1961	15+	Random	3.3	Solomon et al
Nigeria	1987	15+	Random	0	Silman et al
Lesotho	1961	15+	Random	1.8	Moolenburgh et al
United States	1958	18-79	Random	3.1	US Dept of Health
Ireland	1987	18+	Random	0.5	Power et al
England	1958	15+	Random	4.3	Lawrence
Spain	1987	20+	Census	0.5	Carmona et al
United Kingdom	1987	16+	Random	1.2	Symmons et al
India	1987	17+	Household	0.75	Malaviya et al
Iraq	1956	16+	Random	1.3	Al Rawi et al
Oman	1987	16+	Household	0.36	Pountain
Pakistan	1987	15+	Household	0.55	Farooqi and Gibson
Pakistan	1958	16+	Random	0.14	Hameed and Gibson
Saudi Arabia	1987	16+	Random	0.22	Al Dalaan et al
Brazil	1987	17+	Random	0.62	Senna et al
Cuba	1987	17+	Stratified	2.7	Llerena et al
Puerto Rico	1958	15+	Total	0.92	Mendez-Bryan et al
United States	1958	18-79	Random	3.2	US Dept of Health
China	1958	20+	Register	0.34	Wigley et al
China	1958	20+	Register	0.32	Wigley et al
Taiwan	1958	20+	Random	0.26	Chou et al
Taiwan	1958	20+	Random	0.78	Chou et al
Taiwan	1958	20+	Random	0.93	Chou et al
China	1987	17+	Household	0.35	Lau et al
China	1987	16+	Random	0.47	Dai et al
Vietnam	1987	16+	Random	0.28	Hoa et al
China	1961	18+	Household	0.3	Beasley et al
Japan	1961	15+	Random	0.3	Shichikawa et al
Indonesia	1956	15+	Total	0.4	Darmawan et al
Thailand	1987	15-90	Random	0.12	Chaiamnuay et al
Chippewa	1958	18+	Members	7.1	Harvey et al

Eskimos	1987	20+	Register	1.4	Boyer et al
Eskimos	1987	20+	Register	0.6	Boyer et al
Eskimos	1987	20+	Register	1.5	Boyer et al
Eskimos	1987	20+	Register	0.5	Boyer et al
Blackfeet	1958	30+	Total	4.1	Bunim et al
Pima	1958	30+	Total	5.4	Bunim et al
Pima	1961	20+	Total	5.3	Del Puente et al
Pima	1958	15+	Total	3.3	Jacobsson et al
Pima	1958	15+	Total	2.75	Jacobsson et al
Pima	1958	15+	Total	2.05	Jacobsson et al
Pima	1961	15+	Total	5.2	Henrard et al
Pima	1966	15+	Total	5.9	Henrard et al
United States	1958	18-79	Random	4.8	US Dept of Health

Ancestral Group and Subgroup Division

In order to make analysis possible, each population of study had to be placed into specified ancestral groups of *Caucasoid, Negroid or Mongoloid* (Bass 1995). These ancestral groups are already well-established anthropological terms and are based on geographical origins, not skin color (White 2000). They are often used for human identification and are appropriate for the present study to distinguish populations of individuals. In keeping with the terms of this study, each ancestral group was further divided into two subgroups based on where each population study was held. These subgroups are North America and non-North America for each ancestral group.

Population studies included in the *Caucasoid* group include the following countries: Ireland, England, Spain, United Kingdom, India, Iraq, Oman, Pakistan, Saudi Arabia, Cuba, Puerto Rico, Brazil, and the United States. These were further subdivided into two categories: *North America* and *non-North America.* Cuba, Puerto Rico and the United States are included in the *North American* subgroup. Cuba's population as stated in the prevalence study conducted there, was 72.6 percent white (Caucasoid). Puerto Rico's population according to the CIA World Factbook for 2004 is 80.5 percent white

(Caucasoid). Those numbers are high enough to be included in the *Caucasoid North American* subgroup. Ireland, England, Spain, United Kingdom, Brazil, India, Iraq, Oman, Pakistan and Saudi Arabia are part of the *non-North American* subgroup. India's population presented in the study conducted there was considered to be more closely related to *Caucasoid* and so it is included in the *Caucasoid non-North American* subgroup (Malaviya et al. 1993). Brazil's population according to the CIA World Factbook for 2004 is 55 percent white (Caucasoid) and 38 percent mixed black (Negroid) and white (Caucasoid), adequate to be included in the *Caucasoid* group. The most logical ancestral group category to place Iraq, Oman, Pakistan and Saudi Arabia seemed to be *Caucasoid* for they share the closest affinity (Quintana-Murci et al. 2004).

Population studies included in the *Negroid* group include the following countries: South Africa, Nigeria, Lesotho and the United States. These were further subdivided into two categories: *North America* and *non-North America*. Only one study conducted in the United States is included in the *Negroid North American* subgroup. The studies conducted in Nigeria, Lesotho and South Africa are part of the *non-North American* subgroup.

Population studies included in the *Mongoloid* group include the following countries: Vietnam, Thailand, Indonesia, Japan, Taiwan, China, and will all be contained within the subgroup of *Mongoloid non-North American*. Other population studies that will be included in the *Mongoloid* group include: Chippewa, Eskimos, Blackfeet, Pima, and the United States, which are all part of the subgroup of *Mongoloid North American*. The decision was made to classify Native Americans as part of the *Mongoloid* ancestral

group because they are the likely closest genetic match, as Native Americans are thought to have originally migrated from Asia to North America (Dugoujon et al. 2004).

Table 2.2 is a list of each country or population used in this study along with the corresponding prevalence for each. Although 46 prevalence scores are listed only 34 studies were actually used. This difference is due to the fact that some studies were conducted on more than one population or were done at several intervals over many years giving multiple results. The ancestral group for which each country or population has been assigned is also listed. As discussed above, the ancestral groups are *Negroid, Caucasoid,* and *Mongoloid.* Along with the ancestral group, the two subgroups to which each population is assigned are also given which include *North American* and *non-North American.*

Table 2.2 – Groups and Subgroups

	Country	Prevalence of RA (%)	Ancestral Group	Subgroup
1	South Africa	0.87	Negroid	non-North American
2	South Africa	2.2	Negroid	non-North American
3	South Africa	3.3	Negroid	non-North American
4	Nigeria	0	Negroid	non-North American
5	Lesotho	1.8	Negroid	non-North American
6	United States	3.1	Negroid	North American
7	Ireland	0.5	Caucasoid	non-North American
8	United Kingdom	4.3	Caucasoid	non-North American
9	Spain	0.5	Caucasoid	non-North American
10	United Kingdom	1.2	Caucasoid	non-North American
11	India	0.75	Caucasoid	non-North American
12	Iraq	1.3	Caucasoid	non-North American
13	Oman	0.36	Caucasoid	non-North American
14	Pakistan	0.55	Caucasoid	non-North American
15	Pakistan	0.14	Caucasoid	non-North American
16	Saudi Arabia	0.22	Caucasoid	non-North American
17	Brazil	0.62	Caucasoid	non-North American
18	Cuba	2.7	Caucasoid	North American

19	Puerto Rico	0.92	Caucasoid	North American
20	United States	3.2	Caucasoid	North American
21	China	0.34	Mongoloid	non-North American
22	China	0.32	Mongoloid	non-North American
23	Taiwan	0.26	Mongoloid	non-North American
24	Taiwan	0.78	Mongoloid	non-North American
25	Taiwan	0.93	Mongoloid	non-North American
26	China	0.35	Mongoloid	non-North American
27	China	0.47	Mongoloid	non-North American
28	Vietnam	0.28	Mongoloid	non-North American
29	China	0.3	Mongoloid	non-North American
30	Japan	0.3	Mongoloid	non-North American
31	Indonesia	0.4	Mongoloid	non-North American
32	Thailand	0.12	Mongoloid	non-North American
33	Chippewa	7.1	Mongoloid	North American
34	Eskimos	1.4	Mongoloid	North American
35	Eskimos	0.6	Mongoloid	North American
36	Eskimos	1.5	Mongoloid	North American
37	Eskimos	0.5	Mongoloid	North American
38	Blackfeet	4.1	Mongoloid	North American
39	Pima	5.4	Mongoloid	North American
40	Pima	5.3	Mongoloid	North American
41	Pima	3.3	Mongoloid	North American
42	Pima	2.75	Mongoloid	North American
43	Pima	2.05	Mongoloid	North American
44	Pima	5.2	Mongoloid	North American
45	Pima	5.9	Mongoloid	North American
46	United States	4.8	Mongoloid	North American

Figure 1 shows the mean prevalence for each country and population used in this study. Countries and populations that have multiple studies conducted are represented by the average of those scores. As shown in Table 2.2, some groups and subgroups are well represented with several different studies contributing to the average, while others may contain only one study or prevalence score making the average less reliable.

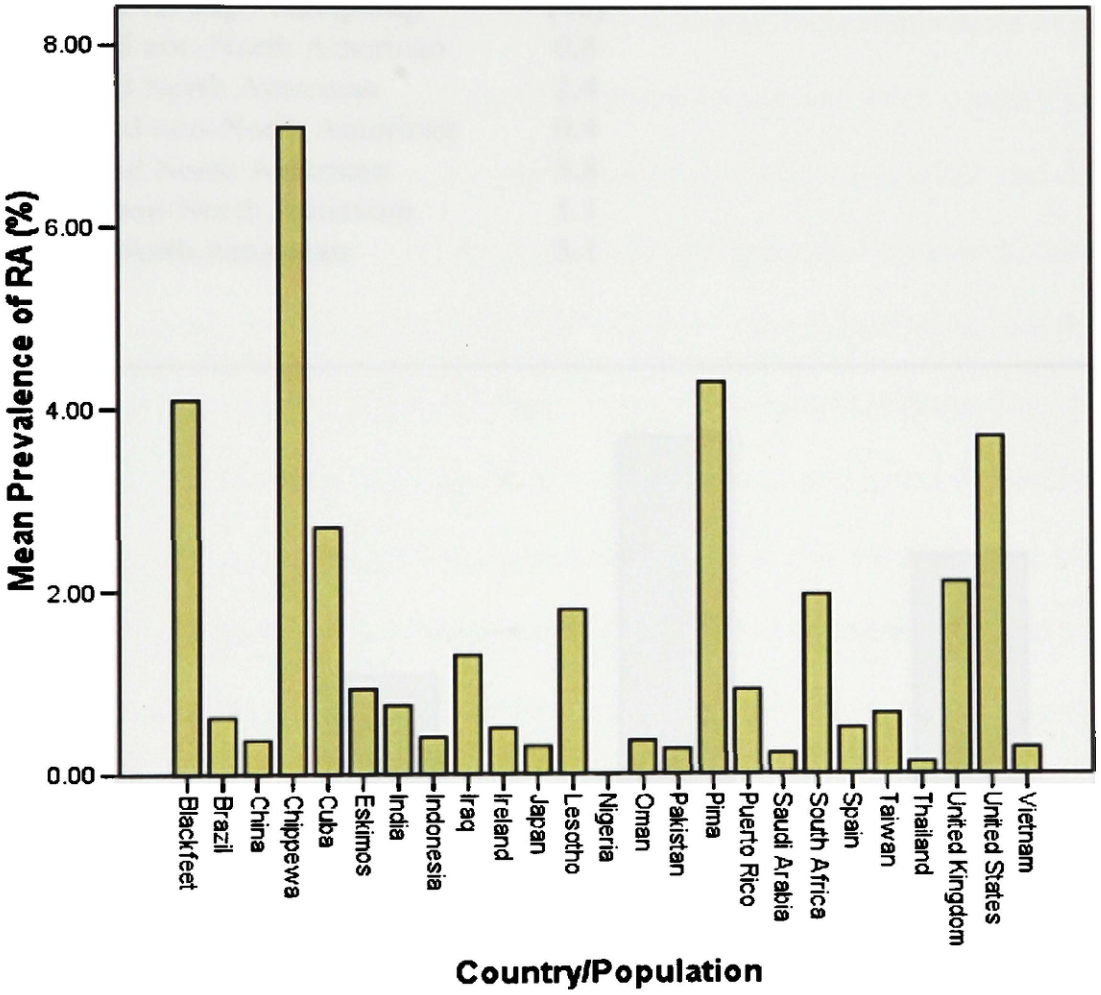

Figure 1 – Average Prevalence of RA per Country/Population

Table 2.3 lists the six ancestral group and subgroup combinations and the average prevalence of rheumatoid arthritis for each. Figure 2 displays the difference in prevalence of rheumatoid arthritis for each of the six groups/subgroups. The prevalence for each group/subgroup is the average of all the scores for that grouping.

Table 2.3 – Prevalence of RA per Group/Subgroup

Ancestral Group / Subgroup	Prevalence (%)
Caucasoid non-North American	0.8
Caucasoid North American	2.4
Mongoloid non-North American	0.4
Mongoloid North American	3.8
Negroid non-North American	1.1
Negroid North American	3.1

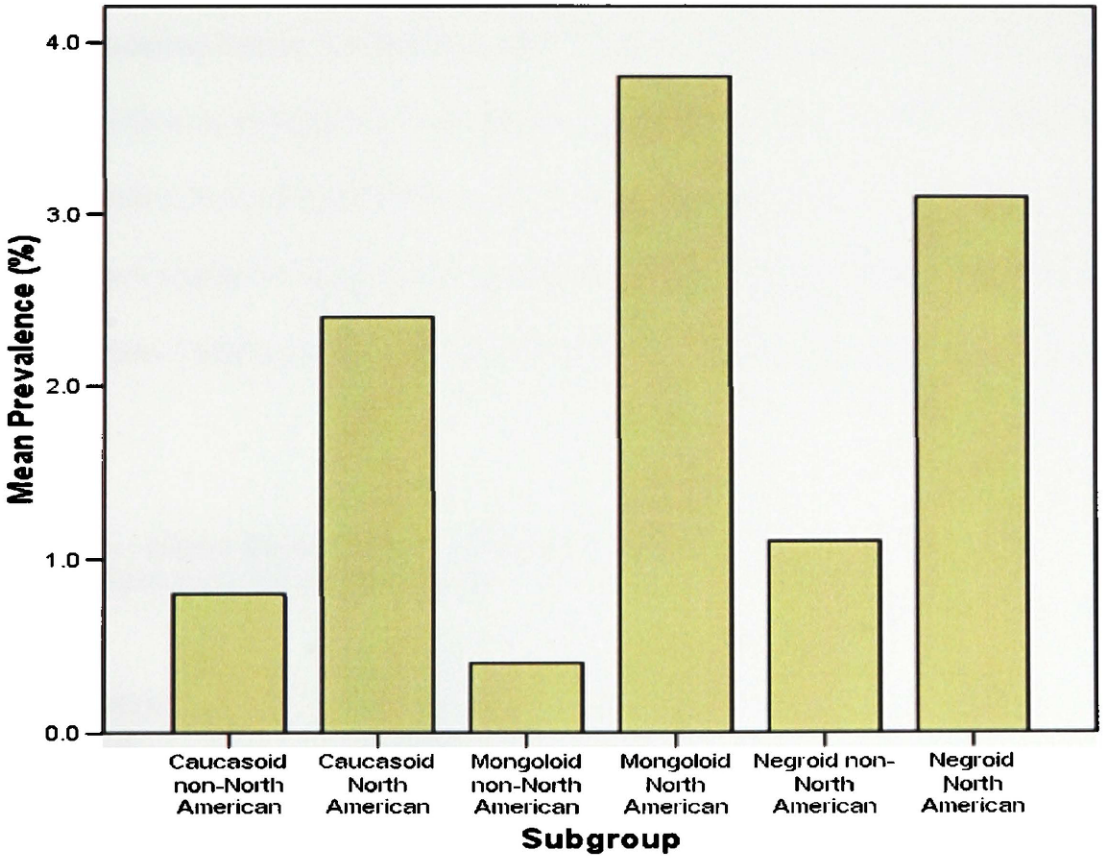

Figure 2 – Average Prevalence of RA per Group/Subgroup

Economic and Demographic Data

It initially appears as though there is an increased prevalence of rheumatoid arthritis in every ancestral group for North America, as compared to non-North American ancestral groups. But the prevalence rate is not telling the whole story of rheumatoid arthritis. There is more to this matter than simply claiming that Americans have an increased prevalence of rheumatoid arthritis. Various economic and demographic issues for each population must be considered when assessing these differences in prevalence.

Numerous statistics and data are available for almost every country in the world, but for the present study only a few select economic and demographic variables are needed. The variables consist of the gross domestic product - per capita, the life expectancy of the total population, the age structure of the population, and the percentage of the population below the poverty line. These were chosen because they measure the quality of life in a country and can affect key socioeconomic issues (www.cia.gov 2004).

Table 2.4 is a list of all the countries included in this study and the gross domestic product - per capita for each of those countries as stated by the CIA World Factbook for 2004. Figure 3 displays the gross domestic product - per capita for each country used in this study.

Table 2.4 – Gross Domestic Product-per capita
(Source: 2004 CIA World Factbook)

	Country	GDP-per capita
1	Ireland	29,800
2	Spain	22,000
3	United Kingdom	27,700
4	India	2,900
5	Iraq	1,600
6	Oman	13,400

7	Pakistan	2,100
8	Saudi Arabia	11,800
9	Brazil	7,600
10	Cuba	2,800
11	Puerto Rico	16,800
12	United States	37,800
13	South Africa	10,700
14	Nigeria	800
15	Lesotho	3,000
16	China	5,000
17	Taiwan	23,400
18	Vietnam	2,500
19	Japan	28,000
20	Indonesia	3,200
21	Thailand	7,400

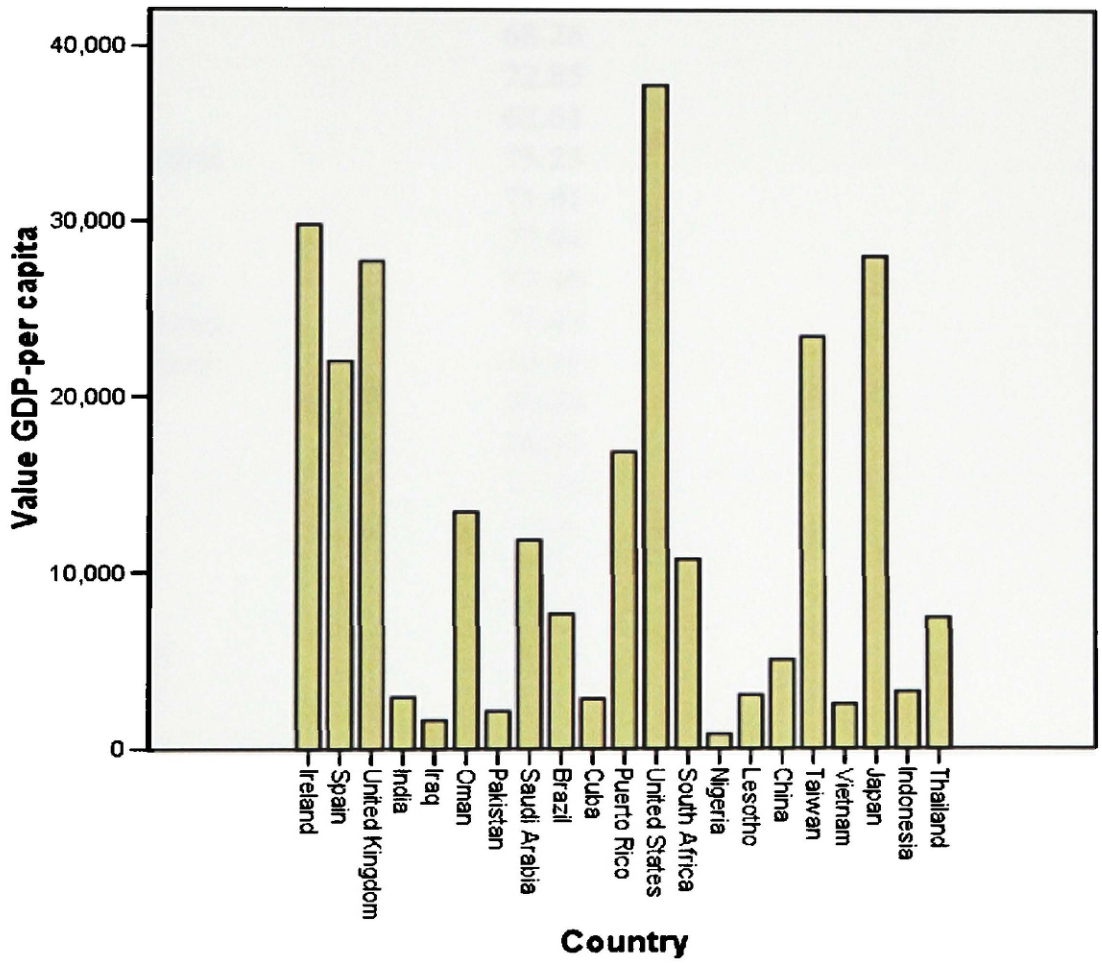

Figure 3 – Gross Domestic Product-per capita for each country
(Source: 2004 CIA World Factbook)

Table 2.5 lists each country used in this study and the life expectancy calculated for the total population of men and women according to the CIA World Factbook for 2004. Figure 4 compares the life expectancy for the total population for each country used in this study.

Table 2.5 – Life Expectancy of the Total Population
(Source: 2004 CIA World Factbook)

	Country	Life Expectancy (Total Population)
1	Ireland	77.36
2	Spain	79.37
3	United Kingdom	78.27
4	India	63.99
5	Iraq	68.26
6	Oman	72.85
7	Pakistan	62.61
8	Saudi Arabia	75.23
9	Brazil	71.41
10	Cuba	77.04
11	Puerto Rico	77.49
12	United States	77.43
13	South Africa	44.19
14	Nigeria	50.49
15	Lesotho	36.81
16	China	71.96
17	Taiwan	77.06
18	Vietnam	70.35
19	Japan	81.04
20	Indonesia	69.26
21	Thailand	71.41

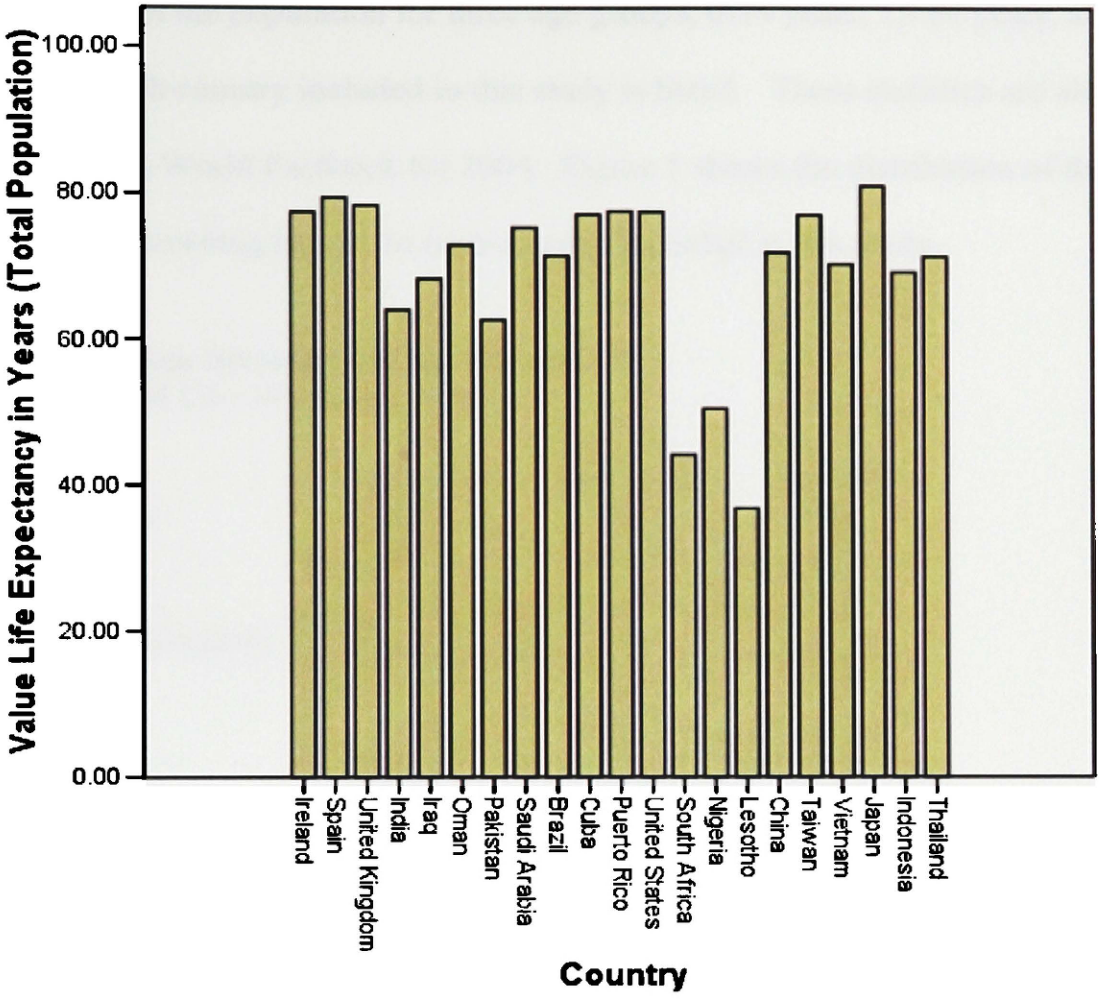

Figure 4 – Life Expectancy of the Total Population for each country
(Source: 2004 CIA World Factbook)

Table 2.6 is a breakdown of how the population is distributed according to age. The percent of the population for three age groups, 0-14 years, 15-64 years, and 65+ years, for each country included in this study is listed. These statistics are also taken from the CIA World Factbook for 2004. Figure 5 shows the distribution of the population according to age for each country included in this study.

Table 2.6 – Age Structure of the Population
(Source: 2004 CIA World Factbook)

	Country	Age 0-14 (%)	Age 15-64 (%)	Age 65+ (%)
1	Ireland	21	67.5	11.5
2	Spain	14.4	68	17.6
3	United Kingdom	18	66.3	15.7
4	India	31.7	63.5	4.8
5	Iraq	40.3	56.7	3
6	Oman	42.4	55.1	2.5
7	Pakistan	40.2	55.8	4.1
8	Saudi Arabia	38.3	59.3	2.3
9	Brazil	26.6	67.6	5.8
10	Cuba	20	69.8	10.1
11	Puerto Rico	22.4	65.4	12.2
12	United States	20.8	66.9	12.4
13	South Africa	29.5	65.3	5.2
14	Nigeria	43.4	53.7	2.9
15	Lesotho	37.3	57.2	5.5
16	China	22.3	70.3	7.5
17	Taiwan	19.9	70.7	9.4
18	Vietnam	29.4	65	5.6
19	Japan	14.3	66.7	19
20	Indonesia	29.4	65.5	5.1
21	Thailand	24.1	68.7	7.3

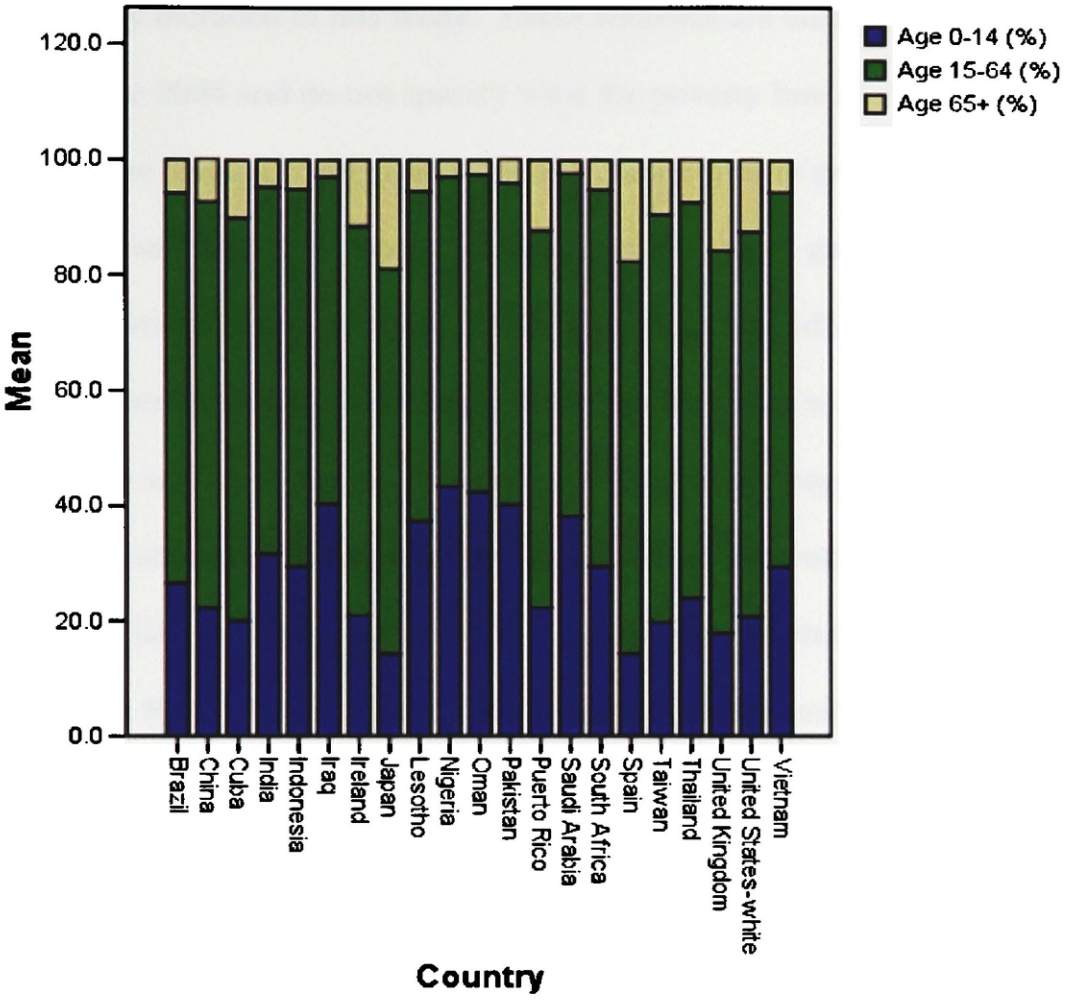

Figure 5 – Age Structure of the Population for each country
(Source: 2004 CIA World Factbook)

Table 2.7 includes the percentage of the population below the poverty line for each country included in this study. These statistics are taken from the CIA World Factbook for 2004 and do not specify what the poverty line is estimated to be for each country. The Factbook only states that the "definitions of poverty vary considerably among nations" and "rich nations generally employ more generous standards of poverty than poor nations" (www.cia.gov 2004). Unfortunately information was not available for several countries used in the present study. Spain, Iraq, Oman, Saudi Arabia, Cuba, Puerto Rico and Japan had no data on the percent of the population below the poverty line and are shown as (NA). Figure 6 compares the percentage of the population below the poverty line for each country included in the present study. The countries of Spain, Iraq, Oman, Saudi Arabia, Cuba, Puerto Rico and Japan are included, but show a value of zero because of lack of information.

Table 2.7 – Percentage of the Population Below the Poverty Line
(Source: 2004 CIA World Factbook)

		Population below poverty line
	Country	**(%)**
1	Ireland	10
2	Spain	NA
3	United Kingdom	17
4	India	25
5	Iraq	NA
6	Oman	NA
7	Pakistan	35
8	Saudi Arabia	NA
9	Brazil	22
10	Cuba	NA
11	Puerto Rico	NA
12	United States	12
13	South Africa	50
14	Nigeria	60
15	Lesotho	49

16	China	10
17	Taiwan	1
18	Vietnam	37
19	Japan	NA
20	Indonesia	27
21	Thailand	10.4

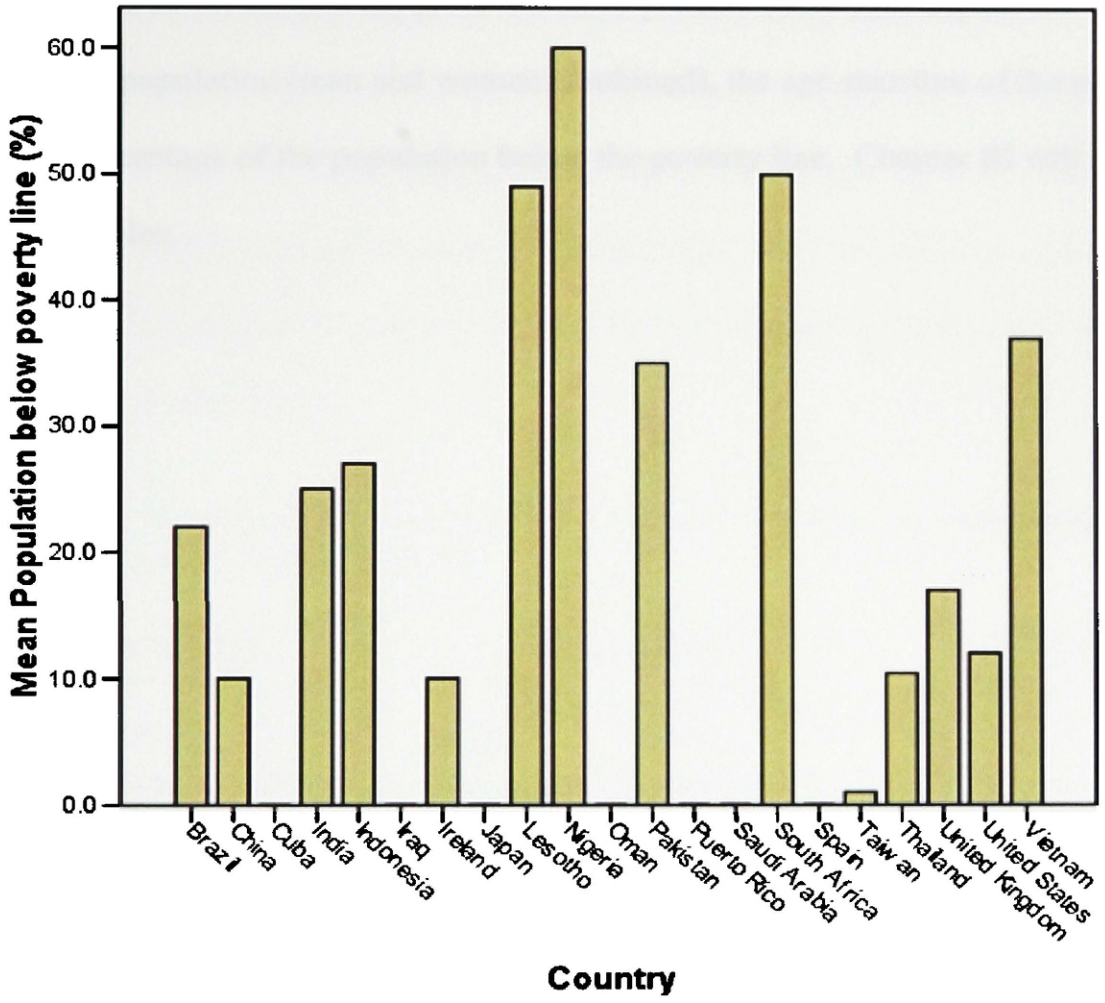

Figure 6 – Percentage of the Population Below the Poverty Line for each country
(Source: 2004 CIA World Factbook)

Conclusion

It is evident from Figure 2 that there is an increased prevalence of rheumatoid arthritis in the three ancestral groups that make up the North American subgroup. To explain this phenomenon, several economic and demographic variables were provided for each country involved in the present study. These variables, taken from the CIA World Factbook for 2004, include the gross domestic product (GDP) per capita, life expectancy of the total population (men and women combined), the age structure of the population, and the percentage of the population below the poverty line. Chapter III will analyze these variables.

CHAPTER III
RESULTS

The present chapter will examine the statistics for gross domestic product - per capita, life expectancy of the total population (men and women), the percentage of the population 65 years and older, and the percentage of the population below the poverty line presented in Chapter II. All four of these variables may potentially contribute to the outcome of the prevalence rates of rheumatoid arthritis for each country included in the present study, although to what degree is not fully understood. To help establish a relationship between the prevalence of rheumatoid arthritis and the four variables, the top five highest and lowest values were tallied for the first three variables just mentioned. The results are as follows:

Table 3.1 – Top Five High/Low values for GDP per capita, Life Expectancy, and % of the Population 65+

GDP-per capita		Life expectancy		% Population 65+	
High	Low	High	Low	High	Low
Ireland	*Iraq*	*Spain*	India	*Spain*	*Iraq*
UK	**Pakistan**	**UK**	**Pakistan**	**UK**	Oman
US	Cuba	*Puerto Rico*	S. Africa	*Puerto Rico*	**Pakistan**
Taiwan	**Nigeria**	**US**	**Nigeria**	**US**	Saudi Arabia
Japan	Vietnam	**Japan**	Lesotho	**Japan**	**Nigeria**

In Table 3.1, the countries that are highlighted in **bold** print are found consistently in all three variables. This includes the United Kingdom, the United States and Japan for the highest values for each of the variables, and Pakistan and Nigeria for the lowest values. The countries that are found in at least two of the variables are *italicized* and

include Spain and Puerto Rico for the highest values and Iraq for the lowest value. Next, the prevalence of each of these countries is applied.

Table 3.2 – Prevalence of RA for the Countries with the Highest and Lowest Values

High	Prevalence	Low	Prevalence
United Kingdom	2.1	Pakistan	0.27
United States	3.7	Nigeria	0
Japan	0.3	Iraq	1.3
Spain	0.5		
Puerto Rico	0.92		

As shown in Table 3.2, for the five countries that most consistently have the highest values, the prevalence rate of rheumatoid arthritis ranges from 0.3 percent to 3.7 percent. The three countries that most consistently have the lowest values have a prevalence rate of rheumatoid arthritis ranging from 0.0 percent to 1.3 percent. It appears as though the prevalence of rheumatoid arthritis can vary substantially despite commonalities shared between countries and is not influenced by any of the three variables above. To further establish what appears to be an absence of a relationship, the Pearson Correlation Test was performed for gross domestic product - per capita, life expectancy of the total population, and the percentage of the population 65 years and older. The results are given below in Table 3.3.

Table 3.3 – Pearson Correlation Test Results

		GDP-per capita	Life expectancy	Age 65+ (%)
Prevalence of RA (%)	Pearson Correlation	0.420	-0.056	0.254
	Sig. (2-tailed)	0.058	0.808	0.267
	N	21	21	21

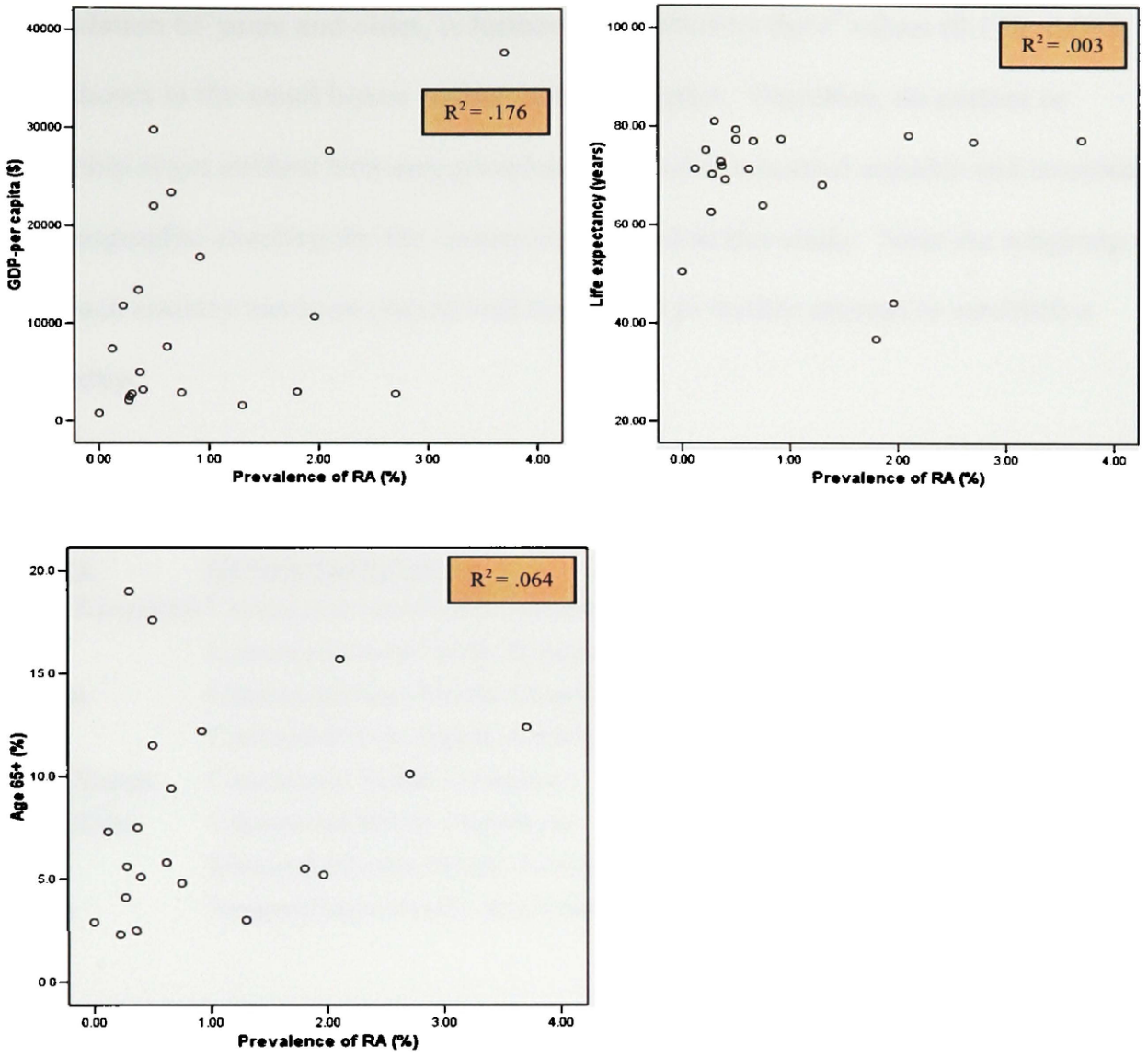

Figure 7 – Scatterplots of the Pearson Correlation Test Results

According to Table 3.3, the correlation between the prevalence of rheumatoid arthritis and gross domestic product - per capita, life expectancy of the total population, and the percentage of the population age 65 years and older, are not significant at the .01 and .05 levels. Figure 7 plots the prevalence of rheumatoid arthritis against the three variables. Many of the points appear to be rather random with several outliers. The absence of a relationship between the prevalence of rheumatoid arthritis and gross domestic product - per capita, life expectancy of the total population, and percentage of

the population 65 years and older, is further established by the r^2 values (0.176; 0.003; 0.064) shown in the small boxes within each scatterplot. Therefore, no pattern or relationship is yet evident between prevalence rate of rheumatoid arthritis and economic and demographic standing for the countries included in this study. Next the subgroup in which each country has been placed will be applied to further attempt to establish a relationship.

Table 3.4 – Group/Subgroup and Prevalence of RA for High/Low Countries

Country	Group/Subgroup	Prevalence	High/Low
United Kingdom	Caucasoid non-North American	2.1	High
Spain	Caucasoid non-North American	0.5	High
Pakistan	Caucasoid non-North American	0.27	Low
Iraq	Caucasoid non-North American	1.3	Low
United States	Caucasoid North American	3.7	High
Puerto Rico	Caucasoid North American	0.92	High
Japan	Mongoloid non-North American	0.3	High
Nigeria	Negroid non-North American	0	Low

In Table 3.4 it appears as if there is no relationship evident between the prevalence of rheumatoid arthritis, group/subgroup, and economic and demographic standing. The five countries with highest values in the above variables represent three subgroups (*Caucasoid non-North American, Caucasoid North American, Mongoloid non-North American*) and the three countries with lowest values represent two subgroups (*Caucasoid non-North American, Negroid non-North American*). The four countries represented in the Caucasoid non-North American subgroup have prevalence rates of rheumatoid arthritis of 0.27, 0.5, 1.3 and 2.1 percent. Of these, there are two high and two low values for the variables discussed above. Unfortunately the high and low values each represent a high and low prevalence of rheumatoid arthritis (0.27%-Low; 0.5%-

High; 2.1%-High; 1.3%-Low). The three other subgroups (*Caucasoid North American, Mongoloid non-North American, Negroid non-North American*) shown in Table 3.4 do not have enough data to attempt to formulate a pattern. In addition, no correlation test could be performed due to the lack of numerical data sets in Table 3.4.

Next, the percentage of the population below the poverty line will be applied. These numbers can only loosely be associated since statistics for several countries were unavailable including four (Spain, Iraq, Puerto Rico, Japan) of the eight that have the top high and low values. The low and high values in this case indicate the opposite of the three variables discussed previously.

Table 3.5 – Top Five Low/High Values for the Percentage of the Population Below the Poverty Line

% Population below poverty line	
Low	High
Ireland	**Pakistan**
US	South Africa
China	**Nigeria**
Taiwan	Lesotho
Thailand	Vietnam

Again in Table 3.5, the United States has one of the lowest values and Pakistan and Nigeria come in with some of the highest values. Unfortunately this reveals little more information. As was done with the previous three variables, the Pearson Correlation Test was performed to further establish what appears to be the absence of a relationship between the prevalence of rheumatoid arthritis and the percentage of the population below the poverty line.

Table 3.6 – Pearson Correlation Test Results

		Below poverty line (%)
Prevalence of RA (%)	Pearson Correlation	-0.055
	Sig. (2-tailed)	0.853
	N	14

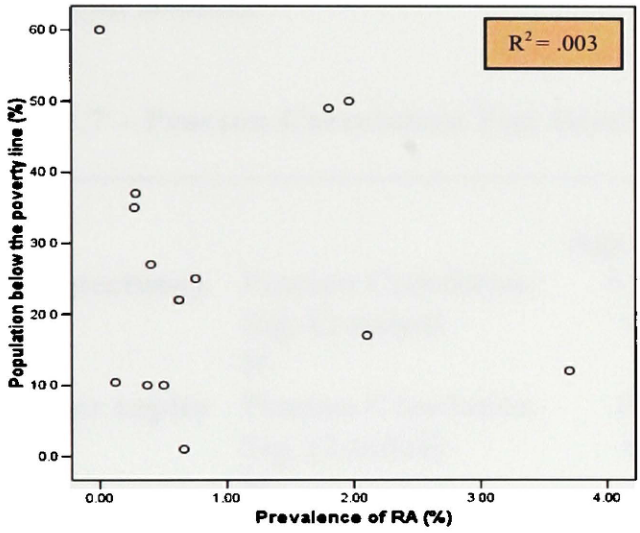

Figure 8 – Scatterplot of the Pearson Correlation Test Results

In Table 3.6 the correlation between the prevalence of rheumatoid arthritis and the percentage of the population below the poverty line is not significant at the .01 or .05 levels, further proving a lack of association between them. Figure 8 plots the prevalence of rheumatoid arthritis against the percentage of the population below the poverty line. As with the other three variables discussed above, the points appear to be random with many outliers. What appears to be an absence of a relationship is further established by the r^2 value of 0.003 shown in the small box within the scatterplot.

Unfortunately this has demonstrated that individually the correlation between the four variables and prevalence of rheumatoid arthritis is insignificant and that there are

some other underlying factors influencing the prevalence rate of rheumatoid arthritis in the studies included here, so a different approach was needed. A correlation test was performed between each of the four variables (gross domestic product - per capita, life expectancy of the total population, percentage of the population 65 years and older, percentage of the population below the poverty line) excluding the prevalence of rheumatoid arthritis.

Table 3.7 – Pearson Correlation Test Results excluding the Prevalence of RA

		Age 65+ (%)	Below poverty line (%)	GDP-per capita
Life expectancy	Pearson Correlation	0.550**	-0.864**	0.447*
	Sig. (2-tailed)	0.010	0	0.042
	N	21	14	21
GDP-per capita	Pearson Correlation	0.521*	-0.584*	
	Sig. (2-tailed)	0.015	0.028	
	N	21	14	
Below poverty line (%)	Pearson Correlation	-0.655*		
	Sig. (2-tailed)	0.011		
	N	14		

** Correlation is significant at the 0.01 level (2-tailed)
* Correlation is significant at the 0.05 level (2-tailed)

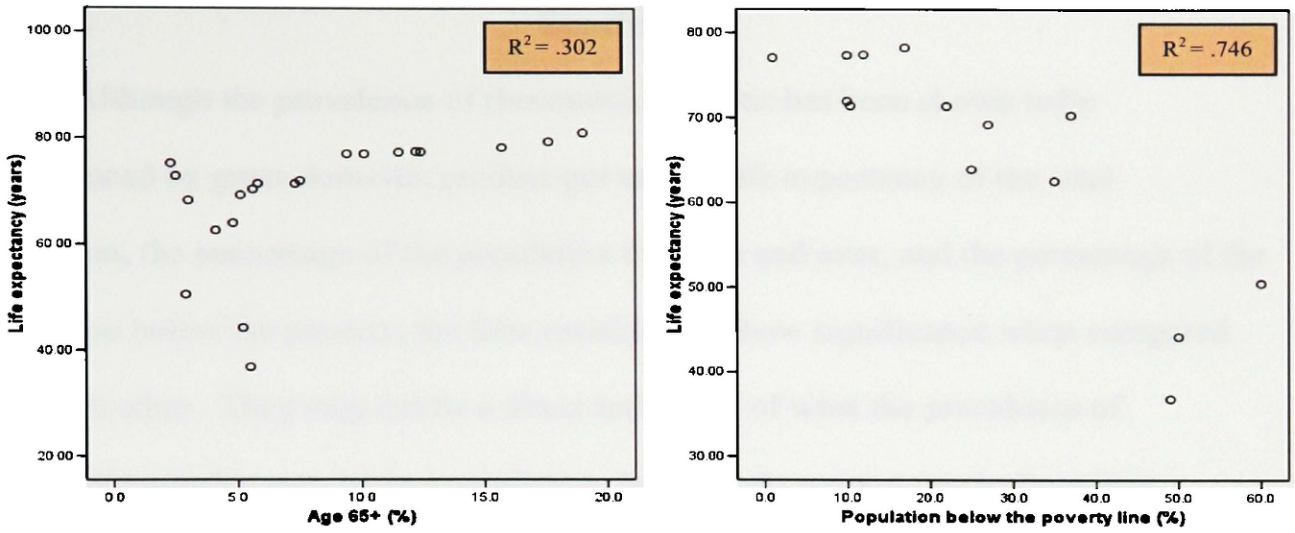

Figure 9 – Scatterplots of the significant results of the Pearson Correlation Test at at the .01 level

As shown in Table 3.7, all combinations had significant correlation results, but only two had significant results at the .01 level. There is a positive correlation between the life expectancy of the total population, and the percentage of the population 65 years and older ($r = 0.550$, $p = 0.010$). This is simply saying the greater the life expectancy of a population, the larger the population 65 years and older will be. There is a negative correlation between life expectancy and the percentage of the population below the poverty line ($r = -0.864$, $p = 0.000$). This is more significant than the previous case. Basically it is stating that the greater the number of individuals in poverty, the lower the life expectancy they will have. Figures 9 plots each of the significant results at the .01 level shown in Table 3.7. The points appear to be less random with fewer outliers, unlike Figures 7 and 8. As demonstrated in Table 3.7 the relationship between these variables is significant and can be further established by the r^2 values of 0.302 and 0.746 respectively.

Conclusion

Although the prevalence of rheumatoid arthritis has been shown to be uninfluenced by gross domestic product-per capita, life expectancy of the total population, the percentage of the population 65 years and over, and the percentage of the population below the poverty, the four variables do show significance when compared with each other. They may not be a direct indication of what the prevalence of rheumatoid arthritis may be in a population, but they do suggest much about how rheumatoid arthritis and other diseases may be handled and treated in that country. Chapter IV will further discuss the impact of the four variables on the prevalence of rheumatoid arthritis and explore other explanations that may have influenced the outcome of the prevalence studies included here.

CHAPTER IV
DISCUSSION

In the previous chapter, the four variables (gross domestic product - per capita, life expectancy of the total population, the percent of the population sixty-five years and older, and the percentage of the population below the poverty line) were examined. The goal of this chapter is to discuss the results of those variables and explore other explanations such as access to medical care, cultural values, communication, and expectations that may clarify the difference in prevalence of rheumatoid arthritis between North American and non-North American populations. This chapter will begin with a discussion of the economic and demographic statistics presented in Chapters II and III.

Economic and Demographic Statistics

The gross domestic product-per capita has shown to be the best predictor of the prevalence of rheumatoid arthritis among the four variables examined in Chapter III (see Table 3.3), but probably does not contribute to the differences between countries/populations. Table 2.4 and Figure 3 in Chapter II show the substantial differences among the countries included in this study and Figure 7 in Chapter III illustrates the randomness and lack of relationship between the two variables. While the gross domestic product-per capita of a country cannot predict whether a population will have a high or low prevalence of rheumatoid arthritis, it can provide insight into the availability of health care and medical services. Each country has limited resources for health care and how these resources are allocated can greatly affect the care that patients receive. Access to and availability of health care can play a large role in the outcome of rheumatoid arthritis in a population (discussed in detail below).

The age structure of the population could also potentially contribute to the difference in prevalence rates between countries/populations. Yet as demonstrated in Chapter III, Table 3.3 and Figure 9, this is not the case with the countries included in this study. The correlation between the percentage of the population 65 years and over and the prevalence of rheumatoid arthritis is insignificant and appears to be unrelated. As shown in Chapter II, Table 2.6 and Figure 5, the age structure for each country varies quite substantially for all three age groups. This is important because a large elderly population (65 years of age and greater) or a large population under 15 years of age will have the tendency to dramatically change the prevalence rate of rheumatoid arthritis for that population. This is due to the fact that rheumatoid arthritis usually has an onset during adulthood. The age structure of a country can also reveal where its economic issues may lie. For instance, if a country has a large elderly population, more money may be devoted towards health care and providing medical services for the aging population. On the other hand, if a country has a large youth population, then more money may be invested into education, and health care may be neglected (www.cia.gov 2004).

The life expectancy of a population may also affect the prevalence of rheumatoid arthritis. As with the age structure of the population, the smaller the percentage of older individuals that make up the population, the lower the prevalence of rheumatoid arthritis should be. As shown in Table 2.5 and Figure 4 of Chapter II, the life expectancy varies greatly for each country ranging from less than 40 years to over 80 years. Unfortunately for this study, life expectancy has not been shown to be a good predictor of the prevalence of rheumatoid arthritis in a population. Chapter III, Table 3.3 and Figure 8 illustrate the lack of relationship between the two variables. The life expectancy for an

individual can have a lot to do with social, political and economic conditions, but is also affected by behavioral choices such as diet and exercise, as well. As people live longer, they are more likely to experience problems with human mechanics and functions, body parts begin to deteriorate or break down resulting in a variety of disorders. This has affected individuals in developed countries for decades. It has only recently become an issue in developing countries as their population has begun to develop chronic diseases due to recent improvements in health care.

The percentage of the population below the poverty line may also potentially contribute to the difference in prevalence of rheumatoid arthritis between countries. Poverty is typically measured in terms of income. As shown in Chapter II, Table 2.7 and Figure 6, poverty varies substantially between countries from one percent to 60 percent. The concept of the poverty can be misleading though. According to the CIA World Factbook, the "definitions of poverty vary considerably among nations" and "rich nations generally employ more generous standards of poverty than poor nations" (www.cia.gov 2004). This makes it much more difficult to determine an association between poverty and rheumatoid arthritis. Table 3.6 and Figure 10 in Chapter III show that in this study poverty is not a good indicator of the prevalence of rheumatoid arthritis in a population. Yet poverty should contribute to the health of nations. Being below the poverty line indicates that the income level is insufficient to sustain a family in terms of food, housing, clothing, medical needs, and various other factors.

Accessibility of Health Care

Accessibility of health care, "a measure of the proportion of a population that reaches appropriate health services" (www.euro.who.int 2004), has significance when

accounting for differences in prevalence of rheumatoid arthritis between countries. Many people in developed and developing countries cannot afford to seek such services or none are provided for them. In most developing countries, medical services are often unavailable, inaccessible or unaffordable. Although, it is worth mentioning that "there are great disparities in wealth and levels of health care achieved in developing countries, thus it is difficult to generalize from one geographical area to another" (Ojanuga and Gilbert 1992:615). This is an important factor when considering treatment and preventative measures for rheumatoid arthritis, and many other diseases as well, for all parts of the world.

Accessibility is a measure of *geographical*, *financial* and *cultural* factors. *Geographical* accessibility is a measure of the degree to which services are available and accessible to a population (www.euro.who.int 2004). In many developed countries, many people are within close proximity to a clinic or hospital. Even in rural areas, it is more likely that a clinic will be only a short drive away. Transportation is also readily available, as almost everyone has access to a vehicle and many towns and cities have inexpensive public transportation (bus, subway). But in many developing countries health care facilities are much less accessible because of distance, lack of transportation or simply the absence of adequate health care facilities. Geographical accessibility may also work in the opposite regard as well. Some individuals may not be able to be contacted by research teams because of the remoteness of where they live. For researchers conducting population surveys on a random sample of individuals, some will be neglected due to the time and effort required to access their location.

Financial accessibility is a measure of the degree a population is able to pay for health care (www.euro.who.int 2004). For instance, even if health care facilities exist and are geographically accessible, many people cannot afford such services and/or do not have health care coverage. Many conditions require expensive medications, frequent physician visits and even hospitalization. For a chronic disease like rheumatoid arthritis, this expense will continue for the duration of the patient's life. Without adequate health insurance or wealth, many may not receive the proper treatment for the disease causing a worse outcome with increased disability. This applies to people all over the world, in developed and developing countries.

Cultural accessibility is a measure of the degree for which cultural taboos limit access to health care (www.euro.who.int 2004) and is important in determining possible risk factors and potential consequences of rheumatoid arthritis for the individual. In many countries, culture plays a large role in the manner in which people carry out their lives. For instance, ones culture may determine whether a woman may receive medical attention from a male doctor or even be permitted to seek such services without the consent of her husband (Ojanuga and Gilbert 1992). According to Ojanuga and Gilbert, women in developing countries "tend to utilize health facilities less than men even though their need for health care is greater" (Ojanuga and Gilbert 1992:614). For women with rheumatoid arthritis this may have a profound affect on their physical ability to maintain the same level of daily activity they had before the disease initiated. Some minority groups may not feel comfortable attending a health care facility that is mainly staffed by those of a different ethnicity or of the majority population. This may be due to feelings of discrimination or because of the absence of common values. Also some

individuals of certain cultures may not seek medical attention for processes that are considered natural, such as childbirth and osteoarthritis (www.euro.who.int 2004). Regardless of the specific cultural reason for restricting access to medical care, the health of many individuals can be affected by their cultural identity.

Accessibility of Health Care in the United States

Although many feel that poor accessibility to health care only affects individuals in developing countries, it is also a problem in the United States, a developed country. Larger countries have the added complication of having to deal with multiple subpopulations with differing beliefs and expectations. The increase in immigrant populations in the United States has recently focused the attention of many towards racial and ethnic health disparities that negatively influence access to health care. This involves multiple causes, such as health care systems, providers, and patients, but some play a larger role than others.

For example, physicians may discriminate against their patients. This can occur consciously or subconsciously based on biases or stereotypes previously formed about populations different from their own. A survey conducted by The Henry J. Kaiser Family Foundation in 1999 found that African Americans were "fourteen times as likely to report that they were treated unfairly because of race when seeking medical care" (Smedley et al. 2003:636). Many other studies have been conducted that support physician bias, with their subject matter pertaining to patient and physician assessment of care, surveys blinded to patient race and ethnicity, and physician responses to white and black patients with identical symptoms. A study, conducted by Shi, claims that even when controlling for sociodemographic and health-status differences, many racial and ethnic minorities

experienced "worse first-contact primary care than whites" in the United States (Shi 1999:1073). Yet not all studies have shown racial and ethnic minorities to be at a disadvantage. Two studies comparing white, African American and/or Hispanic patients with rheumatoid arthritis reported no differences in pain, disability and overall physical function (Jordan 1999).

This disparity goes beyond race or ethnicity and may also lie in socioeconomic status as well. A study conducted in urban California, published in 1995, reports that people living in low-income areas were more likely to be hospitalized for chronic conditions than people living in high-income areas (Bindman et al. 1995). This seems to correlate with their perception about the accessibility of health care as well. Individuals who feel they have poor accessibility to health care are often those who are hospitalized for conditions that could have otherwise been avoided if they had initially sought proper treatment.

Another factor that may contribute to racial and ethnic disparities in health care in the United States is the lack of availability of affordable public or private health insurance. This has continued to be a problem regardless of the establishment of programs such as Medicare and Medicaid. For many this may be due to the overall expense, but for immigrant populations, fear of divulging too much information about oneself or family, or fear of jeopardizing their application for citizenship may also play a role. Unfortunately most of these fears are "based on a misunderstanding of federal policies" (Smedley et al. 2003:648). Several statistics from the National Center for Health Statistics demonstrate this disparity. For example in 2004, 26.3 percent of Hispanics at the time of the interview had been uninsured for more than a year versus

only 6.1 percent of whites at the time of the interview. Many of those who are unemployed or are below the poverty line also find themselves uninsured. In 2004, it was reported that almost 58 percent of currently unemployed adults had been uninsured for part of the year and about one third of currently unemployed adults had been uninsured for more than a year (www.cdc.gov 2004). Unfortunately, insuring the previously uninsured may not overcome the disparity that many minority groups may experience when seeking medical attention in the United States.

The potential for racial and ethnic discrimination still exists and may play a large role in explaining the persistence of disparities in health care in the United States. Efforts must be made in the United States and in all countries "to provide ethnically and culturally competent care and to remove or reduce the many barriers facing racial/ethnic minorities in their access to primary care" (Shi 1999:1074). This differential treatment of minority populations is not unique to the United States. It has been demonstrated that Aboriginal people in Australia, Inuit people in Canada, African immigrants in France, Russian immigrants in Israel, and the non-white majority population in South Africa also face unequal accessibility and content of health care (Smedley et al. 2003).

Other Explanations

Although accessibility of health care may contribute to the uneven reported prevalence data between North American and non-North American populations, it will not determine the prevalence of rheumatoid arthritis. Other factors that may also affect the prevalence data must also be considered, such as cultural values, communication and language barriers, and expectations and attitudes towards modern medicine.

Cultural values and local cultural differences are important considerations when comparing the prevalence of rheumatoid arthritis for all populations. Culture is ingrained into many daily activities for people in developed and developing countries and may affect every aspect of their lives. This may limit many people's willingness to discuss or disclose certain health conditions to a stranger conducting a survey in their area. Many cultures may consider this to be private information that should not be revealed to anyone and may even be kept hidden from family and friends. This is the opposite of many non-immigrant populations living in the United States who lack any relevant cultural restrictions. Some individuals may even have a much greater propensity to report and discuss their health issues with anyone and even manifest some for attention.

Often there are problems with communication with the people involved in the study because of a language barrier. Without an interpreter to assist with the interview or having previously translated the questionnaire, many of those surveyed may misinterpret the questions. This could lead to highly inaccurate results. For example, with languages other than English, problems may occur when trying to differentiate or distinguish levels of pain and disability, as there may not be similar words to describe it. A study conducted in Britain and France reported, "qualitative sociological and anthropological evidence supports the hypothesis of a socially differentiated interpretation of illness" (Aiach and Curtis 1990:271) and it is likely to be even more apparent between developed and developing countries. Those conducting population studies must consider and investigate this issue prior to working in an environment unlike their own. This is important since many researchers may not be from the country or culture they are studying and cannot fully relate to their patients. Time and monetary constraints may

also affect researchers' ability to fully investigate and assess patient's symptoms in situations where language barriers exist. These problems with communication undoubtedly exist with many individuals who seek general medical services as well.

Also attitudes towards and expectations from modern medicine differ between cultures. Some individuals may not seek medical attention from a physician but may look toward a traditional or local healer for medical advice and treatment. Some may feel commercial medicines are not safe and instead treat themselves with herbal supplements which they do not acknowledge as medicine. Others may not reveal that they are taking anything at all for their symptoms. Regardless, not reporting the ingestion of any medicine or consultation with a traditional healer may alter the results of the study due to negative clinical findings of rheumatoid arthritis during the initial interview. Minority patients have also been shown to be "more likely to refuse recommended services, adhere poorly to treatment regimens, and delay seeking care" (Smedley et al. 2003:7). This behavior can be brought on in individuals by a variety of factors mostly due to a mismatch between patient and provider. This affects citizens of the United States as well as all other countries with diverse populations, although it does not fully explain the healthcare disparities faced by many racial and ethnic minorities.

Antiquity and Etiology

Two other factors that may contribute to the difference in prevalence rate of rheumatoid arthritis for North American and non-North American populations include antiquity and etiology. Both were discussed at length in Chapter II. Unfortunately neither is completely understood and both require further investigation and research.

This makes their role in the present study inconclusive but they undoubtedly play a large role in the expression of rheumatoid arthritis.

The prevalence of rheumatoid arthritis in North American ancestral groups is higher than in any other non-North American ancestral group as shown in Chapter II, Figures 1 and 2. The prevalence is especially high with the Native American population (*Mongoloid North American* subgroup). As mentioned in Chapter I, the antiquity of rheumatoid arthritis has yet to be proven, but it may have originated in the Tennessee River Valley of the United States as early as 6500 BC with the Native American population. The correlation between possible place of origin and high prevalence rate should not be overlooked here or in other studies like the present one. Could there be one or a combination of environmental factors that North Americans are exposed to that are absent or very minimal elsewhere? Isolating an environmental stimulant seems almost impossible at this time, as there are many factors to be considered. The lack of knowledge about the etiology of rheumatoid arthritis only makes this question more complicated. Regardless, the proposed geographic area and population of origination of rheumatoid arthritis should be given consideration as a potential factor explaining the increased prevalence of rheumatoid arthritis in North American populations.

The etiology of rheumatoid arthritis should also be considered as playing a role in the difference in prevalence between North American and non-North American populations. The genetic, environmental, hormonal, and immunologic factors of the etiology of rheumatoid arthritis are described in detail in Chapter II. There are many factors that could potentially be contributing to the expression of this disease, so many that determining which one(s) result in the expression of rheumatoid arthritis has thus far

proven to be an impossible task. The problem is there are so many inconsistencies between individuals afflicted with the disease. What appears to cause rheumatoid arthritis in some people is completely absent in others. Its onset can occur in the teens up through the elder years, several levels of severity exist with some individuals having a complete remission of symptoms, and some scientists state that rheumatoid arthritis is not actually an autoimmune disease. The unpredictability and irregularity of rheumatoid arthritis has left many physicians and their patients understandably unsettled. Nonetheless, the etiology of rheumatoid arthritis should be considered a potential factor affecting the inconsistency in prevalence between North American and non-North American populations.

Conclusion

The discussion of several explanations regarding the difference in prevalence of rheumatoid arthritis between North American and non-North American ancestral groups has just been presented. This included economic and demographic variables as well as accessibility to health care, cultural values, communication, expectations, and the antiquity and etiology of rheumatoid arthritis. Any one or a combination of several of these factors could play a significant role in the outcome and expression of rheumatoid arthritis, but how they contribute to the prevalence rate for each of the studies included here is the real question that needs to be answered.

CHAPTER V
CONCLUSIONS

The current chapter seeks to clarify the impact each of the variables discussed in Chapter IV (economic and demographic variables, accessibility of health care, cultural values, problems with communication, expectations and attitudes towards modern medicine and health care, and antiquity and etiology of rheumatoid arthritis) has on the results and conclusion of all of the prevalence studies included in this study.

Summary

Hypothesis 1: The prevalence of rheumatoid arthritis will be lower among the ancestral groups of North American when compared to ancestral groups living on other continents due to the advanced health care available in North America, and more specifically the United States.

Hypothesis 1 was proven false. Considering that the United States is a developed country with some of the most advanced medical care, it was rather unexpected that all three ancestral groups (Caucasoid, Mongoloid, Negroid) in North America had a noticeably higher prevalence of rheumatoid arthritis than all ancestral groups living elsewhere. The prevalence of rheumatoid arthritis in the Mongoloid group of the North American subgroup seems appropriately increased when considering some believe rheumatoid arthritis may have originally began with the Native American population, which makes up the entire subgroup for North America.

Hypothesis 2: The prevalence of rheumatoid arthritis can be partially explained by carefully selected economic and demographic variables for each country addressed in this study.

Hypothesis 2 was proven false. None of the four variables (gross domestic product-per capita, life expectancy of the total population, percentage of the population 65 years and older, and percentage of the population below the poverty line) were found to have influence over or be a good predictor of the prevalence of rheumatoid arthritis for any of the studies included. Substantial variability in the prevalence of rheumatoid arthritis was found between poor and wealthy countries as well as countries with a large young or elderly population.

Hypothesis 3: Studies conducted on the prevalence of rheumatoid arthritis will be influenced by factors that are often not given adequate consideration.

Hypothesis 3 was found to be true. The variability in prevalence of rheumatoid arthritis among the studies was found to be influenced more heavily by communication problems and cultural values than by the disease itself or by the four variables discussed in Hypothesis 2.

Conclusions

The gross domestic product– per capita, life expectancy of the total population, percentage of the population 65 years and older, and the percentage of the population below the poverty line did not appear to play any role in explaining the uneven prevalence of rheumatoid arthritis between North American and non-North American subgroups. Countries that are economically stable and have a significant elderly population can have either a high or low prevalence of rheumatoid arthritis. This also applies to poor nations whose populations rarely live to reach 70 years old. An example that does not fit preconceived ideas about the health of individuals in particular countries is China, which has a life expectancy of about 72 years, a gross domestic product-per

capita of 5,000 dollars, but a prevalence of rheumatoid arthritis of 0.37 percent. Another example is the country of Lesotho, which has a gross domestic product-per capita of 3,000 dollars, a prevalence of rheumatoid arthritis of 1.8 percent but a life expectancy of only about 37 years. Clearly for the prevalence studies included in this study, a connection cannot be made between rheumatoid arthritis prevalence and economic standing for any country. Yet the four variables do show consistency and exhibit regularity among the countries included here. Typically, a country that has a high gross domestic product-per capita and a low percentage of the population below the poverty line will also have a high life expectancy and a high percentage of the population 65 years and older. Unfortunately these four variables do not help to explain the difference in prevalence of rheumatoid arthritis between North American and non-North American populations, but they do provide information about the general health care that should be available to individuals living in each country.

The accessibility of health care was discussed at length in Chapter IV. Regardless of the economic standing of each country included in this study, individuals in the United States and other countries, both developed and developing, face problems with geographical, financial and cultural barriers when seeking medical attention for minor and major health problems. For poor nations with large rural populations, this is not surprising. But the health care in the United States, believed to be one of the best, has been shown to be unavailable and inadequate for many individuals. Mostly immigrant and minority populations as well as individuals with a low socioeconomic status are affected, according to some rather unexpected statistics and studies conducted in the past few years. Considering that poor accessibility of health care affects nearly every

population and country, it is difficult to associate it with any difference in prevalence rate of rheumatoid arthritis found when comparing countries/populations. Therefore it appears to have no impact on the outcome of any of the studies included here or on the present study.

Cultural values exist in many different forms among many different populations. To make the statement that they may affect an individuals' willingness to disclose personal information to a stranger may be too much of a generalization. But for the present argument, it is appropriate. The bulk of the North American data comes from a study conducted in the early 1960s, and several studies on Native American populations exclusively over several decades. The 1960s study, which covers all three ancestral groups, is assumed to not have included a large immigrant population and was predominantly second or third generation Americans. Immigrant populations were probably not neglected, but the response rate from them was almost certainly rather low. The Native American population studies (*Mongoloid North American* subgroup) included here were conducted from the 1960s through the 1990s. These populations have not been living in isolation and have been undoubtedly influenced by American culture. As discussed in Chapter IV, the non-immigrant population living in the United States has a much greater propensity to divulge personal information, in general, than populations living in other developed and developing countries. Therefore, it seems that cultural values can undeniably alter the outcome of population studies conducted in areas where they are prevalent and look to be a significant factor to explain the uneven distribution of rheumatoid arthritis worldwide.

Excellent communication between researcher and participants is essential for accurate results when conducting studies on populations using a different language. An inability to fully comprehend questions and responses may lead to erroneous conclusions based on avoidable misunderstandings. Eliminating the communication or language barrier is solely the responsible of those conducting the population study and should be dealt with long before the study is underway. The issue of communication is not addressed in most of the prevalence studies included here or is at least not disclosed in the published article. Information on the background of the authors involved in the study and any translations taken place with the questionnaire would be helpful to resolve this matter. If even half of the researchers had problems communicating with the participants included in the studies or if the participants had trouble understanding the questionnaire, the potential for inaccurate results exists. When working with prevalence rates that only differ by tenths of a percent, accuracy is crucial. For that reason, the language barrier that may have been present between researcher and participant may have significantly affected the conclusion formed in each of the prevalence studies included, thereby affecting the outcome of this study as well.

The thought of seeking medical attention from modern medical services conjures up many different ideas and feelings from individuals in both developed and developing countries. These attitudes and expectations often result from cultural values or from experiences in the past. Some individuals may choose to seek other alternatives to modern medicine when in need of medical attention including traditional healers or herbal supplements. These individuals would be missed if the prevalence studies used medical records from hospitals and clinics to find those afflicted with rheumatoid

arthritis. But, as part of the criteria created for the present study, all prevalence studies included here must have interviewed a representative or random sample of the population to ensure that all of the defined survey areas were properly sampled. Unless the interview refusal rate for those opposed to modern medicine was high, which is undeterminable, the expectations and attitudes individuals have towards modern medicine should not have affected the outcome of the prevalence studies included and therefore should not affect the conclusion of the present study either.

The antiquity of rheumatoid arthritis is not fully understood, but an increasing number of skeletal remains continue to be found during archaeological excavations. Through analysis, skeletal remains will help to provide further proof of either a European or North American origin. If rheumatoid arthritis did first develop in North America, it may explain why the prevalence rate is considerably higher in Native Americans than in any other population around the world. It may also explain why the prevalence rate of rheumatoid arthritis is higher in all three subgroups of North American than those in non-North American subgroups. But since the origin is not known, it is impossible to connect the antiquity of rheumatoid arthritis with the higher prevalence in North America. As a result, it cannot be presumed to have affected the results of any of the prevalence studies included here.

The etiology of rheumatoid arthritis is essentially unknown as well. Scientists have been researching potential causes for decades but have not found one or a multiple of factors that are consistently found in every individual with rheumatoid arthritis. This has left many individuals afflicted with rheumatoid arthritis and the physicians treating them unsettled. Fortunately many new medications, though very expensive, have been

developed to stop the progress of joint damage rather effectively. Nonetheless, until the etiology of rheumatoid arthritis is uncovered and a cure is eventually found, the etiology cannot be implicated as a potential cause/factor to explain the difference in prevalence of rheumatoid arthritis between North American and non-North American subgroups.

Although all of the potential causal factors discussed in Chapter IV are important to consider when comparing multiple studies conducted on several populations by different investigators, many of them, as discussed, do not play any significant role in the conclusion of the present study. This is not to say that they do not influence the health of the populations being studied, but that they do not contribute to the outcome of this comparison. Of the seven variables discussed only two, cultural values and communication, were found to have considerable affect on the results of the prevalence studies included here.

Concluding Remarks

It is probable that in the future we will see chronic diseases, such as rheumatoid arthritis, become major health concerns, as many of these diseases tend to increase with age. Altering this predicted rise in the number of individuals developing rheumatoid arthritis is necessary to ease the global suffering many could potentially face. A broad knowledge and understanding of rheumatoid arthritis and its prevalence provides the foundation to promote education, research and ultimately prevention. Hopefully the present study and all subsequent studies like it will bring us one step closer to a complete understanding of this complex disease and to reducing the disability so many are already facing.

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