AN EPIDEMIOLOGIC STUDY OF FIBROMYALGIA IN A REPRESENTATIVE COMMUNITY SAMPLE:

THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY (LFES)

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ABSTRACT

A representative community sample of 3395 non-institutionalized adults was surveyed with respect to pain. One hundred community fibromyalgia cases (FC) were confirmed by tender point examination using validated classification criteria; 86 cases were female. The mean age of female FC was 49.2 years, of male FC 39.3 years ($p < 0.02$).

Fibromyalgia (FMS) was found to affect almost five percent of women and between one and two percent of men in London, Ontario. It affected all ages, but was most common in middle age, especially in women. It may affect up to 700,000 Canadian adults. Demographic risk factors for having FMS are middle age, female sex and lower socioeconomic status.

Fibromyalgia cases reported a wide array of symptoms. Most prominent among them, besides widespread pain, were fatigue, severe fatigue lasting 24 hours after minimal activity, and sleep difficulties. Overall, FC reported a greater number and greater severity of symptoms, worse overall health, and more healthy years of life lost than did individuals with chronic widespread musculoskeletal pain (Pain controls, PC) who did not meet the case definition for FMS.

Fibromyalgia cases also reported worse function and more frequent work disability than did PC and matched general population controls (GC). Approximately one

quarter of FMS sufferers were receiving disability pensions. Almost one third reported being disabled. Fibromyalgia cases reported a $4000 net loss of annual income. Demographic risk factors for being disabled included middle age and physically stressful past employment. Pain, fatigue, weakness and cognitive difficulties were the symptoms most often reported to have a negative impact on work capacity. The Fibromyalgia Impact Questionnaire (FIQ) score was the best predictor of self-reported disability, especially at scores below 60% and above 79%.

In Canada, FMS accounts for a conservatively estimated $350 million annually in differential direct health care costs, largely resulting from increased utilization of outpatient physician services. It also results in a significant increase in medication use. Irrespective of whether one views it as a legitimate medical condition or a medicalization of a social phenomenon, the costs of FMS, both at the individual and societal level, suggest that further investigations into its etiology and treatment are warranted.

Keywords: 1) fibromyalgia
2) prevalence
3) clinical characteristics
4) costs

CO-AUTHORSHIP

Each of the five manuscripts contained herein is based upon research which primarily was designed, orchestrated, and analyzed by the author of this doctoral dissertation, Kevin P. White. This includes the development and testing of the survey questionnaires, recruiting and training telephone interviewers and the data entry clerk, monitoring data collection and entry, and all data analyses. Regular feedback was provided by each of the three co-authors. Examination of subjects for fibromyalgia tender points was performed primarily by Dr. Kevin P. White, with a minority of subjects examined by Dr. Manfred Harth. Each of the five manuscripts was authored primarily by Kevin P. White, with editing provided by each of the three co-authors.

EPIGRAPH

"Facts do not cease to exist because they are ignored."

Aldous Huxley

DEDICATION

In memory of my father

Emery Louis White

1924 - 1983

ACKNOWLEDGEMENTS

The seed for this project first was planted in September 1992, while I was using the photo copier in the rheumatology division office at University Hospital. Dr. Manfred Harth entered the office to check his secretary's desk, and we started talking. I already had begun to mull over the prospect of what I then perceived would be a Masters thesis. I told Manfred some of my ideas, including one involving a survey of the general population to determine the prevalence of fibromyalgia (FMS) in London. Somewhat to my surprise, Manfred was immediately very keen on the idea. "I think it could be a very major study," he said.

One week later, I was in the office of Dr. Mark Speechley, who had had no particular research interest in FMS, but who had taught the Introduction to Epidemiology course that I had completed the preceding year, the course that had inspired me to enter the Masters programme. He also encouraged me with respect to a study of FMS prevalence. By October, the three of us were in the rheumatology library, and I was presenting my concept, now better formulated, to both of them. The idea had taken root. By November, Dr. Trüls Østbye had joined us. My decision to ask him to be on my committee had been sparked by a very brief but very positive exposure to him in two epidemiology courses. He, Mark and Manfred continuously have provided me with well-intentioned, constructive criticism that has helped to mold the project, and support that, like water to a plant, has permitted it and me to grow.

Further unwavering support has been provided to me by Dr. David Bell, who has been the chief of the Division of Rheumatology since I arrived in London in 1989, whose leadership resulted in me being appointed first as a research fellow in the Division of Rheumatology in 1991, and later as an Assistant Professor in the Department of Medicine in 1996. Immediately following this latter appointment, I hired a secretary, whose tremendous value to me in my work could never be measured. Also, I have received both warm encouragement and thoughtful advice from numerous other faculty and staff in the Department of Epidemiology and Biostatistics, most notably Dr. Allan Donner, Dr. James Rochon, Dr. John Koval, Dr. Karen Campbell, Larry Stitts and, perhaps most of all, Helen Simpson; has there ever been a departmental secretary more willing and capable to help students? All of this encouragement and advice helped to nourish the project.

Along the way, this initial seed and my passion to learn epidemiology had grown too large to be a Masters project. What was I getting myself into? Initially I had some reservations about having, perhaps, reached to far. But the further I kept reaching, the more support I felt from Mark, Manfred, Truls, and all of the Department. Then, funding support arrived, first from the National Health Research and Development Programme, then from the Arthritis Society and the University of Western Ontario.

My friend, Bill DeYoung eagerly provided his computer expertise to develop the Scantron form that greatly facilitated data entry on almost 3400 subjects. Seven

telephone interviewers were hired to survey these subjects by telephone... without your diligence, the project never would have left the ground. Thanks also to Charlene, Manfred's secretary, who enthusiastically performed data entry and provided me with a vast array of other secretarial services as needed in those days before I could hire my own; and to both Stacey and Tracy, students who provided invaluable services during the course of preparing this dissertation.

More than five years have passed since the first seed was planted. The fruits of labour have included many abstracts, many manuscript submissions for publication and, of course, this dissertation. I am indebted to all of the nurturing support I have received. But, even with that support, I would not have succeeded without the unfailing support of my family. This includes Don and Marie, in-laws par excellence... you have supported Donna and me in all our endeavors, and we always will be grateful. It especially includes my wife and children. Donna, I love you... your love shines down on me and warms my heart. Ashley, Adam, Sam and Patrick... you too are seeds taking shape. My greatest joy has been, and will continue to be, watching you grow.

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INTRODUCTION

1.0 OVERVIEW

Musculoskeletal (MSK) disorders contribute greatly to chronic disability and health services utilization in developed economies. In the USA, an estimated 37 million individuals (14.5% of the U.S. population) suffered from arthritis in 1989.[1] Musculoskeletal disorders account for 15% of work loss days in the USA[2] and 14 -17% of work loss days in Great Britain.[3] In Canada, data suggest that one million adults have physical disabilities secondary to MSK illness, a prevalence of 50.1 per thousand.[4] Sixteen percent of respondents to the 1980 Canadian Health Survey (CHS)[5] and 14 percent to the 1990 Ontario Health Survey (OHS)[6] reported having either arthritis or rheumatism. In each study, 'arthritis and rheumatism' was the most commonly reported cause of chronic disability, and the second most frequent cause of two week disability (after respiratory illness including rhinitis). These findings were consistent across all age

groups. In addition, people affected by arthritis and rheumatism use more health services than the general population,[7] and the costs of MSK illness may be increasing. In 1980, MSK disorders in the U.S. accounted for an estimated $21 billion in health care costs and lost wages, approximately one percent of the country's Gross National Product.[8] A more recent survey, performed between 1990 and 1992, estimated the same costs as $149.4 billion, or 2.5% of the GNP.[9] A recent workshop focused upon estimating the population health impact of arthritis through model building.[10,11] Using this model and the concept of quality adjusted life years (QALY), it was estimated that the typical adult woman with arthritis could be expected to lose 3.3, and an adult man 1.6 healthy years of life.

Fibromyalgia Syndrome (FMS), also known as fibrositis, is a common form of non-articular rheumatism that is associated with chronic generalized musculoskeletal pain, fatigue, and a long list of other complaints.[12] Clinic studies indicate that FMS patients are as adversely affected by their symptoms as patients with rheumatoid arthritis (RA), and more so than osteoarthritis (OA) patients.[13,14,15] For various reasons, including a relative dearth of specific physical, laboratory and radiographic findings, the concept of FMS has met with much skepticism[16,17,18,19] and has attracted much less research interest than other less common musculoskeletal disorders.[20] Despite this, it is diagnosed in 10 to 20 percent of patients seen in outpatient rheumatology clinics in the U.S., Mexico, Spain, and Australia[21,22,23,24] and appears to be one of the three most common disorders diagnosed among new referrals to Canadian rheumatologists.[25]

The primary objectives of this study were to estimate the prevalence and socioeconomic impact of FMS among non-institutionalized Canadian adults. Although a handful of population-based studies have been reported in the English literature, the largest prospective study to date identified only 36 cases of FMS.[26] Moreover, only that one study attempted to address the issue of direct costs of FMS in the general population. The London Fibromyalgia Epidemiology Study (LFES) was designed to identify a sufficiently large representative cohort of random community cases of FMS, in order to estimate point prevalence, clinical characteristics, functional and disability status, and direct and some indirect costs of FMS, in comparison to controls. Data collection occurred between November 1994 and May 1996, during which time 100 community cases of FMS were identified, in addition to controls.

This chapter reviews the English language scientific literature justifying the current research, then outlines the primary and secondary study objectives.

1.1 THE HISTORY OF FIBROSITIS/FIBROMYALGIA

1.1.0 Overview

The literature associated with FMS is rich with opinion and controversy. Although it has been accepted as a valid clinical entity by numerous academic and professional bodies, such as the American College of Rheumatology,[27] still there are those who have called it "an illusionary entity",[18] "a common non-entity",[28] and "the syndrome of feeling out of sorts".[19] It also has been called "an emerging... condition",[16]

referring to an apparent increase in its prevalence, at least within rheumatology clinical practice. Some have warned of an impending 'epidemic'.[29] There are some data to support this. In a 1977 U.S. survey of 826 practicing community and academic rheumatologists, fibrositis accounted for only 2% of patients seen.[30] A chart review of four U.S. community rheumatologists, done in the same year, found fibrositis accounting for 6.1% of new cases.[31] In comparison, a more recent U.S. survey, published in 1983, found 15.9% of new rheumatology patients to have FMS.[32] But these figures must be interpreted with caution. Although it is possible that the increased prevalence of FMS in rheumatology practices reflects an increase in prevalence in the general population, there are other, equally feasible explanations, that can only be explored through epidemiologic studies in the general population.

The primary objectives of this literature review are: 1) to outline the history of fibromyalgia to clarify the current concepts as to the nature of this disorder; 2) to define what is now generally accepted to be the clinical entity called fibromyalgia; 3) to illustrate the limitations in current understanding and the associated controversies with respect to FMS; and 4) to demonstrate the need for continued epidemiologic research to enrich our understanding of etiologic and prognostic factors for this syndrome.

1.1.1 The Early Years

The term 'fibrositis' was first used in 1904 by Dr. William Gowers in a treatise on low back pain.[33] He used it to label what he perceived to be a localized inflammatory process within richly innervated muscle and fibrous tissues. But the concept of chronic pain originating in muscles had appeared in earlier reports, especially in the German medical literature in the mid to late nineteenth century. In those reports, pain was thought to be related to focal areas of "Muskelharten" (muscle hardness)[34,35] or "Muskelschwiele" (muscle callouses)[36] that were palpable by the examiner and very tender. The concept of inflammatory foci within muscle and fibrous tissues initially was supported in a report by Stockman, in which he described inflammatory changes in "white fibrous tissue" of patients with "chronic rheumatism".[37] This finding was not reproduced in several subsequent studies, however, and the inflammatory focus hypothesis gradually fell into disrepute.[38,39]

In the 1930s, the concept that widespread pain could originate within foci in deep connective tissue structures was supported by several studies by Kellgren and Lewis.[40,41,42,43] Using blindfolded volunteers, they demonstrated that saline injection into various structures such as muscles, fascia, and tendons, could result in pain that radiated from the stimulated site to distant parts of the body. The distribution of the radiated pain caused by injecting a specific site was consistent from subject to subject. The pain also was associated with other phenomena, such as referred tenderness and muscle spasm. So

called 'trigger points'[44] or 'taut bands',[45] these characteristic sites of deep structure tenderness became part of the disorder known as myofascial pain syndrome (MPS).

1.1.2 **Fibrositis and Sleep**

In the Bible, Job wrote: "*... and wearisome nights are annointed to me. When I lie down, I say, When shall I arise, and the night be gone? And I am full of tossings to and fro unto the dawning of the day.*" "*... and the days of affliction have taken hold upon me. My bones are pierced in me in the night season; and my sinews take no rest.*"[46]

Smythe and Moldofsky released a series of publications in the late 1970's and early eighties, describing the association between widespread musculoskeletal pain, characteristic points of body tenderness, and a stage IV, non-REM (rapid eye movement) sleep disorder.[47,48,49] In patients with widespread musculoskeletal pain, and in healthy subjects undergoing experimentally-induced stage IV sleep deprivation, there was "an anomalous intrusion of alpha rhythms" into the normal electroencephalographic (EEG) pattern of stage IV delta wave activity. Moreover, twenty-four hours of experimental deprivation of stage IV, but not REM, sleep resulted in widespread musculoskeletal pain and tenderness. They proposed that the label 'fibrositis' be restricted to individuals with widespread musculoskeletal pain and a non-restorative sleep pattern. Previously and for some time afterwards, the term 'localized fibrositis' was used to describe regional muscular pain, and various other non-specific terms such as 'psychogenic rheumatism'[50]

and 'chronic pain syndrome' were used to describe more diffuse muscular pain. There still are proponents of such terminology.[51,52]

1.1.3 **Clinic Studies**

In the 1980's, several researchers attempted to characterize the syndrome called fibrositis as it existed in rheumatology clinics, resulting in several additional sets of diagnostic criteria.[16,53,54,55] Because of further studies that failed to demonstrate any inflammatory process within muscle or fibrous tissue,[38,39] the presumptuous and probably inaccurate term fibrositis was replaced by the more descriptive term 'fibromyalgia', meaning pain in muscles and fibrous tissues. Finally, in 1990, the Fibromyalgia Multicentre Criteria Committee, under the auspices of the American College of Rheumatology (ACR), published classification criteria for fibromyalgia that included a requirement for at least three months of widespread musculoskeletal pain, in addition to tenderness upon digital palpation at a sufficient number of characteristic 'tender points'.[27] These criteria were presented following a multi-centre study of approximately 265 patients previously diagnosed by their rheumatologists as having FMS, and a similar number of age-and sex-matched non-FMS rheumatology clinic controls. Each study subject completed a symptom checklist and was examined by multiple independent observers. The combination of widespread chronic pain and at least eleven tender points (out of 18 palpated sites) was found to be 88.4% sensitive and 81.1% specific for FMS in that study population.

1.2 THE EPIDEMIOLOGY OF FIBROMYALGIA

1.2.0 Fibromyalgia in the Clinic Population

In 1977, Epstein and Henke analyzed the results of a questionnaire that had been mailed out and completed by 826 rheumatologists practicing in the United States.[30] They found a discrepancy in the frequency of certain conditions between university-based and community rheumatology practices: academic rheumatologists reported that tendonitis and bursitis accounted for only 5.7% of their cases, and fibrositis for 2.0%; community rheumatologists reported these diagnoses accounting for 11.6% and 6.0%, respectively. Both academic and community rheumatologists reported that degenerative joint disease and rheumatoid arthritis were the two disorders seen most commonly. Another U.S. survey of four community rheumatologists, which involved an audit of practice records, found FMS to account for 6.1% of new cases, "back syndrome" for 20%, and shoulder tendonitis, bursitis and capsulitis for 9.7%.[31] In 1981, a rheumatologist in Orange County, California reported on the first thousand patients seen in his practice; as in previous surveys, rheumatoid arthritis and degenerative joint disease were the most common disorders seen; myofascial pain syndrome and "psychogenic rheumatism" only accounted for 4.7% and 3.3%, respectively.[56] These figures contrasted with the first year in practice of a rheumatologist in Cleveland, Ohio, for whom FMS accounted for 16% of new patients.[32] Clearly, referral bias and ascertainment bias both may have played a major role in these discrepant figures.

Perhaps as a result of increasing acceptance of the diagnosis of FMS, at least among rheumatologists, more recent rheumatology clinic surveys have generally estimated the percentage of patients with FMS to be between 10 and 20 percent; these include surveys in the United States,[53,55,57] Mexico,[58] Spain,[59] and Australia.[60]

In 1993, White et al undertook a mail survey of a random sample of Canadian rheumatologists.[25] The sampling frame was the 1991 Canadian Rheumatology Association Membership Directory, excluding non-rheumatologists, paediatric rheumatologists, and rheumatologists not currently practicing in Canada. The final sampling list included approximately 250 names, stratified into three geographic regions (Eastern Canada, Ontario, Western Canada), and substratified into small urban (population < 500,000) and large urban (population = or > 500,000) centres, based upon the geographic location of each practice. From this list, 100 rheumatologists were randomly selected for survey. After three mailings, 89 of 100 had responded. The five disorders reported as being most commonly seen were osteoarthritis (28.1% of new patients), FMS (23.4%), mechanical neck or back pain (22.9%), localized soft tissue rheumatism (18.8%), and rheumatoid arthritis (18.4%). Fibromyalgia was among the three most common disorders seen by almost half (48.3%) of all respondents. It was the only disorder perceived by a majority (69.3%) to have increased in frequency within their practices over the previous five years. Only four rheumatologists (4.4%) felt it had decreased over the same 5 years; one of these four reported having made a conscious decision not to see FMS patients, because she had been seeing too many with this

diagnosis. The survey results were consistent across all 6 substrata. A chart audit of 3 surveyed rheumatology practices, performed to estimate the accuracy of self-reported frequencies, found that self-reported estimates of FMS frequency and true frequency differed only by 1.2%.

In addition to being common within rheumatology clinic populations, FMS appears to account for a significant percentage of patients seen in family practice clinics (2.1%),[61] general medicine clinics (5.7%),[54] and hospitals (7.5%).[62]

1.2.1 Potential sources of bias in clinic samples of FMS

There are significant limitations to using clinic or hospital studies to make inferences about the incidence, prevalence and clinical characteristics of a disorder such as fibromyalgia, as is suggested by Wolfe's *fibromyalgia funnel*.[63] In his model, Wolfe argues that individuals in the community who have fibromyalgia are quantitatively and qualitatively different from individuals who become enrolled as subjects in FMS studies. One reason for this is that someone with FMS in the community must pass through several decision filters before she or he can be recognized as a potential study subject. The individual must have symptoms that are severe enough, problematic enough, or of sufficient duration that she seeks medical attention. Where evaluations by a specialist must be arranged by referral from a general practitioner, as in Ontario, the FMS patient must have chronic symptoms that do not respond adequately to initial treatment, or must express sufficient concern that a referral is made. The referral must be made to a centre

in which FMS research is being conducted; perhaps patients with more classic symptoms (or more severe symptoms) are more likely to be referred to a research centre. Once referred, a patient with more severe and/or treatment-resistant symptoms may be more likely to remain a patient in the specialty clinic for a longer duration of time, with more frequent visits; hence, he may have a greater probability of being recruited into a study than someone who is successfully treated or has milder symptoms and is discharged after one or a few visits. That disease in the community tends to be milder and less chronic than disease in specialty clinics already has been shown both for rheumatoid arthritis[64] and for chronic musculoskeletal pain.[65,66]

There also may be demographic factors that influence the likelihood of being recruited into a study. Females are more likely than males to seek medical attention.[67,68,69] Certain age groups receive more medical attention than others.[70] People of different ethnic backgrounds utilize westernized medical care to varying degrees.[71,72] Because illness is a common reason for leaving the work force, it is reasonable to assume that non-working individuals utilize more health care than those who work. In addition, there may be demographic differences in the way in which the diagnosis of FMS is applied. For example, it once was believed that ankylosing spondylitis, an inflammatory arthritis and enthesitis principally involving the axial skeleton, was restricted to males. The diagnosis may not have been considered in many females who otherwise would have met the diagnostic criteria. Recent evidence suggests that ankylosing spondylitis may be as common in females as in males, though there may be sex differences in the clinical presentation of the disease.[73]

1.2.2 **Fibromyalgia in the General Population**

The first general population study of FMS reported in the English medical literature appeared in the Scandinavian Journal of Rheumatology in 1989.[74] As in several of the early studies and for an obvious reason, the investigators did not utilize the 1990 ACR criteria, which limits comparison of these results to more recent studies. In 1985, Jacobsson et al contacted 450 men and 450 women, all aged 50 to 70 years, who previously had been randomly selected from the general population of Malmo, Sweden, to participate in a 1984 health survey. Of the 876 who participated, 450 were examined by a rheumatologist to confirm or exclude a list of rheumatic disorders, 198 completed a mailed questionnaire, 142 underwent a telephone interview, and 47 agreed to have their medical files reviewed; for the remaining 37, there was inadequate information to include them in analysis. Nine cases of *primary FMS*• were reported, of which 5 had been confirmed by examination. Eight of nine (four of five confirmed) cases were female. The prevalence of FMS was similar in the total group of 876 (1.0%, 95% confidence interval [CI] 0.4%, 1.7%) as in the 450 subjects who had been examined by a rheumatologist (1.1%, CI 0.1%, 2.1%).

• *Primary FMS* is fibromyalgia that occurs in the absence of any other significant musculoskeletal disease. *Secondary FMS* occurs in the setting of some other musculoskeletal disease, such as rheumatoid arthritis. The 1990 ACR criteria recommended that the designations of primary and secondary FMS be abandoned.

A major limitation in the study by Jacobsen et al, at least with respect to how FMS currently is defined, are the criteria that were used to confirm and exclude FMS. Yunus' criteria for FMS,[75] published in 1981 and used in the Swedish survey, specifically exclude "patients with aches and pains thought to be related to trauma (obvious or due to repetitive use)" and patients with "clinical evidence of any organic systemic illness". Several recent studies have documented the higher than expected occurrence of FMS in a variety of rheumatic conditions, approaching 50% in patients with RA,[76] lupus[77] and osteoarthritis.[78] Greenfield et al reported on 127 FMS patients seen consecutively either in a university hospital rheumatology clinic or a suburban rheumatology practice; 23% reported having had trauma, surgery or a medical illness coincident with the start of FMS symptoms, and were labeled as having *reactive fibromyalgia.*[79] In a more recent prospective study, 21.6% of neck injury patients developed FMS within twelve months of the traumatic event.[80] Also, Yunus' criteria require that "all relevant investigations including roentgenographs" be normal. However, the frequency of asymptomatic abnormalities on lumbosacral spine radiographs may exceed 50% in the general adult population.[81] Hence, the utilization of these strict exclusion criteria likely resulted in a marked under-estimation of the prevalence of FMS in this population. Also, because only 9 cases of FMS were identified, only 5 of whom were confirmed, little useful information about the demographics or clinical characteristics of these cases can be ascertained.

In 1991, Makela and Heliovaara reported a fibromyalgia prevalence of 0.75%, identifying 54 cases (38 female, 70%) among 7217 adults age 30 or greater in Finland.[82]

Fibromyalgia was more common in women ($p < 0.04$), and its prevalence appeared to steadily rise with age into the 55-64 year age group, before leveling off. Prevalence was inversely proportional to level of education. There are at least three major limitations of this study. The first is that the investigators utilized data that had been collected during the mini-Finland Health Survey, completed between 1977 and 1980, at which time there had been no intent to screen for fibromyalgia. Makela and Heliovaara reviewed the records of the 3434 subjects who had reported moderate or severe musculoskeletal symptoms, and retrospectively assigned the label of FMS using *post hoc* criteria. Second, because the initial examinations all had been performed prior to the publication of any FMS criteria, no validated or widely utilized criteria were used. This casts doubt as to how many of the 54 `cases' would meet currently accepted criteria, and how many of the 3390 non-cases would fail to meet current criteria. Finally, because only subjects with moderate or severe pain were examined, this would eliminate any mild cases of FMS.

Forseth and Gran studied the prevalence of FMS among women aged 20 to 49 years in the small town of Arendal on the South coast of Norway.[83] In 1989 and 1990, all 2498 eligible women residing in Arendal were invited to complete a questionnaire involving several questions on rheumatic complaints; 2038 questionnaires were completed and returned (81.5%). A positive responder was defined as someone who reported having had pain/or stiffness lasting at least 3 months in any one of four body locations: 1) the joints, 2) the muscles, 3) the back, 4) all over. More than half (1165, 57%) gave a positive response, of whom a random 242 (20.8%) were invited for a confirmatory examination. Of these, 217 (89.7%) were examined, and 40 cases of FMS

were identified, for an estimated prevalence of FMS in this population of 10.5%. Of the forty identified cases, nine had abnormal screening laboratory tests (23%), and nine had comorbid conditions, including hypothyroidism (4 cases, 10%), arthritis (2 cases, 5%), and malignancy, trauma and osteoporotic fracture (1 case each).

Before 1992, there had been no reported prospective studies of FMS in anything other than relatively narrow subgroups of the general adult population. At the Second World Congress on Myofascial Pain and Fibromyalgia, Myopain '92, held in Copenhagen, several abstracts were presented addressing the prevalence of FMS in adults. Croft et al[84] surveyed 1340 adults, aged 20-85, selected at random from the population registers of two suburban practices in Cheshire, England. In a mailed questionnaire, 13.2% reported chronic widespread pain the authors felt was consistent with the first ACR criterion for FMS*. No estimate of FMS prevalence could be made, because the presence of fibromyalgia tender points was not confirmed. Also, because these were patient registries, the sampling frames may not have been representative of the general population.

Raspe and Baumgartner[85] randomly selected 541 German residents of Bad Sackingen, of whom 438 (81%) responded to a mailed questionnaire. They used criteria for FMS that have not been published elsewhere, including 34 active tender points and 10

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* Their definition of widespread pain (axial pain plus pain in at least 2 contralateral quadrants of the body) in fact is not equivalent to the 1990 ACR first criterion (pain that is right and left-sided, above and below the waist, axial and peripheral); an individual could have contralateral 2 quadrant pain above but not below the waist, and vice versa.

control points. A subject was classified as having FMS if he or she had tenderness to digital palpation at no fewer than 17 active tender points and at no more than 2 control points. Applying these criteria, they identified 10 cases, and estimated a minimum prevalence of FMS at 1.9%. However, several subsequent clinic studies in FMS patients have documented hyperalgesia* both at classic tender points and control points versus control subjects, thereby invalidating the control points used in the German study.

Lyddell and Meyers[86] interviewed 84% (n = 1102) of all the adults of age 34 years and older in a small South African rural community. Utilizing the 1990 ACR criteria, they estimated the prevalence of FMS to be 3.2%. All cases were female, with a mean age of 45 years.

Abstracts presented at the 1992 Workshop of the Standing Committee on Epidemiology European League Against Rheumatism (EULAR) included estimates of FMS prevalence of 4.8% in 2034 British adults aged 18 to 75 years, and 4.5% in 1105 Polish adults 18 and older.[87]

Two community surveys went beyond just estimating FMS prevalence. They also addressed the clinical characteristics and costs of FMS. In 1993, Prescott et al reported the results of a survey of 1219 Danish adults aged 18 to 79 years. Using a checklist, subjects were asked if they had pain or discomfort in any of 9 body sites. Positive responders, defined as having had pain at no fewer than 3 sites, with pain both above and

* increased tenderness to digital palpation.

below the waist,[♦] were invited to have an examination for fibromyalgia tender points utilizing the 1990 ACR criteria. Examinations were performed on only 65 of 123 positive responders (53%), confirming FMS in 8 females. The estimated minimum prevalence of FMS was 0.66%.[88] Although the absolute number of confirmed FMS cases was too small to analyze for demographic and clinical characteristics, the investigators divided the 44 examined females[▼] into three groups, based upon their fibromyalgia tender point count: 1) 0 to 4 points, N = 22; 2) 5 to 10 points, N = 14; 3) 11 or more points, N = 8. Having more tender points was associated with a higher score on a pain index ($p = 0.002$), more subjective swelling ($p = 0.009$), worse fatigue ($p = 0.004$), more frequent headaches ($p = 0.04$), a perception of worse overall health ($p = 0.001$), and greater difficulty climbing up stairs ($p = 0.004$).[89] Although these results could be subject to the hazards of multiple comparisons, that 6 out of 24 variables were statistically different between groups, all but one at a p level below 0.01, argues against this entirely being explained by chance. It appeared that the fibromyalgia tender point count, in itself, was a predictor of worse overall symptoms and function.

In 1995, Wolfe et al reported on the results of a mailed survey of 3006 adults aged 18 and older living in Wichita, Kansas. Subjects were categorized into four groups according to their responses on the questionnaire. Group 1 subjects (62.4% of the survey sample) had no pain. Group 2 subjects (5.0%) had current musculoskeletal pain that had been present for less than 3 months. Group 3 subjects (20.1%) had current non-

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♦ This does not necessarily meet the first ACR criterion for FMS.

▼ Males were excluded to eliminate sex as a potential confounder.

widespread musculoskeletal pain that had been present for at least 3 months. Group 4 subjects (10.6%) reported at least 3 months of widespread musculoskeletal pain, meeting the first ACR criterion for FMS. The remaining 1.9% had non-musculoskeletal pain.

Subjects from Groups 1, 3 and 4 were invited to participate in a more detailed in-person evaluation including a tender point examination, reporting of current symptoms, and psychological testing using the SCL-90-R symptom checklist[90] and the Arthritis Impact Measurement Scale (AIMS) depression and anxiety scales[91]. This resulted in 391 evaluations, 69% female, 31% male: 91 in Group 1 (no pain), 102 in Group 3 (chronic regional pain), and 193 in Group 4 (chronic widespread pain). Thirty-six cases of FMS were identified, all in Group 4; the sex distribution of cases was not given. The age- and sex-adjusted prevalence of FMS was estimated at 2.0% overall (CI 1.4%, 2.7%), 3.4% in women (CI 2.3%, 4.6%), 0.5% in men (CI 0.0%, 1.0%).[92]

Demographic factors associated with the presence of FMS in the general population were female sex (odds ratio [OR] 9.1; CI 1.8, 46.8), being divorced (OR 4.3, CI 1.0, 18.1), failure to complete high school (OR 3.5, CI 1.0, 11.9), and household income (OR 0.96, CI 0.93, 0.99).

Clinical factors associated with FMS were decreased pain threshold on dolorimetry* testing (OR 4.5, CI 3.2, 7.8), "pain all over" (OR 5.6, CI 2.6, 11.8), subjective joint swelling (OR 4.9, CI 1.4, 17.2), paresthesias (OR 4.8, CI 2.4, 9.8), morning stiffness of greater than 15 minutes duration (OR 4.4, CI 1.5, 13.1), sleep disturbance (OR 3.8, CI 1.2, 12.0), fatigue (OR 3.3, CI 1.1, 10.0), irritable bowel syndrome• (OR 2.5, CI 1.3, 4.9), moderate impairment on the Health Assessment Questionnaire (HAQ) (OR 9.5, CI 3.8, 24.1), severe impairment on the HAQ (OR 9.1, CI 2.0, 167.8), a 1 unit increase in pain on a 3 unit visual analog scale [VAS] (OR 5.2, CI 2.3, 11.5),), a 2 unit increase in pain on a 3 unit VAS (OR 9.1, CI 4.1, 20.1), fair and poor self-reported health status (OR 4.0, CI 1.7, 9.4 and OR 25.6, CI 5.4, 121.2, respectively), and moderate and marked dissatisfaction with health (OR 5.2, CI 1.5, 18.4 and OR 23.8, CI 4.5, 126.7, respectively).

Psychological factors associated with FMS included somatization• (OR 10.3, CI 2.6, 40.7), number of positive items on the symptom checklist (OR 8.0, CI 1.9, 33.7),◆ anxiety (OR 5.1, CI 1.7, 15.4)◆ and (OR 4.9, CI 2.1, 11.2),▾ depression (OR 2.9, CI 1.1, 7.8)◆ and (OR 2.9, CI 1.0, 7.9),▲ increased global severity of psychiatric illness

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* A dolorimeter is a spring-loaded pressure gauge used to measure tenderness at body points. The pressure at which tenderness is elicited is recorded for each body point. The sum of these scores for all body points tested is called the Total Myalgic Score.

• Irritable bowel syndrome was defined as abdominal pain and diarrhea or constipation.

◆ The odds ratio was calculated as the proportion of FMS versus non-FMS cases with a t-score of 60 or greater on the appropriate SCL-90-R psychiatric symptom rating scale.

▾ The odds ratio was calculated as the proportion of FMS versus non-FMS cases with a score of 4.0 or greater on the AIMS Anxiety Scale.

▲ The odds ratio was calculated as the proportion of FMS versus non-FMS cases with a score of 6.0 or greater on the AIMS Depression Scale.

(OR 4.8, CI 1.8, 13.3),◆ history of past or current depression (OR 4.2, CI 1.9, 9.5), prior hospitalization for depression (OR 3.9, CI 1.3, 12.2), current depression (OR 2.6, CI 1.1, 6.3), and family history of depression (OR 2.2, CI 1.1, 4.6). History of prior or current drug therapy for depression approached statistical significance (OR 2.8, CI 1.0, 7.8).

With respect to health service utilization and disability, a greater proportion of persons with FMS versus persons without had visited a physician in the previous 6 months (OR 3.2, CI 1.6, 6.6) and had applied for disability benefits (OR 5.9, CI 2.5, 14.2), but there was no significant difference with respect to current analgesic use (OR 1.0, CI 0.5, 2.3).

Subjects from the three examined groups were pooled to compare females versus males with respect to tender point (TP) counts, dolorimetry scores, and FMS symptoms.[93] Females had a higher mean TP count, a greater likelihood of having 5 or more TP (OR 2.8, CI 1.3, 6.0) and of having 11 or more TP (OR 9.6, CI 2.0, 46.3). Pain threshold, as measured by dolorimetry, was lower in females; controlling for age, the difference between the sexes using linear regression was 2.0 kg/cm^2 (CI 1.4, 2.7). Women also were more likely to have a variety of FMS symptoms than were men: "pain all over" (OR 3.9, CI 1.3, 11.4), fatigue (OR 4.5, CI 2.0, 10.1), sleep disturbance (OR 3.1, CI 1.5, 6.5) and irritable bowel (OR 5.2, CI 1.8, 15.0). The tender point count was correlated more strongly with FMS symptoms than with dolorimetry scores.

Each of the above statistically significant results potentially could be explained by chance because the nominal p value is affected by the multiple comparisons. However, it is extremely unlikely that all of the results were produced by chance, given that 39 statistically significant differences were noted in 48 group comparisons (81%), which is far greater than the 5% expected by chance. Hence, these results were the first to strongly support the notion that FMS, as defined by the 1990 ACR criteria, is a syndrome of multiple symptoms that is clinically distinct from the isolated aches, pains and other complaints of the general population, a case which some critics of FMS have made.[19] The Wichita survey also was the first report to address the issue of FMS costs to society, though it focused upon only a few variables, did not estimate costs in terms of dollar amounts or utilities, and provided no evidence about the validity of these self-reported costs.

The London Fibromyalgia Epidemiology Study (LFES) was designed and begun prior to the publication of the Wichita results, though the study designs are somewhat similar. One limitation of the Wichita study was that only 36 FMS cases were identified. This eliminated the potential for comparison between FMS cases and chronic pain patients without FMS, with respect to demographic, clinical and functional parameters. One of the two primary objectives of LFES was to identify between fifty and one hundred FMS cases. A second limitation of the Wichita study concerns the difficulty of accurately estimating actual health care costs, due to the multiple insurance payer system that exists in the United States. In Ontario, where the Ministry of Health essentially pays for all physicians' fees and hospitalization and laboratory costs, we have the opportunity

to accurately ascertain these direct costs to the health care system, both for FMS cases and non-cases.

1.3 THE CLINICAL CHARACTERISTICS OF FIBROMYALGIA

> "In the morning they asked her how she had slept. "Dreadfully!" said the princess. "I hardly got a wink of sleep all night! Goodness knows what can have been in the bed! There was something hard in it, and now I'm just black and blue all over! It's really dreadful!... Only a real princess could be so tender as that."
>
> *The Princess and the Pea, Hans Christian Andersen*[♣]

1.3.0 Symptoms and signs

The name 'fibromyalgia' stems from the Latin word *fibra*, meaning fiber, and the Greek words *mys* (muscle) and *algos* (pain).[•] The core clinical characteristics of FMS as it occurs in rheumatology clinics are: 1) generalized musculoskeletal pain, felt mostly in muscles, and 2) muscle and fibrous tissue tenderness[94] especially at, but not exclusive to, characteristic fibromyalgia tender points.[95] A subset of FMS patients complain more of joint pain than muscle pain when initially presenting to a rheumatology clinic.[60] Approximately 50% complain of pain that is "all over".[96] This pain frequently is associated with marked stiffness, especially in the morning, but also post-exertional[97] and

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♣ Spink R [translated]: Hans Andersen's Fairy Tales. E.P. Dutton & Co., Inc., New York, NY, 1958.
• Mosby's Medical, Nursing and Allied Health Dictionary, 4th Edition, Mosby Year Book, Inc, St. Louis, MO, 1994.

sometimes lasting all day.[53] Additional sources of pain are headaches, eye pain, sore throat, and abdominal and pelvic pain.

Other characteristic features of FMS are the oftentimes debilitating fatigue and non-restorative sleep pattern, complaints that may be explained by the non-REM sleep disorder reported by Moldofsky.[47] Common additional features are subjective swelling and paresthesias, especially of the hands and feet, Raynaud's phenomenon, anxiety, panic attacks, and depression. Frequent comorbid conditions are migraine headaches, Irritable Bowel Syndrome (IBS), and primary dysmenorrhea.[96] Less frequent comorbid conditions include female urethral syndrome (FUS) and Sicca Syndrome.[98]

In addition to the characteristic fibromyalgia tender points, other findings on physical examination frequently include myofascial trigger points,[98] skin fold tenderness and reactive hyperaemia, and decreased tissue compliance at various musculoskeletal sites.[95] Decreased pain threshold on dolorimetry testing has been proposed as a more objective physical finding than tenderness to digital palpation, but inter-rater reliability for the two techniques is comparable, and dolorimetry testing may be less sensitive.[99] Dolorimetry readings are affected by numerous factors such as the dolorimeter foot plate surface area, dolorimeter scale length, and the rate at which dolorimeter pressure is applied.[100,101]

1.3.1 The Fibromyalgia patient

In clinic studies, the percentage of adult FMS patients who are female ranges from 75 to 87 percent, and the mean age at presentation ranges from the mid thirties to the mid fifties.[16,53,54,55] Estimates of mean duration of symptoms prior to presentation to a rheumatology clinic are between 5 and 8 years, with a range of 0.25 to 24 years prior to diagnosis.[16,53,54,55] However, a study of Israeli school children found FMS in 6.2%,[102] suggesting that it sometimes may have its onset early, only to present to rheumatology clinics later in life. This point again highlights the risk of estimating characteristics of a disease based upon tertiary clinic studies. Referral bias may result in younger patients either being less likely to be referred to a specialist, or perhaps being referred to different specialists than rheumatologists; for example, paediatricians, sports medicine specialists and orthopaedists.

Several patterns of onset have been described. One pattern is an insidious onset without any antedating or precipitating event. A second pattern of onset is much more acute, often appearing to have been precipitated by some event. There are those who suggest that FMS often is caused by some form of traumatic event.[79,103,104,105,106] However, any causal association between trauma and FMS onset remains unproved and highly controversial.[107]

Fibromyalgia may present in association with a variety of psychiatric illnesses. In several studies, FMS patients have scored higher than controls on scales for anxiety,

depression, hypochondriasis and somatization.[108,109,110,111] Some authors have interpreted this as evidence either that psychiatric illness causes FMS or that FMS is a psychiatric illness.[28,112] Caution must be exercised when interpreting the results of these studies, however. First, patients with chronic pain, irrespective of the aetiology, will score abnormally on a number of psychological tests when compared with healthy controls,[108,113] which may result in erroneous results particularly in assessing depression, hysteria and hypochondriasis.[113,114] Second, the majority of patients with FMS do not show significant differences in these scale scores compared with patients with RA.[109,111] Third, the majority of FMS subspecialty clinic patients do not have a psychiatric illness.[16,115] There is evidence that psychiatric diagnoses in FMS patients are related to health care-seeking behaviour, rather than to the illness itself.[116] It may be that the frequency of comorbidity of psychiatric disorders with FMS is very low in the general population; no study yet has addressed this issue. Finally, establishing a causal role of psychiatric illness for FMS requires confirmation of the appropriate temporal relationship of these two disorders; the psychiatric illness must occur prior to the onset of FMS. No longitudinal data are available with respect to this temporal relationship.

The evidence is as strong or stronger that FMS is associated with a variety of other non-psychiatric disorders. Fibromyalgia frequently occurs in the setting of comorbid rheumatic diseases. Up to 65% of rheumatology clinic patients with primary systemic lupus erythematosis (SLE) meet the ACR criteria for FMS,[77] and FMS appears to be a common component of rheumatoid arthritis[76] and osteoarthritis.[78] Men and women who are infected with the human immunodeficiency virus (HIV)[117] and women

with hyperprolactinaemia[118] or thyroid disease[119] appear to have a significantly increased risk of FMS. Women with hyperprolactinaemia have a risk that is fifteen times as great as women without. Males with sleep apnea may or may not have an increased risk of FMS.[120,121] Despite the apparent associations between FMS and various comorbid illnesses in clinic case-control studies, there have been no studies estimating the frequency of comorbid illness in individuals with FMS in the general community. Since FMS appears to be relatively common, it may be that comorbid illness only affects a small percentage of the total FMS population.

In the London Fibromyalgia Epidemiology Study, we collected demographic data on 100 FMS cases from the general population, as well as self-reported information on disease onset, the range, severity and duration of symptoms, and comorbid illnesses. Because of cost constraints, we did not perform investigations to confirm or exclude comorbid conditions. Confirming a diagnosis of rheumatoid arthritis, for example, as a minimum would require testing serum for the presence or absence of rheumatoid factor (RF), and taking radiographic images of the hands, wrists, ankles and feet of any subject in whom RA was suspected by history and examination. Moreover, the absence of RF and radiographic changes would not exclude RA, since these tests commonly are negative early in the course of RA.[122]

1.4 THE FIBROMYALGIA - CHRONIC FATIGUE SYNDROME DEBATE

Like fibromyalgia, there is no diagnostic test that is confirmatory for diagnosing chronic fatigue syndrome (CFS). The U.S. Centers for Disease Control and Prevention (CDC) has endorsed a working definition for CFS, that was published in the Annals of Internal Medicine in 1988. This definition requires that a patient fulfill 1 major and a number of minor criteria, most of which are very subjective symptoms (eg. arthralgias) or non-specific signs (eg. fever).[123] Although the case definition also requires exclusion of other potential causes of fatigue, it is very difficult to exclude FMS because of the striking similarities between these two syndromes. Profound fatigue often is a major complaint among fibromyalgia patients. Diffuse muscle and joint pain are frequent symptoms of CFS, each being one of the 11 minor symptom criteria in the CDC case definition. Each of the first 10 minor symptom criteria for CFS are frequent complaints among FMS patients. The eleventh criterion is an acute onset of symptoms over a few hours to a few days, a pattern that has been described for FMS. Although many consider CFS to be transmitted by an infectious agent, a flu-like or other infectious onset is not required by the 1988 CDC criteria. As with FMS, some people with CFS report a precipitating event such as infection or trauma, while others report a more insidious onset.

Other similarities between FMS and CFS are that each has no known cause, there is no highly effective therapy for either syndrome, the symptoms in both tend to be chronic, and both conditions seem to be more common in women, including the young.[124]

Goldenberg et al examined 27 patients with debilitating fatigue of at least six months duration in a primary care practice.[125] Sixteen of the 27 met the 1988 CDC criteria for CFS; nineteen (70%) met the 1990 ACR criteria for FMS. Hudson et al studied 33 rheumatology clinic patients with FMS, and found that 14 (42%) met the full CDC criteria for CFS, and an additional 9 (27.3%) were within one minor symptom of meeting the CDC criteria.[126] In contrast, Wysenbeek et al reported on 33 FMS clinic patients, of whom 21 (63.6%) reported significant fatigue; however, only 7 (21.2%) met the CDC criteria for CFS.[127] The difference in the results of these two studies could be related to differences in referral patterns at the two centers, hence to referral bias. To date, there have been no reported studies examining the prevalence of comorbidity of FMS and CFS in the general community. A community survey using probabilistic sampling would have the advantage over clinic studies of eliminating referral bias.

1.5 DISABILITY IN FIBROMYALGIA

Some patients with FMS develop disability that is considered severe enough to prevent them from seeking, continuing or resuming gainful employment.[128] Evidence supporting this comes from several sources and countries. A U.S. survey of 620 clinic patients with FMS found that 15% currently received disability payments.[129] A subsequent survey of rheumatology clinics at six different centers across the U.S. revealed that 26.5% of FMS patients were receiving some form of disability compensation.[130] Twenty-four percent of 55 Swedish patients with FMS were receiving

pensions.[131] In a prospective study of 72 British patients, 50% stopped working because of their illness during the four years of follow-up.[132] A 1988 survey in Norway found that FMS was the most frequent single diagnosis for disability pensions.[133] A survey of Canadian insurance company records found that FMS was responsible for 9% of all disability payments, accounting for an estimated $200 million annually.[134]

Patients with FMS report disabilities in activities of daily living (ADL) that are as extensive as those reported by patients with rheumatoid arthritis (RA), and more extensive than those reported by patients with osteoarthritis.[135] They rate their quality of life as lower than either patients with RA or OA.[136] They report lower overall health and functional status and greater pain than patients with RA, OA, systemic lupus erythematosis (SLE) or scleroderma.[137] Moreover, comorbid FMS may significantly adversely affect the quality of life of patients with other rheumatic conditions, such as lupus.[138]

A contributing factor to FMS patients' relatively high self-reported level of disability may be the greater levels of pain and fatigue they report compared to patients with other rheumatic disorders. For example, when compared to patients with RA and Ankylosing Spondylitis (AS), FMS patients report pain that is greater in intensity, more likely to involve the upper extremities, and more continuous; they also report more severe fatigue.[139,140] Various models have been proposed to explain how the interplay between chronic pain and both intrinsic and extrinsic factors might result in chronic disability.[141,142] Despite these attempts, the issue of disability in FMS remains very complex and highly

controversial, largely due to the relative lack of understanding with respect to the pathogenesis of this disorder and chronic pain in general, and great inadequacies in the process of disability evaluation itself.[129]

1.6 CONTROVERSIES IN FIBROMYALGIA

1.6.0 Overview

"In no other field have pseudoscientists flourished as prominently as in the field of medicine."*

Fibromyalgia has been classified as one of several 'functional' disorders, about which there is much heated debate and disagreement. Included among many in this group are chronic fatigue syndrome (CSF), myofascial pain syndrome (MPS), irritable bowel syndrome (IBS), premenstrual syndrome (PMS), and temperomandibular joint dysfunction syndrome (TMJDS). The debate with respect to FMS is focused upon four main issues: 1) Is FMS a real pathophysiologic entity? 2) Is the label 'fibromyalgia' useful or harmful? 3) Is FMS a legitimate potential cause of disability? 4) Can trauma cause or trigger FMS?

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*Gardner M: Fads and fallacies in the name of science. New York, Dover, 1957, pg. 86.

1.6.1 Is Fibromyalgia a real pathophysiologic entity?

Critics of FMS argue that there is no good evidence to support that FMS is anything other than a psychiatric illness or, worse yet, malingering. They finger the subjectivity of the symptoms, the lack of physical findings except the tender points, the potential for patient manipulation of the tender point examination, and the dearth of specific pathophysiologic findings or objective evidence to explain the symptoms. They also highlight the frequent association of FMS with current or past psychiatric illness. As recently as 1989, FMS appeared in a chapter on "Psychogenic Rheumatism" in a prominent rheumatology textbook.[50]

Caution must be exercised in accepting these arguments. First, symptoms are, by definition, subjective.[143,144] Pain and fatigue cannot be measured, other than by patient report, irrespective of the situation in which they occur. To date, scientists can no better measure the pain or fatigue of a patient with cancer or angina than they can of a patient with FMS. Moreover, there is significant evidence that shows a very poor correlation between physical, radiographic, or histopathologic findings and pain. A well described and widely accepted example in the medical literature of pain occurring in the absence of any physical or radiographic changes is polymyalgia rheumatica (PMR), in which patients report diffuse proximal muscle pain and stiffness in the absence of any physical or histologic findings; that their pain is 'real' rarely is questioned, likely because of the dramatic response these patient have to low dose parenteral steroids. Another well

accepted entity in which severe pain is experienced without any documented histopathology is trigeminal neuralgia, a condition which often is treated surgically.

A graphic example of the converse is the Charcot joint, in which massive destruction of a joint and the surrounding bone can occur, producing gross deformity, all in the absence of any pain. This analgesia occurs often despite otherwise normal or near normal sensation in the affected area. In one study on low back pain, the prevalence of pain was no greater in patients with abnormal versus normal radiographs of the lumbosacral spine.[81] Hence, it is inaccurate to assume that the degree of pain can be predicted on the basis of the degree of physical, histologic or radiographic findings.

Is FMS real? The lack of pathophysiologic findings has been taken as evidence of lack of disease by those whose training does not exceed the biomedical model, the world view of cells and molecules. However, there is growing evidence of pathophysiologic changes in FMS patients. These include certain hormonal and other biochemical changes such as abnormal diurinal variations in corticosteroid secretion,[145] low serum levels of somatomedin-C[146] and tryptophan,[147] low cerebrospinal fluid (CSF) levels of 5-hydroxytryptophan,[148] and high CSF levels of substance P.[149] Thermographically measured skin temperature appears to be lower in the back[150] and higher in the hands[151] in FMS patients versus healthy controls, implying some alteration in normal dermal sympathetic activity in FMS. There also appears to be an abnormal sympathetic response to orthostatic stress.[152] Patients appear to have an alteration in brain wave activity in

Stage IV sleep.[47] Two recent studies suggest an alteration in the pattern of cerebral blood flow.[153,154]

It is true that the tender point examination likely could be manipulated by a patient. But the same is true of almost any disorder in which tenderness is utilized as a sign of disease; for example, the joint line tenderness utilized in the diagnosis of RA. One of the purposes of the current study is to see if the tender point examination, by distinguishing between individuals with chronic widespread pain who have eleven or more tender points versus those with fewer than eleven tender points, in itself is predictive of the quantity and severity of symptoms.

1.6.2 **Is the label 'fibromyalgia' useful or harmful?**

Those who feel the label of fibromyalgia is harmful argue that the process of labeling a patient with a particular diagnosis, in itself, creates illness behaviour and disability. In essence, labeling someone as 'diseased' can lead them to take on a 'sick role' and behave as if they are ill.[19,28,155,156] An eloquent case for the risks of labeling has been made by Hadler in the case of 'black lung disease' in the coal mining areas of the United States.[157] There also is evidence in FMS patients that the degree of concern they have about their health is an independent predictor of their overall level of disability.[158]

On the other hand, labeling a condition does not mean that its worst features will occur. There is no evidence to suggest that this is less true of FMS than it is of ischaemic

heart disease or lymphoma. Conversely, labeling with FMS may allay fears that some other, more ominous and even life threatening condition exists. It may reduce the likelihood of expensive, resource consuming and potentially harmful further investigations and treatment Labeling may be necessary for appropriate treatment.. Also, labeling is virtually a requirement, if researchers are to be able to study the clinical entity to determine its risk factors, cause, natural history, and response to treatment.

This study addresses the issue of diagnostic labeling. Among the 100 individuals from the general population we confirmed having FMS, twenty-eight were found not to have been previously diagnosed with FMS. In Chapter 6, we compare the quality and severity of symptoms, and the degree of functional disability in previously diagnosed versus undiagnosed cases. Future follow-up of these 100 cases, outside the context of this doctoral thesis, will assess whether or not labeling previously undiagnosed cases has an effect upon subsequent level of symptoms and disability, and upon subsequent utilization of health services.

1.6.3 **Is Fibromyalgia a legitimate potential cause of disability?**

There may be no issue more contentious in FMS than the issues of disability and the potentially causative role of trauma. These issues have not only medical, but also strong medicolegal implications.

Claims for work disability arise in several ways and involve various parties. A person with FMS may feel the symptoms are severe enough to prevent him or her from continuing gainful employment and may claim payment for disability from a public and/or private insurance agency. If the individual feels that the symptoms arose because of a work-related injury, the worker may apply for Workers' Compensation. If the symptoms are felt to have arisen as a result of a motor vehicle accident, the injured individual may seek compensation either from their own or the offending party's insurer. In any of these settings, the insurer, either public or private, will wish to evaluate these claims. The patient's employer may become involved, either directly or indirectly; the patient and/or insuring third party may request special considerations in returning to work, such as changing the work environment or job requirements. Because of this, disagreements may arise between the patient and the other parties, resulting in misunderstanding, conflict and litigation.

Controversial aspects of the disability evaluation process in FMS include:

1. Lack of acceptance of the diagnosis;
2. Psychological abnormalities, such as anxiety and depression, that frequently accompany FMS and/or chronic pain;
3. The distinction between self-reported and observed disability;
4. The disability evaluation format itself;
5. The lack of validated disability assessment instruments;
6. The uncertain efficacy of treatment;

7. The potential for the disability evaluation and compensation processes to aggravate symptoms and level of disability;
8. The great variance in physician attitudes with respect to FMS and chronic pain;
9. The use of inappropriate evaluation procedures;
10. The role of the workplace in aggravating and alleviating FMS symptoms.

The current study will address the following questions with respect to work disability in FMS:

1. What percentage of individuals in the community with FMS, versus chronic pain without FMS, consider themselves to be work disabled?

2. What percentage report receiving disability pensions?

3. What demographic and clinical factors are most predictive of work disability?

1.6.4 **Can trauma cause or trigger Fibromyalgia?**

An estimated 25% of FMS study subjects recall some event that immediately preceded the onset of their FMS symptoms; most often that event is physical trauma.[79] This trauma either can be major, as in a motor vehicle accident (MVA) or fall, or minor, as in the repetitive trauma that may occur in the work place. Bennett,[105] Greenfield,[79]

Romano[104]and Waylonis[103] all have characterized post-traumatic or 'reactive' FMS. Bennett has claimed that FMS symptoms, if they are to occur, can develop between 6 and 18 months following a traumatic event. Greenfield and Waylonis note that FMS patients whose onset has been traumatic have a worse outcome.

But there are many critics of the concept of post-traumatic FMS, some of whom are quite vocal.[112,159] Until recently, there was no convincing evidence either to support or refute an association between trauma and FMS.[107] In 1997, Buskila et al published the results of a study showing a 21.6% incidence of FMS among Isreali adults in the first year after suffering a neck injury.[80] Further studies are required to verify these results, and to assess the effect of other forms of trauma on FMS incidence.

In LFES, subjects with FMS and pain controls were asked to describe the onset of their symptoms, and whether or not their symptom onset was preceded by a specific, potentially precipitating event. Although these data may be subject to significant recall bias, the results may serve as a spring board for designing further prospective studies to determine risk factors for FMS.

1.7 OBJECTIVES OF THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY (LFES)

1.7.0 Overview

It is obvious from a review of the scientific literature that there exist numerous gaps in our knowledge with respect to the basic epidemiology of FMS, as basic as whether or not it should be considered a clinically distinct entity. The overall objective of the London Fibromyalgia Epidemiology Study (LFES) has been to estimate the prevalence and costs of fibromyalgia syndrome (FMS) as it occurs among non-institutionalized adults in a demographically representative mid-sized Canadian city.

1.7.1 Primary Objectives and Hypotheses

1.7.1.0 Objective #1: To estimate the point prevalence of FMS among non-institutionalized London adults.

A random telephone survey of 3395 non-institutionalized London adults was performed, screening for individuals with chronic, generalized musculoskeletal pain. Individuals with such pain were examined for the presence or absence of FMS, using published criteria. The point prevalence estimate was adjusted for age and sex, utilizing the 1991 London census data. Point prevalence for each sex was estimated for broad age categories (18-34 years, 35-49 years, 50-64 years, and over 64 years) to estimate both the age-specific and peak life time prevalence of FMS.

1.7.1.1 Objective #2: To identify a minimum of fifty randomly-selected confirmed cases of FMS from among the non-institutionalized adult population of London, Ontario.

The primary purpose of identifying at least fifty FMS cases was to be able to compare this group to two internal control groups, with respect to demographic, and clinical and functional variables, and to the same two internal control groups and a large external database with respect to level of health services and medication utilization. The two internal control groups were: 1) non-institutionalized adults with chronic widespread pain in whom FMS has been excluded; and 2) non-institutionalized adults without chronic widespread pain or FMS. The external control group was the database for the Ontario Health Insurance Plan.

The first internal control group was included to assess if and how FMS, as defined by the 1990 ACR criteria, can be distinguished from general, chronic widespread pain. Inclusion of the second internal control group permitted an estimation of the specific impact of FMS on the individual and on society as a whole. For example, it may be that a certain percentage of individuals with FMS admit to frequent headaches. However, an estimated fifteen to forty-five percent of general population adults report frequent severe headaches.[160] It may be that headaches, though common among FMS sufferers, are no more common than in the general adult population. Hence, they should

not be included as part of the fibromyalgia syndrome. Accessing the OHIP database permitted us to estimate direct health care costs in actual dollar amounts.

1.7.2 Secondary Objectives and Hypotheses

1.7.2.1 To develop and test an instrument to screen for FMS in general population studies, that was easy to use and exhibited high sensitivity, specificity, test-retest reliability and positive predictive value (PPV). The results of this analysis are presented in the next chapter.

1.7.2.2 To determine the prevalence of pain, chronic generalized pain, fatigue, debilitating fatigue, and self-reported arthritis and fibromyalgia in the general population, and to compare males and females. The results of this analysis and that of the next two listed secondary objectives are presented in Chapter 3.

1.7.2.3 To determine the effect of demographic variables on the odds of having FMS.

1.7.2.4 To compare males and females, with and without chronic, generalized pain or FMS, with respect to health services utilization.

1.7.2.5 To determine the most common symptoms and most common major symptoms among FMS patients. The results of this analysis and that

of the next two listed objectives are presented in Chapter 4.

1.7.2.6 To determine what demographic and clinical characteristics distinguish FMS from chronic, generalized non-fibromyalgia pain.

1.7.2.7 To compare the clinical characteristics of FMS in males versus females.

1.7.2.8 To determine what demographic and clinical characteristics in FMS patients are predictive of poor function and work disability. The results of this analysis are presented in Chapter 5.

1.7.2.9 To identify a cohort of at least 50 representative cases of FMS from the general population to follow prospectively to determine the natural history of FMS. This prospective study is outside the context of this doctoral dissertation, but has been funded and is underway. Most subjects have been followed for 18 months, as of the time of this writing. The plan is a five year follow-up of the FMS cases, in addition to those controls with widespread musculoskeletal pain in whom FMS was excluded.

Each of the next five chapters, Chapters 2 through 6, is a manuscript that has been submitted for publication in a peer reviewed scientific journal. The first paper, in Chapter 2, describes the development and testing of the screening survey instrument. The second paper presents age- and sex-specific estimates of FMS prevalence. The third paper presents the estimated direct health care costs associated with FMS. The fourth paper presents the results of demographic and clinical comparisons of the 100 cases of FMS confirmed in LFES with two internal control groups. The final paper compares the 100 FMS cases with controls with respect to physical function and work disability status. The final chapter, Chapter 7, is a global summary of the project. In addition, it discusses the study's limitations, and proposes a direction for future research; for example, a prospective five year study is described in which the 100 FMS cases and 76 controls confirmed in LFES are being followed to assess the natural history and long term costs of the illness.

REFERENCES

[1] Lawrence RC, Hochberg MC, Kelsey JL, McDuffie FC, Medsger TA, Felts WR, Shulman LE. Estimates of prevalence of selected arthritic and musculoskeletal diseases in the United States. J Rheumatol 1989;16:427-41

[2] Felts W, Yelin E. The economic impact of the rheumatic diseases in the United States. J Rheumatol 1989;16:867-84

[3] Wood PHN, Badley EM. Rheumatic Disorders. In: Miller DL, Farmer RDT, eds. Epidemiology of Diseases. Oxford: Blackwell Scientific Publications 1982, pp. 333-46

[4] Reynolds DL, Chambers LW, Badley EM, Bennett KJ, Goldsmith CH, Jamieson E, Torrance GW, Tugwell P. Physical Disability among Canadians Reporting Musculoskeletal Diseases. J Rheumatol 1992;19(7):1020-30

[5] Lee P, Helewa A, Smythe HA, Bombardier C, Goldsmith CH. Epidemiology of Musculoskeletal Disorders (Complaints) and Related Disability in Canada. J Rheumatol 1985;12:1169-73

[6] Badley EH, Yoshida K, Webster G, Stephens M. Ontario Health Survey 1990, Working Paper No. 5: Disablement and Chronic Health Problems in Ontario. Ministry of Health Ontario, 1993

[7] Spitzer WO, Harth MH, Goldsmith CH, Norman GR, Dickie GL, Bass MJ, Newell JP. The Arthritis Complaint in Primary Care: Prevalence, Related Disability, and Costs. J Rheumatol 1976;3(1):88-99

[8] Felts W, Yelin E. The Economic Impact of the Rheumatic Disorders in the United States. J Rheumatol 1989;16:867-84

[9] Yelin E, Callahan LF. The economic cost and social and psychological impact of musculoskeletal conditions. Arthritis Rheum 1995;38(10):1351-62

[10] D, Torrance G, Badley E, Bennett KJ, Chambers L, Goldsmith CH, Jamieson E, Tugwell P, Wolfson MC. Reynolds Modelling the Population Health Impact of Musculoskeletal Diseases: Arthritis. J Rheumatol 1993;20(6):1037-47

[11] Tugwell P, Chambers L, Torrance G, Reynolds D, Wolfson M, Bennett K, Badley E, Jamieson E, Stock S, and the Pohem Workshop Group. The Population Health Impact of Arthritis: Workshop Report. J Rheumatol, 1993;20(6):1048-51

[12] Wolfe F. The Clinical Syndrome of Fibrositis. Am J Med 1986;81(3A):7-14

[13] Hawley DJ, Wolfe F. Pain, disability, and pain/disability relationships in seven rheumatic disorders: A study of 1,522 patients. J Rheumatol 1991;18(10):1552-7

[14] Martinez JE, Ferraz MB, Sato EI, Atra E. Fibromyalgia versus rheumatoid arthritis: A longitudinal comparison of the quality of life. J Rheumatol 1995;22(2):270-4

[15] Burckhardt CS, Clark SR, Bennett RM. Fibromyalgia and quality of life: A comparative analysis. J Rheumatol 1993;20(3):475-9

[16] Goldenberg DL. Fibromyalgia Syndrome: An Emerging but Controversial Condition. JAMA 1987;257(20):2782-7

[17] Bruusgaard D, Evensen AR, Bjerkedal T. Fibromyalgia - A New Cause For Disability Pension. Scand J Soc Med 1993;21:116-9

[18] Ochoa JL. Essence, Investigation, and Management of "Neuropathic" Pains: Hopes from Acknowledgement of Chaos. Muscle Nerve 1993;16:977-1008

[19] Hadler NM. The danger of the diagnostic process, in Hadler NM: Occupational Musculoskeletal Disorders. New York, USA, Raven, 1993 pps. 16-33

[20] Wallace DJ. Systemic Lupus Erythematosis, Rheumatology and Medical Literature: Current Trends. J Rheumatol 1985;12:913-5

[21] Marder WD, Meenan RF, Felson DT, Reichlin M, Birnbaum NS, Croft JD, Dore RK, Kaplan H, Kaufman RL, Stobo JD. The Present and Future Adequacy of Rheumatology Manpower. Arthritis Rheum 1991;34:1209-17

[22] Alarcon-Segovia D, Ramos-Niembro F, Gonzales-Amaro RF. One Thousand Private Rheumatology Patients in Mexico City. Arthritis Rheum 1983;26:688-9

[23] Calabozo-Raluy M, Llamazares-Gonzales AI, Munoz-Gallo MT, Alonso-Ruiz A. Sindrome de Fibromialgia (Fibrositis); Tan Frequente Como Desconcido. Med Clin (Barc) 1990;94:173-5

[24] Reilly PA, Littlejohn GO. Peripheral Arthralgic Presentation of Fibrositis/Fibromyalgia Syndrome. J Rheumatol 1992;19:281-3

[25] White KP, Harth M, Speechley M, Ostbye T. The Fibromyalgia in Rheumatology Practice: A Survey of Canadian Rheumatologists. J Rheumatol 1995;22:722-6

[26] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The Prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38:19-28

[27] Wolfe F, Smythe HA, Unus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, Fam AG, Farber SJ, Fiechtner JJ, Franklin CM, Gatter RA, Hamaty D, Lessard J, Lichtbrown AS, Masi AT, McCain GA, Reynolds WJ, Romano TJ, Russell IJ, Sheon RP. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum 1990;33:160-72

[28] Hart FD. Fibrositis (fibromyalgia) A common non-entity? Drugs 1988;35:320-7

[29] Rush PJ, Ameis A. The diseases which have no clothes: fibromyalgia and myofascial syndrome. Hippocrates 1997;3(3):1-5

[30] Epstein WV, Henke CJ. The nature of U.S. rheumatology practice. Arthritis Rheum 1981;24:1177-87

[31] The American Rheumatism Association Committee on Rheumatologic Practice. A description of rheumatology practice. Arthritis Rheum 1997;20(6):1278-81

[32] Mazanec DJ. First year of a rheumatologist in private practice. Arthritis Rheum 1982;25:718-9

[33] Gowers W. Lumbago: It's lessons and analogues. Br Med J 1904;1:117-21

[34] Simons DG. Muscle pain syndromes - Part I. Amer J Phys Med 1975;54:289-311

[35] Simons DG. Muscle pain syndromes - Part II. Amer J Phys Med 1976;55:15-42

[36] Froriep R. On the therapeutic application of electro-magnetism in the treatment of rheumatic and paralytic affections. Translated by Lawrence RM. London, Henry Renshaw, 1850.

[37] Stockman R. The causes, pathology and treatment of chronic rheumatism. Edinb Med J 1904;15:107-16

[38] Kraft GH, Johnson EW, LaBan MM. The fibrositis syndrome. Arch Phys Med Rehabil 1968(3):155-62

[39] Rice, JR. "Fibrositis" syndrome. Med Clin. North Am 1986;70(2):455-68

[40] Kellgren JH. Observations on referred pain arising from muscle. Clin Sci 1938;3:175-90

[41] Kellgren JH. On the distribution of pain arising from deep somatic structures with charts of segmental pain areas. Clin Sci 1939;4:35-46

[42] Kellgren JH, McGowan AJ, Hughes ESR. On deep hyperalgesia and cold pain. Clin Sci 1944;7:13-27

[43] Lewis T, Kellgren JH. Observations relating to referred pain, visceromotor reflexes and other associated phenomoena. Clin Sci 1939;4:47-71

[44] Travell JG, Simons DG. Myofascial pain and dysfunction. The trigger point manual. Baltimore, Williams and Wilkins, 1983.

[45] McCain GA. Diagnosis and treatment of fibromyalgia. In: Cervical Flexion-Extension/Whiplash injuries. Teasell R, Shapiro A (Eds) 1993;7:423-41

[46] Job 7: verses 3-4 and Job 30: verses 16-17.

[47] Moldofsky H, Scarisbrick P, England R, Smythe HA. Musculoskeletal symptoms and non-REM sleep disturbance in patients with 'fibrositis syndrome' and healthy subjects. Psychosom Med 1975;37:341-51

[48] Moldofsky H, Scarisbrick P. Induction of neurasthenic musculoskeletal pain by selective sleep stage deprivation. Psychosom Med 1976;38:35-44

[49] Smythe HA, Moldofsky H. Two contributions to an understanding of the 'fibrositis' syndrome. Bull Rheum Dis 1977;28(1):928-31

[50] Smythe HA. Nonarticular rheumatism and psychogenic musculoskeletal syndromes. In: Arthritis and Allied Conditions 11th edition. McCarty DJ (Ed) Lea & Febiger, Philadelphia, 1989, pps 1241-54

[51] Block SR. Fibromyalgia and the rheumatisms. Common sense and sensibility. Rheum Dis Clin North Am 1993;19(1):61-78

[52] Bohr T. Problems with myofeascial pain syndrome and fibromyalgia syndrome. Neurology 1996;46:593-7

[53] Yunus M, Masi AT, Calabro J, Miller KA, Feigenbaum SL. Primary fibromyalgia (fibrositis): Clinical study of 50 patients with matched normal controls. Semin Arthritis Rheum 1981;11(10):151-71

[54] Campbell SM, Clark S, Tindall EA, Forehand ME, Bennett RM. Clinical characteristics of fibrositis. I. A "blinded" controlled study of symptoms and tender points. Arthritis Rheum 1983;26(7):817-24

[55] Wolfe F, Cathey MA. Prevalence of primary and secondary fibrositis. J Rheumatol 1983;10:965-8

[56] Bohan A. The private practice of rheumatology. The first 1,000 patients. Arthritis Rheum 1981;24(10):1304-7

[57] Marder WD, Meenan RF, Felson DT. The present and future adequacy of rheumatology manpower. Arthritis Rheum 1991; 34: 1204-1217

[58] Alarcon-Segovia D, Ramos-Niembro F, Gonzales-Amaro RF. One thousand private rheumatology patients in Mexico City [letter]. Arthritis Rheum 1983;26:688-9

[59] Calabozo-Raluy, Llamazares-Gonzalez AI, Munoz-Gallo MT, Alonso-Ruiz A. Sindrome de fibromyalgia (fibrositis); tan frequente como desconcido. Med Clin (Barc) 1990;94:173-5

[60] Reilly PA, Littlejohn GO. Peripheral arthralgic presentation of fibrositis/fibromyalgia syndrome. J Rheumatol 1992;19:281-3

[61] Hartz A, Kirchdoerfer E. Undetected fibrositis in primary care practice. J Fam Pract 1987;25:365-9

[62] Muller W. The fibrositis syndrome: diagnosis, differential diagnosis and pathogenesis. Scand J Rheumatol [Suppl] 1987;65:40-53

[63] Wolfe F. Fibromyalgia. Rheum Dis Clin North Am 1990;16(3):681-98

[64] Hochberg MC. Predicting the prognosis of patients with Rheumatoid Arthritis: Is there a crystal ball? J Rheumatol 1993;20(8):1265-7

[65] Macfarlane GJ, Thomas E, Papageorgiou AC, Schollum J, Croft PR, Silman AJ. The natural history of chronic pain in the community: A better prognosis than in the clinic? J Rheumatol 1996;23(9):1617-20

[66] Crook J. The importance of community based epidemiological studies. J Rheumatol 1996;23(9):1500-1

[67] Briscoe ME. Why do people go to the doctor? Sex differences in the correlates of GP consultation. Soc Sci Med 1987;25:507

[68] Waldron I. Sex differences in illness incidence, prognosis and mortality: issues and evidence. Soc Sci Med 1983;17:1107

[69] Chien A, Schneiderman LJ. A comparison of health care utilization by husbands and wives. J Community Health 1975;1:118

[70] Ontario Health Survey 1990 Highlights. Ontario Ministry of Health, September 1992.

[71] Lewis CE, Raczynski JM, Oberman A, Cutter GR. Risk factors and the natural history of coronary heart disease in blacks. Cardiovasc Clin 1991;21(3):29-45

[72] Zuckerman MJ, Guerra LG, Drossman DA, Foland JA, Gregory GG. Health care seeking behaviors related to bowel complaints. Hispanics versus non-Hispanic whites. Dig Dis Sci, 1996;41(1):77-82

[73] Tore Gran J, Husby G. Ankylosing Spondylitis in women. Semin Arthritis Rheum 1990;19(5):303-12

[74] Jacobsson L, Lindgarde F, Manthorpe R. The commonest rheumatic complaints of over 6 weeks' duration in a twelve month period in a defined Swedish population. Scand J Rheumatol 1989;18:361-8

[75] Yunus M, Masi AT, Calabro JJ. Primary fibromyalgia (fibrositis). Semin Arthritis Rheum 1981;11:151-71

[76] Romano TJ. Incidence of fibromyalgia syndrome (FS) in rheumatoid arthritis (RA) patients in a general rheumatology practice. Scand J Rheumatol 1992;[suppl 94]:11

[77] Romano TJ. Coexistence of fibromyalgia syndrome (FS) and systemic lupus erythematosis (SLE). Scand J Rheumatol 1992;[suppl 94]:12

[78] Romano TJ. Presence of fibromyalgia syndrome (FS) in osteoarthritis (OA) patients. Scand J Rheumatol 1992;[suppl 94]:11

[79] Greenfield S, Fitzcharles M, Esdaile JM. Reactve fibromyalgia syndrome. Arthritis Rheum 1992;35(6):678-81

[80] Buskila D, Neumann L, Vaisberg G, Alkalay D, Wolfe F. Increased rates of fibromyalgia following cervical spine injury. A controlled study of 161 cases of traumatic injury. Arthritis Rheum 1997;40(3):446-52

[81] Heslin DJ, Saplys RJ, Brown W. Frequency of asymptomatic abnormalities in the lumbosacral spine. Modern Medicine of Canada 1987;42(6):469-72

[82] Makela M, Heliovaara M. Prevalence of primary fibromyalgia in the Finnish population. BMJ 1991;303:216-9

[83] Forseth KO, Gran JT. The prevalence of fibromyalgia among women aged 20-49 years in Arendal, Norway. Scand J Rheumatol 1992;21:74-8

[84] Croft PR, Schollum J, Rigby AS, Boswell RF, Silman AJ. Chronic widespread pain in the general population. Scand J Rheumatol 1992;[suppl 94]:8

[85] Raspe H, Baumgartner CH. The epidemiology of fibromyalgia syndrome (FMS) in a German town. Scand J Rheumatol 1992;[suppl 94]:8

[86] Lyddell C, Meyers OL. The prevalence of fibromyalgia in a South African community. Scand J Rheumatol, 1992;[suppl 94]:8

[87] The Epidemiology of Fibromyalgia: Workshop of the Standing Committee on Epidemiology European League Against Rheumatism (EULAR), Bad Sackingen, 19-21 November 1992. Br J Rheumatol 1994;33:783-6

[88] Prescott E, Kjoller M, Jacobsen S, Bulow PM, Danneskiold-Samsoe B, Kamper-Jorgensen F. Fibromyalgia in the adult Danish Population: I. A prevalence study. Scand J Rheumatol 1993;22:233-7

[89] Prescott E, Kjoller M, Jacobsen S, Bulow PM, Danneskiold-Samsoe B, Kamper-Jorgensen F. Fibromyalgia in the adult Danish Population: II. A study of clinical features. Scand J Rheumatol 1993;22:238-42

[90] Derogatis LR, Cleary PA. Confirmation of the dimensional structure of the SCL-90. J Clin Psychol 1977;33:981-9

[91] Meenan RF, Gertman PM, Mason JH. Measuring health status in arthritis: The arthritis impact measurement scales. Arthritis Rheum 1980;23:146-52

[92] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38(1):19-28

[93] Wolfe F, Ross K, Anderson J, Russell IJ. Aspects of fibromyalgia in the general population: Sex, pain threshold, and fibromyalgia symptoms. J Rheumatol 1995;22:151-6

[94] Wolfe F. Fibromyalgia: The clinical syndrome. Rheum Dis Clin North Am 1989;15(1):1-18

[95] Granges G, Littlejohn GO. A comparative study of clinical signs in fibromyalgia/fibrositis syndrome, healthy and exercising subjects. J Rheumatol 1993;20(2):344-51

[96] Yunus MB, Masi AT, Aldag JC. A controlled study of primary fibromyalgia syndrome: clinical features and association with other functional syndromes. J Rheumatol 1989;16[suppl 19]:62-71

[97] Bennett RM. Physical fitness and muscle metabolism in the fibromyalgia syndrome: An overview. J Rheumatol 1989;16[suppl 19]:28-9

[98] Yunus MB. Fibromyalgia syndrome and myofascoial pain syndrome: clinical features, laboratory tests, diagnosis, and pathophysiologic mechanisms. Myofascial Pain and Fibromyalgia: Trigger Point Management. Rachlin ES [Ed], Mosby-Year Book, Inc., St. Louis, MO, 1994

[99] Cott A, Parkinson W, Bell MA, Adachi JA, Bedard M, Cividino A, Benson W. Interrater reliability of the tender point criterion for fibromyalgia. J Rheumatol 1992;19(12):1955-9

[100] Smythe HA, Gladman A, Dagenais P, Kraishi M, Blake R: Relation between fibrositic and control site tenderness; effects of dolorimeter scale length and footplate size. J Rheumatol, 1992; 19 (2): 284-289.

[101] White KP, McCain GA, Tunks E. The effects of changing the painful stimulus upon dolorimetry scores in patients with fibromyalgia. J Musculoskel Pain 1993;1(1):43-58

[102] Buskila D, Press J, Gedalia A, Klein M, Neumann L, Boehm R, Sukenik S. Assessment of nonarticular tenderness and prevalence of fibromyalgia in children. J Rheumatol 1993;20(2):368-70

[103] Waylonis GW, Perkins RH. Post-traumatic fibromyalgia. A long-term follow-up. Am J Phys Med Rehabil 1994;73(6):403-12

[104] Romano T. Valid complaints or malingering? Clinical experiences with post-traumatic fibromyalgia syndrome. West Virg Med J 1990;86:198

[105] Bennett RM. Disabling fibromyalgia: Appearance versus reality. J Rheumatol 1993;20:1821-4

[106] Bennett RM. Fibromyalgia and the disability dilemma. A new era in understanding a complex, multidimensional pain syndrome. Arthritis Rheum 1996;39(10):1627-34

[107] Wolfe F. The fibromyalgia syndrome: A consensus report on fibromyalgia and disability. J Rheumatol 1996;23(3):534-9

[108] Wolfe F, Cathey MNA, Kleinheksel SM, Amos SP, Hoffman RG, Young DY, Hawley DJ. Psychological status in primary fibrositis and fibrositis associated with rheumatoid arthritis. J Rheumatol 1984;11:500-6

[109] Scudds RA, Rollman GB, Harth M, McCain GA. Pain perception and personality measures as discriminators in the classification of fibrositis. J Rheumatol 1987;14:563-9

[110] Uveges JM, Parker JC, Smarr KL, McGowan JF, Lyon MG, Irvin WS, Meyer AA, Buckelew SP, Morgan RK, Delmonico RL, Hewitt JE, Kay DR. Psychological symptoms in primary fibromyalgia syndrome: Relationship to pain, life stress, and sleep disturbance. Arthritis Rheum 1990;33:1279-83

[111] Yunus MB, Ahles TA, Aldag JC, Masi AT. Relationship of clinical features with psychological status in primary fibromyalgia. Arthritis Rheum 1991;34:15-21

[112] Bohr TW. Fibromyalgia syndrome and myofascial pain syndrome: Do they exist? Neurologic Clin 1995;13(2):365-84

[113] Merskey H. Physical and psychological considerations in the classification of fibromyalgia. J Rheumatol 1989;15[suppl 19]:72-9

[114] Smythe HA: Problems with the MMPI. J Rheumatol 1984;11:417-8

[115] Mufson M, Regestein QR. The spectrum of fibromyalgia disorders. Arthritis Rheum 1993;36:647-50

[116] Aaron LA, Bradley LA, Alarcon GS, Alexander RW, Triana-Alexander M, Martin MY, Alberts KR. Psychiatric diagnoses in patients with fibromyalgia are related to health care-seeking behaviour rather than to illness. Arthritis Rheum 1996;39(3):436-45

[117] Simms RW, Zerbini CAF, Ferrante N, Anthony J, Felson DT, Craven DE. Fibromyalgia Syndrome in patients infected with Human Immunodeficiency Virus. Am J Med 1992;92:368-74

[118] Buskila D, Fefer P, Harman-Boehm I, Press J, Neumann L, Lunenfeld E, Gedalia A, Potashnik G, Sukenik S. Assessment of nonarticular tenderness and prevalence of fibromyalgia in hyperprolactinemic women. J Rheumatol 1993;20(12):2112-5

[119] Jurell KC, Zanetos MA, Orsinelli A, Tallo D, Waylonis GW. Fibromyalgia: A Study of Thyroid Function and Symptoms. J Musculoskel Pain 1996;4(3):49-60

[120] May KP, West SG, Baker MR, Everett DW. Sleep apnea in male patients with the fibromyalgia syndrome. Am J Med 1993;94:505-8

[121] Fiona D, Esdaile JM, Kimoff JR, Fitzcharles M. Musculoskeletal complaints and fibromyalgia in patients attending a respiratory sleep disorders clinic. J Rheumatol 1996;23(9):1612-6

[122] Van der Heide A, Remme CA, Hofman DM, Jacobs JWG, Bijlsma JWJ. Prediction of progression of radiologic damage in newly diagnosed rheumatoid arthritis. Arthritis Rheum 1995;38(10):1466-74

[123] Holmes GP, Kaplan JE, Gantz NM, Komaroff AL, Schorberger LB, Strauss SE, Jones JF, Dubois RE, Cunningham-Rundles C, Pakwa S. Chronic fatigue syndrome: a working case definition. Ann Intern Med 1988;108:387-9

[124] Goldenberg DL. Fibromyalgia and chronic fatigue syndrome. J Musculoskeletal Pain 1994;2(3):51-5

[125] Goldenberg DL, Simms RW, Geiger A, Komaroff AL. High frequency of fibromyalgia in patients with chronic fatigue seen in primary care practice. Arthritis Rheum 1990;33(3):381-7

[126] Hudson JI, Goldenberg DL, Pope HG, Keck P Jr., Schlesinger L. Comorbidity of fibromyalgia with medical and psychiatric disorders. Am J Med 1992;92(4):363-7

[127] Wysenbeek AJ, Shapira Y, Leibovici L. Primary fibromyalgia and the chronic fatigue syndrome. Rheumatol Int 1991;10(6):227-9

[128] White KP, Harth M, Teasell R. Work disability evaluation and the fibromyalgia syndrome. Semin Arthritis Rheum 1995;24(6):371-81

[129] Cathey MA, Wolfe F, Roberts FK, Bennett RM, Caro X, Goldenberg DL, Russell IJ, Yunus MB. Demographics, work disability, service utilization and treatment characteristics of 620 fibromyalgia patients in rheumatologic practice. Arthritis Rheum 1990;33[suppl]:S10

[130] Wolfe F, Anderson J, Harkness D, Bennett RM, Caro XJ, Goldenberg DL, Russell IJ, Yunus MB. Work and disability status of persons with fibromyalgia. J Rheumatol 1997;24(6):1171-8

[131] Bengtsson A, Henriksson K-G, Jorfeldt L, Kagedul B, Lennmarken C, Lindstrom F. Primary fibromyalgia. A clinical and laboratory study of 55 patients. Scand J Rheumatol 1986;15:340-7

[132] Ledingham J, Doherty S, Doherty M. Primary fibromyalgia syndrome - An outcome study. Br J Rheumatol 1993;32:139-42

[133] Bruusgaard D, Evensen AR, Bjerkedal T. Fibromyalgia - a new cause for disability pension. Scand J Soc Med 1993;21:116-9

[134] McCain GA, Cameron R, Kennedy JC. The problem of long term disability payments and litigation in primary fibromyalgia: The Canadian perspective. J Rheumatol 1989;16[suppl 19]:174-6

[135] Hawley DJ, Wolfe F: Pain, disability and pain/disability relationships in seven rheumatic disorders. J Rheumatol 1991;18:1552-7

[136] Burckhardt CS, Clark SR, Bennett RM. Fibromyalgia and quality of life: A comparative analysis. J Rheumatol 1993;20:475-9

[137] Callahan LF, Smith WJ, Pincus T. Self-reported questionnaires in five rheumatic diseases. Comparisons of health status constructs and associations with formal education level. Arthritis Care Res 1989;2:122-31

[138] Gladman DD, Urowitz MB, Gough J, MacKinnon A. Fibromyalgia is a major contributor to quality of life in lupus. J Rheumatol 1997;24(11):2145-8

[139] Viitanen JV, Kautiainen H, Isomaki H. Pain intensity in patients with fibromyalgia and rheumatoid arthritis. Scand J Rheumatol 1993;22:131-5

[140] Mengshoel AM, Forre O. Pain and fatigue in patients with rheumatic disorders. Clin Rheumatol 1993;12(4):515-21

[141] Gerdle B, Elert J. Disability and impairment in fibromyalgia syndrome: Possible pathogenesis and etiology. Crit Rev Phys Med Rehab 1995;7(3):189-232

[142] Shapiro A, Roth RS. The effect of litigation on recovery from whiplash, in Spine: State of the Art Reviews 1993;7(3):531-56

[143] Mosby's Medical, Nursing and Allied Health Dictionary, 4th Edition; Anderson KN, Anderson LE, Glanze WD, Editors; Mosby - Year Book, Inc., St. Louis, USA., 1994.

[144] Dorland's Illustrated Medical Dictionary 28th Edition, WB Saunders Company. Philadelphia, PA, 1994:1620.

[145] McCain GA, Tilbe KS. Diurnal hormone vaiation in fibromyalgia syndrome. A comparison with rheumatoid arthritis. J Rheumatol 1989;16 (suppl 19):154-7

[146] Bennett RM, Clark SR, Campbell SM, Burckhardt CS. Low levels of somatomedin C in patients with the fibromyalgia syndrome. A possible link between sleep and muscle pain. Athritis Rheum 1992;35(10):1113-6

[147] Yunus MB, Dailey JW, Aldag DC, Masi AT, Jobe PC. Plasma tryptohan and other amino acids in primary fibromyalgia: A controlled study. J Rheumatol 1992;19(1):90-4

[148] Russell IJ, Vaeroy H, Javors M, Nyberg F. Cerebrospinal fluid biogenic amino metabolites in fibromyalgia/fibrositis syndrome and rheumatoid arthritis. Arthritis Rheum 1992;35:550-6

[149] Vaeroy H, Helle R, Forre O, Kass E, Terenius L. Elevated CSF levels of substance P and high incidence of Raynaud's phenomenon in patients with fibromyalgia: New features for diagnosis. Pain 1988;32:21-6

[150] Hau PP, Scudds RA, Harth M. An evaluation of mechanically induced neurogenic flare by infrared thermography in fibromyalgia. J Musculoskel Pain 4(3):3-20

[151] Qiao Z, Vaeroy H, Morkrid L. Electrodermal and microcirculatory activity in patients with fibromyalgia during baseline, acoustic stimulation and cold pressor tests. J Rheumatol 1991;18(9):1383-9

[152] Martinez-Lavin M, Hermosillo AG, Mendoza C, Ortiz R, Cajigas JC, Pineda C, Nava A, Vallejo M. Orthostatic sympathetic derangement in subjects with fibromyalgia. J Rheumatol 1997;24(4):714-8

[153] Mountz JM, Bradley LA, Modell JG, Alexander RW, Triana-Alexander M, Aaron LA, Stewart KE, Alarcón GS, Mountz JD. Fibromyalgia in women. Abnormalities of regional cerebral blood flow in the thalamus and the caudate nucleus are associated with low pain threshold levels. Arthritis Rheum 1995;38(7):926-38

[154] Bradley LA, Alberts KR, Alarcon GS, Alexander MT, Mountz JM, Weigert DA, Liu HG, Blalock JE, Aaron LA, Alexander RW, SanPedro EC, Martin MY, Morell AC. Abnormal brain regional cerebral blood

flow (rCBF) and cerebrospinal fluid (CSF) levels of substance P (SP) in patients and non-patients with fibromyalgia (FM). Arthritis Rheum 1996;39(9)[suppl]:S212

[155] Brena SR, Chapman SL. The 'learned pain syndrome': Decoding a patient's pain signals. Postgrad Med 1981;69:53-64

[156] Chapman SL, Brena SR. Learned helplessness and responses to nerve blocks in chronic low back patients. Pain 1982;14:355-64

[157] Hadler NM. Social security. The process of pensioning the invalid. In: Occupational Musculoskeletal Disorders. Hadler NM (Ed) New York, USA, Raven, 1993 pp 227-48

[158] Robbins JM, Kirmayer LS. Illness, worry and disability in fibromyalgia syndrome. Int J Psychiatry Med 1990;20:49-63

[159] Rush PJ, Ameis A. Trauma and fibromyalgia: Does the punishment fit the crime? [letter] J Rheumatol 1995;22(2):372

[160] Ziegler DK. Headache: Public health problem. Neurol Clin 1990;8(4):781-91

CHAPTER 2

TESTING AN INSTRUMENT TO SCREEN FOR FIBROMYALGIA SYNDROME IN GENERAL POPULATION STUDIES: THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY SCREENING QUESTIONNAIRE (LFESSQ)[i]

2.0 INTRODUCTION

Fibromyalgia syndrome (FMS) increasingly is being recognized as a major cause of morbidity world wide.[1,2] Much of what we know about the syndrome, with respect to clinical characteristics, co-morbid conditions, pathophysiology, and response to treatment, stems from clinic based studies. However, inferences about disease based clinic and hospital studies alone can be biased.[3,4,5]

The first general population study of FMS was a Swedish study reported in 1989.[6] Since then, general population surveys have been performed in Europe,[7,8,9,10,11] South Africa,[12] Israel,[13] the United States,[14] and Canada.[15] Most of these studies were small,

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estimated disease prevalence only, and were inadequate to make inferences about disease characteristics. All were 'point-in-time' studies, so that there are no data with respect to the course of FMS in the community. No study addressed risk factors for disease. Hence, further community-based epidemiological studies are needed.

As the first step in our program in epidemiologic research, we designed an instrument to screen for FMS in general population surveys. To our knowledge, no prior screening instrument has been validated for this purpose. We present the results of several clinic and community sub-studies testing the sensitivity, specificity, positive predictive value (PPV) and test-retest reliability (TRR) of two different versions of the London Fibromyalgia Epidemiology Study Screening Questionnaire (LFESSQ), one utilizing 4 questions on pain, the other adding 2 questions on fatigue.

2.1 METHODS

2.1.0 Designing the LFESSQ

A 6-item questionnaire was designed with 4 items relating to chronic pain and 2 items relating to fatigue. [Figure 1]. The four questions on pain were selected to be in accordance with the distribution of pain required by the 1990 American College of Rheumatology criteria.[16] The two items on fatigue were added after an extensive review of scientific publications on FMS. Prior to testing, the LFESSQ was reviewed for content by six independent rheumatologists, who otherwise did not participate in the study.

2.1.1 **Estimating the sensitivity and specificity of the questionnaire**

We tested sensitivity and specificity in the outpatient rheumatology clinic. Ninety-one subjects were selected from three groups: **1)** 31 consecutive rheumatology clinic outpatients with diagnosed FMS, all meeting the 1990 ACR criteria; **2)** 30 consecutive rheumatology clinic outpatients with rheumatoid arthritis (RA); and **3)** 30 non-patient controls who denied having either FMS or RA; half of these were recruited from hospital staff; half were recruited from a community service organization. The three groups did not differ with respect to mean age. All subjects were female.

The questionnaire was administered verbally by a research fellow. A positive screen was defined in one of two ways: 1) meeting the pain criteria alone, or 2) meeting both the pain and fatigue criteria. Meeting the pain criteria required 'yes' responses to all four questions on pain, and pain on both a right and left sided extremity. Meeting the fatigue criteria required a 'yes' response to both fatigue items. Sensitivity and specificity were measured for both definitions of a positive screen.[17] After completing the questionnaire, each subject was asked to comment on the clarity of the questionnaire.

2.1.2 **Estimating positive predictive value (PPV)**

PPV was studied in a random survey of 3395 non-institutionalized adults (males and females) in London, Ontario, as part of the London Fibromyalgia Epidemiology Study (LFES). For the purposes of this survey, an individual screened positive who met

the pain criteria, with or without the fatigue criteria. Two hundred forty-eight subjects met the pain criteria, and were invited to be examined by a rheumatologist to confirm or exclude FMS, as defined by the 1990 ACR criteria; 176 subjects (71%) agreed to be examined.

PPV was calculated by excluding the 72 subjects who screened positive but declined to be examined, because their disease status was unknown. The PPV was the total number of confirmed FMS cases divided by the number of subjects examined (176).[17] Chi-square analyses were performed to test the hypotheses that PPV is affected: 1) by the subject's sex, and 2) by the patient's age.

2.1.3 **Estimating test-retest reliability (TRR)**

Test-retest reliability[18] was estimated in a general population survey of 672 non-institutionalized adults (males and females) in London, Ontario. Subjects were contacted by random digit dialing and screened by trained interviewers. Of 632 subjects who failed to meet either definition of a positive screen, 50 were randomly selected for retest, of whom 44 agreed to be re-contacted by a second, blinded interviewer within 2 weeks. Of 40 subjects who met either definition of a positive screen, 34 agreed to be re-tested, also by a second, blinded interviewer within 2 weeks.

2.1.4 Confidence Intervals

Ninety-five percent confidence intervals were calculated for all estimates. For estimates approaching zero or 100%, confidence limits were calculated using the logit transformation of the proportion.[19] For estimates equal to 100%, the lower bound was calculated as:

$$(1 - [n/3]) \times 100\%$$ [20]

2.2 RESULTS

2.2.0 Sensitivity and specificity

(Refer to Tables 1 and 2)

All 31 FMS patients screened in the outpatient rheumatology clinic met the screening criteria for pain, a sensitivity of 100% (95% confidence interval [CI] = 90.3%, 100%). Only 29 of 31 met the criteria both for pain and fatigue, a sensitivity of 93.5% (CI = 83.8%, 100%).

Among thirty RA controls, 14 screened positive for pain (specificity = 53.3%, CI = 35.4%, 71.2%), but only 6 screened positive both for pain and fatigue (specificity = 80.0%, CI = 65.7%, 94.3%). None of the 30 non-patient controls screened positive using either definition of a positive screen (specificity = 100%, CI = 90.0%, 100%).

2.2.1 **Positive predictive value (PPV)**

(Refer to Table 2)

For the first 672 subjects involved in LFES, only those subjects who met both the criteria for pain and fatigue were invited to participate in the study; we did this because of the combined criteria's higher specificity in the outpatient clinic. FMS was confirmed in 24 of 34 examined positive screens (PPV = 70.6%, CI = 55.3%, 85.9%).

After an interim analysis, we considered a PPV of 70.6% to be high enough to significantly risk losing some FMS cases who might falsely screen negative. Because of this, after the first 672 subjects, we eliminated the fatigue criteria from the definition of a positive screen; a subject who satisfied only the pain criteria now could screen positive. Utilizing the pain criteria alone to screen for FMS, the PPV of the screening instrument ultimately was estimated at 56.8% overall (100 of 176, CI = 53.0%, 60.6%). The PPV was higher for females than males (73.0% versus 36.0%; odds ratio = 3.01, CI = 1.36, 6.84). The PPV of the questionnaire was not affected by subject age ($X^2 = 46.8$, d.f. 55, $p = 0.78$).

2.2.2 **Test-retest reliability (TRR)**

(Refer to Table 2)

Using either definition of a positive screen (pain alone or pain and fatigue), TRR was 100% (44 of 44, CI = 93.2%, 100%) among those who screened negative. Among those who screened positive, TRR was higher using the pain criteria alone than for the

combined criteria: 95.0% (38 of 40, CI = 88.8%, 100%) versus 81.0% (34 of 42, CI = 69.1%, 92.8%), respectively.

2.2.3 **Discussion**

Our primary objective was to design a screening instrument for FMS that would be useful particularly in the setting of general population surveys. No prior screening instrument has been validated for this purpose. In the medical literature, screening instruments used in most surveys typically are not well described. Similarly, in many reports, the sensitivity, specificity and PPV are not reported, and insufficient data are presented for them to be calculated by the reader. Where it can be calculated, the PPV has been as low as 1.6%,[7] and as high as 12.3%[11] and 18.9%.[14] In no prior survey of FMS has the test-retest reliability of the screening instrument been reported.

We present data on the sensitivity, specificity, PPV and TRR of a screening instrument for FMS that appears to be useful both in clinic and in community surveys. In the outpatient clinic, using the combined pain and fatigue criteria distinguishes rheumatoid arthritis from FMS in 80% of cases, while missing less than 10% of FMS cases. When using the pain criteria alone, the screening test is less specific. We selected RA patients as a control group because of their diffuse pain, and the presumed likelihood that many RA patients without FMS would falsely screen positive in a community telephone survey. Although we did not use other forms of arthritis as controls, we felt that RA patients were most likely to report diffuse, four extremity and axial pain.

That our instrument was effective in distinguishing other rheumatic disorders from FMS is evidenced by the high PPV of the LFESSQ in a survey of 3995 adults. Utilizing the combined criteria resulted in a PPV above 70 percent. This may be too high, given that minimizing false negatives generally is the primary aim of a screening instrument. Using the pain criteria alone still provided a PPV above 50%, which is clearly beyond that reported in any prior survey. With respect to future population surveys, this is advantageous in terms of minimizing sample size requirements, and hence research time and resources.

The design of our study does not allow us to estimate the negative predictive value (NPV) of the pain criteria alone; to do so would require a study in which both positive and negative screens are examined.[17] Nonetheless, given that the 1990 ACR criteria require widespread pain, and that the test-retest reliability of a negative screen was 100%, it is unlikely that many FMS cases in the survey sample falsely screened negative. In other words, the NPV of the LFESSQ pain criteria alone likely approached 100%.

The LFESSQ predicted FMS especially well among women, with a PPV twice as high as among men. This is to be expected, because FMS is more prevalent in women, PPV is related to prevalence, and most of the gain in predictive value occurs with increases at the lowest rates of disease prevalence. It was equally effective at all adult age groups. An additional advantage is that it is brief and can be easily administered by a

lay interviewer. Negative screens usually were identified within one minute, positive screens within two minutes. This is important in telephone surveys, in which the length of the questionnaire appears to be inversely proportional to participation rates.[21] Our telephone survey participation rate approximated 75%.

Hence, the LFESSQ should be a useful screening instrument, especially designed for community surveys, but potentially useful in the clinic as well. Once a subject has screened positive, an examination for fibromyalgia tender points is required to confirm or exclude the diagnosis of FMS. Subsequent clinical examination of negative screens is likely to have a very low diagnostic yield.

Tables and Figures

Figures

Tables

Figure 1: The London Fibromyalgia Epidemiology Study Screening Questionnaire (LFES-SQ)

Pain criteria

1. In the past three months, have you had pain in muscles bones or joints, lasting at least one week?
2. Have you had pain in your shoulders, arms or hands? On which side? Right, left or both?
3. Have you had pain in your legs or feet? On which side? Right, left or both?
4. Have you had pain in your neck, chest or back?

Fatigue criteria

1. Over the past three months, have you often felt tired or fatigued?
2. Does tiredness or fatigue significantly limit your activities?

Meeting the pain criteria requires 'yes' responses to all four pain items, and either 1) both a right and left side positive response, or 2) a both sides positive response. Screening positive for chronic, debilitating fatigue requires a 'yes' response to both fatigue items

Table #1: Testing for sensitivity and specificity of the pain criteria alone versus combined pain and fatigue criteria for the LFES-SQ.

Subject Group	Pain criteria alone			Pain + fatigue criteria	
	screen (+)	screen (-)		screen (+)	screen (-)
FMS patients (N = 31)	31	0		29	2
RA controls (N = 30)	14	16		6	24
non-patient controls (N = 30)	0	30		0	30

Pain criteria alone

Sensitivity among FMS patients = 31/31 = 100%

Specificity among RA patients = 16/30 = 53.3%; among non-patient controls = 30/30 = 100%

Pain + fatigue criteria

Sensitivity among FMS patients = 29/31 = 93.5%

Specificity among RA patients = 24/30 = 80.0%; among non-patient controls = 30/30 = 100%

Table #2: Comparing the pain criteria alone versus combined pain and fatigue criteria for the LFES-SQ.

	Pain criteria alone		Pain + fatigue criteria
Sensitivity[1]	100% (90.3%, 100%)		93.5% (83.8%, 100%)
Specificity[2]			
RA controls	53.3% (35.4%, 71.2%)		80.0% (65.7%, 94.3%)
Healthy controls	100% (90.0%, 100%)		100% (90.0%, 100%)
Test-retest reliability[3]			
Negative screen	100% (93.2%, 100%)		100% (93.2%, 100%)
Positive screen	95.2% (88.8%, 100%)		81.0% (69.1%, 92.8%)
Positive predictive value[4]	56.8% (53.0%, 60.6%)		70.6% (55.3%, 85.9%)

[1] tested in 31 FMS clinic outpatients

[2] tested in 30 RA clinic outpatients and 30 non-patients without rheumatologic diagnoses.

[3] tested among 44 subjects who screened negative and 34 who screened positive randomly selected in a random telephone survey of 672 non-institutionalized adults.

[4] tested in a random telephone survey of 3395 non-institutionalized adults.

REFERENCES

[1] Schochat T, Croft P, Raspe H. The epidemiology of fibromyalgia. Workshop of the standing committee on epidemiology European League Against Rheumatism (EULAR), Bad Sachingen, 19-21 November 1992. Br J Rheumatol 1994;33:783-6

[2] Wolfe F and the Vancouver fibromyalgia consensus group. The fibromyalgia syndrome: A consensus report on fibromyalgia and disability. J Rheumatol 1996;23(3):534-9

[3] Wolfe F. Fibromyalgia. Rheum Dis Clin North Am 1990;16(3):681-98

[4] Felson DT. Epidemiologic research in fibromyalgia. J Rheumatol 1989;16[suppl 19]:7-11

[5] Crook J. The importance of community based epidemiological studies. J Rheumatol 1996;23(9):1500-1

[6] Jacobsson L, Lindgarde F, Manthorpe R. The commonest rheumatic complaints of over 6 weeks' duration in a twelve month period in a defined Swedish population. Scand J Rheumatol 1989;18:361-8

[7] Makela M, Heliovaara M. Prevalence of primary fibromyalgia in the Finnish population. BMJ 1991;303:216-9

[8] Forseth KO, Gran JT. The prevalence of fibromyalgia among women aged 20-49 years in Arendal, Norway. Scand J Rheumatol 1992;21:74-8

[9] Raspe H, Baumgartner CH. The epidemiology of fibromyalgia syndrome (FMS) in a German town. Scand J Rheumatol 1992;[suppl 94]:8

[10] The Epidemiology of Fibromyalgia: Workshop of the Standing Committee on Epidemiology European League Against Rheumatism (EULAR), Bad Sackingen, 19-21 November 1992. Br J Rheumatol 1994;33:783-6

[11] Prescott E, Kjoller M, Jacobsen S, Bulow PM, Danneskiold-Samsoe B, Kamper-Jorgensen F. Fibromyalgia in the adult Danish Population: I. A prevalence study. Scand J Rheumatol 1993;22:233-7

[12] Lyddell C, Meyers OL. The prevalence of fibromyalgia in a South African community. Scand J Rheumatol 1992;[suppl 94]:8

[13] Buskila D, Press J, Gedalia A, Klein M, Neumann L, Boehm R, Sukenik S. Assessment of nonarticular tenderness and prevalence of fibromyalgia in children. J Rheumatol 1993;20:368-70

[14] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38(1):19-28

[15] White KP, Speechley M, Harth M, Ostbye T. The London Fibromyalgia Epidemiology Study: The prevalence of fibromyalgia (FMS) in London, Ontario. Arthritis Rheum 1996;39(9)[suppl]):S212

[16] Wolfe F, Smythe HA, Yunus MB et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia: Report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33(2):160-72

[17] Sackett DL, Haynes RB, Tugwell P. Clinical Epidemiology - A Basic Science for Clinical Medicine, First edition. Little, Brown and Company, Boston/Toronto, 1985

[18] Carmines EG, Zeller RA. Reliability and validity assessment. Sage Publications, Inc. Newbury Park, 1979

[19] Rochon J. The application of the GSK method to the determination of minimal sample sizes. Biometrics 1989;45:193-205

[20] Hanley JA, Lippman-Hand A. If nothing goes wrong, is everything all right? Interpreting zero numerators. JAMA 1983;249(13):1743-5

[21] Schuman H, Presser S. Questions and Answers in Attitude Surveys. Experiments on Question Form, Wording, and Context. Academic Press, Inc. Orlando, 1981

CHAPTER 3
THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY (LFES): THE PREVALENCE OF FIBROMYALGIA SYNDROME (FMS) IN LONDON, ONTARIO[i]

3.0 INTRODUCTION

Fibromyalgia Syndrome (FMS) is diagnosed in 10 to 20 percent of patients seen in rheumatology clinics in the U.S.,[1] Mexico,[2] Spain,[3] and Australia[4] and is one of the three most common disorders diagnosed among new referrals to Canadian rheumatologists.[5] The prevalence of FMS in the adult U.S. population has been estimated at 2.0%.[6] To date, the prevalence of FMS in Canada is unknown. The primary objective of this study was to estimate the point prevalence of FMS among non-institutionalized Canadian adults.

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3.1 METHODS

3.1.0 Phase I: The Screening Survey

London, Ontario is a community of 341,320 persons (1991 census) in Southwestern Ontario. London was selected both for logistic reasons, and because it is demographically representative of other mid-size Canadian cities outside of Quebec.

The screening survey was performed from November 1994 to March 1996, inclusive. The **sampling frame** was a computer-generated list of 19,500 seven digit telephone numbers, equally distributed among the 39 telephone exchanges in London. Each **sampling unit** was a London residence with at least one telephone number, selected by random digit dialing (RDD) (approximately 1% of London households do not have telephone service). One adult (age 18 years plus) per household was eligible to be interviewed.[7]

We wished to estimate overall FMS prevalence with a precision of plus or minus 1.0% with 95% confidence (assuming a true prevalence of 2.0%, and both a 75% Phase I and a 75% Phase II participation rate) and to identify at least 50 confirmed community cases of FMS. We calculated that we required 3375 completed screening interviews.

Subjects screened positive if they reported widespread pain of at least one week's duration over the preceding three months [Figure 1]. Subjects also were asked questions on demographics that were selected from the Ontario Health Survey (OHS).[8]

3.1.1 Phase II: Confirming or excluding FMS

All subjects who screened positive in Phase I were invited to be evaluated by one of two rheumatologists (KPW, MH) to confirm or exclude FMS. The evaluation consisted of questions on the distribution and duration of pain, followed by digital palpation for tenderness at the eighteen fibromyalgia points specified by the American College of Rheumatology (ACR),[9] applying 4 kg pressure at a rate of 1 kg per second. Based upon this examination, subjects were identified either as FMS cases (**FC**) or pain controls (**PC**). In a pilot study of 25 consecutive rheumatology outpatients, 12 with FMS; the two examiners had agreed on the presence or absence of FMS in all cases (κ = 1.00).

3.1.2 Estimating Point Prevalence

Three estimates of point prevalence were calculated. The most conservative estimate was based upon the assumption that the only cases of FMS in the survey sample were those that were confirmed [Estimate #1, Appendix A]. A second estimate adjusts for Phase II non-participation by assuming the same prevalence among positive screens who refused to be examined as among those who were examined [Estimate #2, Appendix A]. A third estimate adjusted both for Phase II non-participation and the number of adults residing in each household[10] [Estimate #3, Appendix A]. All estimates were

adjusted for age and sex by direct age standardization, using 1991 London census data. Ninety-five percent confidence intervals were constructed using logit transformation.[11]

Using subject responses to demographic items in the Phase I telephone interview, we calculated the crude odds of having FMS for each demographic variable, with 95% confidence limits, using SPSS.[12]

3.2 RESULTS

To achieve the required sample size, 16,769 telephone numbers were dialed, resulting in 4,674 eligible contacts, 1279 (27.4%) refusals, and 3,395 completed screening interviews: 2,090 (61.6%) female, 1,290 (38.0%) male; 15 subjects refused to identify their sex and were excluded from further analysis (0.4%). Because the sample sex distribution differed from the 1991 London census (females = 52.7% of adults) all subsequent data analyses were adjusted for age and sex.

Pain and fatigue: Recalling the previous three months, 34.8% of the survey sample reported having had some musculoskeletal pain lasting at least one week: 36.1% of females, and 32.6% of males (Odds ratio [OR] = 1.16, 95% exact confidence limits [CI] = 1.00, 1.35). A much smaller percentage, 7.3% (n = 248), reported having had chronic widespread pain, as defined in Figure 1. Widespread pain also was more commonly reported by females (9.0% versus 4.7%, OR = 2.02, CI = 1.49, 2.77).

More than half of the survey sample, 54.5%, reported having had frequent fatigue over the previous three months and, for 21.5%, this fatigue was debilitating enough to significantly limit their activities. As with chronic pain, females were more likely to report fatigue than were males, 60.0% versus 45.0% reporting frequent fatigue (OR = 1.84, CI = 1.60, 2.13), 25.1% versus 15.3% reporting activity limiting fatigue (OR = 1.86, CI = 1.55, 2.25).

Women were more likely to report previously having been told they had arthritis (26.3% versus 16.6%, OR = 1.80, CI = 1.50, 2.15) and fibromyalgia (8.6% versus 4.9%, OR = 1.83, CI = 1.35, 2.51).

Phase II participants and non-participants: Of 248 subjects (187 females, 60 males, and 1 sex not reported) who screened positive, 176 (71%) agreed to be examined. A somewhat greater percentage of participants versus non-participants were female (79.0% versus 69.4% males) and participants were younger (mean age difference = 3.2 years); otherwise, the two groups were demographically similar. Phase II participants and non-participants did not differ with respect to distribution of pain, the percentage with frequent fatigue (92.0% versus 91.7%), or the percentage with fatigue that significantly limited activities (71.0% versus 63.9%). Age and sex-specific phase II participation rates are presented in Tables 1 and 3.

FMS prevalence in females: Among 184 women who screened positive for chronic widespread pain, 86 cases of FMS were confirmed (mean age = 49.2 years) and a further 31 cases expected (assuming the same percentage with FMS among the 49 Phase II non-participants as among the 137 who were examined) for a total of 117 cases [Table 1]. Not adjusting for Phase II non-participation, point prevalence is 4.2% (4.0%, 4.4%) [Table 2]. Adjusting for non-participation, the estimate is 5.7% (5.5%, 5.9%). Weighting according to the number of adults in each household results in a prevalence estimate of 4.9% (4.7%, 5.1%). In all three estimates, prevalence is one percent or less in women under 25, gradually increases until late middle age, then steadily declines.

FMS prevalence in males: Fourteen cases (mean age = 39.3 years) were identified among 39 male subjects who were examined [Table 3]. The unadjusted, response-adjusted, and response-adjusted plus weighted estimates for FMS prevalence were 1.0%, 1.7% and 1.6%, respectively [Table 4]. Similar to females, the prevalence of FMS in males is approximately one percent in the 18-24 year age group. Unlike females, the prevalence remains low throughout life, between one and two percent. There were no cases identified in men over 64 years.

Overall point prevalence: One hundred cases of FMS were confirmed among the 176 who were examined. The unadjusted, response-adjusted, and response-adjusted plus weighted estimates of FMS prevalence, adjusted both for age and sex, were 2.7% (2.6%, 2.8%), 3.8% (3.7%, 3.9%), and 3.3% (3.2%, 3.4%) respectively.

Odds Ratios for Demographic variables: The demographic characteristics of 100 confirmed FMS cases are presented in Table 5. The likelihood of having FMS was not affected by the number of adults residing in one's household. Less than a high school education was associated with having FMS versus chronic, non-FMS pain (compared to a university degree, OR = 3.45, CI = 2.00, 5.97) as was having an annual household income less than $12,000 (compared to an annual income of no less than $80,000, OR = 2.61, CI = 1.19, 5.71) or being disabled (compared to working or in school, OR = 2.68, CI = 1.04, 6.91).. There were increased odds of having chronic, widespread non-FMS pain (with or without FMS) among those who were divorced or separated (compared to those currently married, OR = 1.95, CI = 1.10, 3.45).

3.3 DISCUSSION

Only since 1989 have researchers reported the prevalence of FMS in the community. Most early studies were in Western Europe, where the prevalence of FMS varied from 0.7% and 0.8% in Denmark[13] and Finland[14] to 2.0% in Germany.[15] Interestingly, the prevalence of FMS in Poland[16] (4.5%) and South Africa (3.2%)[17] appears to be higher than in any Western European country. A possible exception is Norway.[18,19] There are as yet no explanations for the international differences in FMS prevalence, and no published data as to variations within countries.

Prior to 1995, estimates of FMS prevalence in the North American general population were based entirely upon clinic studies; these estimates ranged from 1.0%[20] to 15%.[21] The first reported community prevalence study was performed in Wichita, Kansas,[22] where FMS prevalence was 3.2% in females, 0.5% in males, and 2.0% overall. Of 193 subjects examined, 18.9% (36) were found to meet the ACR criteria for FMS.

We have confirmed 100 cases of FMS in a random, community survey of non-institutionalized adults. We generated three estimates of FMS prevalence, both for females and males.

1) a conservative estimate using only confirmed cases of FMS;
2) an estimate including probable cases of FMS among subjects who screened positive for widespread pain but were not examined, an assumption we justified on the basis of it being impossible to determine whether or not FMS itself enhanced or diminished an eligible subject's likelihood to participate in Phase II, and our own data that shows that Phase II non-participants were demographically and symptomatically similar to participants;
3) an estimate to adjust for over-representation by seniors in the sample.

The three estimates were very similar. An intermediate estimate of FMS prevalence among non-institutionalized females is 4.9% (4.7%, 5.1%) and 1.6% in males (1.3%, 1.9%), for a female to male prevalence ratio of approximately three to one. In our study population, the percentage of FMS cases that are female is 75.0% (71.2%, 79.7%), at the low end of what generally has been reported in clinic studies.[23] Roughly one in

twenty adult females and one in sixty adult males currently have FMS. Besides female sex, risk factors for having FMS versus chronic pain from another source include middle age, low household income, and less than a high school education. These four risk factors also were identified in Wichita.[24]

If London is representative of the adult population of Canada, FMS currently affects almost 700,000 Canadian adults. FMS is approximately four to eight times as common as rheumatoid arthritis,[25] and much more common than systemic lupus.[26]

FMS generally is regarded to be a non-infectious, chronic, non-remitting, non-crippling and non-fatal disorder.[27] This characterization is not supported by our data, especially in females, for whom FMS prevalence steadily rises from age 18 through middle age, then appears to decline steadily. Weighting according to the number of adults residing in each household reduces the increase in prevalence from early to late middle age, probably by limiting over-counting elderly subjects living alone. Nonetheless, the peak FMS prevalence in the 55 to 64 year old age group remains.

There are at least three potential explanations for the observed age effect. The first is that FMS does remit, particularly in individuals over age 64. However, in a ten year, prospective study of FMS clinic patients, there were no cases of complete remission.[28] In an eight year Swedish study of 49 FMS patients, remissions were described as 'rare'.[29]

A second explanation is *selective mortality:* individuals with FMS are more likely to die than age- and sex- matched individuals in the general population. FMS could have a potentially fatal course itself, it could be a *confounder* through association with other, potentially fatal illnesses, or it could reduce survival in other conditions. Clinic studies already have demonstrated that FMS commonly co-exists with lupus[30] and rheumatoid arthritis,[31] diseases with a standardized mortality ratio (SMR) greater than one.

A third hypothesis is that the differences across age groups reflect different years of birth (a *cohort effect)* rather than an age effect per se. Sometime in the past, there may have been an epidemic of FMS, specific to one particular age group. If FMS truly is chronic, non-remitting and non-fatal, then this peak of FMS prevalence would follow this cohort as it ages. Further study of larger samples would permit a more accurate estimation of age, period and cohort effects. Allowing for this possibility, then the 'epidemic of FMS' must be explained, and the potential especially for an infectious or other environmental cause must be re-examined.

It is possible that our study was biased towards confirming FMS in middle-aged, rather than older individuals, if older persons with FMS are less likely to participate either in the initial screening survey or the confirmatory examination. However, several findings make this improbable. First, the representation of people over age 65 in the sample (15.2%) is very close to the proportion of the population in this age group (15.5%). Second, while the proportion of positive screens who participated in Phase II is

lower among those 65 and older (58%) than among those under 65 years (75%), this lower participation rate is insufficient, by itself, to account for the difference in prevalence.

One might argue that the fall in FMS prevalence commencing at age 65 supports the claim that FMS is a product of an over-generous compensation system. This explanation is not supported by the higher prevalence of FMS in Poland and South Africa than in Western Europe and the U.S. Nor is it supported by the gradual decline in FMS prevalence, approximately three percent per decade after age 64, rather than a sharp decline at age 65.

It is possible that the apparent decline of FMS prevalence in those over age 64 is a result of a bias towards selectively surveying well elders at home, as opposed to more ill elders in institutions. In 1991, 6300 Londoners, 1.8% of the population, did not reside in private households. We can estimate the effect of institutionalized adults on FMS prevalence on females age 65 and older. Assume that half of the 6300 institutionalized persons in London are female, and that 50% of these females are 65 or older. If 10% of them have FMS (double the rate in the non-institutionalized) it would inflate the crude estimate of FMS prevalence in women over 64 from 3.6% (2.7%, 4.8%) to 3.7% (2.8%, 4.9%). This compares to a crude prevalence of 8.5% in the 55 to 64 age group (6.8%, 10.6%). Hence, even correcting for a prevalence of FMS among institutionalized females that is double that of non-institutionalized females, there is a statistically significant decline in prevalence in women 65 and older.

In summary, we found FMS to be a common illness, especially among middle-aged women and persons of lower socioeconomic status.

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Figure 1: The LFES Screening Questionnaire (LFES-SQ)

Pain criteria

1. In the past three months, have you had pain in muscles bones or joints, lasting at least one week?
2. Have you had pain in your shoulders, arms or hands? On which side? Right, left or both?
3. Have you had pain in your legs or feet? On which side? Right, left or both?
4. Have you had pain in your neck, chest or back?

Meeting the pain criteria requires 'yes' responses to all four pain items, and either

1) both a right and left side positive response, or **2)** a both sides positive response.

Table 1: Confirmed and estimated female cases of FMS in the survey sample.

	A	B	C	D	E	F (C-D) x (E / D)	G (E + F)
Age Group	**Females in 1991 London census**	**Number (& percent) surveyed**	**Number (+) screens**	**Number (& percent) examined**	**Confirmed FMS cases**	**Estimated unconfirmed FMS cases**	**Estimated Total FMS cases**
18-24	18813	291 (1.5%)	9	6 (67%)	2	1	3
25-34	32815	452 (1.4%)	21	16 (76%)	9	3	12
35-44	27550	474 (1.7%)	46	36 (78%)	26	8	34
45-54	18105	276 (1.5%)	34	27 (79%)	19	5	24
55-64	14770	200 (1.4%)	35	28 (80%)	17	4	21
65-74	13470	216 (1.6%)	31	21 (68%)	11	5	16
75+	10460	143 (1.4%)	10	3 (30%)	2	5	7
Subtotal	135983	2052 (1.5%)	186	137 (74%)	86	31	117
Age unknown	0	38	1	N/A	N/A	N/A	N/A
Total	135983	38	187				

N/A = not applicable

Table 2: The prevalence of FMS in non-institutionalized adult females - London, Ontario

Age Group	= (E / B) from Table 1 *Prevalence if only confirmed* FMS cases counted*	= (G / B) from Table 1 *Prevalence if confirmed &* unconfirmed FMS cases counted**	Prevalence counting confirmed & unconfirmed cases, also weighted by # of adults in each household***
18-24	0.7% (0.1%, 4.5%)	1.0% (0.3%, 3.7%)	0.4% (0.0%, 9.9%)
25-34	2.0% (1.3%, 3.1%)	2.7% (2.0%, 3.7%)	3.2% (2.5%, 4.2%)
35-44	5.5% (4.7%, 6.4%)	7.2% (6.4%, 8.1%)	7.5% (6.7%, 8.4%)
45-54	6.9% (5.6%, 8.4%)	8.7% (7.4%, 10.2%)	6.6% (5.3%, 8.1%)
55-64	8.5% (6.8%, 10.6%)	10.5% (8.7%, 12.3%)	7.9% (6.2%, 10.0%)
65-74	5.1% (3.6%, 7.2%)	7.4% (5.8%, 9.4%)	5.1% (3.6%, 7.2%)
75+	1.4% (0.2%, 9.0%)	4.9% (2.8%, 8.4%)	3.5% (1.6%, 7.4%)
Total****	4.2% (4.0%, 4.4%)	5.7% (5.5%, 5.9%)	4.9% (4.7%, 5.1%)

* The prevalence estimate is the number of confirmed FMS cases in each age group, divided by the number surveyed in that age group.

** The prevalence estimate was adjusted for Phase II non-participation, dividing the estimated total number of FMS cases by the number surveyed in each age group.

*** The prevalence estimate adjusts for Phase II non-participation, and weights according to the number of adults in each household.

**** Estimate adjusted for age using direct age standardization and the 1991 London census.

Table 3: Confirmed and estimated male cases of FMS in the survey sample.

Age Group	A Males in 1991 London census	B Number (& percent) surveyed	C Number (+) screens	D Number (& percent) examined	E Confirmed FMS cases	F (C-D) x (E / D) Estimated unconfirmed FMS cases	G (E + F) Estimated Total FMS cases
18-24	18451	237 (1.3%)	6	6 (100%)	3	0	3
25-34	31090	312 (1.0%)	10	5 (50%)	3	3	6
35-44	25795	288 (1.1%)	18	13 (72%)	4	2	6
45-54	17285	183 (1.1%)	12	6 (50%)	2	2	2
55-64	13695	104 (0.8%)	9	7 (78%)	2	1	3
65-74	10570	94 (0.9%)	4	2 (50%)	0	0	0
75+	5695	53 (0.9%)	0	0	0	0	0
Subtotal	122581	1271 (1.0%)	59	39 (66%)	14	8	22
Age unknown	0	19	1	N/A	N/A	N/A	N/A
Total	122581	1290	60				

N/A = not applicable

Table 4: The prevalence of FMS in non-institutionalized adult males - London, Ontario

Age Group	= (E / B) from Table 3 Prevalence if only confirmed FMS cases counted*	= (G / B) from Table 3 Prevalence if confirmed & unconfirmed FMS cases counted**	Prevalence counting confirmed & unconfirmed cases, also weighted by # of adults in each household***
18-24	1.3% (0.4%, 4.5%)	1.3% (0.3%, 4.5%)	1.0% (0.2%, 4.9%)
25-34	1.0% (0.3%, 3.4%)	1.9% (1.0%, 3.6%)	1.9% (1.0%, 3.6%)
35-44	1.4% (0.5%, 3.6%)	2.1% (1.1%, 3.9%)	2.4% (1.4%, 4.2%)
45-54	1.1% (0.2%, 7.1%)	2.2% (0.8%, 5.6%)	2.5% (1.1%, 5.7%)
55-64	1.9% (0.3%, 12.3%)	2.9% (0.8%, 10.0%)	1.2% (0.0%, 21.5%)
65-74	0.0% (0.0%, 3.2%)	0.0% (0.0%, 3.2%)	0.0% (0.0%, 3.2%)
75+	0.0% (0.0%, 5.7%)	0.0% (0.0%, 5.7%)	0.0% (0.0%, 5.7%)
Total****	1.1% (0.8%, 1.4%)	1.7% (1.4%, 2.0%)	1.6% (1.3%, 1.9%)

* The prevalence estimate is the number of confirmed FMS cases in each age group, divided by the number surveyed in that age group.

** The prevalence estimate was adjusted for Phase II non-participation, dividing the estimated total number of FMS cases by the number surveyed in each age group.

*** The prevalence estimate adjusts for Phase II non-participation, and weights according to the number of adults in each household.

**** Estimate adjusted for age using direct age standardization and the 1991 London census.

Table 5: The demographic profile of confirmed FMS cases.

N =	100
% female	86.0%
mean age (years)	47.8
males	39.3[1]
females	49.2[1]
marital status	
% never married	18.2%
% married	47.5%
% divorced/separated	30.3%
% widowed	4.0%
education	
% < highschool	29.6%
% highschool	24.5%
% some college	23.5%
% some university	10.2%
% university degree	11.2%
% other	1.0%
household income	
% with < $12,000	10.9%
% with $12,000 - $29,999	16.4%
% with $30,000 - $59,999	27.4%
% with $60,000 - $79,999	4.1%
% with > $80,000	4.1%

The response rate was not 100% for all questions.

[1] $p < 0.05$

APPENDIX A: Formulae to calculate FMS Prevalence

Estimate #1: $\frac{\text{confirmed FMS cases}}{\text{total Phase I participants}} \times 100\%$

Estimate #2: $\frac{\text{confirmed FMS cases} + (p \times \text{Phase II refusals})}{\text{total Phase I participants}} \times 100\%$

where p = the proportion of Phase II participants in whom FMS has been confirmed.

Estimate #3: $\frac{\Sigma(\text{confirmed FMS cases} \times n_i) + (p \times \Sigma(\text{Phase II refusals} \times n_i)}{\Sigma(\text{Phase I participants} \times n_i)} \times 100\%$

where n_i = the number of adults living in the 'i^{th}' household.

REFERENCES

[1] Marder WD, Meenan RF, Felson DT, Reichlin M, Birnbaum NS, Croft JD, Dore RK, Kaplan H, Kaufman RL, Stobo JD. The present and future adequacy of rheumatology manpower. Arthritis Rheum 1991;34:1209-17

[2] Alarcon-Segovia D, Ramos-Niembro F, Gonzales-Amaro RF. One thousand private rheumatology patients in Mexico City. Arthritis Rheum 1983;26:688-9 [letter]

[3] Calabozo-Raluy M, Llamazares-Gonzales AI, Munoz-Gallo MT, Alonso-Ruiz A. Sindrome de fibromialgia (fibrositis); Tan frequente como desconcido. Med Clin (Barc) 1990;94:173-5

[4] Reilly PA, Littlejohn GO. Peripheral arthralgic presentation of fibrositis/fibromyalgia syndrome. J Rheumatol 1992;19:281-3

[5] White KP, Harth M, Speechley M, Ostbye T. Fibromyalgia in rheumatology practice: A survey of Canadian rheumatologists. J Rheumatol 1995;22:722-6

[6] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The Prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38:19-28

[7] O'Rourke D, Blair J. Improving random respondent selection in telephone surveys. Journal of Marketing Research 1983;20:428-32

[8] Badley EH, Yoshida K, Webster G, Stephens M. Ontario Health Survey, 1990. Working Paper Number 5. Disablement and chronic health Problems in Ontario. Health Canada

[9] Wolfe F, Smythe HA, Unus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, Fam AG, Farber SJ, Fiechtner JJ, Franklin CM, Gatter RA, Hamaty D, Lessard J, Lichtbrown AS, Masi AT, McCain GA, Reynolds WJ, Romano TJ, Russell IJ, Sheon RP. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum 1990;33:160-72

[10] Scheaffer RL, Mendenhall W, Ott L: Elementary Survey Sampling, Fourth Edition. PWS-Kent Publishing Co., Boston, MA, 1990

[11] Rochon J. The application of the GSK method to the determination of minimum sample sizes. Biometrics 1989;45:193-205

[12] SPSS, release 6.1. Copyright © SPSS Inc., 1989-1994

[13] Prescott E, Kjoller M, Jacobsen S, Bulow PM, Danneskoild-Samsoe B, Kamper-Jorgensen. Fibromyalgia in the adult Danish population. Scand J Rheumatol 1993;22:233-7

[14] Makela M, Heliovaara M. Prevalence of primary fibromyalgia in the Finnish population. BMJ 1991;303(7):216-9

[15] Raspe H, Baumgartner CH. The epidemiology of the fibromyalgia syndrome (FMS) in a German town. Scand J Rheumatol 1992; S94:8

[16] Schochat T, Croft P, Raspe H. The epidemiology of fibromyalgia. Workshop of the standing committee on epidemiology, european league against rheumatism (EULAR), Bad Sackingen, 19-21 November 1992. Br J Rheumatol 1994;33:783-6

[17] Lyddell C, Meyers OL. The prevalence of fibromyalgia in a South African community. Scand J Rheumatol 1992;S94: 8

[18] Forseth KO, Gran JT. The prevalence of fibromyalgia among women aged 20-49 years in Arendal, Norway. Scand J Rheumatol 1992;21:74-8

[19] Forseth KO, Gran JT, Husby G. A population study of the incidence of fibromyalgia among females aged 26 - 55 years. Arthritis Rheum 1997;40(9):S44

[20] Wallace DJ. Systemic lupus erythematosis, rheumatology and medical literature: Current trends. J Rheumatol 1985;12:913-5

[21] Gerecz-Simon EM, Kean WF, Watson-Buchanon W. New criteria for the classification of fibromyalgia. Can J Diagnos (February) 1990:80-96

[22] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38(1):19-28

[23] Goldenberg D. Fibromyalgia syndrome. An emerging but controversial condition. JAMA 1987;257(20):2782-6

[24] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38(1):19-28

[25] Spector TD. Epidemiology of rheumatic diseases: Rheumatoid arthritis. Rheum Dis Clin North Am 1990;16(3):513-37

[26] Schur PH. Clinical features of SLE. In: Textbook of Rheumatology, 3rd Ed., Kelley WN, Harris ED Jr, Ruddy S, & Sledge CB (eds). WB Saunders Co., Harcourt Brace Jovanovich, Inc., Philadelphia, USA, 1989

[27] Wolfe F and the Vancouver fibromyalgia consensus group. The fibromyalgia syndrome: A consensus report on fibromyalgia and disability. J Rheumatol 1996;23(3):534-9

[28] Kennedy M, Felson DT. A prospective long-term study of fibromyalgia syndrome. Arthritis Rheum 1996;39(4):682-5

[29] Bengtsson A, Backman E. Long-term follow up of fibromyalgia patients. Scand J Rheumatol 1992;S94:98

[10] Romano TJ. Coexistence of fibromyalgia syndrome (FMS) and systemic lupus erythematosis. Scand J Rheumatol 1992;S94:12

[31] Romano TJ. Incidence of fibromyalgia syndrome (FMS) in rheumatoid arthritis (RA) patients seen in a general rheumatology practice. Scand J Rheumatol 1992;S94:11

CHAPTER 4
THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY (LFES): DIRECT HEALTH CARE COSTS OF FIBROMYALGIA SYNDROME (FMS) IN LONDON, ONTARIO[i]

4.0 INTRODUCTION

Musculoskeletal (MSK) disorders contribute greatly to chronic disability and health services utilization in developed economies. In the USA, an estimated 37 million individuals (14.5% of the U.S. population) suffered from arthritis in 1989.[1] Musculoskeletal disorders account for 15% of work loss days in the USA[2] and 14 -17% of work loss days in Great Britain.[3] In Canada, one million adults have physical disabilities secondary to MSK illness, a prevalence of 50.1 per thousand.[4] Sixteen percent of respondents in the 1980 Canada Health Survey (CHS)[5] and 14 percent in the 1990 Ontario Health Survey (OHS)[6] reported having either arthritis or rheumatism. In each study, 'arthritis and rheumatism' was the most commonly reported cause of chronic disability, and the second most frequent cause of two week disability (after respiratory illness including rhinitis). These findings were consistent across all adult age groups. In

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addition, people affected by arthritis and rheumatism use more health services than the general population,[7] and the costs of MSK illness may be increasing. In 1980, MSK disorders in the U.S. accounted for an estimated $21 billion in health care costs and lost wages, equivalent to approximately one percent of the country's Gross National Product.[8] A more recent survey, performed between 1990 and 1992, estimated the same costs as $149.4 billion, or 2.5% of the GNP.[9]

Fibromyalgia Syndrome (FMS), also known as fibrositis, is a common form of non-articular rheumatism associated with chronic generalized musculoskeletal pain, fatigue, and a long list of other complaints.[10] Clinic studies indicate that FMS patients are as adversely affected by their symptoms as patients with rheumatoid arthritis (RA), and more so than osteoarthritis (OA) patients.[11,12,13] For several reasons, including a relative dearth of specific physical, laboratory and radiographic findings, the concept of FMS has met with much skepticism,[14,15,16] and has attracted less research interest than other less common musculoskeletal disorders.[17]

We sought to identify between 50 and 100 individuals living in the community with confirmed FMS, in order to estimate direct health care costs for individuals with FMS, compared to several general population control groups. Previous population-based samples from other countries generally have been too small to assess costs. To our knowledge, our 100 confirmed community cases of FMS represent the largest cohort of community FMS cases reported. These cases will be compared to: 1) 76 general population controls with chronic widespread musculoskeletal pain in whom FMS has

been excluded; 2) 135 group-matched general population controls without chronic widespread pain; and 3) 384 pair-matched general population controls from the Ontario Health Insurance Plan (OHIP) billing database.

4.1 METHODS

This was a three phase study. **Phase I** was a random telephone survey of non-institutionalized adults to identify possible cases of FMS. In **Phase II**, individuals with widespread, chronic pain were examined to identify FMS cases and collect additional health data. In **Phase III**, we compared direct health care costs in FMS cases versus controls. The protocol was approved by the Review Board for Research involving Human Subjects at the University of Western Ontario, London, Ontario.

4.1.0 Phase I: Screening for chronic widespread pain

The **target population** was London, Ontario, a community of 341,320 persons (1991 census) in Southwestern Ontario. London was selected because it is demographically representative of other mid-size Canadian cities outside of Quebec.

Phase I data were collected from November 1994 to March 1996, inclusive. The **sampling frame** was a computer-generated list of 19,500 seven digit telephone numbers, equally distributed among the 39 telephone exchanges in London. Each **sampling unit** was a London residence with at least one telephone number, selected by random digit

dialing (RDD) (approximately 1% of London households do not have telephone service). One person per household was eligible to be interviewed, that being the adult (age 18 years plus) with the most recent birthday as of the date of initial telephone contact; this method for subject selection has been validated previously.[18]

A **sample size** of 3375 completed screening interviews would allow for 80% power to detect a $200 or greater difference in annual OHIP spending between study groups.

Subjects screened positive if they reported widespread pain of at least one week's duration over the preceding three months; details of the screening phase and instrumentation are presented elsewhere.[19] Subjects also were asked questions on demographics selected from the Ontario Health Survey (OHS).[20]

4.1.1 Phase II: Confirming or excluding FMS; data collection

All subjects who screened positive in Phase I were invited to be evaluated by one of two rheumatologists (KPW, MH) to confirm or exclude FMS. The evaluation consisted of questions on the distribution and duration of pain, followed by digital palpation for tenderness at the eighteen fibromyalgia points specified by the American College of Rheumatology (ACR),[21] applying 4 kg pressure at a rate of 1 kg per second. Based upon the results of the examination, subjects were identified either as FMS cases (**FC**) or pain controls (**PC**). In a pilot study of 25 consecutive rheumatology clinic

outpatients, 12 with FMS, the two examiners had agreed on the presence or absence of FMS in all cases ($\kappa = 1.00$).

FC and PC then completed a detailed health questionnaire, including: 1) 12 items on the use of medications and drugs over the preceding 4 weeks, selected from Section B of the Ontario Health Survey (OHS) questionnaire; and 2) 18 items on the use of health services over the preceding 12 months, and the preceding 14 days, from Section C of the OHS.

For each **FC** confirmed in Phase II, two general controls (**GC**) without chronic, generalized pain, matched for age and sex, were selected during subsequent telephone interviews. The same Phase II Health Questionnaire that was completed by all FC and PC subjects was mailed to all GC subjects, accompanied by an introductory letter, an information letter and consent form, and a pre-addressed, pre-stamped envelope. General control subjects who had not returned the completed questionnaire were re-contacted by telephone within three weeks.

4.1.2 **Phase III: Estimating Direct Health Care Costs**

All FC, PC and GC subjects were asked to participate in a group comparison of annual health services costs to the provincially managed, public health insurance program, the Ontario Health Insurance Plan (OHIP). In Ontario, OHIP is the primary

source of reimbursement for physician, laboratory and imaging services, and also covers many services provided by non-physician health care providers. The OHIP detailed claims file for each consenting subject was entered to access all individual billing claims for the twelve months of 1994, the year prior to Phase II data collection. For each subject, health care utilization for the year 1994 was calculated as **1)** the quantity of health services used in 1994, and **2)** the cost, in 1994 Canadian dollars, of health services billed in 1994. Claims then were subdivided into: **1)** reimbursement of physicians, **2)** reimbursement of other health care professionals, **3)** laboratory costs, and **4)** radiology costs. These costs then were aggregated for the three groups.

4.1.3 **Phase III Data Analysis**

The SAS statistical package[22] was used to analyze group differences in mean annual number of services and annual OHIP costs, using 1) linear regression adjusted for age and sex and 2) where appropriate, the Wilcoxon Rank Sum test to adjust for non-homogeneous group variances. Post-hoc testing, for parametric and non-parametric analyses, respectively, involved: 1) Scheffe's test to adjust for groups of different sizes, and 2) the Kruskal-Wallis test. Fibromyalgia cases also were compared to age-, sex- and geographically-matched controls from the OHIP database, with four OHIP controls (**OC**) randomly selected for each FC. Group means for annual number of services and annual OHIP costs were compared using Student's t-test for paired samples; the mean of each matched group of four OC subjects was calculated and compared to the correspondingly matched FC subject.

4.2 RESULTS

To achieve the required sample size, 16,769 telephone numbers were dialed, resulting in 4674 eligible contacts, of whom 1279 (27.4%) refused to participate. This resulted in 3,395 completed screening interviews: 2,090 (61.6%) female, 1,290 (38.0%) male; 15 subjects refused to identify their sex and were excluded from further analysis (0.4%). Because the sample sex distribution differed from the 1991 London Census (females = 52.7% of adults) all subsequent data analyses were adjusted for age and sex, where appropriate.

Among the 3395 subjects who were screened, 248 screened positive for widespread musculoskeletal pain and were invited to be examined; 176 (71%) agreed. Of these, 100 were found to meet the ACR criteria for FMS.

Direct Health Care Costs: Although 100 FC ultimately were identified, only 86 had been confirmed by the end of the telephone survey. Hence, 172 subjects (two controls per FC) were recruited to the GC group; 135 completed questionnaires were returned (78.5%). The three internal study groups (FC, PC and GC) were similar in mean age (47.8, 47.2 and 44.5 years, respectively; NS). Fewer PC were female (67% versus 86% and 82% in the FC and GC groups, respectively; $p < 0.003$). FC generally were less educated than GC ($p < 0.05$). Otherwise, the groups were demographically similar [Table 1].

Annual utilization of OHIP sponsored health services and direct health care costs billed to OHIP are presented in Table 2. Five FC, 9 PC and 41 GC refused to participate in this part of the study. The 41 GC who refused to participate were slightly younger than the 94 GC who did participate in Phase III (39.1 versus 46.0 years, $p = 0.01$); they were not different with respect to sex distribution, marital status, education level or household income. They also did not differ with respect to mean duration of symptoms, severity of pain or fatigue, number of symptoms, number of major symptoms, or FIQ score.

Health services and direct costs were highest for the FC group, both with respect to total annual costs and costs for each of the four cost sub-categories. Consistently, PC had the second highest annual use of services and costs, followed by pair-matched subjects from the OHIP database (OC), with the GC having the lowest annual use of services and costs. The mean annual total number of health services used was 53.2 for FC, and 39.8, 28.6 and 24.9 respectively for the remaining three groups: PC, OC and GC ($F = 9.46$, d.f. 255, $p < 0.0001$). Annual costs were \$1028 (standard deviation = \$1182) for FC, and \$751, \$536 and \$463 for the other three groups, respectively ($F = 8.28$, d.f. 255, $p < 0.0003$). In both instances, the statistical difference in group means was between the FC and GC groups. Details regarding specific services utilized are presented in Table 2.

FC subjects reported more frequent visits over the preceding year to see physicians than either PC or GC subjects ($p < 0.0001$) [Table 3]; similar results were obtained when subjects recalled the previous two weeks ($p < 0.0001$). They also reported more visits to physician specialists over the preceding year than the GC group ($p < 0.003$). Males with FMS reported more annual visits to an emergency department than males in either control group ($p < 0.005$). Fibromyalgia cases and pain controls used a greater number of prescription drugs ($p < 0.0001$), and consumed both prescription ($p < 0.0001$) and over the counter (OTC) ($p < 0.0001$) drugs on more days over the prior two weeks than did subjects in the GC group.

4.3 DISCUSSION

To our knowledge, only one other community-based survey has reported on health service utilization and costs associated with FMS. Wolfe et al found that 36 confirmed cases of FMS randomly surveyed in Wichita Kansas reported utilizing more health services than did the general population.[23] In a subsequent clinic study of FMS patients at six centers across the U.S., including Wichita, the average FMS patient utilized $2,274 U.S. annually.[24] Hospital costs were more than twice that for outpatient visits.

Our 100 FMS cases reported using more medications and health services than either of two control groups, including those with chronic widespread pain without FMS. The differences in medication use were both for prescribed and over-the-counter medication. The difference in self-reported health services use primarily was for

physician services, rather than services by other health professionals. These differences were present both for one year and two week recall. Most of the services utilized were provided on an outpatient basis, the average individual with FMS spending only two days as a hospital inpatient per year, compared to twelve outpatient visits to physicians annually.

It is somewhat surprising that males, not females with FMS, utilized emergency department services more than did controls. It may be that males were less likely to utilize the services of their family physicians; males with FMS reported somewhat fewer visits to their family physicians over the preceding year (6.9 versus 9.6 visits for females). More numerous or more severe symptoms might lead certain patients to seek emergency care, rather than the care of their family physician, but there were no sex differences in symptom quantity or severity.

Direct health care costs incurred by the Ontario Health Insurance Plan (OHIP) were higher for FMS cases than any of the three control groups, including those with chronic widespread pain without FMS. The total cost of health services rendered to FMS cases was $1028 annually (1993 Canadian dollars). This excludes a number of health services not reimbursed by OHIP, such as visits to dentists, psychologists, physiotherapists in private practice, and certain alternative health practitioners, and certain elective procedures such as cosmetic surgery. It excludes the costs of medications, which can be considerable. It also excludes other, difficult to measure direct costs such as those for clinic staffing and maintenance.

Accepting these limitations to our data, we still can measure accurately the difference between annual reimbursement costs for FMS cases versus general population controls from the OHIP database, which was $493 per annum. Multiplied by an estimated 700,000 adults with FMS Canada wide,[25] this represents almost $350 million in net direct health care costs attributable to FMS across Canada in 1993. The lion's share of this was for physician services, approximately $250 million annually. The estimated reimbursements for other health professionals, laboratory and radiology services were $21 million, $41 million, and $23 million, respectively. These costs are only a percentage of the actual costs of FMS, which also would include indirect costs such as lost income and insurance pensions, the last of which has been estimated as high as $200 million annually.[26] Data from the U.S. 1990-1992 National Health Interview Survey (NHIS) suggest that somewhat less than 50% of the costs of musculoskeletal illness are direct health care costs.[27] If this is true for FMS, then the net annual cost of FMS in Canada likely exceeds $700 million.

In summary, we found FMS to result in substantial expenses, at least to the health care system. Irrespective of whether one views it as a legitimate medical condition or a medicalization of a social phenomenon, the costs of FMS suggest the need for further investigations into its etiology and treatment.

List of Tables

Table 1: A demographic comparison of FMS cases (FC), Pain controls (PC), and General controls (GC).

	FC	PC	GC
N =	100	76	135
mean age (years)	47.8	47.2	44.5
% female**	86.0%	67.1%	81.5%
marital status			
% never married	18.2%	17.1%	28.8%
% married	47.5%	42.1%	32.7%
% divorced/separated	30.3%	36.8%	28.8%
% widowed	4.0%	3.9%	8.7%
education*			
% < highschool	29.6%	18.4%	15.0%
% highschool	24.5%	34.2%	30.7%
% some college or university	33.7%	34.2%	25.2%
% university degree	11.2%	11.8%	28.3%
household income			
% with < $12,000	10.9%	9.4%	4.0%
% with $12,000 - $29,999	16.4%	18.9%	11.9%
% with $30,000 - $59,999	27.4%	20.8%	24.6%
% with $60,000 - $79,999	4.1%	13.2%	15.1%
% with > $80,000	4.1%	7.5%	10.3%

The response rate was not 100% for all questions.

* $p < 0.05$, ** $p < 0.005$

Table 2: Services reimbursed and amount paid in 1993 by Ontario Health Insurance Plan (OHIP)

	FC	PC	GC	f probability * Pr > f	OC	t probability** Pr > t
N =	95	67	94		380	
Physician services						
# services	27.5	22.3	14.1	NS	15.8	NS
amount paid	$781	$571	$353	p < 0.005	$414	p < 0.002[1]
Other provider services						
# services	4.5	5.7	2.0	NS	2.0	NS
amount paid	$55	$68	$26	NS	$25	NS
Laboratory services						
# services	18.0	9.2	7.5	p < 0.0003	9.3	p < 0.003[2]
amount paid	$116	$61	$44	p < 0.003	$57	NS
Radiology services						
# services	2.6	2.0	1.3	NS	1.4	p < 0.005[3]
amount paid	$71	$47	$39	NS	$38	p < 0.004[3]
Total services						
# services	53.2	39.8	24.9	p < 0.0001	28.6	p < 0.0003[4]
amount paid	$1,028	$751	$463	p < 0.0003	$536	p < 0.0003[4]

All analyses were Bonferoni corrected; statistical significance if $p < (0.05 / 10) \doteq 0.005$

* FC, PC and GC are independent samples; were compared by linear regression, adjusted for age and sex.

** FC and OC are interdependent samples; were compared by paired Student's t test.

[1] FC > GC, OC [2] FC > GC [3] FC > OC [4] FC > PC, GC, OC

Table 3: One Year Utilization of Health Services by Group: FC, PC, GC

Service	mean services used FC	PC	GC
N =	100	76	135
visits to all MDs** [1]	12.1	6.9	4.3
visits to specialists* [1]	2.9	1.1	1.0
visits to psychiatry	3.0	2.3	1.7
visits to therapists	8.1	7.0	3.4
visits to other health professionals	7.4	3.5	2.2
hospital days	2.0	0.3	0.4
current prescribed medications** [2]	2.8	1.9	0.9

All statistical analyses were Bonferroni corrected, with significance at $p < 0.005$.

* $p < 0.005$, ** $p < 0.0001$

[1] FC > PC and GC [2] FC > PC > GC

REFERENCES

[1] Lawrence RC, Hochberg MC, Kelsey JL, McDuffie FC, Medsger TA(Jr), Felts WR, Shulman LE. Estimates of prevalence of selected arthritic and musculoskeletal diseases in the United States. J Rheumatol 1989;16:427-41

[2] Felts W, Yelin E. The economic impact of the rheumatic diseases in the United States. J Rheumatol 1989;16:867-84

[3] Wood PHN, Badley EM. Rheumatic Disorders. In: Miller DL, Farmer RDT, eds. Epidemiology of Diseases. Oxford: Blackwell Scientific Publications 1982, pp. 333-46

[4] Reynolds DL, Chambers LW, Badley EM, Bennett KJ, Goldsmith CH, Jamieson E, Torrance GW, Tugwell P. Physical disability among Canadians reporting musculoskeletal diseases. J Rheumatol 1992;19(7):1020-30

[5] Lee P, Helewa A, Smythe HA, Bombardier C, Goldsmith CH. Epidemiology of musculoskeletal disorders (complaints) and related disability in Canada. J Rheumatol 1985;12:1169-73

[6] Badley EH, Yoshida K, Webster G, Stephens M. Ontario Health Survey 1990, Working Paper No. 5: Disablement and chronic health problems in Ontario. Ministry of Health Ontario, 1993

[7] Spitzer WO, Harth MH, Goldsmith CH, Norman GR, Dickie GL, Bass MJ, Newell JP. The Arthritis complaint in primary care: Prevalence, related disability, and costs. J Rheumatol 1976;3(1):88-99

[8] Felts W, Yelin E. The economic impact of the rheumatic disorders in the United States. J Rheumatol 1989;16:867-84

[9] Yelin E, Callahan LF. The economic cost and social and psychological impact of musculoskeletal conditions. Arthritis Rheum 1995;38(10):1351-62

[10] Wolfe F. The clinical syndrome of fibrositis. Am J Med 1986;81(3A):7-14

[11] Hawley DJ, Wolfe F. Pain, disability, and pain/disability relationships in seven rheumatic disorders: A study of 1,522 patients. J Rheumatol 1991; 18(10):1552-7

[12] Martinez JE, Ferraz MB, Sato EI, Atra E. Fibromyalgia versus rheumatoid arthritis: A longitudinal comparison of the quality of life. J Rheumatol 1995;22(2):270-4

[13] Burckhardt CS, Clark SR, Bennett RM. Fibromyalgia and quality of life: A comparative analysis. J Rheumatol 1993;20(3):475-9

[14] Bruusgaard D, Evensen AR, Bjerkedal T. Fibromyalgia - A new cause For disability pension. Scand J Soc Med 1993;21:116-9

[15] Ochoa JL. Essence, investigation, and management of "neuropathic" pains: Hopes from acknowledgement of chaos. Muscle Nerve 1993;16:977-1008

[16] Hadler NM. Occupational musculoskeletal disorders. Raven Press, New York, 1993:16-33

[17] Wallace DJ. Systemic lupus erythematosis, rheumatology and medical literature: Current trends. J

Rheumatol 1985;12:913-5

[18] O'Rourke D, Blair J. Improving random respondent selection in telephone surveys. Journal of Marketing Research 1983;20:428-32

[19] White KP, Speechley M, Harth M, Ostbye T. Testing an Instrument to Screen for Fibromyalgia (FMS) in General Population Surveys. (Proceedings of the 124th Annual Meeting of the American Public Health Association, November 17-21, 1996, New York, New York.)

[20] Badley EH, Yoshida K, Webster G, Stephens M. Ontario Health Survey, 1990. Working Paper Number 5. Disablement and chronic health Problems in Ontario. Health Canada

[21] Wolfe F, Smythe HA, Unus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, Fam AG, Farber SJ, Fiechtner JJ, Franklin CM, Gatter RA, Hamaty D, Lessard J, Lichtbrown AS, Masi AT, McCain GA, Reynolds WJ, Romano TJ, Russell IJ, Sheon RP. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum 1990;33:160-72

[22] SAS Release 6.12, 1996. SAS Institute Inc., Cary, North Carolina, USA

[23] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum, 1995;38(1):19-28

[24] Wolfe F, Anderson A, Harkness D, Bennett RM, Caro XJ, Goldenberg DL, Russell IJ, Yunus MB. A prospective, longitudinal, multicenter study of service utilization and costs in fibromyalgia. Arthritis Rheum 1997;40(9):1560-70

[25] White K, Speechley M, Harth M, Østbye T. The London Fibromyalgia Epidemiology Study (LFES): Estimating the Number of Canadian Adults with Fibromyalgia (FMS). (Proceedings of the 1997 American College of Rheumatology 61st National Meeting, November 8-12, 1997, Washington, DC.) Arth Rheum 1997;40(9):S5187

[26] McCain G, Cameron R, Kennedy JC. The problem of longterm disability payments and litigation in primary fibromyalgia: The Canadian perspective. J Rheumatol 1989;16[suppl 19]:174-6

[27] Yelin E, Callahan LF. The economic cost and social and physical impact of musculoskeletal conditions. Arthritis Rheum 1995;38(10):1351-62

CHAPTER 5
THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY (LFES): COMPARING THE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS IN 100 RANDOM COMMUNITY CASES OF FIBROMYALGIA SYNDROME (FMS) VERSUS CONTROLS[1]

5.0 INTRODUCTION

Fibromyalgia (FMS) may have existed for centuries. It may have affected the biblical writer, Job.[1] However, it was not until the 1970's that a concerted effort was made to characterize FMS. These early studies focused upon the clinical features of FMS among patients presenting to rheumatology clinics,[2,3,4,5] which resulted in a series of diagnostic and classification criteria for FMS.[6]

There are limitations to using clinic or hospital studies to make inferences about the clinical characteristics of a chronic disorder such as FMS. First, subspecialty clinic and hospital populations are not representative of the general population. In general, females are more likely than males to seek medical attention.[7,8] Certain age groups

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[1] A version of this chapter will be submitted for publication to *Arthritis and Rheumatism.*
White KP, Speechley M, Harth, Østbye T. The London Fibromyalgia Epidemiology Study (LFES): Comparing the demographic and clinical characteristics in 100 random community cases of fibromyalgia syndrome (FMS) versus controls. 1997.

receive more medical attention than others.[9] Because illness is a common reason for an individual to leave the workforce, it is reasonable to assume that non-working individuals will be more ill and hence use more health services than those who work; this has been called the *healthy worker effect*.[10] Different ethnic backgrounds utilize westernized medical care to varying degrees.[11,12] Second, evidence suggests that chronic musculoskeletal pain tends to be milder and less chronic in the community than in specialty clinics.[13,14] The same is true for rheumatoid arthritis.[15] Third, psychiatric distress may play a major role in health care seeking behaviour among patients with FMS and other disorders;[16,17] relying solely on clinic data may result in an erroneous association between psychological distress and the illness of interest, when in fact the true association is between psychiatric distress and health care seeking behaviour. Taking such considerations into account, Frederick Wolfe has described eloquently the *fibromyalgia funnel*,[7] a model in which individuals in the community who have FMS are quantitatively and qualitatively different from individuals who become enrolled as subjects in clinical studies.

To date, only two published, controlled studies have described the clinical characteristics of FMS in the general population.[18,19] These reports describe 8 and 36 individuals with FMS, respectively. In the first, all 8 subjects were female. Both studies are limited by the relatively small number of confirmed FMS cases. We present data on 100 randomly-selected, confirmed community cases of FMS (FC), with respect to demographic and clinical characteristics. We compare these 100 FC to two cohorts of similarly recruited controls. Our objective was to identify demographic and clinical

features that distinguish FMS from chronic widespread pain that does not meet FMS case criteria.

5.1 METHODS

5.1.0 Subject recruitment and data collection

The study involved three groups:

1. 100 FMS cases (**FC**), confirmed in an examination by a rheumatologist (either KPW or MH), using the 1990 American College of Rheumatology (ACR) classification criteria;[20]

2. 76 pain controls (**PC**) with recent widespread musculoskeletal pain of at least 3 months duration (widespread pain defined as pain above and below the waist, on the right and left side of the body, and involving both the axial and peripheral skeleton), in whom FMS was excluded by examination;

3. 135 general controls (**GC**) without recent widespread musculoskeletal pain, group matched with FMS cases for age and sex.

All FC, PC and GC were recruited in a three phase, cross-sectional telephone survey of non-institutionalized adults. The **target population** was London, Ontario, a community of 341,320 persons (1991 census) in Southwestern Ontario. London was

selected because it is demographically similar to other mid-size Canadian cities and Canada on the whole outside of Quebec. Subjects in these groups were recruited as part of a random digit dialing telephone survey of 3,395 non-institutionalized London adults. The survey method and the screening instrument have been described in detail elsewhere.[21,22]

The initial telephone interview included 10 questions on demographics (sex, birth year, birth month, marital status, number of adults residing in the household, work status, number of months working in past 12 months, full-time or part-time work status, highest education level achieved, and estimated annual household income), all following the Ontario Health Survey (OHS) format.

Among 3,395 subjects who completed the telephone interview, 248 screened positive for chronic, widespread musculoskeletal pain. All 248 were invited to be examined by a rheumatologist; 176 (71%) agreed and were examined for fibromyalgia tender points. Based upon this examination, we identified 100 **FC** and 76 **PC**. In addition, each subject's hands were examined for evidence of osteoarthritis (OA), rheumatoid arthritis (RA), other arthritis, or other musculoskeletal pathology. After this examination, FC and PC completed a more detailed health questionnaire.

For each of the 86 **FC** who had been confirmed by the time the telephone survey was completed, two age- and sex-matched internal controls were recruited to be general population controls (**GC**) during subsequent telephone interviews. All GC were mailed

the same Health Questionnaire that was completed by FC and PC, accompanied by an information letter and consent form, and a pre-addressed, pre-stamped envelope. Subjects who had not returned the completed questionnaire were re-contacted by telephone within three weeks; 135 of 172 questionnaires (78.5%) were returned completed.

The questionnaire completed by all FC, PC and GC included:

1. one item to verify birth date;

2. four items on prior diagnoses of arthritis, rheumatism, fibromyalgia or other medical illnesses, and one item on past surgical procedures; because of cost constraints, we did not perform investigations to confirm or exclude co-morbid conditions;

3. five questions on general health from the OHS, with items on overall health, usual level of happiness, and usual pain experience, all on 5 point Likert scales, and items on level of life stress and satisfaction with health on 4 point Likert scales;

4. seven questions on women's health issues, from the OHS;

5. eight questions on the onset, course and severity of pain and fatigue, including 100 mm visual analog scales for pain and fatigue severity;

6. a 41 item checklist of symptoms, derived from a review of the clinical literature on fibromyalgia and chronic fatigue syndrome; construct validity was assessed by two independent rheumatologists with research interests in FMS; subjects were asked to rate each symptom as absent, a minor problem or a major problem over the preceding two weeks;

7. four 100 mm visual analog scales for severity of morning tiredness, stiffness, anxiety and depression.

5.1.1 Data Analysis

For the purpose of group comparisons, the three groups, FC, PC and GC were considered to be independent of each other; although subjects in the GC group had been matched with FC subjects, they were group-matched, rather than pair-matched. Where appropriate, all analyses were adjusted for age and sex. SPSS[23] or SAS[24] were used for data management and analysis.

Univariate analysis: For demographic characteristics, nominal data were analyzed using Pearson chi-square, for males alone, females alone, and males and females together. In all instances, there was no difference in the results for men versus women, so the data

are presented for males and females together. We initially treated ordinal data as continuous, solely to determine if either age or sex were co-variants, using Analysis of Co-Variance (ANCOVA). Age was a covariate for almost all of the ordinal demographic variables. Only for household income was sex a covariate. Mantel-Haenszel chi-square test for linear trend was performed for each ordinal demographic variable, adjusting for age by creating subsets by 15-year age groups. For household income, males and females initially were analyzed separately; since there was no difference in the results for the two sexes, the results for males and females are presented together. Continuous variables were analyzed using ANCOVA. Where a group effect was found, we performed One-Way Analysis of Variance (ANOVA), with Scheffe's test for groups of unequal size post hoc. Because sex was a covariate for age, the results of One-Way ANOVA are presented for males and females separately.

For clinical characteristics, the group comparison of primary interest was FC versus PC. Data first were analyzed for males and females separately, using Pearson's chi-square. Because no sex differences were noted, further analyses combined males and females. A group comparison of secondary interest was females versus males with FMS.

Multivariate analysis: To determine which demographic and clinical characteristics distinguish FMS from non-FMS widespread pain, hierarchical logistic regression was performed on subjects in the FC and PC groups, using the presence or absence of FMS as the dependent variable. Independent variables tested included age and sex, and all demographic and clinical variables found to have group differences at $p < 0.10$ on univariate analysis. The results of two different methods for regression, forward conditional and backward conditional, were similar, but not identical; a final model was constructed using those variables shared by both methods.

5.2 RESULTS

5.2.0 Demographic Characteristics (univariate analyses): FC Versus Controls

The mean age of 100 FC was 47.8 years, with an age range of 19 to 86 years. FC were similar to PC in mean age (mean difference = 0.6 years) [Table 1]. Eighty-six percent of FC were female, compared to 67.1% of PC ($X^2 = 10.05$, df 2, $p < 0.01$). FC, PC and GC differed with respect to education level (Mantel-Haenzsel $X^2 = 20.65$, df 10, $p < 0.05$); a greater percentage of FC had less than a high school education (29.6% versus 18.4% and 15.0%, respectively), and more GC had a university degree (28.3% versus 11.2% and 11.8%, respectively). The three groups were not different with respect to marital status or annual household income.

Females with FMS were no different than either PC or GC with respect to prior pregnancies, deliveries or contraceptive use; there were no differences between the three groups with respect to mean age at first pregnancy.

5.2.1 **Clinical Characteristics (univariate analyses): FC versus controls**

FC females had an average of 14.4 fibromyalgia tender points, while males had 14.1. These numbers were quite different than female and male PC, who had a mean of 6.7 and 4.4 tender points, respectively ($t = 21.0$, df 174, $p < 0.001$). [Table 2]. On 100 mm VAS, FC reported a greater severity of pain ($f = 13.5$, df 1, 235, $p < 0.0001$) and fatigue ($f = 18.4$, df 1, 235, $p < 0.0001$) than either control group. The mean duration of symptoms was 11.1 years for females, and 9.0 years for males, but this was not different from controls. Despite a mean 11.0 years of symptoms, only 28 of 100 FC previously had been diagnosed with FMS.

Slightly more than half of the FC reported the onset of their symptoms as having occurred over more than one week, compared to slightly less than half of the PC. No more FC than PC recalled a specific event that precipitated their symptoms; slightly less than half in each group reported such an event. Dating back to the time of their onset of symptoms, four times as many FC reported a worsening versus an improvement of symptoms over time, but FC and PC did not differ with respect to their perceived course of symptoms since onset.

FC reported a mean 22.6 symptoms and 9.1 major symptoms on a 41 symptom checklist, compared to 15.9 and 4.0 respectively for PC, and 8.1 and 1.1 respectively for GC ($f = 116.5$, df 2, 308, $p < 0.0001$; and $f = 88.5$, df 2, 308, $p < 0.0001$) [Table 3]. The range with respect to the total number of symptoms reported was 4 to 41 among FC; for major symptoms, zero to 27. FC reported worse overall health, more unhappiness, a greater effect of pain on activities, more dissatisfaction with health (all at $p < 0.0001$) and more life stress ($p < 0.005$) than either control group.

The most commonly reported symptoms among FC, besides musculoskeletal pain, were fatigue (100%), non-restorative sleep (92%), weakness (90%), insomnia (84%), numbness in hands and/or feet (82%), headaches (82%), increased irritability (81%), severe fatigue lasting 24 hours after minimal activity (77%), panic attacks (77%), pain worse in cold weather (74%), depression (72%), difficulties with concentration (71%) and dizziness (70%). Despite 70% reporting dizziness, only 6% reported fainting in the previous 2 weeks.

The most common major symptoms were pain (77.3%), fatigue (77.3%), severe fatigue lasting 24 hours after minimal activity (77.0%), non-restorative sleep (65.7%), and insomnia (56.0%) [Table 4].

At a Bonferroni corrected $p < 0.001$, ten symptoms were found on univariate analysis to distinguish FC from PC: fatigue, severe fatigue lasting 24 hours after minimal

activity, weakness, non-restorative sleep, cervical adenopathy, pain, panic attacks, difficulties with memory, and insomnia.

Sixty-four percent of FC, 59% of PC and 19% of GC reported having previously been told they had arthritis ($p < 0.0001$). Nine FC (9.0%, CI = 5.8%, 13.7%; 7 female) reported having been diagnosed previously with RA, all of whom had evidence of RA on examination of their hands. One PC reported having been diagnosed with RA, and another with Juvenile RA (a total of 2 out of 76; 2.6%); neither had physical evidence in their hands to support these diagnoses. Sixteen percent of FC and 19.7% of PC reported having been diagnosed with OA; 22.0% of FC and 35.8% of PC had hand evidence of OA. There were no statistical differences between FC and PC with respect to the self-reported or confirmed prevalence of RA or OA. Two FC had been diagnosed by a rheumatologist as having systemic lupus erythematosis. One PC had been diagnosed with Sjogren's Syndrome.

5.2.2 **Males versus females with FMS**

Females with FMS were almost 10 years older than males with FMS (49.2 versus 39.3 years; $t = 2.5$, df 98, $p < 0.02$). [Table 5]. The age range also differed for males (20 - 59 years) versus females (19 - 86 years) with FMS ($X^2 = 23.2$, df 13, $p = 0.04$). Females reported more major symptoms on the 41 symptom checklist (9.6 versus 6.4, respectively; $f = 6.0$, df 1,82, $p = 0.02$). In no other way were females with FMS significantly different from males with FMS. Our analysis included logistic regression,

with all 41 checklist items as independent variables. Only two symptoms, axillary adenopathy ($p = 0.003$) and dizziness ($p = 0.006$) even approached the Bonferroni adjusted $p < 0.001$. The total number of major symptoms, which had been statistically different on univariate analysis, was not retained in the multivariate model ($p = 0.02$).

5.2.3 **Multivariate analysis**

On forward conditional regression, six variables remained in the FMS model: weakness ($p = 0.0003$), pain severity ($p = 0.0008$), glandular swelling in the neck ($p = 0.003$), severe fatigue lasting 24 hours after minimal activity ($p = 0.004$), severity of depression ($p = 0.02$), and shortness of breath ($p = 0.04$). On backward conditional regression, six variables remained in the model: pain severity ($p = 0.004$), severe fatigue lasting 24 hours after minimal activity ($p = 0.006$), weakness ($p = 0.008$), glandular swelling in the neck ($p = 0.01$), sex ($p = 0.01$), and self-reported general health ($p = 0.05$). The model created from the four variables shared by each of the above models correctly predicts 64.5% of PC and 82.8% of FC. Converting pain severity from a continuous (zero to 100 on a 100 mm scale) to an ordinal variable (pain from zero to 24 = 1, from 25 to 49 = 2, etc.), and both weakness and glandular swelling to dichotomous variables (the symptom has been a major problem or not over the previous two weeks), the model correctly predicts 79.8% of FC and 77.3% of PC. Among females, the sensitivity of the model is higher (84.7% versus 64.3% for males), but its specificity lower (58.8% versus 100.0%).

5.3 DISCUSSION

Although it has been accepted as a valid clinical entity by numerous academic and professional bodies, such as the American College of Rheumatology,[20] there are some who argue that FMS is no more than an extension of the non-specific aches and pains experienced by the otherwise healthy general population, exacerbated perhaps by psychological distress and/or an inability to cope.[25,26,27] Some have argued that the term '*fibromyalgia*' be discarded, in favour of 'a less emotive term', such as '*rheumatism*'.[28] We sought to determine if there were demographic or clinical characteristics that might distinguish FMS from other forms of chronic, generalized pain.

Chronic, widespread pain, with or without FMS, appears to exist in adults at all ages. In our sample, the youngest FC and PC both were 19 years old; the oldest were 86 and 78, respectively. There was no difference in mean age between the two groups. A somewhat greater percentage of FC were female. Those with FMS were less likely to have completed high school than PC. Both groups with chronic widespread pain (FC and PC) were less likely than the general population to have completed a university degree. This final finding may be the result of sampling error, since the 28.3% of GC with a university degree is much higher than the 15.7% of adults reporting a university degree in the 1991 London census.[29] Otherwise, FC and PC were demographically similar to the general population.

Despite only 28% having been previously diagnosed, the average subject with FMS had had symptoms for eleven years. Among the 72 subjects not previously diagnosed, the mean duration of symptoms was 10.3 years (standard deviation 8.9 years). Our study does not provide an explanation for the long delay in diagnosis, but it highlights the potential risk in making inferences about FMS based upon the results of subspecialty clinic studies. There was no difference between FC and PC in the duration of symptoms. Nor was there any difference between these subject groups with respect to the nature of symptom onset; for both groups, roughly half recalled some precipitating event. Although FC and PC did not differ statistically, the nine percent prevalence of RA among FC suggests that RA may be more common in persons with FMS than in the general population; a previous study demonstrated a high prevalence of FMS in RA patients.[10] More than four times the proportion of FC had worsened as opposed to improved clinically since symptom onset. This was different than the course reported by PC, in which an equal number reported each outcome. However, this difference may be, at least partly, an artifact, since a percentage of individuals with FMS who improve may cease to meet the ACR criteria for the condition.

Males and females with FMS did not differ with respect to clinical parameters, including the tender point count. The small number of male FC may have resulted in type II error in some instances. However, there was no detectable trend that would suggest that males were more or less symptomatic. On the five OHS general health questions, males reported feeling worse on two items, better on one, and the same on two. On six visual analog scales to rate the severity of specific symptoms, males reported

being more symptomatic on two items, and less symptomatic on four. As type I error may have resulted when comparing the clinical courses between FC and PC, similarly, type II error may have resulted when comparing clinical characteristics between males and females, if males have a higher pain threshold on digital palpation and hence are more likely to be classified as PC than females. To test for this, we compared all 22 males and 119 females who had 7 or greater tender points. We chose 7 points to include males and females with somewhat fewer than the 11 tender points required to meet the case criteria, but with at least three tender points more than general controls. Again, there were no differences in clinical characteristics or trends that would suggest that one sex was more symptomatic than the other.

FC reported more major symptoms and more symptoms overall than PC. But the range of symptoms among FC was great; one FC reported no major symptoms and only 4 symptoms overall on a 41 symptom checklist; another FC reported 27 and 41, respectively. From this, one can infer that there is considerable variability in the reporting of clinical severity of FMS.

Besides pain, the most common symptoms reported by FC were fatigue, non-restorative sleep, weakness, and insomnia. The most common major symptoms were pain, fatigue, severe fatigue lasting 24 hours after minimal activity, non-restorative sleep, and insomnia. Virtually all symptoms on a 41 symptom checklist were reported more commonly by FC than PC. However, only four demographic or clinical variables remained in a model distinguishing FC from PC, after multivariate testing. They were:

weakness (reported by 90.0% of FC and 63.2% of PC), pain severity (mean VAS score 66.1 versus 50.1), glandular swelling in the neck (reported by 53.0% of FC and only 28.9% of PC), and severe fatigue lasting 24 hours after minimal activity (reported by 77.0% of FC and only 30.3% of PC). One model using these four variables was approximately 80% sensitive and specific for FC versus PC.

These data suggest that, although individuals in the community with FMS complain of the same spectrum of symptoms as individuals with chronic widespread pain of other sources, there are certain features that may distinguish these two groups. That these features include pain severity, fatigue and self-reported weakness is not surprising, given prior descriptions of FMS in clinic studies.[6] That the fourth distinguishing feature was self-reported glandular swelling in the neck is unexpected, since it has not been considered a prominent complaint or physical finding in this syndrome. In our study, we made no attempt to confirm or exclude objective swelling in the neck, nor to characterize it.

Many symptoms were reported less commonly by our study subjects with FMS than subjects in previous clinic studies.[5] As with rheumatoid arthritis,[15] it may be that FMS is milder in the general population than in subspecialty clinics. Certain symptoms that have been attributed to FMS were decidedly uncommon in our study group. Syncope, pain with urination, pain with defecation, fevers, dry eyes, and facial swelling all were reported by less than a third of FC. And only five of 41 symptoms on the checklist were reported by the majority as having been major problems over the

preceding two weeks: pain, fatigue, severe fatigue lasting 24 hours after minimal activity, non-restorative sleep, and insomnia. This argues against our sample of FMS cases being non-specific complainers.

Is FMS merely an extension of the usual aches and pains of the general population? Our data suggest that FMS may be different than other sources of chronic, generalized pain. It is reasonable to assume that there would have been even greater differences had FMS cases been compared to individuals with chronic focal pain. However, chronic, widespread pain with and without FMS appears to affect all segments of the adult population, and we did not detect any clinical characteristic that, in itself, was both highly sensitive and specific for FMS. Perhaps the feature that best combines sensitivity and specificity is severe fatigue lasting 24 hours following minimal activity, which we found to be 77.3% sensitive, and 69.7% specific. It may be that this feature should be added to the diagnostic criteria for FMS. Further research clearly is needed, both to confirm that the results of the current study can be replicated in different populations, and to search for more objective markers of disease.

List of Tables

Table 1: A demographic comparison of FMS cases (FC), Pain controls (PC), and General population controls (GC) in LFES.

	FC	PC	GC
N =	100	76	135
mean age (years)	47.8	47.2	44.5
males	39.3	43.8	36.4
females	49.2	48.9	46.4
% female[1]	86.0%	67.1%	81.5%
mean # adults in household	2.1	1.8	2.1
marital status			
% never married	18.2%	17.1%	28.8%
% married	47.5%	42.1%	32.7%
% divorced/separated	30.3%	36.8%	28.8%
% widowed	4.0%	3.9%	8.7%
education[2]			
% < highschool	29.6%	18.4%	15.0%
% highschool	24.5%	34.2%	30.7%
% some college	23.5%	23.7%	17.3%
% some university	10.2%	10.5%	7.9%
% university degree	11.2%	11.8%	28.3%
% other	1.0%	1.3%	0.8%
household income			
% with < $12,000	10.9%	9.4%	4.0%
% with $12,000 - $29,999	16.4%	18.9%	11.9%
% with $30,000 - $59,999	27.4%	20.8%	24.6%
% with $60,000 - $79,999	4.1%	13.2%	15.1%
% with > $80,000	4.1%	7.5%	10.3%
reproductive history (females)			
% previously pregnant	89.4%	82.4%	80.7%
% having delivered a child	84.7%	78.4%	78.0%
% having taken oral contraceptives	11.0%	17.6%	7.5%
mean # of pregnancies	2.9	2.9	2.5
mean # of deliveries	2.5	2.3	2.2
mean age at first pregnancy(years)	23.1	23.7	24

The response rate was not 100% for all questions.

[1] $p < 0.01$ [2] $p < 0.05$

Table 2: A comparison of pain, fatigue and tender point count in 100 FC, 76 PC and 135 GC

		females			males		
	FC	PC	GC	FC	PC	GC
N =	86	51	110	14	25	25
Mean severity of pain*[1]	66.1	50.1	39.5	69.4	54.6	34.8
Mean severity of fatigue*[1]	65.9	47.7	33.9	65.7	44.4	39.2
Mean duration of pain &/or fatigue (years)	11.1	9.3	10.6	9.0	13.5	5.1
Mean number of tender points**[1]	14.4	6.7	n/a	14.1	4.4	n/a
Pain onset[2] < 24 hours	25.0%	42.0%	n/a	30.8%	44.0%	n/a
1 - 7 days	19.0%	12.0%	n/a	7.7%	20.0%	n/a
> 1 week	56.0%	46.0%	n/a	61.5%	36.0%	n/a
Precipitating event	43.0%	31.4%	n/a	50.0%	56.0%	n/a
Course of pain since onset						
improved	11.6%	23.5%	n/a	0.0%	20.8%	n/a
unchanged	39.5%	47.1%	n/a	42.9%	58.3%	n/a
worse	48.8%	29.4%	n/a	57.1%	20.8%	n/a

* as measured on a 100 millimeter visual analog scale

** out of 18 1990 ACR classification criteria tender points

The response rate was not 100% for all questions.

[1] $p < 0.0001$ [2] $p < 0.05$

Table 3: A general health comparison of FMS cases (FC), Pain controls (PC) and General population controls (GC)

	FC	PC	GC
N =			
mean # of symptoms on 41-SCL[1]	22.6	15.9	8.1
mean # of major symptoms on 41-SCL[1]	9.1	6.5	1.1
Self-rated general ill health[a 1]	3.8	3.0	2.1
Self-rated unhappiness[b 1]	2.4	1.8	1.4
Self-rated pain interference[c 1]	4.0	3.3	2.2
Self-rated life stress[d 2]	3.0	2.8	2.6
Self-rated dissatisfaction with health[e 1]	3.0	2.4	1.8

[1] $p < 0.0001$, [2] $p < 0.005$

[a] 1 = excellent, 2 = very good, 3 = good, 4 = fair, 5 = poor.

[b] 1 = happy & interested in life, 2 = somewhat happy, 3 = somewhat unhappy, 4 = unhappy with little interest in life, 5 = so unhappy that life is not worthwhile.

[c] 1 = free of pain & discomfort, 2 = pain or discomfort that does not prevent any activities, 3 = pain or discomfort that prevents a few activities, 4 = pain or discomfort that prevents some activities, 5 = pain or discomfort that prevents most activities.

[d] 1 = not at all stressful, 2 = not very stressful, 3 = fairly stressful, 4 = very stressful.

[e] 1 = very satisfied, 2 = somewhat satisfied, 3 = not too satisfied, 4 = not at all satisfied.

Table 4: The clinical characteristics of FMS (FC) versus pain controls (PC) and general population controls (GC).

Symptoms	% reporting symptom as a major problem in the past 2 weeks		
	FC	PC	GC
Fatigue	77.3	37.3[1]	29.0
Severe fatigue lasting > 24 hours after minor activity	77.0	30.3[1]	11.9
Weakness	44.0	10.5[1]	2.3
Non-restorative sleep	65.7	32.9[1]	9.8
Cervical lymphadenopathy	23.0	2.6[2]	0.8
Insomnia	56.0	28.0[2]	8.2
Pain	77.3	50.7[2]	13.3
Difficulties with memory	35.0	11.8[2]	3.7
Hands/feet hurt more in cold	45.0	19.7[2]	2.2
Difficulties with concentration	34.0	11.8[3]	2.2
Abdominal pain	26.3	7.9	3.0
Increased irritability	35.0	14.5	1.5
Hypersomnia	23.0	6.6	1.5
Anxiety	28.3	10.5	5.2
Hands/feet change colour in cold	22.2	6.6	0.8
Chills	17.2	4.0	0.0
Chest pains	17.0	3.9	1.5
Personality change	26.3	10.5	0.0
Depression	33.0	16.0	3.8
Paresthesias in hands or feet	31.0	14.5	7.5
Palpatations	20.0	6.8	3.0
Panic attacks	19.2	6.7	4.5
Dizziness	26.0	11.8	3.0
Eye pain	16.0	5.3	0.7
Dry mouth	21.2	9.2	0.7
Axillary lymphadenopathy	10.1	2.6	0.8
Blurred vision	14.0	5.3	0.7
Nocturnal cramps	24.0	13.3	2.2
Difficulty focussing	16.0	7.9	0.7
Weight loss	6.1	1.3	1.5
Abdominal cramps	14.3	6.6	3.0
Pain with defacation	6.1	1.3	2.2
Diarrhea	10.1	3.9	0.7
Facial swelling	9.0	3.9	1.5
Dyspnea	22.2	14.7	2.3
Urinary frequency (> 5x/day)	32.0	23.7	7.5
Pain with urination	6.1	2.7	0.0
Weight gain	12.0	7.9	3.0
Syncope	1.0	0.0	0.0
Dry eyes	10.0	6.7	0.7
Constipation	12.0	9.2	7.5
Jaw pain	9.2	6.7	0.7
Headaches	32.3	30.3	12.7
Fevers	4.1	3.9	0.0

FC versus PC compared by chi-square analysis. Statistical analyses Bonferroni corrected to $p < 0.001$

Symptoms listed in order of ascending p values

[1] $p < 0.0001$ [2] $p < 0.0005$ [3] $p < 0.001$

Table 5: A clinical comparison of 86 female and 14 male FMS cases.

	females	males
Mean age (years)	49.2	39.3[1]
Age Range (years)	19 - 86	20 - 59[2]
Number of tender points	14.4	14.1
Number of symptoms on 41-SCL	22.8	21.8
Number of major symptoms on 41-SCL	9.6	6.4[1]
Self-rated general ill health[a]	3.8	3.9
Self-rated unhappiness[b]	2.3	2.6
Self-rated pain interference[c]	4.0	4.0
Self-rated life stress[d]	2.0	2.0
Self-rated dissatisfaction with health[e]	3.0	2.8
Severity of pain*	65.2	66.8
Severity of fatigue*	76.1	72.9
Severity of morning fatigue*	73.0	66.5
Severity of stiffness*	68.9	69.6
Severity of depression*	54.0	48.5
Severity of anxiety*	58.3	54.0
Onset associated with a precipitating event	43.0%	50.0%
% totally disabled	29.1%	42.9%
% receiving disability pension or compensation	23.3%	42.9%

* As reported on 100 mm visual analog scales

** Pearson chi-square on 5-year age groups by sex

Simple linear regression, adjusted for age.

[1] $p = 0.02$, [2] $p = 0.04$

[a] 1 = excellent, 2 = very good, 3 = good, 4 = fair, 5 = poor.

[b] 1 = happy & interested in life, 2 = somewhat happy, 3 = somewhat unhappy, 4 = unhappy with little interest in life, 5 = so unhappy that life is not worthwhile.

[c] 1 = free of pain & discomfort, 2 = pain or discomfort that does not prevent any activities, 3 = pain or discomfort that prevents a few activities, 4 = pain or discomfort that prevents some activities, 5 = pain or discomfort that prevents most activities.

[d] 1 = not at all stressful, 2 = not very stressful, 3 = fairly stressful, 4 = very stressful.

[e] 1 = very satisfied, 2 = somewhat satisfied, 3 = not too satisfied, 4 = not at all satisfied.

REFERENCES

[1] Job 7: verses 3-4 and Job 30: verses 16-7.

[2] Yunus M, Masi AT, Calabro JJ, Miller KA, Feigenbaum SL. Primary fibromyalgia (fibrositis): Clinical study of 50 patients with matched normal controls. Semin Arthritis Rheum 1981;11(1):151-71

[3] Campbell SM, Clark SR, Tindall EA, Forehand ME, Bennett RM. Clinical characteristics of fibrositis: I. A "blinded", controlled study of symptoms and tender points. Arthritis Rheum 1983;26(7): 817-24

[4] Goldenberg DL. Fibromyalgia syndrome: An emerging but controversial condition. JAMA 1987;257(20):2782-7

[5] Wolfe F. Fibromyalgia: The clinical syndrome. Rheum Dis Clin North Am 1989;15(1):1-17

[6] Wolfe F. Fibromyalgia. Rheum Dis Clin North Am 1990;16(3):681-98

[7] Briscoe ME. Why do people go to the doctor? Sex differences in the correlates of GP consultation. Soc Sci Med 1983;25:507

[8] Chien A, Schneiderman LJ. A comparison of health care utilization by husbands and wives. J Community Health 1975;1:118

[9] Badley EM, Yoshida K, Webster G, Stephens M. Disablement and chronic health problems in Ontario. A report on the 1990 Ontario Health Survey. Ministry of Health, September 1993.

[10] Mausner JS, Kramer S. Epidemiology - An Introductory Text, 2nd Edition. W.B. Saunders, Philadelphia, PA. 1985, pp. 319-20

[11] Zuckerman MJ, Guerra LG, Drossman DA, Foland JA, Gregory GG. Health care seeking behaviors related to bowel complaints. Hispanics versus non-hispanic whites. Dig Dis Sci 1996;41(1):77-82

[12] Raczynski JM, Taylor H, Cutter G, Hardin M, Rappaport N, Oberman A. Rose questionnaire responses among black and white inpatients admitted for coronary heart disease: findings from the Birmingham-BHS Project. Ethn Dis 1993;3(3):290-302

[13] Macfarlane GJ, Thomas E, Papageorgiou AC, Schollum J, Croft PR, Silman AJ. The natural history of chronic pain in the community: A better prognosis than in the clinic? J Rheumatol 1996;23(9):1617-20

[14] Crook J. The importance of community based epidemiological studies. J Rheumatol 1996;23(9):1500-1

[15] Hochberg MC. Predicting the prognosis of patients with Rheumatoid Arthritis: Is there a crystal ball? J Rheumatol 1993;20(8):1265-7

[16] Aaron LA, Bradley LA, Alarcon GS, Alexander RW, Triana-Alexander M, Martin MY, Alberts KR. Psychiatric diagnoses in patients with fibromyalgia are related to health care-seeking behavior rather than to illness. Arthritis Rheum 1996;39(3):436-45

[17] Smith RC, Greenbaum DS, Vancouver JB, Henry RC, Reinhart MA, Greenbaum RB, Dean HA, Mayle JE. Psychosocial factors are associated with health care seeking rather than diagnosis in irritable bowel

syndrome. Gastroenterology 1990;98(2):293-301

[18] Prescott E, Kjoller M, Jacobsen S, Bulow PM, Danneskiold-Samsoe B, Kamper-Jorgensen F. Fibromyalgia in the adult Danish population: II. A study of clinical features. Scand J Rheumatol 1993;22(5):238-42

[19] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38(1):19-28

[20]Wolfe F, Smythe HA, Unus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, Fam AG, Farber SJ, Fiechtner JJ, Franklin CM, Gatter RA, Hamaty D, Lessard J, Lichtbrown AS, Masi AT, McCain GA, Reynolds WJ, Romano TJ, Russell IJ, Sheon RP. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum 1990;33:160-72

[21] White KP, Speechley M, Harth M, Ostbye T. The London fibromyalgia epidemiology study (LFES): The prevalence of fibromyalgia syndrome (FMS) in London, Ontario [unpublished manuscript].

[22] White KP, Speechley M, Harth M, Ostbye T. Testing an instrument to screen for fibromyalgia syndrome in general population studies: The London fibromyalgia epidemiology study screening questionnaire (LFESSQ)

[23] SPSS, release 6.1. Copyright © SPSS Inc., 1989-1994

[24] SAS, release 6.12. Copyright © SAS Institute Inc., 1996. Cary, NC, U.S.A.

[25] Ochoa JL. Essence, investigation, and management of "neuropathic" pains: Hopes from acknowledgment of chaos. Muscle Nerve 1993;16:977-1008

[26] Hart FD. Fibrositis (fibromyalgia): A common non-entity? Drugs 1988;35:320-7

[27] Hadler NM. Occupational musculoskeletal disorders. Raven Press, New York, 1993:16-33

[28] Block SR. Fibromyalgia and the rheumatisms. Common sense and sensibility. Controversies Clin Rheumatol 1993;19(1):61-78

[29] Statistics Canada. Profile of census tracts in London, Sarnia-Clearwater and Windsor, Part A. Ottawa: Industry, Science and Technology Canada, 1992. 1991 Census of Canada. Catalogue number 95-346

[30] Romano TJ. Incidence of fibromyalgia syndrome (FMS) in rheumatoid arthritis (RA) patients seen in general rheumatology practice. Scand J Rheumatol 1992;S94:11

CHAPTER 6
THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY (LFES): A COMPARISON OF SELF-REPORTED FUNCTION AND WORK DISABILITY IN 100 RANDOM COMMUNITY CASES OF FIBROMYALGIA SYNDROME (FMS) VERSUS CONTROLS[i]

6.0 INTRODUCTION

Fibromyalgia syndrome (FMS) is associated with severe chronic pain and fatigue, in addition to numerous other symptoms.[1] Many patients report levels of disability severe enough to prevent them from seeking, continuing or resuming gainful employment. A U.S. survey of 620 clinic patients with FMS found that 15% currently received disability payments, and 25% considered themselves totally disabled.[2] In another U.S. survey of 1604 FMS patients at six centers across the U.S., more than 16% reported receiving Social Security disability payments, and an additional 10% reported receiving some other form of disability payments.[3] Twenty-four percent of 55 Swedish patients with FMS were receiving pensions.[4] In a longitudinal four year study of 72 British patients, 50%

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[i] A version of this chapter was submitted for publication to *Arthritis and Rheumatism*.
White KP, Speechley M, Harth M, Østbye T. The London Fibromyalgia Epidemiology Study (LFES): A comparison of self-reported function and work disability in 100 random community cases of fibromyalgia syndrome (FMS) versus controls. 1998.

stopped working because of their illness.[5] A 1988 survey in Norway found that FMS was the most frequent single diagnosis for disability pensions.[6] A survey of Canadian insurance company records found that FMS was responsible for 9% of all disability payments, accounting for an estimated $200 million annually.[7]

Patients with FMS report disabilities in activities of daily living (ADL) that are as high as those reported by patients with rheumatoid arthritis (RA), and higher than those reported by patients with osteoarthritis.[8] They rate their quality of life as lower than patients either with RA or OA.[9] They report lower overall health and functional status and greater pain than patients with RA, OA, systemic lupus erythematosis (SLE) or scleroderma.[10]

A contributing factor to FMS patients' relatively high self-reported level of disability may be the greater levels of pain and fatigue they report compared to patients with other rheumatic disorders.[11,12] Various models have been proposed to explain how the interplay between chronic pain and both intrinsic and extrinsic factors might result in chronic disability.[13,14] Despite this, the issue of disability in FMS is complex and controversial, largely due to the relative lack of understanding of the pathogenesis of this disorder and chronic pain in general, and great inadequacies in the process of disability evaluation itself.[15]

We present the results of a comparison of 100 representative cases of FMS from the general population with 76 chronic pain controls, and 135 general population controls

with respect to self-reported functional status and work disability. Using regression analysis, we have tested for demographic and clinical variables that are predictive of functional status and work disability.

6.1 METHODS

6.1.0 Subject recruitment and data collection

The study involved three subject groups:

1) 100 FMS cases (**FC**), confirmed in an examination by a rheumatologist (either KPW or MH), using the 1990 American College of Rheumatology (ACR) classification criteria;[16]

2) 76 pain controls (**PC**) with recent widespread musculoskeletal pain (defined as pain above and below the waist, on the right and left side of the body, and involving both the axial and peripheral skeleton) of at least 3 months duration, in whom FMS was excluded by examination;

3) 135 general controls (**GC**) without recent widespread musculoskeletal pain, group-matched with FMS cases for age and sex.

All FC, PC and GC were recruited in a three phase, cross-sectional telephone survey of non-institutionalized adults. The **target population** was London, Ontario, a

community of 341,320 persons (1991 census) in Southwestern Ontario. London was selected because it is demographically similar to other mid-size Canadian cities and Canada on the whole outside of Quebec. Subjects in these groups were recruited as part of a random digit dialing telephone survey of 3,395 non-institutionalized London adults. The survey method and the screening instrument have been described in detail elsewhere.[17,18]

The initial telephone interview included 10 questions on demographics (sex, birth year, birth month, marital status, number of adults residing in the household, work status, number of months working in past 12 months, full-time or part-time work status, highest education level achieved, and estimated annual household income), all selected from the Ontario Health Survey (OHS).

Among 3,395 subjects who completed the telephone interview, 248 screened positive for chronic, widespread musculoskeletal pain. All 248 were invited to be examined by a rheumatologist; 176 (71%) agreed and were examined for fibromyalgia tender points. Based upon this examination, we identified 100 **FC** and 76 **PC**. In addition, each subject's hands were examined for evidence of osteoarthritis (OA), rheumatoid arthritis (RA), other arthritis, or other musculoskeletal pathology. After this examination, FC and PC completed a more detailed health questionnaire.

For each of the 86 **FC** identified before completion of the telephone survey, two randomly selected age- and sex-matched internal controls were recruited to be general population controls (**GC**) during subsequent telephone interviews. All eligible GC were mailed the same Health Questionnaire that was completed by all FC and PC subjects, accompanied by an introductory letter, an information letter and consent form, and a pre-addressed, pre-stamped envelope. Subjects who had not returned the completed questionnaire were re-contacted by telephone within three weeks. Of 172 questionnaires mailed, 135 (78.5%) were returned completed.

The questionnaire completed by all FC, PC and GC included:

1) one item to verify birth date;

2) four items on prior diagnoses of arthritis, rheumatism, fibromyalgia or other medical illnesses, and one item on past surgical procedures; because of cost and ethical constraints, we did not perform investigations to confirm or exclude co-morbid conditions;

3) five questions on general health from the OHS, with items on overall health, usual level of happiness, and usual pain experience, all on 5 point Likert scales, and items on level of life stress and satisfaction with health on 4 point Likert scales;

4) eight questions on the onset, course and severity of pain and fatigue, including 100 mm visual analog scales for pain and fatigue severity;

5) a 41 item checklist of symptoms, which we derived from a review of the clinical literature on fibromyalgia and chronic fatigue syndrome; construct validity was assessed by two independent rheumatologists with research interests in FMS; subjects were asked to rate each symptom as absent, a minor problem or a major problem over the preceding two weeks;

6) the Fibromyalgia Impact Questionnaire (FIQ), a validated measure of functional status and disease impact in FMS clinic patients;[19]

7) the mobility and agility indices from the 1986 Health and Activity Limitation Survey (HALS).[20]

6.1.1 **Data Analysis**

The three study groups were treated as statistically independent samples. For inter-group comparisons of nominal and ordinal variables, we used chi-square analysis, adjusted for sex. For inter-group comparisons of continuous variables, we used analysis of co-variance, with sex and age as covariates. Crude odds of reporting disability were calculated for each demographic and clinical variable. For variables with more than two ordinal categories, we performed the Mantel-Haentzel test for linearity. Hierarchical

logistic regression was performed with self-reported work disability as the dependent variable. To this model we added, sequentially, those demographic, general health and pain descriptor variables found to have a crude odds ratio confidence interval lower bound of greater than 1.00 on univariate testing, followed by those items on the 41 symptom checklist that were reported by a majority of subjects to have been a major symptom over the preceding 2 weeks. In total, this resulted in 19 independent variables entered into a logistic model on 264 subjects (47 subjects had incomplete data and were excluded from the model). Similarly, hierarchical linear regression was performed with the FIQ score as the dependent variable, 17 independent variables (variables intrinsic to the FIQ, such as pain and fatigue severity on 100 mm visual analog scales, were excluded) and 311 subjects.

Healthy Years of Life Lost (HYLL) were calculated by subtracting quality adjusted life years (QALY) from life expectancy. Each subject's life expectancy was determined from 1990 Ontario Life Tables for males and females. QALY were calculated as the sum:

(Age at symptom onset) + [(Years of symptoms + Expected years of life) x (Marker state utility weight)]

The marker state and corresponding utility weight for each subject were derived using that subject's responses to the HALS mobility and agility indices, and matching the HALS score to the Musculoskeletal Health Status Classification Scheme[21]. The QALY

was adjusted to account for past changing marker states (hence, changing utility weights) over time, based upon the subject's recollection of the duration of each limitation. We made no attempt to adjust for possible future changes in marker states, due to an absence of data for this purpose. We assumed that each subject's utility weight was 1.00 immediately prior to the onset of their pain and fatigue; only one of 176 subjects reported significant limitations prior to the onset of their pain and fatigue, this being related to congenital blindness.

6.2 RESULTS

FC differed with respect to both control groups with respect to mean FIQ score [Table 1]. A greater percentage reported having spent most of at least one day in bed over the previous two weeks because of their health, and they spent more days in bed than either control group. Roughly three out of four (74.0%) reported at least one day in the previous two weeks during which their health caused them to reduce their usual activities, compared to 57.9% of PC and 25.2% of GC ($p < 0.00001$). Almost two thirds of FC reported having had to reduce their work or school hours since the onset of their pain (versus 28.9% and 8.9% for PC and GC, respectively; $p < 0.001$); 31.0% reported being work disabled (versus 10.5% and 2.2%; $p < 0.00001$); and 26.0% were receiving some form of disability pension (versus 9.2% and 3.0%, $p < 0.00001$). The same percentage of FC as PC reported having suffered a reduction in income since the onset of their pain and/or fatigue (47.5% versus 42.1%). The self-reported mean annual change of

income since the onset of symptoms was minus $ 4091.31 for FC versus minus $286.45 for PC (NS).

Females with chronic widespread pain were no different than males with respect to the likelihood of being disabled (crude odds ratio [OR] = 1.14; 95% confidence intervals [CI] = 0.47, 2.74) [Table 2]. Compared to the age group 18 to 34 years, the odds of being disabled increased through middle age, to 5.67 in the 35 to 49 year age group (CI = 1.22, 26.33), and 8.43 in the 50 to 64 year age group (CI = 1.80, 39.49). Then it appeared to decline in persons age 65 years and older (OR = 1.43, CI = 0.19, 10.96). The odds of being disabled was not affected by marital status or education level.

Both the level of physical stress associated with one's most recent employment, and the amount of heavy lifting associated with that position had a significant effect on the likelihood of being disabled [Table 2]. The level of emotional stress associated with prior employment did not have a statistically significant effect.

Individuals in whom FMS was confirmed were four times as likely to be disabled as those in whom FMS was excluded (OR = 4.00, CI = 1.71, 9.36) [Table 3]. Other clinical parameters associated with an increased risk of being disabled were 1) tenderness at 15 or greater fibromyalgia tender points (OR = 6.08, CI = 1.59, 23.23); 2) pain severity of 75 mm or greater on a 100 mm VAS (OR = 17.54, CI = 2.18, 141.23); 3) severity of anxiety of 75 mm or greater on a 100 mm VAS (OR = 3.15, CI = 1.19, 8.33); 4) 31 or more symptoms on the 41 symptom checklist [41-SCL] (OR = 8.63, CI = 1.86,

40.01); 5) 11 to 20 major symptoms on the 41-SCL (OR = 3.84, CI = 1.74, 8.47); 6) 21 or more major symptoms on the 41-SCL (OR = 16.26, CI = 1.61, 164.74); 7) poor to fair self-rated general health (OR = 5.31, CI = 2.26, 12.46); 8) general unhappiness (OR = 3.31, CI = 1.58, 6.94); 9) overall dissatisfaction with health (OR = 7.24, CI = 2.66, 19.69); 10) a FIQ score of 50 to 74 on a 100 point scale (OR = 5.43, CI = 2.66, 19.69); and 11) a FIQ score greater than 75 (OR = 35.00, CI = 8.70, 140.87). Evidence of OA, RA or both on examination of the hands was neither correlated with disability nor FIQ score.

Among the 100 confirmed cases of FMS, 87% reported that pain affected their ability to work in a major way. Eighty percent reported major work limitations due to fatigue, 73.0% due to weakness, and 51.0% due to difficulties with memory and concentration. A minority attributed major work limitations to headaches, anxiety, depression, paresthesias, eye problems, dyspnea, abdominal complaints, other pain or other problems [Table 4].

On multivariate testing, four variables distinct from the FIQ items themselves, remained in the model for FIQ score: the number of major symptoms on the 41-SCL, the overall level of satisfaction with health, the number of fibromyalgia tender points, and the highest level of education achieved [Table 5]. This model explained 80.0% of the variance in the FIQ score. When tested separately, responses to the intrinsic FIQ items all remained in a linear regression model for FIQ score, all at a level of $p < 0.0001$,

except for the number of days having missed work, which remained in the model at a level of $p = 0.0004$.

Four variables remained in a logistic regression model for disability status: FIQ score ($p < 0.0001$); a subject previously having been told she or he had FMS ($p = 0.01$); non-restful sleep as measured on a 3 point ordinal scale ($p = 0.03$); and a history of high physical stress with prior employment ($p = 0.04$) [Table 6].

On a scatter plot of FIQ score versus disability status among the 94 FC either previously or currently employed, no FC had a FIQ score less than 20. The disability rate was 25.0% for FIQ scores between 20 and 39 inclusive ($n = 12$), 7.7% between 40 and 59 ($n = 26$), 36.4% between 60 and 79 ($n = 44$), and 83.3% for scores of 80 and above ($n = 12$). When the three subject groups were combined, the disability rate among 287 previously or currently employed subjects was zero for FIQ scores below 20 ($n = 72$), 5.3% between 20 and 39 ($n = 76$), 9.4% between 40 and 59 ($n = 64$), 34.9% between 60 and 79 ($n = 63$), and 83.3% for scores of 80 or greater ($n = 12$) ($p < 0.0001$ by Pearson X^2). [Figure 1].

6.3 DISCUSSION

Our data confirm that FMS, more so than chronic widespread pain alone, is a disabling illness, at least in the eyes of those with FMS (31% claimed total disability) and those insurers who approve disability pensions for individuals with FMS (26% of

FMS cases were receiving either partial or total disability compensation.). FMS results not only in work disability, but in loss of function in activities of daily living. This is true both for males and females, especially in middle age, and among individuals with a history of physically demanding employment. Why the disability rate appears to decline after age 64 is unclear. One possible explanation is that those 65 and older do not consider themselves to be disabled, because they are no longer eligible for disability pensions. Another possibility is that FMS tends to become less symptomatic in the elderly. This second possibility is supported by our own data that show the prevalence of FMS to decline steadily after age 64, but is refuted by data that show no difference in the severity of pain or fatigue, FIQ score, or number of major symptoms between FC 64 years old and below and those 65 and above.

Why a history of physically stressful employment increases the risk of current disability also cannot be addressed by our study results. It is an effect above and beyond that explained by education level. Trauma associated with heavy manual labor may be a causal or triggering factor. In prior reports, between 25% and 50% of FMS sufferers recalled an event precipitating symptoms, in most cases trauma.[22,23] Cervical spine trauma is associated with a one year incidence of FMS approaching 25%.[24] Repetitive traumas have been implicated in a variety of musculoskeletal syndromes, including carpal tunnel syndrome (CTS)[25,26,27] and repetitive strain injury (RSI).[28] However, our findings also can be explained by suggesting that the physical demands of heavy labor prevent ongoing employment in those who already have FMS. Both hypotheses warrant further study.

The association between FMS-related disability and prior heavy labour argues against a '*healthy worker effect*'. If FMS only causes disability among those who already are physically fragile or ill, then a history of heavy labour should be protective against subsequent disability from FMS. We observed the opposite. Hence, FMS itself appears to be the cause of disability, rather than prior illness. This supports our use of a utility weight of 1.00 for subjects prior to the onset of their pain and fatigue. It also argues against the '*crumbling skull*' hypothesis suggested by some critics of FMS, that is, that the 'aches and pains' only become disabling in those with a long history of physical fragility. Admittedly, we made no attempt to verify past employment among subjects. It is possible that there was a bias towards recalling a higher level of work-related physical stress among those currently disabled. Interestingly, however, there was no significant association between past employment emotional stress and current disability.

It is not surprising that those who are disabled report a greater number and greater severity of symptoms, in addition to worse overall perception of physical and mental health. Pain, fatigue and weakness are considered by those with FMS as the factors most significantly limiting work performance. This is consistent with previously published clinic studies.[29,30] On logistic regression, the FIQ score is the most useful predictor of self-reported disability status. However, there is considerable overlap in FIQ scores between those who report disability and those who do not. It is interesting to note that this overlap is for FIQ scores between 60 and 79. Below this, a small minority report being disabled. Above this, almost all report being disabled. We believe that our data

may be a first step towards developing more objective guidelines for the practitioner assessing FMS patients for disability.

Many would argue that self-reported disability is not the same as an actual inability to function in the workplace. We have not attempted to validate the FIQ, or any other model, as a measure of functionality in the workplace. To date, there exists no validated measure of workplace disability for any musculoskeletal illness.[14] The current study serves only to identify what factors may affect work performance, factors that may in turn be used to construct an instrument to formally measure workplace function. Such an instrument then would require testing for accuracy and precision.

Having previously been told one had FMS remained in our model as a predictor of self-reported work disability. Some have argued that labeling someone with FMS itself can be a cause of disability.[31,32,33,34,35] Hadler has made an eloquent case for the adverse effect of diagnostic labeling in 'black lung disease'.[36] Our data neither refute nor support a labeling hypothesis. It also is possible that those with more severe loss of function are more likely to achieve a diagnosis. The effect of diagnostic labeling on function and disability is being studied in greater detail in a five year prospective study of the subjects identified in LFES.

In summary, FMS commonly results in significant self-reported loss of function and work disability, both for males and females, especially during middle age and in

individuals who have worked in physically demanding jobs. Pain, fatigue and weakness appear to be the most problematic symptoms. Currently, the FIQ is the best measure of self-reported function and work disability. Ongoing research is needed, not just in FMS but in all musculoskeletal illness, to develop an accurate and precise measure of workplace disability.

LIST OF TABLES AND FIGURES

Tables

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Table 1: Comparing FC, PC and GC with respect to functional and work disability status.

	FC	PC	GC	Statistical significance
Number of subjects	100	76	135	
Mean age (years)[a]	47.8	47.2	44.5	$p < 0.02$
Age range (years)[b]	19 - 86	19 - 78	21 - 87	
% female[b]	86.0%	67.1%	81.5%	$p < 0.007$
Mean FIQ score[c]	61.2	41.6	21.9	$p < 0.00001$
% reporting having spent most of a day in bed in past 2 weeks[b]	58.0%	26.3%	12.6%	$p < 0.00001$
mean number of days in bed in past 2 weeks[c]	2.0	0.4	0.3	$p < 0.001$
% reporting having reduced usual activities due to health in past 2 weeks[b]	74.0%	57.9%	25.2%	$p < 0.00001$
mean number of days usual activities reduced in past 2 weeks[c]	4.7	3.1	1.1	$p < 0.01$
% reporting having worked less due to health problems[b]	65.0%	28.9%	8.9%	$p < 0.001$
% reporting being work disabled[b]	31.0%	10.5%	2.2%	$p < 0.00001$
% reporting receiving a disability pension[b]	26.0%	9.2%	3.0%	$p < 0.00001$
HYLL due to pain and/or fatigue[c]	13.5	7.0	2.2	$p < 0.0001$

[a] Group comparisons by analysis of variance (ANOVA)

[b] Group comparisons by Pearson chi-square test (X^2)

[c] Group comparisons by analysis of co-variance (ANCOVA) adjusted for sex and age

HYLL = healthy years of life lost

Table 2: Demographic characteristics and their effects on the odds of being disabled

Demographic Variables	Categories	OR	95% confidence intervals
Sex	male	1.00	n/a
	female	1.14	0.47, 2.74
Age	18 - 34	1.00	n/a
	35 - 49	5.67	**1.22, 26.33**
	50 - 64	8.43	**1.80, 39.49**
	65 +	1.43	0.19, 10.96
Marital Status	Never married	1.00	n/a
	Married	0.89	0.32, 2.46
	Separated or divorced	1.15	0.39, 3.34
	Widowed	0.40	0.07, 2.20
Education	University degree	1.00	n/a
	Some university	1.62	0.31, 8.48
	College	1.10	0.24, 4.95
	High school	1.64	0.40, 6.64
	Less than high school	3.27	0.82, 13.02
Physical stress of last employment	very low	1.00	n/a
	intermediate	1.87	0.52, 6.66
	high	8.94	**2.79, 28.72**
Amount of heavy lifting at last employment	no heavy lifting	1.00	n/a
	infrequent heavy lifting	1.58	0.50, 5.02
	some heavy lifting	1.76	0.59, 5.25
	much heavy lifting	4.13	**1.39, 12.30**
Emotional stress of last employment	very low	1.00	n/a
	intermediate	0.77	0.25, 2.36
	high	2.26	0.79, 6.47

Table 3: Clinical characteristics and their effects on the odds of being disabled

Clinical Variables	Categories	OR	95% confidence intervals	Mantel-Haentzel test for trend in proportions
FMS	confirmed	1.00	n/a	n/a
	excluded	4.00	1.71, 9.36	
Number of tender points	0 - 5	1.00	n/a	p = 0.001
	6 - 10	0.98	0.21, 4.45	
	11 - 14	2.53	0.65, 9.89	
	15 - 18	6.08	1.59, 23.23	
Severity of pain on 100 mm VAS	0 - 24	1.00	n/a	p < 0.00001
	25 - 49	0.46	0.03, 7.81	
	50 - 74	6.18	0.75, 50.73	
	75 - 100	17.54	2.16, 141.23	
Severity of fatigue on 100 mm VAS	0 - 24	1.00	n/a	p = 0.004
	25 - 49	0.79	0.14, 4.44	
	50 - 74	1.67	0.33, 8.47	
	75 - 100	3.60	0.71, 18.28	
Severity of depression on 100 mm VAS	0 - 24	1.00	n/a	p = 0.09
	25 - 49	1.13	0.39, 3.26	
	50 - 74	0.87	0.29, 2.59	
	75 - 100	2.41	0.97, 6.02	
Severity of anxiety on 100 mm VAS	0 - 24	1.00	n/a	p = 0.001
	25 - 49	0.10	0.01, 0.88	
	50 - 74	0.88	0.29, 2.64	
	75 - 100	3.15	1.19, 8.33	
Number of symptoms on 41 item checklist	0 - 10	1.00	n/a	p = 0.002
	11 - 20	1.59	0.41, 6.24	
	21 - 30	2.79	0.74, 10.56	
	31 - 41	8.63	1.86, 40.01	
Number of major symptoms on 41 item checklist	0 - 10	1.00	n/a	p = 0.00003
	11 - 20	3.84	1.74, 8.47	
	21 - 30	16.26	1.61, 164.74	
Self-rated general health	good - excellent	1.00	n/a	n/a
	poor - fair	5.31	2.26, 12.46	
Happiness	happy	1.00	n/a	n/a
	unhappy	3.31	1.58, 6.94	
Self-rated life stress	fairly - very stressful	1.00	n/a	n/a
	not very - not at all stressful	2.45	0.80, 7.48	
Overall satisfaction with health	somewhat - very satisfied	1.00	n/a	n/a
	not too - not at all satisfied	7.24	2.66, 19.69	
FIQ score	0 - 49	1.00	n/a	p < 0.00001
	50 - 74	5.43	1.75, 16.79	
	75 - 100	35.00	8.70, 140.87	

Table 4: Among 100 FMS cases, symptoms perceived to influence ability to work in a major way.

Symptom	% reporting symptom limiting ability to work
Pain in muscles, bones or joints	87.0%
Fatigue	80.0%
Weakness	73.0%
Problems with memory & concentration	51.0%
Headaches	48.0%
Anxiety	45.0%
Depression	45.0%
Numbness or tingling	41.0%
Eye problems	33.0%
Problems with breathing	28.0%
Abdominal complaints	19.0%
Other pain	15.0%
Other problems	7.0%

Table #5: Variables predicting FIQ score in a linear regression model

Variable	R^2	statistical significance
Number of major symptoms	0.54	$p < 0.0001$
Level of satisfaction with health[1]	0.50	$p < 0.0001$
Number of tender points	0.31	$p < 0.0001$
Highest education level achieved[1]	0.06	$p = 0.002$
Overall Model	0.80	$p < 0.0001$

[1] on a 5 point ordinal scale

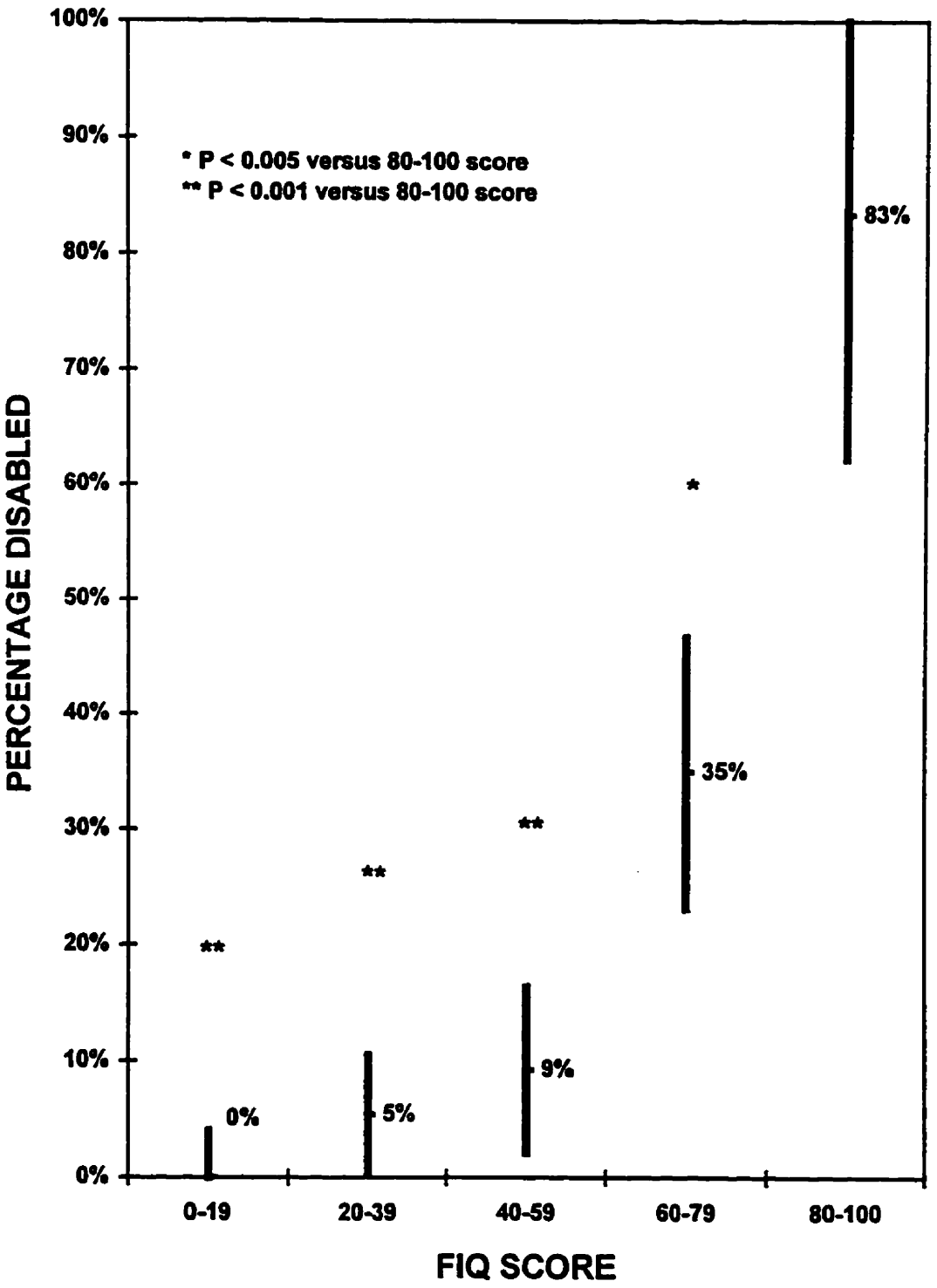
Table #6: Variables predicting work disability in a logistic regression model

Variable	statistical significance
FIQ score	$p < 0.0001$
Previously told they had FMS	$p = 0.01$
Unrestful sleep[1]	$p = 0.03$
Physical stress with prior employment[2]	$p = 0.04$
Overall Model	$p < 0.0001$

[1]Measured on a 3 point ordinal scale

[2]Measured on a 4 point ordinal scale

Figure 1: Percentage disabled by FIQ score
N = 287 (94 FC, 70 PC, 123 GC)



REFERENCES

[1] Wolfe F. The clinical syndrome of fibrositis. Am J Med 1986;81(3A):7-14

[2] Cathey MA, Wolfe F, Roberts FK, Bennett RM, Caro X, Goldenberg DL, Russell IJ, Yunus MB. Demographics, work disability, service utilization and treatment characteristics of 620 fibromyalgia patients in rheumatologic practice. Arthritis Rheum 1990;33[suppl]:S10

[3] Wolfe F, Anderson J, Harkness D, Bennett RM, Caro XJ, Goldenberg DL, Russell IJ, Yunus MB. Work and disability status of persons with fibromyalgia. J Rheumatol 1997;24(6):1171-8

[4] Bengtsson A, Henriksson K-G, Jorfeldt L, Kagedul B, Lennmarken C, Lindstrom F. Primary fibromyalgia. A clinical and laboratory study of 55 patients. Scand J Rheumatol 1986;15:340-7

[5] Ledingham J, Doherty S, Doherty M. Primary fibromyalgia syndrome - An outcome study. Br J Rheumatol 1993;32:139-42

[6] Bruusgaard D, Evensen AR, Bjerkedal T. Fibromyalgia - a new cause for disability pension. Scand J Soc Med 1993;21:116-9

[7] McCain GA, Cameron R, Kennedy JC. The problem of long term disability payments and litigation in primary fibromyalgia: The Canadian perspective. J Rheumatol 1989;16[suppl 19]:174-6

[8] Hawley DJ, Wolfe F. Pain, disability and pain/disability relationships in seven rheumatic disorders. J Rheumatol 1991;18:1552-7

[9] Burckhardt CS, Clark SR, Bennett RM. Fibromyalgia and quality of life: A comparative analysis. J Rheumatol 1993;20:475-9

[10] Callahan LF, Smith WJ, Pincus T. Self-reported questionnaires in five rheumatic diseases. Comparisons of health status constructs and associations with formal education level. Arthritis Care Res 1989;2:122-31

[11] Viitanen JV, Kautiainen H, Isomaki H. Pain intensity in patients with fibromyalgia and rheumatoid arthritis. Scand J Rheumatol 1993;22:131-5

[12] Mengshoel AM, Forre O. Pain and fatigue in patients with rheumatic disorders. Clin Rheumatol 1993;12(4):515-21

[13] Gerdle B, Elert J. Disability and impairment in fibromyalgia syndrome: Possible pathogenesis and etiology. Crit Rev Phys Med Rehab 1995;7(3):189-232

[14] Shapiro A, Roth RS. The effect of litigation on recovery from whiplash, in Spine: State of the Art Reviews, 1993;7(3):531-56

[15] White KP, Harth M, Teasell RW. Work disability evaluation and the fibromyalgia syndrome. Semin Arthritis Rheum, 1995;24(6):371-81

[16] Wolfe F, Smythe HA, Unus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, Fam AG, Farber SJ, Fiechtner JJ, Franklin CM, Gatter RA, Hamaty D, Lessard J, Lichtbrown AS, Masi AT, McCain GA, Reynolds WJ, Romano TJ, Russell IJ, Sheon RP. The American

College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum 1990;33:160-72

[17] White KP, Speechley M, Harth M, Ostbye T. The London fibromyalgia epidemiology study (LFES): The prevalence of fibromyalgia syndrome (FMS) in London, Ontario [unpublished manuscript]

[18] White KP, Speechley M, Harth M, Ostbye T. Testing an instrument to screen for fibromyalgia syndrome in general population studies: The London fibromyalgia epidemiology study screening questionnaire (LFESSQ)

[19] Burckhardt CS, Clark SR, Bennett RM. The fibromyalgia impact questionnaire: Development and validation. J Rheumatol 1991;18:728-33

[20] Statistics Canada: Health and Activity Limitation Survey - 1991 User's Guide

[21] Reynolds DL, Torrance GW, Badley EM, Bennett KJ, Chambers LW, Goldsmith CH, Jamieson E, Tugwell P, Wolfson MC. Modeling the population health impact of musculoskeletal diseases: Arthritis. J Rheumatol 1993;20:1037-47

[22] Greenfield S, Fitzcharles MA, Esdaile JM: Reactive fibromyalgia syndrome. Arthritis Rheum 1992;35(6):678-81

[23] White KP, Speechley M, Harth M, Ostbye T. The London Fibromyalgia Epidemiology Study (LFES): Comparing the demographic and clinical characteristics in 100 random community cases of fibromyalgia syndrome (FMS) versus controls. [unpublished manuscript]

[24] Buskila D, Neumann L, Vaisberg G, Alkalay D, Wolfe F. Increased rates of fibromyalgia following cervical injury. Arthritis Rheum 1997;40(3):446-52

[25] Barnhart S, Demers PA, Miller M, Longstreth WT Jr, Rosenstock L. Carpal tunnel syndrome among ski manufacturing workers. Scand J Work Environ Health 1991;17(1):46-52

[26] Tanaka S, Wild DK, Seligman PJ, Halperin WE, Behrens VJ, Putz-Anderson V. Prevalence and work-relatedness of self-reported carpal tunnel syndrome among U.S. workers: analysis of the Occupational Health Supplement data of 1988 National Health Interview Survey. Am J Ind Med 1995;27(4):451-70

[27] Osorio AM, Ames RG, Jones J, Castorina J, Rempel D, Estrin W, Thompson D. Carpal tunnel syndrome among grocery store workers. Am J Ind Med 1994;25(2):229-45

[28] Hocking B. Epidemiological aspects of 'repetition strain injury' in Telecom Australia. Med J Aust 1987:147;218-22

[29] Viitanen JV, Kautiainen H, Isomaki H. Pain intensity in patients with fibromyalgia and rheumatoid arthritis. Scand J Rheumatol 1993;22:131-5

[30] Mengshoel AM, Forre O. Pain and fatigue in patients with rheumatic disorders. Clin Rheumatol 1993;12(4):515-21

[31] Hadler NM. The danger of the diagnostic process, in Hadler NM (ed): Occupational Musculoskeletal Disorders. New York, NY, Raven Press, 1993, pp. 16-33

[32] Hart FD. Fibrositis (fibromyalgia). A common non-entity? Drugs, 1988;35:320-7

[33] Block SR. Fibromyalgia and the rheumatisms. Common sense and sensibility. Rheum Dis Clin North Am 1993;19(1):61-78

[34] Carette S. Fibromyalgia 20 years later: What have we really accomplished? J Rheumatol 1995;22(4):590-4

[35] Robbins JM, Kirmayer LS. Illness, worry and disability in fibromyalgia syndrome. Int J Psychiatry Med 1990;20:49-63

[36] Hadler NM. Social security. The process of pensioning the invalid. In: Occupational Musculoskeletal Disorders, Hadler NM (Ed). New York, NY, Raven Press, 1993, pp. 227-48

CHAPTER 7
SUMMARY

7.0 OVERVIEW

Prior surveys from Europe, South Africa and the U.S. have shown FMS to affect between 0.5% and 5.0% of the general adult population.[1,2,3,4,5,6,7,8] With one exception, the number of FMS cases confirmed in each of these studies was inadequate to allow for analyses with respect to age- and sex-specific prevalence, disease characteristics, functional status, disability status, and health services utilization. In the U.S. study,[8] these analyses were performed on 36 confirmed cases of FMS. Estimates of health service utilization were by subject self-report only, and no data have been published on the estimated costs of these services.

LFES has been an attempt to identify a representative community sample of adult FMS cases large enough to permit analyses with respect to age- and sex-specific prevalence, disease characteristics, functional status, disability status, and direct health

care costs. In a survey of 3395 non-institutionalized adults residing in London, Ontario, we confirmed FMS in 100 individuals, whom we compared both with internal and external control groups. Because we identified 86 female and 14 male cases, we were able to compare females and males with FMS with respect to clinical severity. Our estimate of direct health care costs is supported by data from the Ontario Health Insurance Plan (O.H.I.P.) on annual services used and costs of services for FMS cases and controls. In London, Ontario, FMS appears to have a significant impact, both on affected individuals and at a societal level.

7.1 BRIEF SUMMARY OF RESULTS

7.1.1 FMS prevalence

FMS is common. It affects almost five percent of adult women and between one and two percent of adult men in London. In adult women, it affects all ages, though it appears to be most common in middle age. Our data on age-related prevalence are less clear for men.

Although a greater percentage of women than men have FMS, females and males do not appear to differ with respect to clinical presentation. The two sexes do not differ in number of symptoms, symptom severity, or overall level of health. Females with FMS may be older, on average. They also report more symptoms as having been a major problem over the preceding two weeks.

7.1.2 **FMS and the individual**

FMS impacts the individual in several ways. Persons with FMS report a wide variety of symptoms. Most prominent among them, besides widespread pain (which is required for the diagnosis), are fatigue, severe fatigue lasting 24 hours after minimal activity, and sleep difficulties. Individuals with FMS report a greater number and greater severity of symptoms, worse overall health, and more healthy years of life lost than individuals with chronic widespread musculoskeletal pain (Pain controls, PC) who do not meet the case definition for FMS. Four clinical characteristics appear to distinguish FC from PC: weakness, pain severity on a 100 millimeter visual analog scale, glandular swelling in the neck, and severe fatigue lasting 24 hours after minimal activity.

Approximately one quarter of FMS sufferers are receiving disability pensions, and almost one third report being disabled. There may be a considerable net loss of income among persons with FMS. Demographic risk factors for being disabled include middle age and physically stressful past employment. Pain, fatigue, weakness and cognitive difficulties are the symptoms most often reported to have a negative impact on work capacity. The Fibromyalgia Impact Questionnaire (FIQ) score appears to be the best predictor of self-reported disability. The FIQ score, itself, is best predicted by overall number of major symptoms, overall satisfaction with health, tender point count, and level of education.

7.1.3 FMS and society

FMS also has a major impact at a societal level. If London is representative of the Canadian population with respect to prevalence of FMS, our figures suggest that as many as 700,000 Canadian adults may be affected. If this estimate is accurate, it means that, in Canada, FMS accounts for a conservatively estimated $350 million annually in differential direct health care costs, largely resulting from increased utilization of outpatient physician services. It also is associated with a significant increase in medication use.

7.2 A COMPARISON OF LFES TO EARLIER STUDIES

Among previously published surveys, only in Wichita have prevalence estimates been given for males and females separately. These estimates were 3.4% in women (CI 2.3%, 4.6%), and 0.5% in men (CI 0.0%, 1.0%),[8] slightly lower than the estimates for London. In Wichita, prevalence rose steadily with age through age 79, compared to the peak in prevalence we observed in women 55 to 64 years old in London. However, because of the relatively small number of confirmed FMS cases in the Wichita study, the confidence limits for age-specific prevalence were large; for example, prevalence was estimated between 4.6 and 9.5 percent for women age 60 to 69, and between 4.8 and 10.0 percent for women age 70 to 79. The study lacked the statistical power to detect differences in prevalence between age groups. In contrast, we were able to show a statistically

significant decline in FMS prevalence in women 65 to 74 years old versus women 55 to 64, and a similar decline for women 75 and older.

In both LFES and the Wichita study, demographic risk factors for having FMS were female sex, less than a high school education, and low household income. The U.S. study also found an association between having FMS and being divorced. In LFES, being divorced was associated with an increased odds both for having FMS or chronic, widespread pain without FMS.

In both the Wichita and London studies, individuals meeting the case definition for FMS reported a greater number and severity of symptoms, both physical and psychological, than others with chronic pain. In both studies, FMS cases utilized more health services. Our data suggest that the largest component of provincially funded direct health care costs is physician reimbursement, especially for out-patient services. Medication costs were not calculated, but our data on self-reported use of medications suggests that these costs also are higher for individuals with FMS.

7.3 QUESTIONS RAISED BY LFES

The findings of the London Fibromyalgia Epidemiology Study (LFES) raise several questions. Among them, are the following:

7.3.1 Why does the prevalence of FMS appear to decline in those over age 64, especially in women?

In only one prospective study of FMS patients in a subspecialty clinic has there been follow-up beyond four years.[9] To our knowledge, prior to LFES there were no reported data on the natural history of FMS in the community. Despite this, it has been characterized as a non-remitting, non-deforming, non-fatal disorder.[10] Is this accurate? Our data on prevalence, that show a steady decline in FMS prevalence in women after age 64, suggest otherwise. This decline withstands adjustment for the number of adults per household, and for a potential 100% increase in the prevalence of the disorder among institutionalized versus non-institutionalized elders.

Our results could be biased if there were under-representation of the over age 64 population in our sample, especially if our sampling tended to exclude elders with FMS who either were unwilling or unable to participate in the study. However, the over age 64 population was not under-represented in the screening survey sample; in fact, the subgroup 65 to 74 years of age was slightly over-represented. In addition, there were no demographic or clinical differences noted between subjects who screened positive and were examined for FMS, and those who screened positive but refused to be examined. These two observations argue against a bias towards excluding elderly FMS cases. Likely, there truly is a decline in FMS prevalence in the elderly.

Why is there a decline in FMS prevalence over age 64? A similar decline has been reported in the prevalence of chronic low back pain.[11] One scenario is that FMS is associated, either directly or indirectly, with an increased risk of mortality. Until recently, rheumatoid arthritis (RA) was not considered to be a fatal illness. There now are data that suggest that the life expectancy of the average RA patient may be shortened significantly.[12,13,14,15]

FMS has been associated, in the clinic population, with a variety of other illnesses, some of which are associated with increased mortality, such as RA and systemic lupus erythematosis (SLE).[16] Many patients with chronic pain suffer from depression or other psychological distress, that may increase mortality risk through a variety of mechanisms, such as suicide, malnutrition, and impaired immune function.[17,18] FMS appears to be associated with decreased household income, which also has been associated with increased mortality.[19,20,21] If FMS causes decreased income as our data suggest, then early mortality may be an indirect outcome of the condition via its effect on income.

It also is possible that the pathophysiologic process responsible for the development of FMS and/or chronic pain, itself, is associated with increased mortality. Currently, our understanding of the pathophysiologic basis of chronic pain is too limited to test this hypothesis.

Another explanation for the reduction in FMS prevalence in the elderly is that the decline is, either partially or totally, the result of an increased risk of institutionalization in elders with FMS. If so, the apparent decline is at least partially erroneous, caused because a disproportionate number of elders with FMS were ineligible because of their institutionalization. We have shown that it would require a several-fold increase in FMS among the institutionalized elderly to account for the apparent decline in FMS prevalence in those over age 64. This is unlikely. Also, although it may be reassuring if FMS did not increase mortality, such a strong association between it and institutionalization would be alarming in itself.

A third, and more favorable scenario is that FMS, although lasting for many years in many, does remit with time, at least in some. Most clinic studies have found FMS generally to have a poor prognosis over time, with little improvement in most, worsening in a significant percentage, and rare remissions.[22,23,24,25,26,27,28] Two recent studies suggest a more favorable outcome.[9,29] Kennedy and Felson reported on 39 FMS patients selected for a follow-up interview ten years after having been diagnosed in clinic. At the time of follow-up, the mean age of subjects was 55 years. Four had died; six had been lost to follow-up. Of the remaining twenty-nine, 55% reported feeling well or very well in terms of symptoms, and only 7% felt they were doing poorly. On the other hand, the subjects did not report much difference from earlier evaluations, and there were no remissions among the 29 cases.

In the second study, 44 patients treated at one of two private rheumatology practices in Melbourne, Australia were re-assessed two years after diagnosis. At follow-up, 21 (47%) no longer met the case criteria for FMS. One potential source of bias in the study was that the diagnostic criteria used to confirm FMS changed during the course of follow-up. In 1988, the 1990 ACR criteria did not exist. The investigators utilized criteria proposed by Smythe and Moldofsky, that required pain to digital palpation at 12 of 14 sites, chronic, diffuse achiness and non-restorative sleep.[30,31] In the Smythe criteria, there were no specifications as to the distribution or duration of pain. According to the 1990 ACR criteria, one must have had pain that has persisted for no less than three months, and the distribution of pain must be axial and peripheral, above and below the waist, and on both the right and left sides of the body. Possibly, many of the FMS cases entered into the Australian study in 1988 had had pain of less than 3 months duration, and of a more limited distribution. Hence, the apparent high remission rate may have been the result of a significant percentage not having had FMS, as now defined, at the time of entry into the study.

Irrespective of the course of FMS in clinic studies, there is evidence in other musculoskeletal conditions that disease symptoms tend to be more severe and more chronic in subspecialty clinic patients than in the general population.[32,33,34] It may be that FMS does remit (either in terms of meeting the case definition, or in terms of FMS symptoms) in the general population. Further study is warranted to determine if remissions do occur, how frequently, after what duration of symptoms, when in the life cycle, and if there are predictors of subsequent remission.

Another explanation of the peak prevalence of FMS in middle age is that of a cohort effect. According to this hypothesis, the decline in prevalence in the elderly is the result, not of any deviation in the chronic nature of the condition, but of some past peak rate of exposure of a given age cohort to a causal or triggering factor. Such a theory suggests that there are environmental factors that can cause or trigger FMS, factors to which certain age cohorts have been more or less exposed. To date, no such environmental factors have been identified, except possibly trauma.[35] Further research is warranted to identify potential risk factors for FMS, and to determine their causal role in this condition.

We have begun a five year prospective study of the 100 confirmed FMS cases identified in LFES to estimate the incidence of remission in community cases of FMS. In addition, we are following prospectively the 76 LFES pain controls to determine the incidence of FMS in this presumably high risk group, and to identify baseline characteristics that are predictive of the subsequent development of FMS.

7.3.2 **What is the effect of labeling someone with the diagnosis of FMS?**

Among the 176 subjects who were examined in LFES, having been told one had FMS was one of four variables in the multivariate model to predict work disability. Critics have argued that the diagnostic label *fibromyalgia,* itself causes illness behaviour and disability,[36,37,38,39,40] as in the case of 'black lung disease' in the United States.[41] Our

data neither refute nor support this hypothesis. It also is possible that those with more severe loss of function are more likely to pursue a diagnosis. To date, there are no data to suggest that labeling someone with FMS will cause any more illness behaviour than labeling someone with some other disease, such as ischaemic heart disease or rheumatoid arthritis. However, the issue of iatrogenic illness caused by a diagnostic label is important, both to the individual patient, and to society as a whole. This is especially true if the diagnostic label is commonly applied. Further study of this issue clearly is warranted, not only for FMS, but for other diagnoses as well.

In the five year prospective study mentioned above, we also are studying the effect of diagnostic labeling on function and disability in the 100 confirmed FMS cases and 76 controls we identified in LFES. We will compare the clinical course of the 72 FC not previously diagnosed with FMS (in whom we identified FMS) with the 28 FC in whom FMS previously had been diagnosed.

7.3.3 **Is there a more cost efficient way to manage the FMS patient?**

Differential direct health care costs for FMS probably exceed $350 million annually in Canada. As is stated below in Section 7.5.1, there is reason to believe that this is an under-estimate of the true differential direct costs. Despite these substantial costs, there is little evidence that treatment results in significant improvement,[42] and no clinical trial has demonstrated a benefit of treatment beyond three months.

It is unclear whether or not labeling someone with FMS increases illness behaviour. Similarly, it also is unclear how administering treatment to such patients affects illness behaviour and utilization of health care resources. It is possible that attempts to treat may lead to escalating health care seeking behaviour and resultant direct health care costs. To date, data generally support the likelihood that treating patients results in modest improvement, at least in the short term. To date, there are no data that support the hypothesis that treating such patients makes them more dependent on the health care system. It is plausible that appropriately labeling and treating such patients decreases health care service utilization and costs.

What the high health care costs of FMS do suggest is a need for further study to better understand this condition, and the effects of labeling and treating it. In this time of increasing fiscal constraints, it also may be important to identify what treatments are most and least cost-efficient, to develop an improved understanding of where and why cost-inefficient treatments are being utilized, and to study how to influence the use of such treatments. Our data suggest that physician services are the largest component of direct costs. Cost-efficiency analyses likely should begin with treatments initiated by physicians, rather than by other health care practitioners, since altering the diagnostic and treatment practices of physicians likely would have the greatest effect on costs.

7.4 STRENGTHS OF LFES

The primary strengths of LFES were the probability sample, examination for FMS tender points of all consenting individuals who screened positive for chronic, widespread pain using a reliable case definition, the large number of FMS cases confirmed, and access to the O.H.I.P. data base to estimate direct health care costs. Further, for reasons noted below, the prevalence estimates likely are conservative - at least as high as reported.

7.5 LIMITATIONS OF LFES

Several potential sources of bias may have affected LFES, and hence affected our estimates of FMS prevalence and costs.

7.5.1 Biases due to sampling method, including response bias

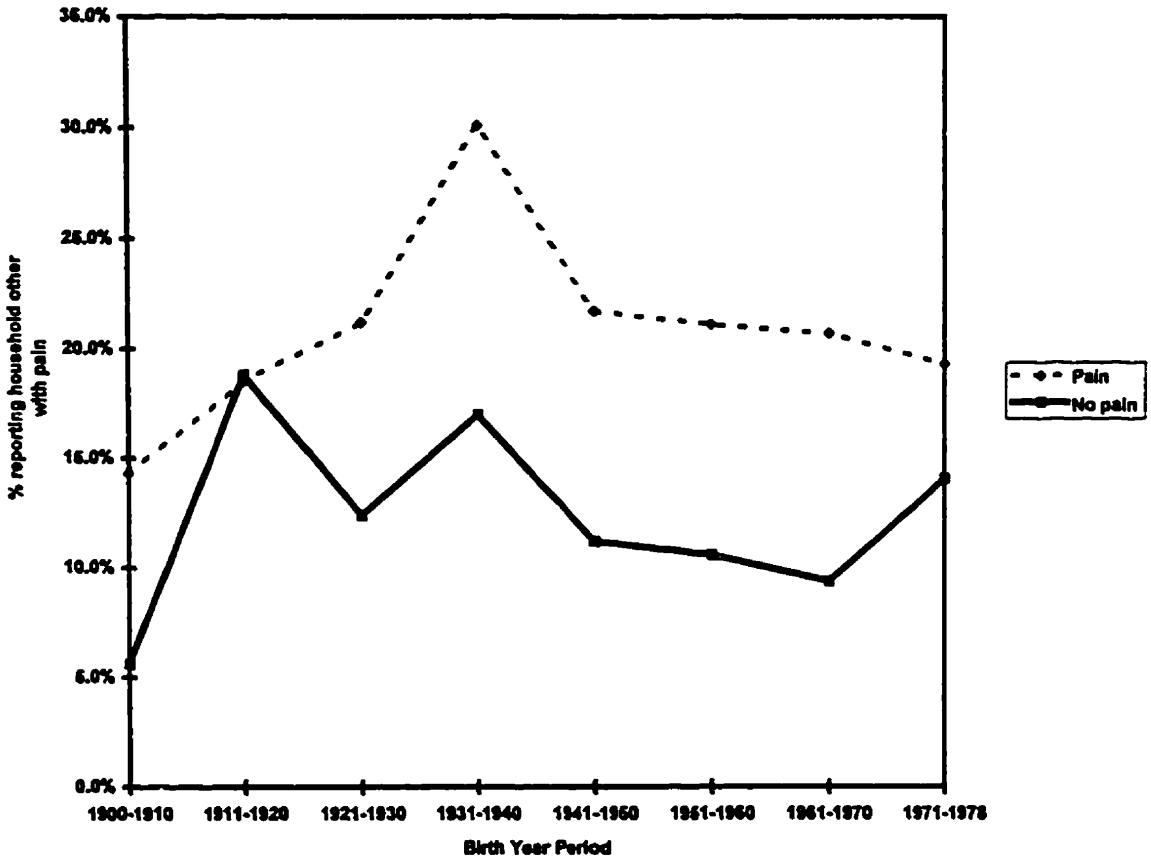
First, it is possible that the survey sample was not representative of the study population. However, other than for sex distribution, for which we adjusted during data analysis, we found no major demographic discrepancies between our sample and the 1991 London census. Nonetheless, having FMS itself may have influenced the likelihood of being sampled. We found that a greater percentage of FMS cases reported being disabled than did subjects in either internal control group. The greatest difference was between FMS subjects (FC) and the general controls (GC) who represent over 90% of the

survey sample. It is reasonable to expect that disabled individuals would be more likely to be at home to receive a telephone call than those not disabled, particularly for telephone calls during the day. This tendency to preferentially interview disabled non-working versus healthy working individuals could falsely elevate estimates of FMS prevalence. We attempted to minimize this by having the interviewers call each selected telephone number in a systematic way at five different times of the day and week. Almost two thirds of completed interviews were performed in the evening, when it is expected that most working individuals would be at home.

It is possible that having chronic widespread pain oneself, or having a member of the household who has chronic widespread pain, would make someone more likely to agree to participate in a study on chronic pain, perhaps in an attempt for that person to find an explanation for their symptoms. This tendency also could falsely elevate the estimate of FMS prevalence. There are at least three ways in which this might occur. First, the initial contact person in a given household might be influenced either to participate themselves or to recruit whomever else is the eligible subject in that household, if someone living there has chronic pain and/or FMS. Second, the initial contact person might falsely claim to be the eligible subject, if they themselves have chronic pain and/or FMS. Third, the initial contact person might defer to some other person in the household, who is in fact not the eligible adult according to the next birthday method, because of that individual's chronic pain and/or FMS.

The first occurrence is the least likely, since all seven interviewers reported that potentially eligible Phase I subjects almost always terminated the telephone conversation before any information was given on the survey's objectives, usually within the first ten seconds of the conversation. If the third scenario occurred frequently, one would expect that Phase I subjects reporting pain would less frequently identify another household member with pain than Phase I subjects not reporting pain, after adjusting for age and sex. In our survey sample, the reverse was true. A greater percentage of subjects with pain identified other household members with pain. This was true for all age groups in both sexes, except for individuals born between 1911 and 1920, for whom there was no difference between subjects with and without pain (Figure 7-1).

FIGURE 7-1: The percentage of Phase I subjects with and without pain reporting household others with pain, by birth year



Unfortunately, we cannot rule out the possibility that the second scenario, that is, that the initial contact person might falsely claim to be the eligible subject, created bias in our results. However, it also is possible that having FMS might have decreased one's ability or willingness to participate. Individuals with severe pain and disability due to pain and/or FMS may have been less capable or willing to answer the telephone or complete the interview. If they screened positive, they might have been less willing or able to agree to be examined. For example, the FMS cases we identified spent a mean of 2.0 days in bed over the preceding two weeks, compared to 0.4 days for pain controls, and 0.3 days for general controls. Eligible subjects whose health requires them to spend more days in bed might be less willing or capable of traveling to a hospital clinic to be examined and to complete a one hour written questionnaire. It also may be that subjects previously diagnosed with FMS would have had less incentive than others to want to participate in the confirmatory examination, since they already have received an explanation for their symptoms.

Other factors may have tended to reduce the estimates of FMS prevalence and costs. For example, our study excluded institutionalized adults. To date, there are no published data on the prevalence of FMS in institutions. Given that the institutionalized generally are more ill than the general population, it is reasonable to assume that the prevalence of FMS is greater among the institutionalized in any given age category. That we excluded institutionalized adults is a potential source of bias in LFES, likely falsely reducing the prevalence estimate. In addition, the costs of treating any given illness among the institutionalized may be greater. Excluding the institutionalized with

its disproportionately high costs of this group could have resulted in a disproportionately low estimate of FMS-related costs. However, 98.5% of the population live outside of institutions.

We also excluded individuals less than 18 years old, even though FMS may affect a sizable percentage of children.[43] Including children might significantly have increased our estimate of healthy years of life lost (HYLL). However, there were practical and ethical considerations associated with including children that we felt were best to avoid. From a practical stand point, there currently are no widely accepted diagnostic criteria for FMS in children. In addition, obtaining a history of chronic, widespread pain could be inaccurate and unreliable in the very young, especially in a telephone interview. From an ethical stand point, until FMS has been better characterized among the clinic paediatric population, and until there is at least a reasonable degree of agreement among no less than paediatric rheumatologists as to how to diagnose it, identifying a child as having FMS may result in unnecessary frustration and fear both for the child and parents.

7.5.2 **Biases arising from measurement**

Our estimate of direct costs likely is low, because the Ontario Health Insurance Plan (OHIP) does not reimburse for the services provided by an array of health care providers, including dentists, psychologists, physiotherapists in private practice, and alternative care practitioners. There is some evidence that FMS patients are frequent consumers of alternative medical interventions,[44] but our FMS cases reported much

greater utilization of physician than non-physician services. The apparent discrepancy between our study and theirs may be because there is recall bias in a study such as ours, with subjects more likely to recall or admit to the use of physician than non-physician services. It also may be the result of the difference between a clinic and community sample.

The OHIP database we accessed also did not include the cost of medications. Our FMS cases used, on average, 2.8 prescribed medications, compared to 1.9 and 0.9 medications for pain controls and general controls, respectively. If the average cost of a prescription is $50.00 per month, this alone translates into over a one thousand dollar annual difference between individuals with FMS and the general population, which in turn can be extrapolated to $700 million in prescribed medication costs in Canada annually.

We made no attempt to measure overhead costs, such as the proportional costs of operating a clinic or emergency department for FMS-related problems. We excluded them, because such costs are difficult to measure, and the methods for this are controversial.[45] Nonetheless, excluding them will result in a reduced estimate of direct costs.

In general, the net effect of sampling and measurement bias probably was a conservative error in the estimates both of prevalence and costs. We estimated that the net annual direct health care costs of FMS were between $300 and $350 million in

Canada. Given all of the costs we did not measure, likely the true estimate is much greater. Adding to this the indirect costs of what appears to be a very disabling illness, and we feel we can conclude accurately that FMS places a large economic burden on Canadian society at least as large as estimated.

7.6 DIRECTIONS FOR FUTURE RESEARCH

To clarify some of the questions raised by LFES, several studies by the LFES research group already are in progress or in the development stages. All studies undertaken by the research group receive approval from the University of Western Ontario Review Board for Research on Human Subjects.

7.6.1 The London Fibromyalgia Epidemiology Study - Phase IV (LFES-IV)

As mentioned above, we have begun a five year follow-up of the 100 subjects in whom FMS was confirmed, and the 76 subjects in whom FMS was excluded by examination in LFES. Follow-up will be at 18 month intervals, consisting of a brief musculoskeletal examination to determine whether or not a subject meets the case definition of FMS, and to assess for other forms of arthritis involving the hands, followed by completion of a detailed health questionnaire. The primary objectives are to estimate the incidence of remission (both in terms of the case definition and in terms of resolution of pain) of FMS in the 100 FC over five years, and to estimate the incidence of FMS among the 76 PC. Secondary objectives include: 1) determining the overall natural

history of FMS and chronic, widespread pain with respect to symptom severity, function, work disability, and health care services utilization; 2) determining the effect of labeling an individual with FMS on symptom severity, function, work disability, and health care services utilization; and 3) testing the sensitivity to change of the tender point examination.

7.6.2 Fibromyalgia in the Amish Communities of Southwestern Ontario (FACSO)

In many ways, the Amish community in North America is culturally isolated and distinct from the rest of the population.[46] There are several reasons to study the prevalence of FMS in the Amish. First, in accordance with Amish law, members do not utilize municipal, provincial/state or federal disability compensation systems. Generally, the only recourse for a disabled community member is to request financial or other assistance from the bishop of the local congregation, who then appeals for donations from congregation members. Congregations are small, their size limited because all services take place within the homes of congregation members. Hence, funds are limited, and not dispensed anonymously. There also is a very strong work ethic and sense of independence among the Amish. For these and other reasons, it is uncommon for community members to seek financial assistance related to physical disability. If FMS is a litigation or compensation-driven ailment, it should be uncommon in the Amish.

Second, the Amish are uncommonly exposed to the forms of high speed trauma, such as motor vehicle collisions (MVC), that appear to precipitate some cases of FMS,[35] because they do not own motor vehicles, usually traveling by horse and buggy. Third, almost all Amish have less than a high school education; traditionally, formal schooling ends after the eighth grade. If a lower level of education is a causative factor for FMS, then the prevalence of FMS in the Amish should be high. Fourth, extremely well documented genealogy records exist for the Amish. The primary objective of this study is to determine if FMS is as prevalent among Amish adults as in rural and major urban non-Amish controls. A secondary objective is to compare Amish cases and control cases of FMS with respect to clinical characteristics and functional status. This study has been funded and is in the field.

7.6.3 Perspectives in post-traumatic pain: A survey of Canadian general practitioners, orthopaedists, physiatrists and rheumatologists

Data collection has begun in a survey of approximately 780 practicing physicians across Canada, within four specialties: rheumatology, orthopaedics, physiatry, and general practice. The objective of this study is to determine the effect of certain patient-specific and physician-specific variables on the acceptance or rejection of the concept of post-traumatic fibromyalgia. Each randomly selected subject has been mailed one of six different versions of a case scenario involving post-traumatic chronic pain. The scenario is followed by questions about perceived likelihood of post-traumatic fibromyalgia, and

perceived risk factors for developing chronic post-traumatic pain. This study is underway.

7.6.4 The Post-MVC (motor vehicle collision) fibromyalgia incidence study (PMFIS)

We propose to study the one year incidence of FMS in individuals who have been involved in a MVC, and in two control groups, to determine if MVC-related trauma is a significant risk factor for FMS. If such trauma significantly increases the risk of subsequent FMS, this could have implications with respect to future research. Because a variety of physiologic abnormalities already have been documented in FMS patients, these physiologic parameters could be evaluated in individuals immediately post-trauma, prior to the onset of FMS, and prospectively as FMS symptoms develop, in an attempt to determine the causal direction of events. Also, since a MVC is a relatively dramatic event for which a large subset of individuals seek medical care, it is an observable risk factor that could lead to research to improve clinical outcomes through earlier disease detection and treatment. Finally, there may be identifiable baseline characteristics among post-MVC patients that are predictive of poorer clinical outcome and higher health services utilization. This would have implications in terms of targeting those post-MVC patients at highest risk for developing FMS, that they might be included in clinical trials on aggressive early or preventative treatment. It also would have implications for future allocation of health care resources.

The study will involve individuals who have presented to emergency rooms (ER) immediately following motor vehicle related trauma, in addition to two control groups: those presenting to ER with minor lacerations, and those presenting to ER with upper respiratory infections. After identification of eligible subjects who consent, baseline demographic and clinical data will be collected. Subjects then will be followed prospectively at quarterly intervals over one year to compare the one year incidence of FMS in each group, and to identify risk factors for developing FMS, poor outcome, and high health care services utilization.

7.7 CONCLUSIONS

FMS is common. It affects almost one in twenty Canadian adult females, and up to one in sixty adult males. It appears to have a major impact on function and the ability to work, and places a large economic burden on Canadian society. Despite high direct medical costs, treatment generally is ineffective or only modestly effective. Until there is a clear understanding of the cause and/or a cost-effective, simple and safe cure for this condition, there will be a need for continued epidemiologic research on FMS.

REFERENCES

[1] Jacobsson L, Lindgarde F, Manthorpe R. The commonest rheumatic complaints of over 6 weeks' duration in a twelve month period in a defined Swedish population. Scand J Rheumatol 1989;18:361-8

[2] Makela M, Heliovaara M. Prevalence of primary fibromyalgia in the Finnish population. BMJ 1991;303:216-9

[3] Croft PR, Schollum J, Rigby AS, Boswell RF, Silman AJ. Chronic widespread pain in the general population. Scand J Rheumatol 1992;[suppl 94]:8

[4] Raspe H, Baumgartner CH. The epidemiology of fibromyalgia syndrome (FMS) in a German town. Scand J Rheumatol, 1992;[suppl 94]:8

[5] Lyddell C, Meyers OL. The prevalence of fibromyalgia in a South African community. Scand J Rheumatol 1992;[suppl 94]:8

[6] Workshop of the Standing Committee on Epidemiology European League Against Rheumatism (EULAR). The Epidemiology of Fibromyalgia. Bad Sackingen, 19-21 November 1992. Br J Rheumatol 1994;33:783-6

[7] Prescott E, Kjoller M, Jacobsen S, Bulow PM, Danneskiold-Samsoe B, Kamper-Jorgensen F. Fibromyalgia in the adult Danish Population: I. A prevalence study. Scand J Rheumatol 1993;22:233-7

[8] Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38(1):19-28

[9] Kennedy M, Felson DT. A prospective long-term study of fibromyalgia syndrome. Arthritis Rheum 1996;39(4):682-5

[10] Wolfe F. The fibromyalgia syndrome: A consensus report on fibromyalgia and disability. J Rheumatol 1996;23(3):534-9

[11] Papageorgiou AC, Croft PR, Ferry S, Jayson MI, Silman AJ. Estimating the prevalence of low back pain in the general population. Evidence from the South Manchester Back Pain Survey. Spine 1995;20(17):1889-94

[12] Cobb S, Anderson F, Bauer W. Length of life and cause of death in rheumatoid arthritis. N Eng J Med 1953;249:553-6

[13] Symmons DPM. Mortality in rheumatoid arthritis. Br J Rheumatol 1988;27[suppl 1]:44-54

[14] Pincus T. Is mortality increased in rheumatoid arthritis (RA)? J Musculoskel Med 1988;5:27-46

[15] Wolfe F, Mitchell DM, Sibley JT, Fries JF, Block DA, Williams CA, Spitz PW, Haga M, Kleinheksel SM, Cathey MA. The mortality of rheumatoid arthritis. Arthritis Rheum 1994;37:481-94

[16] Dubois EL. Causes of death in systemic lupus erythematosis. In: Lupus Erythematosis, 2nd edition. Dubois EL (Ed), 1976, pp. 633-40

[17] Irwin M, Patterson T, Smith TL, Caldwell C, Brown SA, Gillin JC, Grant I. Reduction of immune function in life stress and depression. Biol Psychiatry 1990;27(1):22-30

[18] Leonard BE, Song C. Stress and the immune system in the etiology of anxiety and depression. Pharmacol Biochem Behav 1996;54(1):299-303

[19] Fiscella K, Franks P. Poverty or income inequality as predictor of mortality: longitudinal cohort study. BMJ 1997;314(7096):1727-8

[20] Hahn RA, Eaker ED, Barker ND, Teutsch SM, Sosniak WA, Krieger N. Poverty and death in the United States. Int J Health Serv 1996;26(4):673-90

[21] Jessop EG. Deprivation and mortality in non-metropolitan areas of England and Wales. J Epidemiol Community Health 1996;50(5):524-6

[22] Wolfe F. Disability and the dimensions of distress in fibromyalgia. J Musculoskel Pain 1993;1:65-88

[23] Greenfield S, Fitzcharles MA, Esdaile JM. Reactive fibromyalgia syndrome. Arthritis Rheum 1992;35:678-81

[24] Cathey MA, Wolfe F, Roberts FK, Bennett RM, Caro X, Goldenberg DL, Russell IJ, Yunus MB. Demographics, work disability, service utilization and treatment characteristics of 620 fibromyalgia patients in rheumatologic practice. Arthritis Rheum 1990;33[suppl]:S10

[25] Wolfe F, Anderson J, Harkness D, Bennett RM, Caro XJ, Goldenberg DL, Russell IJ, Yunus MB. Health status and disease severity in fibromyalgia. Results of a six-center longitudinal study. Arthritis Rheum 1997;40(9):1571-9

[26] Ledingham J, Doherty S, Doherty M. Primary fibromyalgia syndrome - An outcome study. Br J Rheumatol 1993;32:139-42

[27] Bruckle W, Muller W. Course and topography of pain in generalized fibromyalgia. J Rheumatol 1991;50:19-28

[28] Hawley DJ, Wolfe F, Cathey MA. Pain, functional disability, and psychological status: A twelve month study of severity in fibromyalgia. J Rheumatol 1988;15:1551-6

[29] Granges G, Zilko P, Littlejohn GO. Fibromyalgia syndrome - Assessment of the severity of the condition 2 years after diagnosis. J Rheumatol 1994;21:523-9

[30] Smythe HA, Moldofsky H. Two contributions to understanding of the "fibrositis" syndrome. Bull Rheum Dis 1977;28(1):928-31

[31] Smythe HA. Nonarticular rheumatism and psychogenic musculoskeletal syndromes. In: Arthritis and Allied Conditions, 11th edition, McCarthy DJ (Ed). Lea & Febiger, Philadelphia, 1989

[32] Hochberg MC. Predicting the prognosis of patients with Rheumatoid Arthritis: Is there a crystal ball? J Rheumatol 1993;20(8):1265-7

[33] Macfarlane GJ, Thomas E, Papageorgiou AC, Schollum J, Croft PR, Silman AJ. The natural history of chronic pain in the community: A better prognosis than in the clinic? J Rheumatol 1996;23(9):1617-20

[34] Crook J. The importance of community based epidemiological studies. J Rheumatol 1996;23(9):1500-1

[35] Buskila D, Neumann L, Vaisberg G, Alkalay D, Wolfe F. Increased rates of fibromyalgia following cervical spine injury. A controlled study of 161 cases of traumatic injury. Arthritis Rheum 1997;40(3):446-52

[36] Hadler NM: The danger of the diagnostic process. In: Occupational Musculoskeletal Disorders, Hadler NM (Ed). New York, NY, Raven Press, 1993, pp. 16-33

[37] Hart FD. Fibrositis (fibromyalgia). A common non-entity? Drugs 1988;35:320-7

[38] Block SR. Fibromyalgia and the rheumatisms. Common sense and sensibility. Rheum Dis Clin North Am 1993;19(1):61-78

[39] Carette S. Fibromyalgia 20 years later: What have we really accomplished? J Rheumatol 1995;22(4):590-4

[40] Robbins JM, Kirmayer LS. Illness, worry and disability in fibromyalgia syndrome. Intl J Psychiatry Med 1990;20:49-63

[41] Hadler NM. Social security. The process of pensioning the invalid. In: Occupational Musculoskeletal Disorders, Hadler NM (Ed), New York, NY, Raven Press, 1993, pp. 227-48

[42] Wolfe F. Fibromyalgia: Whither treatment? J Rheumatol 1988;15(7):1047-9

[43] Buskila D, Press J, Gedalia A, Klein M, Neumann L, Boehm R, Sukenik S. Assessment of nonarticular tenderness and prevalence of fibromyalgia in children. J Rheumatol 1993;20(2):368-70

[44] Pioro-Biossett M, Esdaile JM, Fitzcharles MA. Alternative medicine use in fibromyalgia syndrome. Arthritis Care Res 1996;9:13-9

[45] Drummond MF, Stoddart GL, Torrance GW. Cost analysis in Methods for the Economic Evaluation of Health Care Programmes. Drummond MF, Stoddart GL, Torrance GW (Eds) Oxford University Press, Oxford, 1993, pp. 39-73

[46] Hostetler JA. Amish Society, 3rd Edition. The Johns Hopkins University Press, Baltimore and London, 1980

APPENDIX A
PROCEDURES

A.0 INTRODUCTION

The overall objective of this study was to estimate the prevalence and socioeconomic impact of fibromyalgia syndrome (FMS) in the general population, both

in terms of direct costs and disease burden. Direct costs include medication use and the utilization of health care services. Disease burden included general health, specific health-related problems, and functional and disability status.

This appendix presents the procedures used to collect data in somewhat more detail than that presented in any of the preceding manuscripts (Chapters 2 through 6). Data analysis will be presented somewhat briefly, as it has been covered in greater detail within each manuscript. Appendix B contains a copy of the questionnaires and the data recording forms used in LFES.

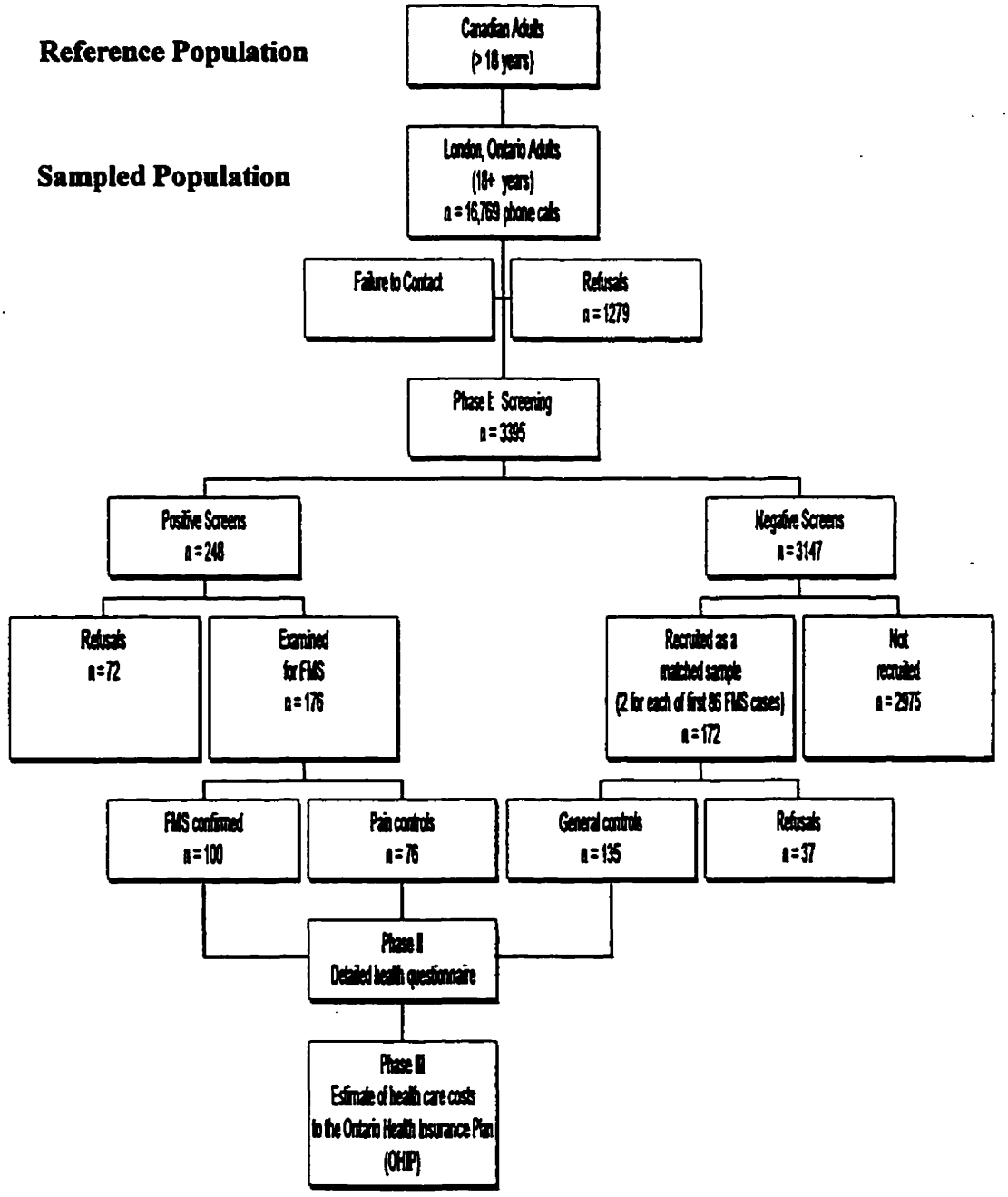
A.1 OVERVIEW

The study was designed as a three phase, cross-sectional point-in-time survey of adults residing in London, Ontario. Phase I was a telephone screening survey to identify possible cases of FMS. In Phase II, individuals who screened positive in Phase I were invited to attend a personal interview and a brief physical examination by a rheumatologist in order to confirm or exclude FMS and to provide additional data. Phase III involved a review of Ontario Health Insurance Program records to allow for an anonymous comparison of FMS cases with age- and sex-matched internal and age-, sex-, and geographically-matched external controls with regards to annual health services costs billed to the provincial insurance plan. Figure A-1 is a flow chart illustrating the overall study design.

FIGURE A-1: Study Design

THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY

POPULATION HIERARCHY



A.2 PHASE I: SCREENING FOR FMS

A.2.0 Objectives

The objectives of Phase I were twofold. First, to identify a sample of individuals who have chronic generalized musculoskeletal pain, and hence could have FMS. Second, to obtain demographic data on the entire survey sample so that demographic data could be compared with the 1991 London city census data.

A.2.1 Selection of Subjects

A.2.1.1 The survey population

The target population was London, a community of 341,020 persons (1991 census) in Southwestern Ontario.[1] Canada's tenth largest city, it is the business, financial and academic hub for a largely agricultural area. Its per capita income is slightly above average, and its unemployment rate slightly below average for Canadian urban centres.[2] London was chosen as the survey site because it is demographically similar, with respect to sex, age and language distribution, to other mid-size Canadian cities and the Canadian population as a whole, excluding Quebec [Table A-1]. Also, London is frequently targeted in marketing surveys, because it is felt to be representative of English Canadian markets.

TABLE A-1: Demographics of all mid-size Canadian cities outside Quebec, 1991 (population 100,000 - 499,999)

City (N = 12)	Population	% female	% < 35 yrs	% > 64 yrs	% English
Halifax	320501	51.3%	56.1%	9.1%	90.1%
Kitchener	356420	50.7%	55.9%	10.2%	79.4%
London	**381522**	**51.7%**	**53.5%**	**12.1%**	**92.4%**
Oshawa	240104	50.3%	56.2%	9.0%	87.3%
Regina	191692	51.2%	56.5%	10.9%	93.9%
Saint John	124981	51.7%	53.5%	12.4%	89.1%
St. John's	171859	51.3%	57.6%	9.3%	95.2%
Saskatoon	210023	51.5%	58.2%	10.3%	93.1%
Sudbury	157610	56.5%	53.0%	10.4%	59.8%
Thunder Bay	124427	50.6%	51.5%	13.3%	91.2%
Victoria	287897	52.1%	45.9%	18.6%	91.7%
Windsor	262075	51.3%	52.1%	12.8%	76.0%
Weighted mean[1]		51.6%	54.1%	11.6%	86.8%
Median		51.3%	54.7%	10.7%	90.7%
London's rank	**1**	**4**	**7**	**5**	**4**
London's difference from mean		0.1%	-0.6%	0.5%	5.6%
London's difference from median		0.4%	-1.2%	1.4%	1.8%

[1] Each percentage weighted by the population of the corresponding community before calculating the mean.

A.2.1.2 The sampling frame

The sampling frame was a computer-generated list of 19,500 seven digit telephone numbers, from the 39 telephone exchanges within London. To create this list, 39 computer files were created, one for each telephone exchange. Within each file, five hundred non-repeating random numbers from '0000' to '9999' were generated. The final list was generated from a programme in which 19,500 numbers were randomly selected from the master list of (39 prefixes x 500 numbers per prefix =) 19500 numbers. Hence, this list included an equal number of numbers with each of the 39 telephone prefixes. This is important, as illustrated in the following example. If twenty-five percent of numbers with the prefix '430' belong to households in which at least one eligible subject resides, then the probability of dialing the number of an eligible subject is twenty-five percent each time a '430' number is dialed. And if ten percent of numbers with the prefix '432' belong to households in which at least one eligible subject resides, then the probability of dialing the number of an eligible subject is ten percent each time a '432' number is dialed. By having an equal number of '430' and '432' numbers within the sampling frame, the probability of contacting any given eligible subject is not affected by the frequency of numbers with a given prefix within the sampling frame, but only by the proportion of numbers with each prefix that belong to eligible subjects. In this way, except for households with no residence phone or multiple phone numbers, the probability of selecting any given household is equal across the sampling population.

This last point can be illustrated with the following example. Household A has one telephone number, with the prefix '433'. Household B also has one telephone number, with the prefix '434'. Assume that every one of the 10,000 numbers with the prefix '433', 433-0000 to 433-9999, had been assigned, each to one household at the time of our survey. The probability of any given household being telephoned by one of our interviewers was 500 (the number of 433 numbers randomly selected for the master list) divided by 10,000 households, which equals 5 percent. Now assume that only 10 percent of the 10,000 numbers with the prefix '434', 434-0000 to 434-9999, had been assigned, each to one household at the time of our survey; hence there are 1000 households with a telephone number with the prefix '434'. The probability is that only 50 active numbers (10%) would be within the master list of 500. The probability of any given household being telephoned by one of our interviewers would have been 50 (the number of 434 numbers randomly selected for the master list) divided by 1000 households, which also equals 5 percent.

A.2.1.3 The sampling unit

The sampling unit was defined as a residence in London with at least one telephone number. Units were selected by random digit dialing (RDD), utilizing the computerized list of random telephone numbers. RDD has the advantages over directory sampling of increasing randomness and accessing unlisted numbers.[3]

After a number had been selected and interviewer-to-person contact made, the initial question asked was: "Have I reached you on a home phone?" A 'No' response resulted in polite termination of the interview. Non-residences which were dialed were not included in data collection, except to record the number of calls in each category, residence versus non-residence, for later inclusion in a response rate table. Included in the definition of non-residence numbers were: 1) not in service numbers, 2) business numbers, 3) fax numbers, 4) dormitories and university residences, 5) hospitals and nursing homes, and 6) car phones.

Two potential biases existed that would have influenced the probability of any given household being selected for interview. First, telephone surveys necessarily eliminate otherwise eligible households with no telephone. This likely would result in under-representation of individuals recently arrived in London, and individuals of lower socioeconomic class. Fortunately, less than two percent of Canadian households have no telephone.[4]

A second potential source of bias is double counting. Double counting occurs when a given household has more than one telephone line. A household with two telephone lines has twice the probability of being randomly selected as a household with only one. Double counting is most likely to occur in higher income households, leading to over-representation of this group. We tried to minimize double counting by classifying car phones and portable phones as non-residence numbers, but were otherwise unable to

eliminate this potential bias. Likely, only a small percentage of London households have more than one telephone line; in Canada, there are 9.6 million telephones categorized as residential and 13.7 million telephones total, compared to 11.2 million households.[5]

A.2.1.4 The sampling element

The eligible sampling element per household was that adult (defined as a person of at least age 18 years) with the most recent birthday as of the date of the initial telephone contact. The birthday method for subject selection has been validated by O'Rourke and Blair.[6] It was decided to choose one respondent per household because of concern over enumerating the prevalence denominator by any other method. By randomly selecting just one resident per household, the denominator becomes the number of households successfully contacted, which is much more easily determined and verified than estimating the sum of adults from all households selected.

A.2.2 **Estimate of Sample Size**

Sample size was calculated to fulfill the two primary objectives of this study: first to achieve a precision of plus or minus 1.0% in the prevalence confidence interval, assuming a true prevalence of FMS in the study population of 2.0%, and that both a 75% Phase I participation rate and a 75% Phase II participation rate could be achieved (with these assumptions, a sample size of 1400 initial contacts was estimated); second, to

identify at least 50 confirmed cases of FMS from the community sample, given the same two participation rate assumptions (a sample size of 4464 initial contacts was estimated).

The decision to confirm 50 cases of FMS was made to permit estimation of mean age with bounds of plus and minus 3 years with 95% confidence, and also to allow for 80% power to detect a $200 or larger difference in annual ministry of health spending between study groups.

Of these two estimates for sample size, the larger was selected and rounded off to 4500. These calculations are included in Figure A-2.

FIGURE A-2: SAMPLE SIZE CALCULATION

A-2.1. Sample size to determine the prevalence of FMS with a precision of plus and minus 1.0 percent for confidence bounds (B)

$$n = \frac{Npq}{(N-1)D + pq}$$

where $N = 381{,}000$ (population of London)

$p = 0.02$ (estimated from results of earlier prevalence studies)

$q = (1 - p) = 0.98$

$D = (B^2/4) = (0.01)^2/4$

$= 0.000025$

$$n = \frac{7468}{9.53 + 0.02} = 782$$

Additional Assumptions:

1. Seventy-five percent Phase I response rate; response rate is defined as the number of subjects who participate in the study divided by the number of subjects with whom actual interviewer contact is made; this 75% estimate is slightly more conservative than the 78.5% response rate reported in the first stage of the study of O'Toole et al.[7]

2. Seventy-five percent Phase II response rate; response rate is defined as the number of subjects who agree to participate in Phase II divided by the total number of positive screen subjects invited to participate; this 75% estimate is slightly more conservative than the 80.0% response rate reported for medical evaluation in the study by O'Toole et al.

Correction Factor:

$CF = 0.75 \times 0.75$ (based on assumptions 1 and 2)

$= 0.56$

Final Sample Size Estimate $= 782/0.56 = 1400$

Figure A-2: Sample Size Estimation (cont'd)

A-2.2. Sample size to identify 50 confirmed cases of FMS.

Assumptions:

1. Prevalence of FMS is 2.0 percent.
2. Correction factor is 0.56. (See above)

Sample Size Estimate:

$$n = \frac{50}{(0.02) \times (0.56)}$$

$$n = 4464$$

A-2.3: Sample size to estimate mean age of confirmed cases of FMS with a precision of plus and minus 3 years for confidence bounds (B).

Assumptions:

1. Variance is 125.1; this was derived from a retrospective chart review of 109 confirmed clinic cases of FMS.

2. Ninety-five percent confidence.

Sample Size Estimation:

$$n = \frac{s^2}{(B/1.96)^2}$$

$$= \frac{125.1}{(3.0/1.96)^2}$$

$$= 53.3$$

A.2.3 **Data Collection**

Data gathering was conducted by telephone interview using trained interviewers. This method was chosen over mailed questionnaire and face-to-face interview for several reasons. The most important reason for choosing the telephone survey method over a mailed questionnaire is to increase control over which person per household is selected as the respondent. The birthday method has been validated as providing a relatively random sample, except for minor disproportion as to month of birth. We were concerned that, despite instructions to the contrary, a self-administered questionnaire would tend to be handed to whomever in a household has the most interest in the questionnaire subject area (for example, someone with chronic musculoskeletal pain and fatigue) rather than to the individual with a most recent birthday; this would result in an overestimation of disease prevalence. Also, persons with limited literacy skills may be reluctant or unable to complete a self-administered questionnaire. Finally, the interviewer-subject rapport that can develop in a telephone survey may improve response rates.

The telephone survey method was chosen over personal interviews because the screening questionnaire was not so long or complicated that it warranted the added expense of or personal risks to in-person interviewers. There was no material that respondents must view to answer questions. Finally, RDD likely results in a more complete sampling frame than a list of London residences.

The major disadvantage to the telephone survey method is that Canadians are becoming inundated with telemarketing disguised as academic research, and are justifiably less trusting of telephone interviews. We attempted to allay this mistrust by clearly stating at each interview's outset the investigators and purposes of the survey. Other procedures to increase response rates, besides using trained interviewers and keeping the questionnaire as brief, interesting and non-threatening as possible, were used:

Before Initial Contact Had Been Made:

1. Data collection was not performed during the last two weeks of December and the first two weeks of July, because of very low response rates reported during those time intervals in the Ontario Health Survey[8].

2. If a selected telephone number was dialed and no one answered, or if the line was repeatedly busy, that number was dialed a minimum of 5 times before declaring it a non-response. These 5 times were at systematically different hours of the day and days of the week, including at least one weekend day. The outcome of each dialing was recorded on a Dialing Record Form (Appendix B).

3. If initial contact was with an answering machine, a brief message was left stating the sponsors of the survey, the survey's intent, and the interviewer's

intended time to call back. The same message was left if initial contact was with someone not eligible to be in the survey, such as a child or baby sitter.

After Initial Contact Had Been Made:

1. If a subject was unable to complete the survey at the time of initial contact, a later time was arranged as per their preference and convenience.

2. Subjects who either were unwilling or unable to respond over the telephone were given the option of having the questionnaire mailed to them. The latter case might have occurred if a subject was willing to participate, but too hearing impaired to complete the survey over the telephone. In fact, this situation did not arise during the course of the survey.

3. Subjects who were uncertain about participating were given the option of telephoning a specific University number to verify the intent of the study, with the understanding that the principal investigator would call back within one week. Several potential subjects were re-contacted in this way, and all later participated in the survey.

A.2.4 **Interviewers and Data Recording**

Interviewers were selected on the basis of the quality of their speaking voices and their experience in the health sciences. Over the course of the study, a total of seven interviewers participated, no more than four at any given time. All were female, between the ages of twenty and forty. To ensure uniformity in data collection, each interviewer was pre-trained in data collection and recording. She was instructed to read the introduction, questionnaire and closing verbatim. Because of inadequate funds to hire translators, subjects who could not understand and speak English were excluded. Answers were recorded by the interviewers on a Phase I Data Record Form (Appendix B). Data collection and recording was monitored on a regular basis. Over the course of the study, the seven interviewers were monitored in person on several occasions during interviews, and the results of their Dialing Record Forms (Appendix B) compared quarterly. Phase I participation rates for the 7 interviewers varied from 69% to 84%, with five of seven between 72% and 75%. There were no appreciable differences in the dialing results (for example, percentage of numbers resulting in business calls) between the 7 interviewers [Table A-2].

All data were edited by the principal investigator (KPW), then entered into a survey-specific data base programme (Epi Info[9]) as soon as possible. Included in Epi Info is a 'check' file to ensure that entered data fits into a reasonable range of data values. Also, a 10% sample of early data was entered into the data base programme twice, which confirmed a rate of data entry error of less than 1.0%.

TABLE A-2: A comparison of seven telephone interviewers

Table A-2: Dialing Record Results - LFES Phase I

	Interviewer Number							
	1	2	3	4	5	6	7	Total
Not in Service #	45.0%	44.0%	41.0%	39.0%	37.0%	38.0%	42.0%	42.0%
Business #	17.0%	14.0%	13.0%	14.0%	16.0%	15.0%	15.0%	15.0%
Ringing/Voice Message/Fax	4.0%	7.0%	12.0%	16.0%	9.0%	16.0%	15.0%	15.0%
Subjects	25.0%	18.0%	18.0%	20.0%	29.0%	17.0%	20.0%	20.0%
Refusals	4.0%	8.0%	6.0%	7.0%	8.0%	11.0%	8.0%	8.0%
non-English	1.0%	1.0%	1.0%	1.0%	0.0%	1.0%	1.0%	1.0%
Other	5.0%	6.0%	6.0%	1.0%	1.0%	2.0%	1.0%	1.0%
Participation rate*	85.0%	71.0%	76.0%	73.0%	79.0%	59.0%	76.0%	74.0%

* The percentage of eligible subjects who participate in the screening survey (= subjects / [subjects + refusals])

A.2.5 **The Screening Questionnaire**

The survey instrument was an 18 item questionnaire [Appendix B] starting with 6 items about pain and fatigue, followed by 1 item each about past history of arthritis and FMS, and 10 items on demographics. The validation of this survey instrument has been presented previously in Manuscript #1, Chapter 2.

A subject who screened negative, but who had responded 'yes' to the question "Have you ever been told, by a doctor or anyone else, that you had a condition called fibrositis or fibromyalgia?", was re-contacted by a rheumatologist (KPW) within 1 week of their initial interview, in order to confirm their earlier responses to the pain and fatigue items. This was done to reduce the risk that previously diagnosed FMS cases who misunderstood the screening questions would be missed. Such a subject who screened positive, upon re-testing within 1 week, was considered a positive screen, and was invited into Phase II. During the course of the study, 70 such subjects (42 female, 28 male) were identified and re-contacted. None of these subjects screened positive upon re-testing.

A.2.6 **Data Entry and Editing**

We developed a Scantron form [Appendix B] to record Phase I data. This eliminated human error in, and reduced costs for data entry, since a data entry clerk would not be required. A pilot study was performed involving four trained interviewers recording data both on a standard data entry form and on a Scantron form. Data from the

standard forms were entered manually by our data entry clerk; Scantron data were entered utilizing an ocular scanner. The error rate for data recording on 30 subjects was identical using the two different forms, at approximately 1.0%. Manual data entry had an error rate also of approximately 1.0%, versus 0.017% using the Scantron form. It was concluded that using the Scantron form would reduce the overall error in data entry and recording.

Passing completed Scantron forms through the ocular scanner resulted in a data file, which was edited by the principal investigator (KPW) using a DOS editor.

A.3 PHASE II: CONFIRMING FMS, DATA COLLECTION

A.3.0 Objectives

The first objective of Phase II was to confirm or exclude the diagnosis of FMS among subjects who had screened positive in Phase I. This would result in two study groups: first, positive screens in whom FMS has been confirmed (FMS cases, FC); and second, positive screens in whom FMS has been excluded (pain controls, PC). A second objective was to generate a third study group, consisting of general population controls matched with FMS cases for age and sex.

The final objective was to collect data from subjects in all three groups on demographics, on symptom prevalence, onset and severity, on functional and work

disability status, and on medication and health services utilization, to allow for group comparisons.

A.3.1 **Selection of Subjects**

All subjects who screened positive in Phase I were invited to participate in Phase II, to be evaluated by one of two rheumatologists (KPW and MH) in the outpatient rheumatology clinic at University Hospital, and to complete a detailed questionnaire. Interviewers were trained to identify positive screens at the time of the initial interview, and to invite such subjects to participate in Phase II. This timing was chosen to reduce losses to follow-up, and to take advantage of the rapport developed between subject and interviewer during the interview.

Subjects who agreed to participate in Phase II were re-contacted within 2 weeks by the principal investigator (KPW). Again, the nature of their proposed participation in Phase II was explained. If a subject gave verbal consent, an appointment was scheduled for as soon as possible (usually within 1 month), at a time most convenient to them, including evenings and weekends. To further improve participation rate, subjects were informed that they would be reimbursed for all transportation and parking expenses relating to the Phase II appointment. During the course of the study, two recruited subjects moved away from London after having been recruited in Phase I and having screened positive. Both were offered full travel expenses to and from University Hospital, and both participated in Phase II. Each subject who agreed to participate in

Phase II was given two telephone numbers to call, should they have questions or concerns, and given detailed directions to the outpatient clinic. Subjects were reminded of their appointment by telephone the evening prior to that appointment.

In addition, for each case of FMS confirmed in Phase II, two randomly selected age- and sex-matched internal controls were recruited into Phase II, by the following method. Given age and sex data on a given confirmed case of FMS, each interviewer was instructed to recruit the next two age- and sex-matched respondents who screened negative in Phase I. If a subject refused, the next matched respondent was asked to participate, and so on until two subjects agreed. This was done to ensure two matched internal control subjects recruited for each confirmed case of FMS. Controls were not required to attend the University Hospital outpatient clinic, but were asked to complete a questionnaire that was mailed to them within two weeks, accompanied by an introductory letter, an information letter and consent form, and a pre-addressed, pre-stamped envelope. Subjects who had not returned the completed questionnaire were re-contacted by telephone within three weeks by the principal investigator. At that time, they were asked if they intended to return the questionnaire, and if they had any questions with respect to it.

A.3.2 **Data Collection**

Each subject first was interviewed by a rheumatologist to confirm their responses to the Phase I survey. The rheumatologist then obtained a brief medical history to identify other musculoskeletal and non-musculoskeletal disorders.

After the medical history, the rheumatologist performed a brief musculoskeletal examination, consisting of an examination of hands and any painful peripheral joints, and digital palpation for tenderness at the eighteen fibromyalgia points specified by the American College of Rheumatology (ACR).[10]

After the examination, subjects completed a more detailed Phase II Health Questionnaire (Appendix B), asking about disease symptoms, symptom onset and severity, medication use, health services utilization, functional status and disability status. This questionnaire consisted of questions selected from the Ontario Health Survey about demographics, two week and one year disability, medication use and health services utilization, in addition to several disease-specific questions about FMS. Functional status was assessed using published pre-validated questionnaires: the mobility and agility indices from the 1986 Health and Activity Limitation Survey (HALS)[11] and the Fibromyalgia Impact Questionnaire (FIQ).[12]

This same Phase II Health Questionnaire was mailed to all subjects in the internal control group, with the exception of Part II, Section One, which deals with pain and

fatigue.

A.3.3 **Data Editing and Entry**

All Phase II data were edited by the principal investigator prior to data entry. For subjects who attended the University Hospital clinic, the questionnaire was reviewed in the presence of the subject, to confirm that no question had been skipped unintentionally, and that all questions had been answered correctly. On those occasions where a numerical answer was given as a range, the subject was asked to specify a single whole number; if the subject could not specify a single whole number, or in the case of questionnaires returned by mail (general controls) the mean of the range was recorded. If the mean was not a whole number, then a coin flip determined if the answer was rounded up to the nearest whole digit (heads) or down (tails); this was done to reduce the risk of biasing numerical responses up or down.

In those instances where a response was not recorded and not retrievable, a missing value was entered, except in the case where the answer could be logically inferred from another recorded response. For example, if a subject had not seen any specialists over the preceding twelve months, then it was assumed that the same subject could not have seen a specialist over the preceding two weeks.

After initial editing, data were entered by a trained data entry clerk into the statistical programme Epi Info. After data entry, the principal investigator re-edited the data in the DOS editor to ensure that missing data were accounted for.

A.4 RELIABILITY AND VALIDITY OF THE DATA

The reliability of data collection was enhanced by several methods. Interviewers were monitored during data collection by an independent observer at random intervals; 20 interviews were selected randomly for monitoring from the first hundred performed by each interviewer, and thereafter 50 of each thousand. Test-retest reliability was estimated by having two different interviewers contact the same 50 subjects one month apart, using the same questionnaire; these 50 subjects were randomly selected from the first 200 participants. Epi Info possesses a check file that ensures reliability of data entry by checking data for acceptable ranges, and by permitting double entry of data. A random 10% of data was double entered.

The content validity of both the Phase I and the Phase II questionnaires was reviewed by two epidemiologists with expertise in population studies and two rheumatologists with expertise in fibromyalgia. As much as possible, pre-validated questions from the O.H.S. and H.A.L.S. were used. The FIQ questionnaire also has been validated in the literature. Criterion-related validity was determined for the screening questionnaire at pre-testing, when sensitivity and specificity were found to be 93.3% and

between 80.0% and 100%, respectively.

The face validity of the Phase I questionnaire was tested in two pilot studies, one by personal interview, one by telephone survey, when none of 30 and 15 subjects, respectively, found any difficulty understanding any item or any word.

Each subject who screened positive had FMS confirmed or excluded by one of two rheumatologists who were blinded to the Phase I survey result. Inter-rater agreement between the two rheumatologists on the presence or absence of FMS was optimized by pre-training using a standardized dolorimeter. A pilot study was performed to estimate the Kappa statistic for inter-rater agreement on 25 subjects, recruited consecutively in the outpatient rheumatology clinic at University Hospital; a kappa of 0.70 was considered satisfactory; a lower result would obligate retraining. Of 25 recruited subjects, 12 had FMS and 13 had other rheumatic disorders. Each rheumatologist was blinded to the diagnosis rendered by the other examiner. Using the 1990 American College of Rheumatology classification criteria for fibromyalgia, there was agreement between the two examiners on all 25 subjects (kappa = 1.00).

A.5 PHASE III: ESTIMATING HEALTH SERVICES UTILIZATION

A.5.0 Objectives

The primary objective of Phase III was to estimate the annual utilization of health care services, and thereby the direct costs to the Ministry of Health per confirmed case of FMS, as compared to two internal and one external control group.

A.5.1 Selection of Subjects

All confirmed cases of FMS, pain controls and general controls who participated in Phase II were asked for consent to participate in an anonymous group comparison of annual health services costs to the Ontario Health Insurance Plan (O.H.I.P.). An external control group was randomly selected from the O.H.I.P. database, four age-, sex-, and geographically-matched subjects for each confirmed case of FMS.

A.5.2 Data Collection

A list of confirmed FMS cases and internal control subject names and O.H.I.P. insurance numbers was mailed, with accompanying letters of consent, to the Ministry of Health. The detailed claims file was entered to access all individual billing claims for the twelve months of 1994. The year 1994 was selected as the year prior to Phase II data collection, since the first Phase II subjects were examined in January of 1995. An

external control group was randomly constructed from the claims file, four subjects matched for age, sex and the London geographic area for each confirmed case of FMS.

For each subject in each of the four groups (FMS cases, pain controls, general controls and external controls), health care utilization for the year 1994 was calculated as the sum of all billing claims, including consultation fees, hospital fees, procedure fees, and laboratory expenses. The sum of costs for all subjects in each group was divided by the number of subjects in that group to determine the mean subject health services expenditure for the year 1994.

A.6 DATA ANALYSIS

A.6.0 Overview

To avoid the effect of multiple testing on the Type I error rate, analysis was restricted to a *priori* hypotheses. Post-hoc analyses were performed only when overall between group differences were observed. All data were analyzed using the statistical software program Epi Info Version 6, SPSS 6.1[13] or SAS 6.12.[14] Regression models were tested using both forward and backward methods, to ensure that each model was robust.

A.6.1 Validation of the Survey Sample

Because Phase I utilized a computer-generated list of random telephone numbers, it was assumed that a significant number of these numbers would be non-eligible. Non-eligible numbers were categorized by reason for ineligibility, and a table constructed of these results [See Table A-2, page 201].

In order to have confidence in the generalizability of our survey results, the demographic profile of respondents was compared to 1991 London census data for adults aged 18 and over, by constructing sex-adjusted graphs of age distribution. More than sixty percent of our survey sample (2090 of 3395) were female, which is a considerably greater percentage than the percentage of adults recorded as female in the 1991 London census. This sex distribution is similar to that reported in other Canadian surveys.[8,11] Our sample was very representative with respect to age, however (Table A-3). All analyses were adjusted for sex, where appropriate.

A.6.2 Validity and Reliability of the Screening Instrument

As previously discussed, the test-retest reliability of the screening questionnaire was examined in the first quarter analysis of Phase I data, and was found to be 100% for negative screens. Thus we could be 100% confident (C.I. 93.2%, 100%) that no subjects

falsely screened negative because of week-to-week differences in their responses. Further discussion of the reliability and validity of the screening instrument is in Chapter 2.

TABLE A-3: A comparison of the survey sample with 1991 London census data by age

TABLE A-3: Sex and age distribution of the LFES telephone survey sample (Phase I) compared to the 1991 London census.

Males	London		LFES		Difference
20-24[1]	13885	11.8%	186	15.2%	3.5%
25-29	15980	13.5%	163	13.4%	-0.1%
30-34	15110	12.8%	148	12.1%	-0.7%
35-39	13425	11.4%	147	12.0%	0.7%
40-44	12370	10.5%	141	11.6%	1.1%
45-49	9515	8.1%	94	7.7%	-0.4%
50-54	7770	6.6%	89	7.3%	0.7%
55-59	6965	5.9%	60	4.9%	-1.0%
60-64	6730	5.7%	44	3.6%	-2.1%
65-74	10570	9.0%	94	7.7%	-1.3%
75+	5695	4.8%	53	4.3%	-0.5%
	118015	100.0%	1220	100.0%	0.0%

Females	London		LFES		Difference
20-24[1]	14435	11.0%	241	12.0%	1.1%
25-29	16755	12.7%	221	11.0%	-1.7%
30-34	16060	12.2%	231	11.5%	-0.7%
35-39	14475	11.0%	275	13.7%	2.7%
40-44	13075	9.9%	199	9.9%	0.0%
45-49	10035	7.6%	161	8.0%	0.4%
50-54	8070	6.1%	116	5.8%	-0.3%
55-59	7465	5.7%	88	4.4%	-1.3%
60-64	7305	5.6%	112	5.6%	0.0%
65-74	13470	10.2%	218	10.9%	0.6%
75+	10460	7.9%	143	7.1%	-0.8%
	131605	100.0%	2005	100.0%	0.0%

[1] Table excludes subjects 18-19 years old, because there are no accurate census data readily available containing this information.

A.6.3 **Estimate of Point Prevalence**

The details of the point prevalence estimates for males and females are presented in Chapter 3.

To estimate point prevalence, one major assumption had to be accepted or rejected, which could affect greatly the final estimate. It is that the only cases of FMS in the eligible sample were those cases that actually were confirmed by examination. This assumption is composed of three minor assumptions: first, that there were no cases of FMS among the 1279 eligible subjects who refused to participate in the Phase I screening interview; second, that there are no individuals with FMS among the 3147 subjects who screened negative for chronic widespread pain in Phase I; and third, that there are no individuals with FMS among the 72 eligible subjects who screened positive for chronic widespread pain in Phase I, but refused to participate in the Phase II examination. These three minor assumptions combined result in an estimate of FMS equal to the equation A.6.3.1:

A.6.3.1 (confirmed cases of FMS) / (total eligible subjects) x 100%

This produces a minimal (conservative) estimate of point prevalence; the true value of point prevalence could be no lower than the lower bound of this estimate.

The first minor assumption, that there are no individuals with FMS among the 1279 eligible subjects who refused to be interviewed in Phase I, accounts for the possibility that individuals with pain, and therefore potentially with FMS, would be more likely to agree to participate in a survey asking about pain. However, this assumption must be rejected for several reasons. First, it is impossible to adjust this estimate of point prevalence for age and sex, since the age and sex of the 1279 eligible subjects who refused to be interviewed in Phase I is unknown. Secondly, although it may be that individuals with pain would be more likely to agree to participate in a survey asking about pain, this does not mean that all persons with pain will participate. In fact, many may choose not to participate because their pain makes it difficult for them to spend time on the telephone. Also, all of our interviewers reported that the large majority of the eligible subjects who refused to participate in Phase I did so before the interviewer had had an opportunity to mention the intent of the survey; these individuals likely would not have known that they would be asked questions about pain.

In rejecting this assumption, it was decided to eliminate eligible subjects who refused to participate in Phase I from the denominator in the estimate of point prevalence. This results in the estimate of point prevalence A.6.3.2:

A.6.3.2 (confirmed cases of FMS) / (total Phase I participants) x 100%

The second minor assumption, that there are no individuals with FMS among the 3147 eligible subjects who screened negative for chronic widespread pain in Phase I, is

supported by the requirement for chronic widespread musculoskeletal pain in the 1990 ACR criteria we utilized to define FMS, and by the test-retest reliability of 100% we found among persons who screened negative.

The third minor assumption, that there are no individuals with FMS among the 72 eligible subjects who screened positive for chronic widespread pain in Phase I, but refused to participate in the Phase II examination, accounts for the possibility that persons with FMS might be more likely to agree to be examined than persons without FMS. This is supported by our own results, that approximately 70% of FMS cases were undiagnosed prior to the Phase II examination; hence these individuals might be highly motivated to obtain a explanation for their symptoms. Second, persons with FMS had worse symptoms, more dissatisfaction with their health, and more functional limitations than persons without FMS but with chronic widespread pain; this also could result in higher motivation to potentially obtain an explanation through participating in Phase II. Also, because the age and sex is known for virtually all subjects who screened positive, there would be no difficulty in adjusting for age and sex.

Conversely, several subjects who screened positive refused to participate in Phase II because they had already had the diagnosis of FMS confirmed. Others refused to participate because they were in too much discomfort to travel to University Hospital. This suggests that FMS may actually have prevented some eligible subjects from being examined to confirm or exclude FMS. Because it is impossible to determine the degree to which FMS itself enhanced or diminished an eligible subject's likelihood to participate

in Phase II, we assumed that the proportion of persons with FMS was the same in eligible subjects who did not participate in Phase II as it was in eligible subjects who did participate. This is supported by our results that show that Phase II participants and non-participants were not demographically different, nor were they different with respect to the distribution of their pain, or the presence and severity of fatigue; these results are discussed in Chapter 3. Rejecting the third minor assumption results in the following estimate of point prevalence, equation A.6.3.3:

A.6.3.3: (confirmed FMS cases + (p x Phase II refusals)) / (total Phase I participants) x 100%

where p = the proportion of Phase II participants in whom FMS has been confirmed

After direct age standardization, using the 1991 London census as the reference population, a further adjustment was made, weighting subjects by the number of adults residing in each particular household. This was done to reduce the risk of over-estimating FMS prevalence in the elderly, who would be most likely to reside alone. Ninety-five percent confidence intervals were constructed for the prevalence of FMS in the general adult population, using the logit transformation of the proportion, to correct for a proportion approaching zero.[15]

A.6.4 Estimate of Lifetime Prevalence

The lifetime prevalence of FMS is the proportion of individuals in a population who will develop this condition in their lifetime. Prevalence for females and for males within each decade of life was calculated using Phase I and Phase II data and data from the 1991 London census. A graph of prevalence by decade of life was constructed for each sex. If FMS is presumed to be a chronic, non-remitting, non-fatal disorder, then the prevalence should increase steadily throughout life.

A.6.5 Measures of Demographics and General Health

The demographic profile of confirmed cases of FMS was examined, including sex, mean age, marital status, education level, employment status, and annual household income. Data on these variables were compared with corresponding data from the survey sample, using Analysis of Variance (ANOVA) for continuous data, Pearson's Chi-squared for nominal data, and the Mann-Whitney test for ordinal data.

Subjects in Phase II were categorized into Group 1) FMS Cases, subjects who met the 1990 ACR criteria for FMS; and two internal control groups: Group 2) Pain Controls, subjects in whom FMS had been excluded after screening positive in Phase I; and Group 3) General Population Controls, subjects randomly entered as internal controls into Phase II who screened negative in Phase I, age- and sex-matched for each confirmed FMS case.

General health measures including satisfaction with health, satisfaction with life, level of happiness, degree of pain, and level of life stress were compared for FMS cases (Group 1), each of the two internal control groups (Groups 2 and 3), and an age- and sex-matched sample from the OHS, using the Mann-Whitney test for ordinal data.

A.6.6 **Measures of Specific Symptoms**

Student's t-test was performed to test the null hypothesis that FMS cases have no more pain and no more fatigue on 100 millimeter visual analog scales than Pain Controls.

Odds ratios were constructed to see which other symptoms on a 42-symptom check list were more common among FMS cases than among Pain Controls.

A.6.7 **Estimate of Functional and Work Disability Status, and Healthy Years of Life Lost (HYLL)**

The Fibromyalgia Impact Questionnaire (FIQ) is a ten item instrument that asks about abilities to perform various household tasks, about how well the individual has felt, about how many days have been missed from work, and about the severity of pain, fatigue, anxiety and depression, all within the context of the preceding seven days.[16] Items are weighted equally and summed to produce a total (FIQ) score, from zero to 10; the higher the score, the greater the impact of FMS symptoms upon that individual.

Internal groups 1, 2 and 3 were compared with respect to their mean FIQ score, using Analysis of Variance (ANOVA) to identify differences, and Scheffe's test to identify where group differences lie; Scheffe's test was used because of the different sizes of the three subject groups.

The Health Activities and Limitations Survey (HALS) mobility and agility indices[17] together are comprised of ten items asking about an individual's ability to perform various activities of daily living (ADL); each item consists of three questions, in order to determine the degree of difficulty one has with a particular ADL, and how long that difficulty has existed. Each item is weighted equally as zero (no difficulty) to 1 (unable to do).

Mean Quality Adjusted Life Years (QALY) were calculated for the FMS cohort and each of the two internal control cohorts, utilizing individual scores on the 10 HALS mobility and agility indices, the unadjusted 1991 Standard life table for Canadians,[18] and the description of marker states from the Musculoskeletal Health Status Classification Scheme in accordance with the method described by Reynold's et al.[19] Healthy Years of Life Lost were calculated for each group, as the difference between the group mean expected life expectancy and the group mean QALY.

Work disability status was ascertained from responses to two specific questions on the Phase II questionnaire: 1) asking if a person considers him/herself totally disabled and 2) asking if that individual is currently working. Subjects who considered

themselves totally disabled and who were not working were defined as `work disabled'. The proportion of individuals in each internal group (Groups 1, 2 and 3) were compared using Pearson's Chi-Square Analysis.

A.6.8 **Estimate of Medication and Health Services Use**

The Phase II Questionnaire contains all of the questions from the Ontario Health Survey (OHS) on health services and drug utilization. This includes questions on one year and two-week recall with respect to visits to the spectrum of health professionals, including general physicians, specialist physicians, nurses, therapists, chiropractors, psychologists, councilors and social workers, as well as a listing for 'other' health professionals. It includes questions on use of hospital services, including emergency and inpatient services. It includes questions on 2 week and 1 months recall with respect to use of prescription and non-prescription medications. These data were analyzed so as to calculate an overall mean estimate of health services utilization (excluding laboratory and radiograph services) for each of the three internal control groups in terms of 1995 Canadian dollars, and these means were compared with an age and sex-matched sample from the OHS database using ANOVA and Scheffe's test.

Phase III data were used to compare 1994 mean annual health services costs to the Ontario Health Insurance Plan (O.H.I.P.) for each of the three internal study groups as well as an O.H.I.P. supplied external cohort of age-, sex-, and geographically-matched controls, again using ANOVA and Scheffe's test.

A.6.9 **Regression Analysis of Functional Status and Work Disability**

Simple multiple regression analysis was performed, with the FIQ score as the dependent variable, and demographic, symptom, and functional status measures as independent variables, to see which variables contribute significantly to variance in functional status.

Logistic regression analysis was performed, with work disability status as the dependent variable, defined as zero (not disabled) or '1' (disabled). Again, demographic, symptom, and functional status measures were the independent variables.

For each model, the cutoff for each variable was set at 0.05. Analysis was performed both by backward elimination and forward selection methods, to ensure that each model was resistant to changing the statistical programme and regression method used.

REFERENCES

[1] Statistics Canada, Profiles Census Canada 1991: London Part I, Ottawa, 1993

[2] The 1997 Canadian Global Almanac, Colombo JR (Ed); MacMillan Canada, Toronto, 1997, pp. 41

[3] Lepkowski JM. Telephone Sampling Methods in the United States. In: Telephone Survey Methodology. Groves RM, Biemer PP, Lyberg LE, Massey JT, Nicholls WL, Waksberg J (Eds). John Wiley and Sons, New York, 1988

[4] The 1997 Canadian Global Almanac, Colombo JR (Ed); MacMillan Canada, Toronto, 1997: page 84

[5] The 1997 Canadian Global Almanac, Colombo JR (Ed); MacMillan Canada, Toronto, 1997: page 224

[6] O'Rourke D, Blair J. Improving Random Respondent Selection in Telephone Surveys. J Marketing Res 1983;20:428-32

[7] O'Toole BI, Battistutta D, Long A, Crouch K. A Comparison of Costs and Data Quality of Three Survey Methods: Mail, Telephone and Personal Home Interview. Am J Epidemiol 1986;124:317-28

[8] Badley EH, Yoshida K, Webster G, Stephens M. Ontario Health Survey 1990. Working Paper No. 5: Disablement and Chronic Health Problems in Ontario

[9] Dean AG, Dean JA, Burton AH, Dicker RC. Epi Info Version 5: a word processing, database, and statistics program for epidemiology on microcomputers. USD, Incorporated, Stone Mountain, Georgia, 1990

[10] Wolfe F, Smythe HA, Unus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, Fam AG, Farber SJ, Fiechtner JJ, Franklin CM, Gatter RA, Hamaty D, Lessard J, Lichtbrown AS, Masi AT, McCain GA, Reynolds WJ, Romano TJ, Russell IJ, Sheon RP. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum 1990;33:160-72

[11] Statistics Canada. Health and Activity Limitation Survey - 1991 User's Guide

[12] Burckhardt CS, Clark SR, Bennett RM. The fibromyalgia impact questionnaire: Development and validation. J Rheumatol 1991;18:728-33

[13] SPSS for Windows, Release 6.1 (24 Jun, 1994) Copyright © SPSS Inc., 1989-1994

[14] SAS for Windows, Release 6.12, Copyright © 1989-1996, Cary, NC, USA

[15] Rochon J. The Application of the GSK Method to the Determination of Minimum Sample Sizes. Biometrics 1989;45,193-205

[16] Burckhardt CS, Clark SR, Bennett RM. The Fibromyalgia Impact Questionnaire: Development and Validation. J Rheumatol 1991;18(5):728-33

[17] Statistics Canada. Health and Activity Limitation Survey. A User's Guide. Ottawa, Ontario: Statistics Canada, 1989

[18] Statistics Canada. Detailed life tables, Ontario, 1990-1992, males and females. Life Tables, Canada and Provinces 1990-1992; Cat. No. 84-537:22-5

[19] Reynolds D, Torrance G, Badley E, Bennett KJ, Chambers L, Goldsmith CH, Jamieson E, Tugwell P, Wolfson MC. Modeling the Population Health Impact of Musculoskeletal Diseases: Arthritis. J Rheumatol 1993;20(6):1037-47

THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY (LFES)

APPENDIX B

Table of Contents

Page

THE SCREENING QUESTIONNAIRE

Page 1

Opening Statement

Hello.
Have I reached *(7 digit number)*?

Yes ❑ Have I reached you at home?	No ❑ I'm sorry. I have misdialed. Goodbye. (Hang up)
Yes ❑ (see statement below.)	No ❑ I'm sorry. I am looking for a household. Goodbye. (Hang up)

This is _ *(your name)* from the University of Western Ontario. I am speaking on behalf of the London Fibromyalgia Epidemiology Study, a research group in the Departments of Medicine and Epidemiology at the University. Right now we are conducting a very brief telephone survey in London to find out some things about arthritis and rheumatism. Your telephone number was selected completely at random. We are not selling anything, and we are not asking for money. The questions we are asking are very important, because we are studying a type of rheumatism that appears to be very common. We would just like to ask a few questions that will take about five minutes to answer.

To do this, what I'd like to do is speak to the person, currently living in your home, who has had the most recent birthday. He or she must be at least 18 years old. Who would that be?

(If all birthdays not known) Of the birthdays you know, who has had the most recent birthday?

Can I speak to that person?

<u>If available</u>	<u>If unavailable</u>
(See statement below.)	What would be a good time to catch him/her?

Page 2

This is _ *(your name)* from the University of Western Ontario. I am speaking on behalf of a research group in the Departments of Medicine and Epidemiology at the University. Right now we are conducting a very brief telephone survey in London to find out some things about arthritis and rheumatism. Your telephone number was selected completely at random from the phone book. We are not selling anything, and we are not asking for money. The questions we are asking are very important, because we are studying a type of rheumatism that appears to be very common. We would just like to ask a few questions that will take about five minutes to answer. If you agree to answer them, confidentiality will be respected at all times; your answers will be recorded without using your name, and your name will never appear when we publish the results of our survey; results will be published for those who respond as a whole.

Do you have time to answer these questions now, or would it be better that I call back at another time?

If now	If later
(Proceed to questionnaire)	What would be a better time to catch you?

Page 3

Screening Health Questionnaire

Date_____ **Subject #**_____ **Interviewer #**_____
dd/mm/yy

PART A

As I mentioned earlier, our main purpose in this survey is to find out about arthritis and rheumatism. The first few questions deal with whether or not you have any type of arthritis or rheumatism pain.

1. **In the past three months have you had pain in muscles, bones or joints that has lasted more than one week?** Yes / No

   If No, skip to Question 5.

I would like to find out about where you have had pain in the past three months? I would like you to answer yes or no to each of these questions.

2. **Have you had pain in your shoulders, arms or hands?** Yes / No
   (If Yes): On which side: your right side, your left side or both sides of your body?

3. **Have you had pain in your in your legs or feet?** Yes / No

   (If Yes) On which side: your right side, your left side or both sides of your body?

4. **Have you had pain in your neck, back or chest?** Yes / No

---

I would now like to ask some questions about tiredness or fatigue.

5. **Over the past three months have you often felt tired or fatigued?** Yes / No

   If No, skip to Question 7.

---

6. **Does this tiredness or fatigue <u>significantly</u> limit your activities?** Yes / No

7. **Have you ever been told, by a doctor or anyone else, that you had some form of arthritis?** Yes / No

8. **Have you ever been told, by a doctor or anyone else, that you had a condition called fibrositis or fibromyalgia?** Yes / No

---

PART B

It is important that I obtain a little bit of information about each of person who completes this survey in order to group your answers with other people who are similar to you. So the last few questions are about yourself.

9. **Because we are speaking over the phone and I can't see you, to make positively sure I have to ask you this question. Are you are a man or a woman?**

10. **In what year were you born?** _____

11. **In what month is your birthday?** _____

12. **Which of the following answers describes you?**

    1. Never married.
    2. Married right now, including common law marriage.
    3. Married before, but now separated or divorced.
    4. Widowed.
    5. Other. Can you explain?

13. **Including children, how many people live in your household?**

In our study, we are interested in whether or not your working situation affects your risk of having arthritis or rheumatism. I have just a couple of questions about your working situation.

14. **What has been your main activity during the last 12 months?**

    1. Working at a job.
    2. Looking for work.
    3. Going to school.
    4. Keeping house.
    5. Retired.
    6. Other (Could you explain?)

    Let me repeat that list for you.

Page 5

15. **During how many of the last 12 months have you been working?**
_____ (0-12)

16. **Was the work mostly full-time or mostly part-time?**

1. Full-time.
2. Part-time.

Another one of the reasons for our study is to see if how much schooling a person has had effects how likely they are to get arthritis or rheumatism. To do this, I would just like to ask you about your level of schooling.

17. **What is the highest level of education you have completed? I will give you a list of choices.**

1. Did not finish high school.
2. Completed secondary or high school.
3. Attended community college, technical college, CEGEP,or a nursing programme.
4. Some university, not completed.
5. A university degree.
6. Other. Can you please explain.

Let me repeat that list for you.

I have one final question. We are interested in seeing if a person's level of income affects how likely they are to get arthritis or rheumatism. To do this, I would just like to ask you, in general terms, how much money your household made, including everybody's work, pensions, disability cheques and so on, in the past year. I'll give you a list to choose from, so you don't have to be specific. The question is:

18. **How much money did your household make in the past year? Here is the list of choices.**

1. No income
2. Less than $12,000.
3. At least $12,000, but less than $30,000.
4. At least $30,000, but less than $60,000.
5. At least $60,000, but less than $80,000.
6. $80,000 or more.
7. Don't know or can't say.

I'll repeat the list.

Closing Statement for Subjects who Screen Negative

I would like to thank you very much for taking the time to answer all of these questions. This thanks comes not only from me, but also from all of the persons on our research team at the University of Western Ontario. I hope you have a very nice day.

Closing Statement for Subjects who Screen Positive

I would like to thank you very much for taking the time to answer all of these questions. This thanks comes not only from me, but also from all of the persons on our research team at the University of Western Ontario.

One final thing is that, based upon your answers to the questions I asked about pain and fatigue, you are of extreme interest to us. Would you be willing to come to University Hospital to be seen in our clinic by two specialists in arthritis and rheumatism? Before you answer, let me tell you what it would involve. To start with, the whole visit would take about one hour and we would reimburse you for transportation and parking costs. We would arrange a time to suit your time schedule, including evenings or weekends. You can come with a family member or friend if you would like. The visit would include a brief medical examination of your muscles and joints by a specialist. There are no needles or instruments used. Then you would be asked to complete a written questionnaire. The questionnaire would take approximately one half hour to complete.

Would you be willing to participate in that part of our study?

If yes:

I will need to have your full name so that our secretary can call you to arrange a time for your visit to our clinic.

Again, I'd like to thank you very much for taking the time to answer all of our questions, and for agreeing to visit our clinic. Our secretary will call you in the next few days to arrange a time. What is the best time of the day for her to call you?

Thank you. Goodbye.

If no:

Again, I would like to thank you very much for taking the time to answer all of our questions. I hope you have a very nice day. Thank you. Goodbye.

DIALING RECORD FORM

DATE: _____ **OPERATOR:** _____

Telephone Number	Attempt AM	PM	HS	WE	FNL	Notes	Result
1.						ans machine adults out ringing message	not in svc business # refused sbjt#
2.						ans machine adults out ringing message	not in svc business # refused sbjt#_____
3.						ans machine adults out ringing message	not in svc business # refused sbjt#_____
4.						ans machine adults out ringing message	not in svc business # refused sbjt#_____
5.						ans machine adults out ringing message	not in svc business # refused sbjt#_____
6.						ans machine adults out ringing message	not in svc business # refused sbjt#_____
7.						ans machine adults out ringing message	not in svc business # refused sbjt#_____
8.						ans machine adults out ringing message	not in svc business # refused sbjt#_____
9.						ans machine adults out ringing message	not in svc business # refused sbjt#_____
10.						ans machine adults out ringing message	not in svc business # refused sbjt#_____

PHASE I DATA RECORD FORM

Screening Health Questionnaire

Date _____ **Subject #**_____ **Interviewer #**_____
dd/mm/yy

Time contacted: a.m. ❑ afternoon ❑ p.m. ❑

PART A

1.	**Pain in past 3 months**	Yes	❑	No	❑	
2.	**Shoulders, arms or hands?**	Yes	❑	No	❑	
	Which side?	Right	❑	Left	❑	Both ❑
3.	**Legs or feet?**	Yes	❑	No	❑	
	Which side?	Right	❑	Left	❑	Both ❑
4.	**Neck, back or chest?**	Yes	❑	No	❑	
	i. **Meets Pain criteria**	Yes	❑	No	❑	
5.	**Fatigue?**	Yes	❑	No	❑	
6.	**Fatigue limiting activities?**	Yes	❑	No	❑	
7.	**Arthritis?**	Yes	❑	No	❑	
8.	**Fibromyalgia?**	Yes	❑	No	❑	

PART B

9.	**Month born** _____							
10.	**Year born** _____							
11.	**Sex**	1. **Male** ❑		2. **Female** ❑				
12.	**Marital status**	**1**	**2**	**3**	**4**	**5**		
13.	**Number in household**	_____						
14.	**Employment status**	**1**	**2**	**3**	**4**	**5**	**6**	
15.	**Months working in past year**	_____						
16.	**Full-time/part-time**	**1**	**2**					
17.	**Schooling**	**1**	**2**	**3**	**4**	**5**	**6**	
18.	**Household income**	**1**	**2**	**3**	**4**	**5**	**6**	**7**

The London Fibromyalgia Study (LFES)

Information Letter

You have been asked to participate in this study so that researchers at University Hospital can learn more about a condition called fibromyalgia syndrome or fibrositis. You have been selected because of your responses to questions about pain and fatigue in a recent telephone interview.

If you decide to participate, it will involve about one hour of your time. During that hour, a rheumatologist (arthritis specialist) will ask you some health questions, and then will perform a very brief examination of your hands and the muscles around your neck, elbows, low back and hips, and knees. During this examination, no needles or instruments will be used. After the examination, you will be asked to complete a 25 page written questionnaire, that will take about 30 to 40 minutes to finish.

The findings on examination and your responses to all questions will be kept strictly confidential, by labelling your records only by a number (not your name), and storing them in a locked room.

Should you decide not to participate, this will not affect your future care at University Hospital in any way.

Please feel free to ask questions before signing the attached consent form.

Kevin P. White, M.D.
Mark Speechley, Ph.D.
Manfred Harth., M.D.
Truls Ostbye, M.D., M.P.H.

Consent Form

I have read the attached information letter regarding the London Fibromyalgia Epidemiology Study (LFES) and agree to participate.

_____ _____

Name Date

_____

Witness

PHASE II HISTORY AND PHYSICAL EXAMINATION

Subject #_____ **Group #:** **1 (FMS case)**
2 (Pain control)
3 (General control)

Examiner **1 KW**
2 MH **Date_____**

Sex: **1. Male** **2. Female**

Birthdate: **Day____** **Month ____** **Year____**

Age: **____Years**

PAIN AND FATIGUE

The first few questions deal with whether or not you have any type of arthritis or rheumatism pain.

1. **In the past three months have you had pain in muscles, bones or joints that has lasted more than one week?**

   Yes ❑ No ❑

   If No, skip to Question 5.

---

2. **Have you had pain in your shoulders, arms or hands?**

   Yes ❑ No ❑

   If yes, on which side? your right side ❑

   your left side ❑

   both sides ❑

3. **Have you had pain in your in your legs or feet?**

   Yes ❑ No ❑

   If yes, on which side? your right side ❑

   your left side ❑

   both sides ❑

4. **Have you had pain in your neck, back or chest?**

   Yes ❑ No ❑

---

5. **Over the past three months have you often felt tired or fatigued?**

Yes ❑ No ❑

6. **Does tiredness or fatigue <u>significantly</u> limit your activities?**

Yes ❑ No ❑

7. **Have you ever been told, by a doctor or anyone else, that you had some form of arthritis?**

Yes ❑ No ❑

8. **If yes, what type(s):** _____

_____

_____

9. **Have you ever been told, by a doctor or anyone else, that you had some form of rheumatism?**

10. **If yes, what type(s):** _____

_____

_____

11. **Have you ever been told, by a doctor or anyone else, that you had a condition called fibrositis or fibromyalgia?**

Yes ❑ No ❑

12. **If yes, who told you?**

a. **Your family doctor?** ❑
b. **A specialist doctor?** ❑
c. **A therapist?** ❑
d. **Someone else (Who?)** ❑

13. **Do you have, or have you had any other significant illnesses in your life that required treatment?**

Yes ❑ No ❑

14. **List:** _____

_____

_____

15. **Have you ever had any surgeries?** Yes ❑ No ❑

16. **List:** _____

_____

_____

PHYSICAL EXAMINATION

Pertinent physical findings

(circle one)

1. normal exam
2. evidence of rheumatoid arthritis (RA)
3. evidence of osteoarthritis (OA)
4. evidence of both RA and OA
5. evidence of other arthritis
6. other findings

Fibromyalgia tender points _____

PHASE II QUESTIONNAIRE

PART ONE: GENERAL HEALTH ISSUES

This part of the questionnaire asks about general health issues. These questions are the same questions asked in the recently completed Ontario Health Survey, which involved 35,000 Ontario households. We would like to compare your answers to those given by other people in Ontario. Section A asks about your general health, section B about medicines you take, and section C about your contacts with health professionals. Section D should be answered by women only.

Please answer each question by placing an 'x' in the appropriate circle, circling the appropriate response or filling in the blank, as indicated.

SECTION A: YOUR HEALTH (OHS: Q1-5)

A | Your Health

1. **In general, compared to other persons your age, would you say your health is...**

   1 ○ Excellent
   2 ○ Very good
   3 ○ Good
   4 ○ Fair
   5 ○ Poor

2. **Which one of the following best describes how you usually feel?**

   1 ○ Happy and interested in life
   2 ○ Somewhat happy
   3 ○ Somewhat unhappy
   4 ○ Unhappy with little interest in life
   5 ○ So unhappy that life is not worthwhile

3. **Which one of the following sentences best describes the effect of pain or discomfort you usually experience?**

   1 ○ Free of pain and discomfort
   2 ○ Pain or discomfort that *does not* prevent any activities
   3 ○ Pain or discomfort that prevents a *few* activities
   4 ○ Pain or discomfort that prevents *some* activities
   5 ○ Pain or discomfort that prevents *most* activities

4. **As a whole, would you describe your life as ...**

   6 ○ Very stressful
   7 ○ Fairly stressful
   8 ○ Not very stressful
   9 ○ Not at all stressful

5. **How satisfied are you with your health?**

   1 ○ Very satisfied
   2 ○ Somewhat satisfied
   3 ○ Not too satisfied
   4 ○ Not at all satisfied

SECTION B: MEDICINE AND DRUGS (OHS: Q7-8)

B | Medicine and Drugs

7. In the past 4 weeks did you take any of the following?

		Did you take this on the advice of a doctor or dentist?	Did you take this at least once a week in the past 4 weeks?
a) Pain relievers (for example: Aspirin, Advil, Tylenol)	01 ○ Yes → 02 ○ No	03 ○ Yes 04 ○ No →	05 ○ Yes 06 ○ No
b) Medicine for the heart or blood pressure	07 ○ Yes → 08 ○ No	09 ○ Yes 10 ○ No →	11 ○ Yes 12 ○ No
c) Stomach remedies or laxatives	13 ○ Yes → 14 ○ No	15 ○ Yes 16 ○ No →	17 ○ Yes 18 ○ No
d) Tranquilizers or sleeping pills (for example: Valium, Diazapam, Librium)	19 ○ Yes → 20 ○ No	21 ○ Yes 22 ○ No →	23 ○ Yes 24 ○ No
e) Penicillin or other antibiotics	25 ○ Yes → 26 ○ No	27 ○ Yes 28 ○ No →	29 ○ Yes 30 ○ No
f) Cough or cold remedies	31 ○ Yes → 32 ○ No	33 ○ Yes 34 ○ No →	35 ○ Yes 36 ○ No
g) Allergy medicine, or antihistamines	37 ○ Yes → 38 ○ No	39 ○ Yes 40 ○ No →	41 ○ Yes 42 ○ No
h) Codeine, Demerol or Morphine	43 ○ Yes → 44 ○ No	45 ○ Yes 46 ○ No →	47 ○ Yes 48 ○ No
i) Anti-depressants	49 ○ Yes → 50 ○ No	51 ○ Yes 52 ○ No →	53 ○ Yes 54 ○ No
j) Diet pills or stimulants	55 ○ Yes → 56 ○ No	57 ○ Yes 58 ○ No →	59 ○ Yes 60 ○ No
k) Vitamins	61 ○ Yes → 62 ○ No	63 ○ Yes 64 ○ No →	65 ○ Yes 66 ○ No

8. How many different types of prescription drugs have you taken in the last 4 weeks? ☐☐ Number

SECTION C: CONTACTS WITH HEALTH PROFESSIONALS

1. **Have you seen or talked to any of the following health professionals about your health during the past twelve months? Please circle the appropriate response.**

a)	**Your general practitioner or family doctor?**	**Yes**	**No**
	If yes, how many times?	_____	
b)	**A specialist?**	**Yes**	**No**
	If yes, how many times?	_____	
c)	**A nurse?**	**Yes**	**No**
	If yes, how many times?	_____	
d)	**A pharmacist or druggist?**	**Yes**	**No**
	If yes, how many times?	_____	
e)	**A physiotherapist?**	**Yes**	**No**
	If yes, how many times?	_____	
f)	**A chiropractor?**	**Yes**	**No**
	If yes, how many times?	_____	
g)	**A psychologist, social worker or other counsellor?**	**Yes**	**No**
	If yes, how many times?	_____	

i) **Some other health professional?** **Yes** **No**

If yes, how many times? _____

What type of health professional(s)?

_____ _____

_____ _____

_____ _____

2. **During the past twelve months, have you gone to an emergency room at a hospital because of your health?**

Yes **No**

If yes, how many times? _____

---

3. **Have you been admitted to a hospital during the past twelve months?**

Yes **No**

If yes, how many times? _____

4. **In total, how many nights did you spend in a hospital during the past twelve months?**

_____ **nights.**

5. **Have you seen or talked to any of the following health professionals about your health during the past two weeks (14 days)? Please circle the appropriate response.**

a) **Your general practitioner or family doctor?** **Yes** **No**

If yes, how many times? _____

b) **A specialist?** **Yes** **No**

If yes, how many times? _____

c) **A nurse?** **Yes** **No**

If yes, how many times? _____

d) **A pharmacist or druggist?** **Yes** **No**

If yes, how many times? _____

e) **A physiotherapist?** **Yes** **No**

If yes, how many times? _____

f) **A chiropractor?** **Yes** **No**

If yes, how many times? _____

g) **A psychologist, social worker or other counsellor?** **Yes** **No**

If yes, how many times? _____

i) **Some other health professional?** **Yes** **No**

If yes, how many times? _____

What type of health professional(s)?

_____ _____

_____ _____

_____ _____

6. **During the past two weeks (14 days), did you stay in bed all or most of the day because of your health?**

Yes **No**

If yes, how many days? _____

7. **What was the health problem responsible for your staying in bed?**

_____

10. **Was this the result of an accident or injury?** **Yes** **No**

11. **Were there any other days during those 14 days that you cut down on things you usually do because of your health?**

Yes **No**

If yes, how many days? _____

12. **What was the health problem responsible for your cutting down on the things you usually do?**

_____

13. **Was this the result of an accident or injury?** **Yes** **No**

14. **During those same 14 days, did you use any prescription drugs or prescription medications?**

Yes **No**

If yes, how many days? _____

15. **What was/what were the health problem(s) for which you took this medication?**

_____

_____

16. **During those 14 days, did you use any non-prescription drugs or medications; for example, pain relievers, ointments, vitamins or cough or cold remedies?**

Yes **No**

If yes, how many days? _____

17. **What was/what were the health problem(s) for which you took this medication?**

_____

_____

18. **Are you covered by any kind of government or private insurance plan which pays for all or part of the cost of prescribed medication or other health services? Do not include OHIP.**

Yes No Don't know

SECTION D: WOMEN'S HEALTH ISSUES

1. **Do you take either of the following types of pills?**

   a) **Oral contraceptives (either as a method of birth control or to regulate your menstrual cycle, or for another reason?**

   Yes **No**

   b) **Female hormones (as a treatment for menopausal disorders, infertility or for another reason?)**

   Yes **No**

2. **Have you ever been pregnant?** **Yes** **No**

   If yes, how many times have you been pregnant? _____

   How old were you at the time of your first pregnancy? _____

3. **Have you ever given birth to a child?** **Yes** **No**

   If yes, how many children have you had? _____

PART TWO: SPECIFIC HEALTH ISSUES

This second part of the questionnaire deals in greater detail with pain and fatigue. These questions were designed by researchers at the University of Western Ontario.

Also, because we want to compare your answers with persons who are similar to you, we will ask you a few questions about your personal background.

For each question, please circle the appropriate response or, where necessary, fill in the blank.

PART ONE

SECTION ONE: YOUR PAIN AND FATIGUE

We are interested in finding about more about your pain and fatigue, including how they started, how severe they are, and what other symptoms you have. The following questionnaire will take approximately fifteen minutes to complete. Please answer each question as carefully as you can.

1. **In what year, did you first start to develop the pain and fatigue that you have now?** _____

2. **If this year, how many months ago?** _____

---

3. **How quickly did your pain start? (Please circle the appropriate response).**

   a. **Over less than 24 hours.**

   b. **Over more than 24 hours but less than one week.**

   c. **Over more than one week.**

4. **When your pain started, was there something that happened, an illness, an accident, a surgery, or otherwise, that triggered the start of your pain?**

   Yes **No**

5. **If no, skip to question 5. If yes, briefly describe what it was that triggered your pain?**

   _____

   _____

6. **IN THE PAST WEEK, how much pain have you had in either your muscles, bones or joints ON AVERAGE? (Please put an 'x' on the following line to describe the severity of your pain).**

No Pain **Severe Pain**

7. **IN THE PAST WEEK, how much fatigue have you had ON AVERAGE?**

No Fatigue **Severe Fatigue**

8. **Since your pain and fatigue started, do you feel your overall condition has improved, worsened or stayed the same?**

1. Improved **2. Worsened** **3. Stayed the same**

PART ONE

SECTION TWO: OTHER HEALTH PROBLEMS

We are interested in finding out if you have other health problems. Please read the following list and circle the appropriate number to indicate whether each of the following has been no problem, a minor problem, or a major problem for you over the past two weeks.

		No	Minor	Major
9.	**Night time muscle cramps?**	1	2	3
10.	**Headaches?**	1	2	3
11.	**Eye pain?**	1	2	3
12.	**Jaw pain?**	1	2	3
13.	**Chest pains?**	1	2	3
14.	**Belly pains?**	1	2	3
15.	**Pain when you pass urine?**	1	2	3
16.	**Pain when you pass stool?**	1	2	3
17.	**Weakness?**	1	2	3
18.	**Numbness or tingling in your hands or feet?**	1	2	3
19.	**Fevers?**	1	2	3
20.	**Chills?**	1	2	3
21.	**Weight loss?**	1	2	3
22.	**Weight gain?**	1	2	3
23.	**Blurred vision?**	1	2	3
24.	**Difficulty focussing?**	1	2	3
25.	**Dry eyes?**	1	2	3

		No	Minor	Major
26.	**Dry mouth?**	1	2	3
27.	**Swollen glands around the face?**	1	2	3
28.	**Painful glands in the neck?**	1	2	3
29.	**Painful glands under the arms?**	1	2	3
30.	**Hands or feet change colour in cold weather?**	1	2	3
31.	**Hands or feet hurt more in cold weather?**	1	2	3
32.	**Heart racing or pounding?**	1	2	3
33.	**Shortness of breath?**	1	2	3
34.	**Diarrhea?**	1	2	3
35.	**Constipation?**	1	2	3
36.	**Belly cramps?**	1	2	3
37.	**Having to pass urine more than five times per day?**	1	2	3
38.	**Difficulty concentrating?**	1	2	3
39.	**Problems with memory?**	1	2	3
40.	**Increased irritability?**	1	2	3
41.	**Personality change?**	1	2	3
42.	**Depression?**	1	2	3
43.	**Anxiety?**	1	2	3
44.	**Panic attacks?**	1	2	3
45.	**Feeling dizzy or light-headed**	1	2	3

		No	Minor	Major
46.	**Fainting?**	1	2	3
47.	**Difficulty sleeping?**	1	2	3
48.	**Sleeping too much?**	1	2	3
49.	**Waking up unrested?**	1	2	3

50. **Do you ever have severe fatigue lasting more than 24 hours after some activity you used to be able to do easily?**

Yes **No**

SECTION THREE: WORK ISSUES

51. **Before you started having pain and fatigue, what was your working situation? (Please circle the answer or answers that describes what your situation was).**

1. **Working full time.**
2. **Working part time.**
3. **Looking for work.**
4. **Taking care of the home.**
5. **Full time student.**
6. **Part time student.**
7. **Partial disability.**
8. **Complete disability.**
9. **On strike.**
10. **Retired.**
11. **Other (please explain) _____**

52. **If you were working, either full or part time, before you started having pain and fatigue, how much heavy lifting did you have to do at your job?**

1. **Much heavy lifting.**
2. **Some heavy lifting.**
3. **Infrequent heavy lifting.**
4. **No heavy lifting.**
5. **You were not working full or part time.**

53. **How would you rate the physical stress associated with that job?**

1. **Very low.**
2. **Intermediate.**
3. **High.**
4. **You were not working full or part time.**

54. **How would you rate the mental stress associated with that job?**

1. **Very low.**
2. **Intermediate.**
3. **High.**
4. **You were not working full or part time.**

55. **Briefly describe what work you did.**

1. **Not working.**
2. _____

_____

56. **Have you had to reduce your work or school hours because of your pain and fatigue?**

Yes **No**

IF NO, THEN STOP HERE

57. **If yes, are you currently totally disabled and unable to work in any way?**

Yes **No**

58. **For how long, in months or years, have you been disabled?** _____

59. **Are you receiving any form of disability cheque, either from the government or from an insurance company?**

Yes **No**

60. **If so, are you getting a full disability cheque or a partial disability cheque?**

Full **Partial**

61. **Do you think you will ever be able to work full time again?**

Yes **No**

62. **If you are not already doing so, do you think you will ever be able to work part time again?**

Yes **No**

Which of the following problems affect your ability to work IN A MAJOR WAY? (Please circle Yes or No)

63. **Pain in muscles, bones or joints?** **Yes** **No**

64. **Headaches?** **Yes** **No**

65. **Pain elsewhere (where?)** _____

66. **Numbness or tingling?** **Yes** **No**

67. **Fatigue** **Yes** **No**

68. **Weakness?** **Yes** **No**

69. **Problems with your eyes?** **Yes** **No**

70. **Problems with breathing?** **Yes** **No**

71. **Problems with your belly?** **Yes** **No**

72. **Problems with concentrating or your memory?** **Yes** **No**

73. **Anxiety?** **Yes** **No**

74. **Depression?** **Yes** **No**

75. **Other? Please list.** _____

_____

76. **From the time you first developed pain and fatigue until now, has your personal income increased, decreased or remained the same? (Circle one answer).**

1. **Increased.**
2. **Decreased.**
3. **Remained the same.**
4. **Don't know or can't say.**

IF YOUR PERSONAL INCOME HAS CHANGED...

Please estimate how much it has changed (per month or per year, whichever you find easier to estimate)?

77. **$_____ per month.**

or

78. **$_____ per year.**

PART THREE

You are almost finished. These last three pages ask about how much difficulty you have performing particular tasks around your home.

Please read each question carefully and check the appropriate answers.

The Fibromyalgia Impact Questionnaire

For the next 10 questions, please think about how you have been over the past ONE WEEK.

1. We are interested in how your health has affected your ability to perform certain duties around the home OVER THE PAST WEEK. We would like to know if your health has prevented you from doing certain tasks or chores, such as shopping. Please read the following list and answer whether or not you can NEVER perform a certain task because of your health, whether you can perform it only OCCASIONALLY because of your health, whether you can perform it MOST TIMES, or whether you can ALWAYS perform this task as you wish or need to.

	Always	Most times	Occasionally	Never
1. Were you able to:				
a. Do shopping	0	1	2	3
b. Do laundry with a washer and dryer	0	1	2	3
c. Prepare meals	0	1	2	3
d. Wash dishes/cooking utensils by hand	0	1	2	3
e. Vacuum a rug	0	1	2	3
f. Make beds	0	1	2	3
g. Walk several blocks	0	1	2	3
h. Visit friends/relatives	0	1	2	3
i. Do yard work	0	1	2	3
j. Drive a car	0	1	2	3

2. Of the 7 days in the past week, how many days did you feel good?

0 1 2 3 4 5 6 7

3. How many days in the past week did you miss work because of your health? (If you don't have a job outside the home, please leave this item blank.)

0 1 2 3 4 5

Please answer the following questions by placing an 'X' somewhere on each line.

4. When you did go to work, how much did your health interfere with your ability to do your job?

No problem ——— Great difficulty

5. How bad has your pain been?

No pain ——— Very severe pain

6. How tired have you been?

No tiredness ——— Very tired

7. How have you felt when you got up in the morning?

Awoke well rested ——— Awoke very tired

8. How bad has your stiffness been?

No stiffness ——— Very stiff

9. How tense, nervous or anxious have you felt?

Not tense ——— Very tense

10. How depressed or blue have you felt?

Not depressed ——— Very depressed

Notes to Reviewers: The following list is of the ten HALS mobility and agility questions, which are included on the following pages.

The mobility index asks about:

1. ability to walk
2. ability to carry an object for 10 meters
3. ability to move from room to room
4. ability to stand for long periods

The agility index asks about:

1. ability to bend
2. ability to dress and undress
3. ability to get in and out of bed
4. ability to cut toenails
5. ability to use fingers to grasp or handle objects
6. ability to cut food

The Musculoskeletal Health Status Classification Scheme utilizes these 10 questions and defines the following levels of disability:

1. mild disability: 2 limitations
   utility weight = 0.76

2. moderate disability: 5 limitations
   utility weight = 0.64

3. severe disability: 9 limitations
   utility weight = 0.34

Questions on mobility:

The next few questions are about your ability to move around.

---

1. **Do you have any difficulty walking 350 meters or 400 yards without resting (about three city blocks, about half a kilometer or a quarter of a mile)?**

    1. **Yes**
    2. **No**

2. **At what age did you first have difficulty doing this?**

    Age ____ years (if less than 1 year, enter zero)

3. **Are you completely unable to do this?**

    1. **Yes, completely unable.**
    2. **No, able.**

---

4. **Do you have any difficulty carrying an object of 4.5 kg for 10 meters or 10 pounds for 30 feet (for example, carrying a bag of groceries)?**

    1. **Yes**
    2. **No**

5. **At what age did you first have difficulty doing this?**

    Age ____ years **(if less than 1 year, enter zero)**

6. **Are you completely unable to do this?**

    1. **Yes, completely unable.**
    2. **No, able.**

---

7. **Do you have any difficulty moving from one room to another?**

   1. **Yes**
   2. **No**

8. **At what age did you first have difficulty doing this?**

   Age ____ years (if less than 1 year, enter zero)

9. **Are you completely unable to do this?**

   1. **Yes, completely unable.**
   2. **No, able.**

---

10. **Do you have any difficulty standing for more than 20 minutes?**

    1. **Yes**
    2. **No**

11. **At what age did you first have difficulty doing this?**

    Age ____ years (if less than 1 year, enter zero)

12. **Are you completely unable to do this?**

    1. **Yes, completely unable.**
    2. **No, able.**

Questions on flexibility and agility.

The next few questions deal with flexibility and agility. Again, we are asking about difficulties that have lasted or are expected to last 6 months or more.

---

13. **When standing, do you have any difficulty bending down and picking up an object from the floor (for example, a shoe)?**

    1. **Yes**
    2. **No**

14. **At what age did you first have difficulty doing this?**

Age ____ years (if less than 1 year, enter zero)

15. **Are you completely unable to do this?**

1. **Yes, completely unable.**
2. **No, able.**

---

16. **Do you have any difficulty dressing and undressing yourself?**

1. **Yes**
2. **No**

17. **At what age did you first have difficulty doing this?**

Age ____ years (if less than 1 year, enter zero)

18. **Are you completely unable to do this?**

1. **Yes, completely unable.**
2. **No, able.**

---

19. **Do you have any difficulty getting in and out of bed?**

1. **Yes**
2. **No**

20. **At what age did you first have difficulty doing this?**

Age ____ years (if less than 1 year, enter zero)

21. **Are you completely unable to do this?**

1. **Yes, completely unable.**
2. **No, able.**

---

22. **Do you have any difficulty cutting your own toenails? (That is, is it physically difficult for you to cut your own toenails?)**

    1. **Yes**
    2. **No**

23. **At what age did you first have difficulty doing this?**

    Age ____ years (if less than 1 year, enter zero)

24. **Are you completely unable to do this?**

    1. **Yes, completely unable.**
    2. **No, able.**

---

25. **Do you have any difficulty using your fingers to grasp or handle (such as using pliers or scissors)?**

    1. **Yes**
    2. **No**

26. **At what age did you first have difficulty doing this?**

    Age ____ years (if less than 1 year, enter zero)

27. **Are you completely unable to do this?**

    1. **Yes, completely unable.**
    2. **No, able.**

---

28. **Do you have any difficulty cutting your own food?**

    1. **Yes**
    2. **No**

29. **At what age did you first have difficulty doing this?**

    Age ____ years (if less than 1 year, enter zero)

30. **Are you completely unable to do this?**

    1. **Yes, completely unable.**
    2. **No, able.**

THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY
(LFES)
PHASE III

Information Letter

There is some evidence that the amount of research dollars dedicated to FMS is too low, compared to the overall effect of this disorder on Canadian health care.

One of the major objectives of the **London Fibromyalgia Epidemiology Study** is to estimate the impact of fibromyalgia syndrome (FMS) on the health services system. To do this, we would like to compare the amount of health services (for example, visits to doctors, blood tests, and X-rays) that FMS patients use in a year, compared to other people in the general population of London and Ontario.

You and approximately 200 others in this study are being asked to give us permission to have your name and health card number sent to a researcher at the Ministry of Health (M.O.H.). He will, in turn, sum up all of the health services used in 1993 by the persons with FMS in our study, in comparison with other persons in the study. He will then provide us with a group average, per person cost of health services for persons with FMS in 1993, which we can then compare with the group average, per person cost of health services for persons without FMS in 1993. Please note that your identity and what services you used will not be released by O.H.I.P. to the researchers in our group; we are only interested in group averages.

To ensure your confidentiality, your name will never be used in any presentations or publications of our data. In fact, the actual amount of health services you individually used in 1993 will not leave the Ministry of Health; all we will be sent are the group averages. As with all previous parts of the LFES, all records will be kept in a locked file cabinet, and no part of this study will enter your doctors' or hospital charts.

Should you decide that you do not want to participate in this part of the study, in no way will it effect your further care at University Hospital. Should you have questions about the study, please call 663-3861 for further information.

Kevin P. White, M.D.
Mark Speechley, Ph.D.

THE LONDON FIBROMYALGIA EPIDEMIOLOGY STUDY
(LFES)
PHASE III

Consent Form

I _____ understand that researchers in the Departments of Medicine and Epidemiology and Biostatistics at the University of Western Ontario will involve me in a study wherein my computerized Ontario Health Insurance Programme (O.H.I.P.) detailed claims file will be reviewed. I understand that my file will be reviewed to determine what health services I used in 1993.

I authorize the Ministry of Health to release this information from the O.H.I.P. detailed claims file to the research team directed by Dr. Kevin P. White.

If I have any further questions, I may reach Dr. Kevin White at 663-3861. I have been given a copy of this consent form.

Dated in London, Ontario, this day of _____, 199__.

_____ _____
Name Printed **Signature**

_____
O.H.I.P. number

_____ _____
Witness name **Signature**

CONSENT TO BE RECONTACTED FOR FUTURE STUDIES

Subject #_____

Fibromyalgia confirmed	Yes	No
Agrees to participate in future studies	Yes	No

Name: _____

Phone: _____

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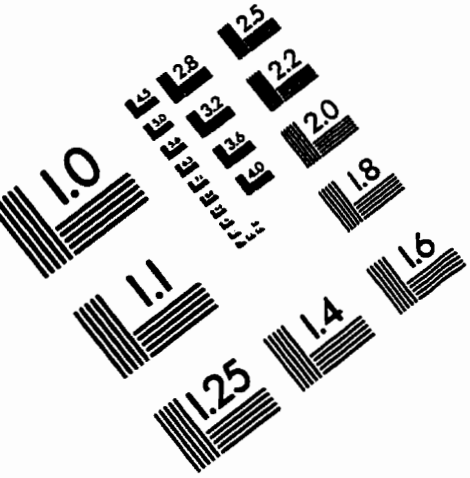
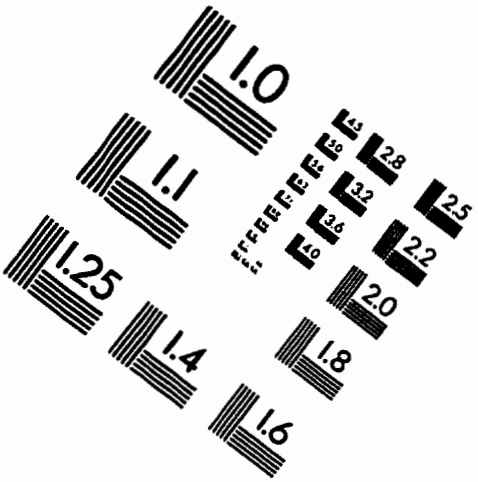
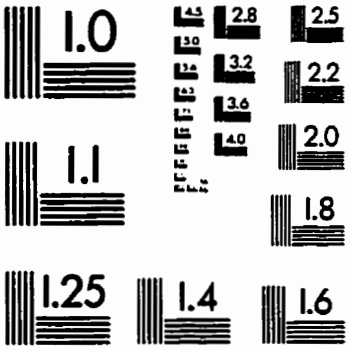
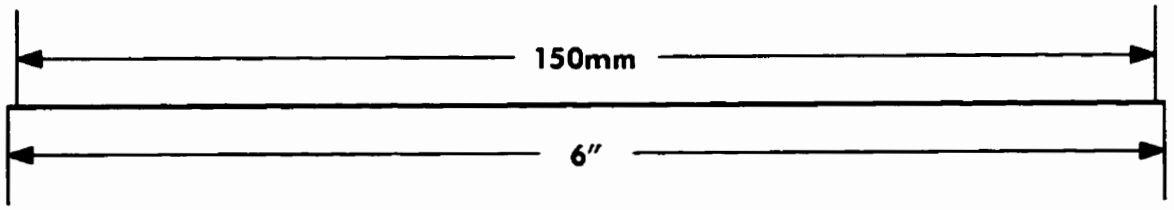
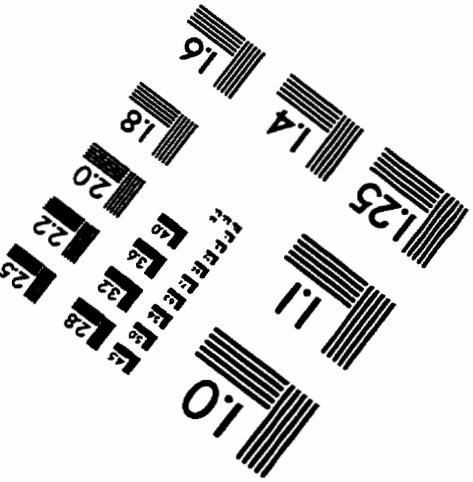
TEST TARGET (QA-3)

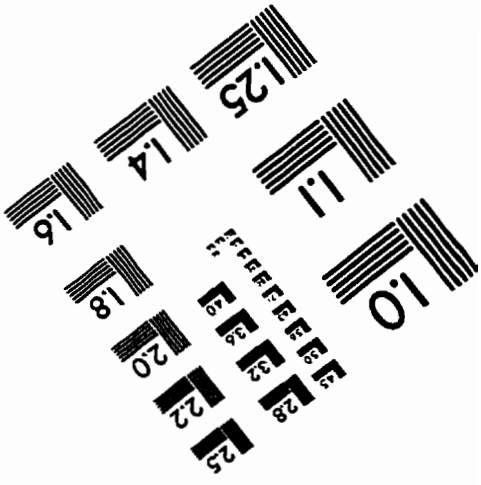












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