THE USE OF FUZZY ANALYSIS IN EPIDEMIOLOGY

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ABSTRACT

Inherent in much of epidemiology is the concept of ambiguity of expression. Both the data gathered and the questions asked may have a subjective element in them. By applying traditional statistical methods to such information, overly precise statements may be made. Fuzzy analysis, on the other hand, was specifically designed to incorporate the subjectivity associated with human responses and questions.

In this paper, fuzzy analysis is briefly described. Some of its methods are applied to several application areas of epidemiology to help characterize both the disease component as well as the risk factor aspects of epidemiology. The appropriateness of the methods are discussed and further research areas are indicated.

CHAPTER 1 INTRODUCTION

Fuzzy sets were first developed by Professor L. A. Zadeh in 1965. Other than for a few specialists, little attention was paid to fuzzy sets for the first decade. Recently, however, there has been a rapid growth in the number of researchers and papers devoted to them. This may be due to the following situation. It has been said that there are three conditions which are necessary for the establishment of a new field. These conditions are: a societal need, a new methodology (both ideas and techniques) and attractiveness to researchers.

The first condition, that of need, may be clearly seen from both mechanistic and human points of view. Advanced technology is closely connected with people's lives. Indeed, the connection between artificial intelligence and "thought", which is the essence of humanity, by itself has a great influence. For ordinary people to deal with artificial intelligence systems, it is necessary that computers understand the language of humans. However, there is an enormous amount of ambiguity in ordinary language, and it cannot be dealt with by standard logical processing. A new, logical tool which may express ambiguity is necessary, and fuzzy sets can be considered appropriate in this case. Furthermore, the interaction between people and technology can be quite complicated. It actually requires a partnership among the natural sciences, the humanities, and the social sciences. These fields have previously

progressed independently. Fuzzy sets are a communication medium that speaks to both the logical nature of the sciences and the complexity of the humanities and social sciences. It is reasonable to assume that the societal need for fuzzy sets will grow in the future.

The second condition is a new methodology. Fuzzy set theory, which at first was viewed only as a technique for mathematically expressing linguistic ambiguity, is now established as a mathematical measure for a large variety of ambiguous phenomena, including the concept of probability. Furthermore, a logical system for expressing and interpreting ambiguity is being established; few points of ambiguity remain in fuzzy set theory. If this systematization is made use of, enormous theoretical developments which bring together opposing concepts, such as subjectivity and objectivity, vagueness and precision, macro and micro viewpoints, and emotion and logic, become possible. This in turn allows new areas of application to be considered which further enhances the unique methodology.

The third condition for the establishment of a new area is for it to be an interesting field of study. The interest generated could be, as is the case for fuzzy analysis, in both theoretical methodology and practical applications. As a mathematical system, fuzzy sets expand current frameworks and build a world which takes in new concepts. This has interested theoretical researchers for quite some time. However, few practical applications existed. With its utilization

in control systems and artificial intelligence, fuzzy sets have begun to interest practical planners as well.

The previously mentioned three conditions are somewhat complementary. That is, if a new methodology is developed, a desire to make some kind of use of it will come along. If examples of practical use grow, the interest of society will be aroused and needs will arise. This process becomes the stimulus for further theoretical development. The recent, sudden expansion of fuzzy sets means that they have come to this point.

Subjectivity is a frequently encountered element in epidemiological data. This element is present, for example, in questionnaires which require respondents to subjectively assess how much, and how frequently, they have been exposed to specific substances. Opinion sometimes exists in the determination of a disease condition and classification of case status. Traditionally, the information generated by such subjective judgments has been analyzed through the use of various statistical techniques. However, this treats answers given by opinion as if they were little different from more objective laboratory measurements, and does not fully recognize the marked difference between subjective and objective information. Opinion is rarely a focused, precise, and single quantity. It instead may be ambiguous, imprecise, and multi-level. Indeed, opinion has an inherently two-dimensional hierarchical structure; there is not merely the alphanumeric answer, but there is also the degree of belief associated with that answer. All too frequently, the gathering of

subjective data stops with this first dimension of an "answer", but the second dimension of the belief strength is equally important. The degree of conviction contributes information on how closely the response conforms to the individual's assessment of the behavior under study. Thus, the alphanumeric answer has a necessary, but frequently forgotten, link to the strength of belief in that response.

General procedures used in epidemiology produce one question - one answer results under the requirement that the response be a single, fixed quantity. They do not allow for the ambiguity of several answers held with differing degrees of belief. This artificially narrows the spectrum of response and may result in the loss of relevant information. Fuzzy numbers provide one approach to remedy this limitation, since they represent the entire response spectrum. Fuzzy numbers explicitly characterize subjectivity by joining the alphanumeric answer with the respondent's degree of belief. The portrayal of subjective uncertainty is a central difference between ordinary numbers and fuzzy numbers. Statistical randomness of ordinary numbers is customarily dealt with via probability theory. True (non-degenerate) fuzzy numbers, on the other hand, are often considered in the realm of possibility theory (Vila and Delgado, 1983). The two approaches of probability and possibility are formulated under different mathematical axioms, and thus, they have more than merely a semantic difference. Probability describes the statistical inexactness, due to the occurrence of random events, that is caused by some chance mechanism.

Possibility is the inexactness, due to human judgment, which is based on the imprecision of perception or language (Dubois and Prade, 1988).

The current research examines the use of fuzzy analysis in epidemiology. Fuzzy numbers are utilized to depict the rather nebulous disease of Lupus and to characterize the highly subjective symptoms of Attention Deficit Disorder (ADD). Specifically, a diagnosis of Lupus may be warranted when a patient experiences at least four out of eleven general criteria. However, several of the criteria such as fatigue, pain, and depression not only are highly subjective, but their relative contribution toward a diagnosis of Lupus is somewhat dependent upon a physician's judgment. Thus, the opinions of both a patient and a physician must be assimilated in order to help generate a final diagnosis. As will be seen later, this is readily done through the use of fuzzy numbers. Similarly, the guidelines which are used to establish a diagnosis of Attention Deficit Disorder are somewhat vague. Indeed, many of the criteria employ linguistic terms such as "often", "easily", and "frequently". The rigidity of ordinary numbers make them ill-equipped to capture the nuances of such terms. Fuzzy numbers, on the other hand, were specifically designed to portray this subjectivity. When the subjectivity extends across several experts, as is the case for ADD where a final diagnosis may be dependent upon the opinions of physicians, parents and teachers, a meaningful way of consolidating the judgments is important. A fuzzy integration of opinion will be presented later in the dissertation.

Although a few applications of fuzzy analysis in medicine exist, primarily in the areas of cardiology and cancer, neither Lupus nor Attention Deficit Disorder have been investigated. However, as may be seen from the previous descriptions of both syndromes, these diseases would appear to benefit, in a variety of ways, from fuzzy analysis. Toward this end, five methods of fuzzy analysis were selected from the literature. The procedures were chosen for their potential applicability in Lupus and Attention Deficit Disorder evaluations and for their diverse approaches to assimilate subjective assessments. In addition to the new application areas for these methods, two of the procedures have been substantially modified to increase the ease of interpretation and the ease of computation.

One of these altered methods is the FLMCM algorithm. This procedure combines a patient's assessment of his/her symptom with a physician's appraisal of the relative worth of the symptom to the diagnosis of disease. The combination of the two assessments, across symptoms, is a fuzzy weighted average. However, in the original algorithm, unnecessary complications and confusions arose when a redundant set was used to keep track of criteria which had been evaluated. Additionally, the original iterative scheme was sometimes ill-behaved because criteria which had been previously accepted were occasionally rejected through the use of a second index set. The monotonic nature of left and right membership functions should preclude this erratic

behavior. The revised FLMCM algorithm is presented and it is applied to the consideration of SLE determination.

In ADD, it is important to know the relative effectiveness of various treatment schemes. Therefore, a pairwise comparison of treatment effectiveness between symptoms may be done. This results in the calculation of a matrix of efficacy percentages. However, to obtain the maximal and minimal levels of effectiveness, a modification of the notion of eigen-fuzzy sets is invoked. Eigen-fuzzy sets were originally used by Gerstenkorn and Rakus (1994) in an expert system on inflammation assessment and treatment. Since treatment effectiveness in ADD will be considered only in the case of symptom disappearance, the full power of eigen-fuzzy sets need not be used. Instead, the problem reduces to finding the appropriate maximum or minimum of a given column or row in the effectiveness matrix. This new reduction in computational complexity will be utilized in assessment of treatment effectiveness for ADD.

Three other methods, with little or no modification, will be used to analyze the new application areas of Lupus and Attention Deficit Disorder. The first method, originally used to aggregate several pathologists assessments of tumor pathology, combines experts' opinions through a mixed linear combination. This procedure will be applied to ADD assessment. The second method uses a rule-based approach to characterize the risk, in this case, of a child for ADD. Medical experts define certain linguistic criteria which are indicative of ADD and children are assessed on those criteria. The third method uses a distance-

based approach to categorize a patient with respect to suspected pathology for Lupus. The distance between the membership function for a suspected Lupus patient and the membership function for someone with definite Lupus will be calculated for each criterion. Distances will then be summed and normalized across criterion. Both the rule and distance based approaches previously were used to assess cardiovascular disorders.

In addition to the new application areas and modified methods for fuzzy analysis, a new computer program was created to rank patients with respect to risk for a given disease. The program, based upon an algorithm created by Kirkwood and Sarin (1985), is an extensive modification of that algorithm. Procedures were implemented to help cope with inconclusive rankings and missing data, and there are both batch and interactive versions of the program. Although the program is extremely general, and potentially could be applied to rank objects with respect to a variety of criteria, it was used to assess the risk of a patient having Lupus. After the new application areas and methods are presented, the dissertation concludes with a specification of further areas of research.

CHAPTER 2 DISEASES CONSIDERED: LUPUS

2.1 DESCRIPTION OF LUPUS

Although lupus was considered to be a rare disease, at one time, it is now recognized as being much more common. Indeed, in a study which used data from 1965, the prevalence rate for white females was 17/100,000 (Siegel and Lee, 1973). However, a study in the 1980s determined that the prevalence rate was 54/100,000 (Michet et al, 1985). This change may be due to improved diagnostic techniques and greater awareness of the disease by physicians. It has been estimated that more than 500,000 Americans, of which 90% are women, have lupus. Additionally, approximately sixteen thousand new cases are diagnosed each year (Dibner and Colman, 1994). As a general rule, lupus afflicts women who are between the ages of fifteen and sixty. Specifically, in the 15-44 year old age group, the age-specific incidence rate has been estimated to be 3.8 per 100,000 (Siegel and Lee, 1973). In the 25-44 year old age group, the rate is 6.3 per 100,000 (Michet et al, 1985). Similarly, in the 35-54 year old age group, the rate is 7.0 per 100,000 (Hochberg, 1985). In the 45-64 year old age group, the rate is 15.9 per 100,000 (Nived, Sturfelt, and Wollheim, 1985). Lupus also tends to be more prevalent in Asian, African-American, and Hispanic women than in Caucasian women (Dibner and Colman, 1994). A study conducted among women living in San Francisco determined a fourfold greater prevalence among African-American women than Caucasian women

(Fessel, 1974). Although the cause of excess morbidity from SLE among African-Americans is not known, it has been suggested that it may be due to environmental, rather than genetic, factors (Hochberg, 1989). For Caucasians and Asian-Americans, estimated age-adjusted prevalence rates of 10.3 and 22.4 per 100,000 have been obtained (Catalano and Hoffmeier, 1989).

The symptoms for lupus are numerous and diverse, and unfortunately, there is no single diagnostic test which positively confirms the presence of the disease. Indeed, even the general term of "lupus" is somewhat misleading for it actually refers to three different types of autoimmune diseases. These diseases are discoid lupus, SLE, and drug-induced lupus.

Definition 2.1.1 (Discoid Lupus): Discoid Lupus is primarily a skin disease which is characterized by a rash that usually appears somewhere on the head. In most cases, this disease does not result in other symptoms, and it does not affect any internal organs. Its most typical serious consequence, when the skin disease is left untreated, is permanent scarring and baldness. In about ten percent of the cases, discoid lupus will develop into a mild form of SLE (Dibner and Colman, 1994).

Definition 2.1.2 (SLE - Systemic Lupus Erythematosus): SLE is the most severe form of all those diseases which have been grouped together as "lupus". It may have a devastating effect on the skin, joints, and tendons

(connective tissue) as well as other body organs. Because of the involvement of connective tissue, SLE is often considered to be a "connective tissue disease". However, lupus has also been called a "collagen vascular disease" because the inflammation of blood vessels (vasculitis) is a common complication.

Definition 2.1.3 (Drug-Induced Lupus): Certain drugs may trigger lupus-like symptoms or lupus attacks in people who have had no prior history of the disease. These drugs include hydralazine, which is used to treat hypertension, and procainamide, which is used to treat irregular heartbeat. In most cases, once the drug is discontinued, the lupus-like symptoms gradually disappear. There appears to be a genetic predisposition for drug-induced lupus which may be related to the way in which certain medications are metabolized in the body (Dibner and Colman, 1994).

Consideration of the different types of lupus may be important. For example, mortality from all forms of lupus, based upon data from the National Center for Health Statistics for 1968-1978, showed no significant differences by race, region, or year (Lopez-Acuna, Hochberg and Gittelsohn, 1982). However, if only SLE was considered, mortality rates were three times higher among African-Americans and two times higher among Asian-Americans when compared with Caucasians. The rates were respectively 8.4, 6.8, and 2.8 per

million person-years for African-Americans, Asian-Americans, and Caucasians (Kaslow, 1982).

A variety of etiologic factors for SLE have been considered. These factors may be grouped into three areas: endocrine-metabolic, environmental, and genetic. For example, a case-control study (Hochberg and Kaslow, 1983) was used to examine the influence of endocrine-metabolic factors. Seventy-four women with SLE and an equal number of age- , race- , and neighborhood-matched controls were interviewed to ascertain menstrual, sexual, and reproductive histories (prior to the time of diagnosis for the SLE patients). There were no significant differences between cases and controls in age at menarche, age at first intercourse, use of oral contraceptives, or history of infertility. However, a history of miscarriages was significant. Indeed, the odds ratio associated with miscarriage was 2.7 (95% confidence interval of 1.4-5.2). An even greater risk was determined for women who had been pregnant on one or more occasions without having had a live birth. The estimated odds ratio was 17.3 (95% confidence interval of 13.4-21.2).

A viral etiology has long been hypothesized for SLE (Phillips, 1981). Yet, no definite viral etiology has been found (Boumpas, 1986). A more likely environmental factor for SLE are chemicals. The use of certain drugs has been mentioned previously as inducing lupus-like symptoms. A recent case-control study (Freni-Titulaer et al, 1989) was used to determine exposure to occupational and environmental factors, including medications specifically

associated with drug-induced lupus and other chemicals with similar chemical and metabolic structures. Forty-four cases with connective tissue disease, of which 23 patients had SLE, and eighty-eight age- , sex- , and race-matched controls were included in the study. Matched univariate analyses showed significant associations between connective tissue disease and the use of hair dyes, use of hair permanent solutions, and use of hair spray. In a multivariate analysis, the use of hair dyes continued to be significant with an odds ratio of 7.1 (95% confidence interval of 1.9-26.9).

Strong evidence exists for a link between genetic factors and SLE. Indeed in a case-control study (Hochberg et al, 1978), the presence of SLE among first-degree relatives of 77 SLE patients and age- , sex- , and race-matched controls without a history of rheumatic disease was examined. SLE occurred in nine of 541 first-degree relatives of SLE patients. However, SLE was present in only one of 540 first-degree relatives of controls. This results in a relative risk of 8 (95% confidence interval of 6.7-9.3). Studies with twins have demonstrated a greater concordance rate among monozygotic than among dizygotic twin-pairs. This provides additional evidence of a genetic contribution to the occurrence of SLE (Deapen et al, 1986). Thus, there appear to be a wide variety of factors which may induce lupus. This may be partly due to the ambiguity of some characteristics and the subjectivity inherent in some symptoms of lupus.

2.2 GENERAL SYMPTOMS OF LUPUS

One of the numerous reasons why lupus is such a frustrating disease for both a physician to diagnosis and for a person to understand is that every woman with lupus may experience the illness in a different way. The following are some common, but rather non-specific, symptoms.

Symptom 1: FATIGUE

Of all the symptoms of lupus, fatigue is the one which is most common. According to some rheumatologists, the fatigue and achiness which some lupus patients experience may be compounded by fibromyalgia. Although the fibromyalgia syndrome is also present in non-lupus patients, recent studies have shown that it occurs in more than half of all lupus, particularly SLE, patients (Dibner and Colman, 1994).

Symptom 2: PAIN

Lupus patients often cite almost flulike aches and general, rather than localized, pain. In some cases, the muscle soreness may seem comparable to that which may occur after a vigorous workout. However, the pain characterized by other patients is almost arthritic in nature. Indeed, some lupus patients suffer

from arthritis and experience specific pain and/or swelling in their joints, particularly in the smaller joints of the hands and feet. This pain may subside during the day but worsen at night.

Symptom 3: RASHES

A variety of rashes can be seen in lupus patients. Some of the rashes may result in scarring, but the most common is a general red facial rash. This type of rash is called a malar or wolf's mask rash. Because of its shape, it is also termed a butterfly rash.

Symptom 4: SUN SENSITIVITY

After prolonged sun exposure, a majority of women with lupus, particularly SLE, report that several of their symptoms appear to increase. These symptoms include rash, fever and achiness.

Symptom 5: HAIR LOSS

Particularly during periods of active disease or during disease flare-ups, lupus patients may notice more hair loss. Although the loss of hair may be somewhat uniform, patches of hair loss may also be noted.

Symptom 6: FEVER

The presence of fever is another symptom for people with lupus. Some women with lupus may have a constant low-grade fever near 100°F. On the other hand, some develop an intermittent high fever. The fever may increase in severity at night and lessen during the day.

Symptom 7: CHEST PAIN

A sharp pain which results from inflammation of the lining of the heart or lungs is frequently noted by lupus patients.

Symptom 8: COLD HANDS AND FEET

About twenty percent of all women who have lupus also experience Raynaud's syndrome which is characterized by a sensitivity to cold in the extremities. When exposed to cold, the fingertips could turn white and the nail beds could turn a bluish color. When rewarmed, the fingers become red. Raynaud's syndrome may cause a deep, tingling sensation in the hands and feet. However, emotional stress can also provoke such episodes.

Symptom 9: DEPRESSION

Many lupus patients experience severe depression. This is most frequently characterized by both a sense of helplessness and hopelessness.

Symptom 10: EDEMA OR SWELLING

For some patients, the first sign of lupus may be swelling in the ankles and legs or around the eyes. This symptoms could be an indication of a lupus-induced kidney disease.

Symptom 11: DRY EYES, DRY MOUTH

Many women with lupus experience Sjogren's syndrome. In this syndrome, autoantibodies attack the glands which produce saliva and other lubricants. This loss of natural moisture results in dry eyes or dry mouth.

Symptom 12: PREMENSTRUAL FLARES

Many women report that, regardless of the symptoms which they experience, the symptoms worsen prior to their menstrual periods. This may indicate that an endocrinal factor is important in the etiology of lupus.

2.3 GENERAL DIAGNOSTIC PROCEDURES FOR SLE

2.3.1 INTRODUCTION

Since no single symptom or medical test conclusively and exclusively yields a diagnosis of SLE, a physician must carefully appraise each patient to ascertain whether her particular combination of symptoms, laboratory results,

and physical findings warrant a diagnosis of SLE. As with many diseases, a precise, painstaking examination by a physician is a crucial first step toward the establishment of a diagnosis. Specific blood tests may also help confirm the diagnosis. Although in some cases an experienced physician may be able to diagnose SLE at the initial visit, most cases are much trickier, even for the most skilled practitioners. This is due to the fact that other illnesses have features which are similar to lupus. In fact, physicians have called lupus a "great imitator" because of the wide range of conditions it may mimic.

Depending on the patient's symptoms, other diseases which may be diagnosed rather than lupus include certain connective tissue diseases, such as rheumatoid arthritis, and certain infectious diseases, such as Lyme, syphilis, tuberculosis (TB), mononucleosis, and even AIDS. Doctors also have to eliminate from consideration such blood disorders as leukemia and lymphoma, such neurologic disorders as multiple sclerosis, and such psychiatric disorders as schizophrenia. In addition, lupus may initially be confused with chronic fatigue syndrome and fibromyalgia. Because of the diversity of diseases with which lupus may be confused, a patient may be extremely frustrated through the lack of a proper diagnosis. Unfortunately, it may be months or even years before a physician can eliminate the other possibilities and say with any certainty, "You have lupus."

In all likelihood, to determine if a person has lupus, a doctor has referred to the Criteria for SLE (officially known as the Revised Criteria for the

Classification of Lupus, developed in 1982 by the American College of Rheumatology). It is a list of the eleven abnormalities which are most specific for SLE. Unfortunately, most of the symptoms on the list may also apply to patients with other autoimmune or connective tissue disorders as well as other completely unrelated diseases. As a general rule, if a patient has had four or more of the eleven criteria, but not necessarily all at the same time, she may be diagnosed as having SLE. Few patients actually ever develop all eleven conditions. Additionally, some patients are diagnosed as having lupus when they have had fewer than four of the criteria. Thus, when it comes to lupus, in general, and SLE, in particular, the exception may be the rule. The following list outlines the eleven criteria. There is a brief description of how the given criterion is used by a physician in a determination of SLE.

2.3.2 SPECIFIC DIAGNOSTIC CRITERIA

Criteria 1: MALAR RASH

About half of all SLE patients eventually develop the malar, or butterfly-shaped, rash over the cheeks and bridge of the nose (Dibner and Colman, 1994). The rash usually consists of red, raised bumps which may itch or be uncomfortable. However, on some patients, it will appear more like a red flush. The malar rash may be hot to the touch and it may worsen during periods of active disease. For some people, the rash may be milder in the morning and

more severe later in the day. Although the precise cause of the malar rash is unknown, it usually appears on those parts of the face which are most exposed to the sun. This suggests that the sun may either trigger or at least aggravate the rash. In addition, biopsies of these rashes show that there are significant deposits of antibodies in the dermis, the deep layer of skin. Because there is usually an inflammation of blood vessels, an autoimmune response may also be at work. The malar rash may disappear either spontaneously or with treatment and does not cause any scarring.

Criteria 2: DISCOID RASH

The discoid rash, which may affect about twenty-five percent of all SLE patients (Dibner and Colman, 1994), consists of individual, round, scaly spots which frequently occur on the face. Discoid rash resembles psoriasis. Unlike a psoriasis lesion which is red, the surface of a discoid rash appears to have a cluster of small blackheads. If untreated, the discoid rash can leave scars. The discoid rash may also be aggravated by sun exposure and tends to worsen during spring and summer. Similar to a malar rash, a discoid rash biopsy reveals inflammatory cells in the affected areas. Discoid lupus, in which the patient only has discoid rash and does not have any other organ involvement, is a separate disease and should not be confused with SLE discoid rash. However, about ten percent of all patients with discoid lupus will eventually go on to develop SLE (Dibner and Colman, 1994).

Criteria 3: PHOTOSENSITIVITY

Most SLE patients exhibit photosensitivity which means they are highly sensitive to the sun and other forms of light. But the precise relationship between photosensitivity and SLE is not fully understood. One possibility is that the sun might damage the deoxyribonucleic acid (DNA) in the skin. This might make the DNA appear to be abnormal to the immune system. Thus, the immune system would make autoantibodies to DNA, which might lead to inflammation and tissue damage (Dibner and Colman, 1994). Typically, sun exposure will trigger a rash but it may also result in fever, fatigue, joint pain, and other symptoms of SLE. In some cases, sun exposure may even induce the onset of kidney disease. Many lupus patients are also sensitive to light emitted from fluorescent bulbs (UVB) and halogen lamps (UVA).

Criteria 4: ORAL ULCERS

As many as 40 percent of all SLE patients may have small erosions that resemble cold sores (Dibner and Colman, 1994). These are typically found on the hard palate of the mouth. Oral ulcers, which are caused by inflammation, are usually painless, and the patient is often totally unaware of them.

Criteria 5: ARTHRITIS

Most SLE patients will suffer from a form of arthritis which does not damage bones but it will cause swelling and inflammation of joints and ligaments. These arthritis symptoms may be temporary or chronic, and they will often worsen during periods of active disease.

Criteria 6: SEROSITIS, PLEURITIS, PERICARDITIS, PERITONITIS

At least half of all SLE patients have serositis, the painful inflammation of the linings which cover the lungs, heart, or the abdominal cavity (Dibner and Colman, 1994). Pleuritis happens when the lining of the lungs becomes inflamed and can result in chest pain, especially when breathing in. Pericarditis is the inflammation of the tissue surrounding the heart and may cause similar chest pain. Frequently, this pain may become more acute when lying down and improve when sitting or leaning forward. During a physical examination, a doctor may hear an abnormal sound which suggests an inflammation and perhaps a buildup of fluid around the heart or lungs. These conditions may also be detected by a chest X-ray, an electrocardiogram (EKG), or an echocardiogram. Peritonitis, which occurs less frequently than pleuritis or pericarditis, is the inflammation of the lining of the abdominal cavity and can result in acute abdominal pain. It is often difficult to distinguish between the pain of peritonitis and appendicitis. These symptoms, in the presence of some of the other criteria, may suggest a diagnosis of lupus.

Criteria 7: RENAL DISORDER

Most SLE patients have some form of kidney abnormality which may range from protein leakage into the urine (often a somewhat mild condition) to the breakdown of the kidney's ability to remove toxins from the blood (a severe impairment). However, only about half of lupus patients will suffer permanent kidney damage (Dibner and Colman, 1994). Because they are usually painless and symptomless, kidney disorders are frequently detected after a urine analysis shows an abnormally high protein level or the presence of white or red blood cells.

Criteria 8: NEUROLOGIC ABNORMALITIES

About 50 percent of SLE patients develop problems of the central nervous system (CNS) at some time. Twenty-five percent of all patients have neurologic problems at the time of diagnosis (Dibner and Colman, 1994). Involvement of the CNS in SLE may cause a wide variety of disorders. These range from acute seizures, psychosis, and depression to chronic forms of confusion and memory loss.

Criteria 9: HEMATOLOGIC ABNORMALITIES

There are four hematologic abnormalities, or disorders of blood cells, that are common in SLE patients. Unfortunately, these conditions may also be a sign of another problem. The abnormalities are caused by autoantibodies

which attack particular kinds of blood cells. The following are the major forms of blood disorders which are found in lupus patients.

Hemolytic anemia: This condition occurs when a patient makes antibodies against her own red blood cells. This causes their removal by scavenger cells in the spleen or liver. If untreated, hemolytic anemia may be quite serious.

Thrombocytopenia: This condition is characterized by a low number of platelets, or clotting cells (less than 100,000 platelets per cubic millimeter). It is caused by autoantibodies that destroy these cells in the spleen. A severe drop in platelets can result in catastrophic bleeding.

Leukopenia: This condition occurs when the white blood cell count is low (below 4,000 cells per cubic millimeter). It is usually not a serious condition but may indicate that lupus is active.

Lymphocytopenia: This is characterized by the lymphocyte count being low. It is not considered to be serious and rarely, by itself, does it impede the body's ability to fight infection.

Any one of, or combination of, these four blood abnormalities counts as 1 point toward the eleven diagnostic criteria.

Criteria 10: IMMUNOLOGIC ABNORMALITIES

There are four antibodies, found in the blood, that when combined with other symptoms may suggest a diagnosis of SLE.

Anti-DNA antibodies: Many SLE patients produce antibodies against their own DNA or genetic material.

The lupus erythematosus cell preparation (LE prep): The LE cell is found in the blood of 90 percent of patients with active SLE. However, it may also be found in patients with other autoimmune disorders including rheumatoid arthritis, scleroderma, and Sjogren's syndrome. The LE cell test was the first laboratory test designed to detect SLE, but it is not as specific as more recent tests and is no longer widely used.

Antibodies to Sm (Smith): These autoantibodies, named after the patient in which they were first identified, are directed against a protein found in the cell nucleus. Between thirty and forty percent of all SLE patients have antibodies to Sm (Dibner and Colman, 1994). The anti-Sm antibody test is highly specific for SLE, meaning that it is extremely rare for it to be found in people with other disorders. Therefore, if a patient tests positive for anti-Sm antibodies, that person is likely to be diagnosed with SLE.

False-positive serologic test for syphilis: About 20 percent of SLE patients will test positive for syphilis, although SLE appears to be totally unrelated to this or any other venereal disease. The false positive test occurs when certain SLE patients produce antibodies that can be similar to those

produced by a patient trying to fight off syphilis. Syphilis also causes an inflammation of blood vessels and many other symptoms that are similar to SLE. Great care must be taken to distinguish between the two if the syphilis test is positive.

Any one of the above immunologic abnormalities counts as 1 point toward the eleven criteria.

Criteria 11: ANTINUCLEAR ANTIBODIES (ANA)

About 95 percent of all lupus patients test positive for ANA, that is, for autoantibodies to cell nuclei. However, a positive ANA may also be found in patients with other autoimmune disorders as well as in people who are on certain medications, and it may even be seen in some completely symptomless, healthy people. Therefore, a positive ANA test, by itself, does not yield a valid diagnosis of lupus. An ANA test reports furnish two pieces of information: a titer and a pattern. The titer is a number which tells how many times a patient's blood must be diluted to obtain a sample which is free of ANA. A titer of 1:80 is usually, but not always, considered positive. Lower titers are not normally significant. The higher the titer, the more antibody which is present in the blood. An ANA titer may vary throughout the course of the disease and it does not necessarily reflect the severity of the condition. The pattern refers to the way in which the autoantibodies arrange themselves. The ANA pattern may help

differentiate SLE from other conditions that may cause a positive ANA result. A smooth, homogenous pattern is frequently seen in patients who are taking certain types of drugs, who have a connective tissue disease, or who are healthy despite the positive ANA. A speckled pattern is most common in SLE and other connective tissue diseases. The peripheral pattern or rim is usually found only in SLE.

Only five of the eleven criteria for determining a diagnosis of SLE rely on numbers obtained from laboratory tests and even the numeric results may be somewhat ambiguous. The rest can only be determined by information obtained through the interaction between a patient and her physician.

2.3.3 DIAGNOSTIC PROCESS

Step 1: FAMILY MEDICAL HISTORY

Perhaps the most crucial portion of a doctor's examination is the exchange of information between patient and doctor. At the initial meeting, the physician will commonly ask for a family medical history to determine if there could be a genetic predisposition to a particular problem. For example, if a patient suffers from arthritic-type pain or extreme fatigue, a determination should be made as to whether a close blood relative (a parent, sibling, grandparent, aunt, or first cousin) had ever experienced similar symptoms or had ever been diagnosed with a related disorder. Seemingly unrelated illnesses, such as

kidney disease, high blood pressure, arthritis, or blood clots, could be valuable clues in helping a physician make an accurate diagnosis.

Step 2: PERSONAL MEDICAL HISTORY

A brief but concise list of current symptoms should be presented to the physician along with a list of previous surgical procedures, blood transfusions, allergies, serious illnesses, fevers, skin rashes, or unexplained hair loss. The physician also needs to know if symptoms get worse after any particular activity or during any part of the day. Very often, with SLE, patients feel worse later in the day or when they are fatigued. Patients with arthritis may feel stiff or sore in the morning upon awakening.

Medications or infections in the recent past may also be an important factor. For example, a person may not think that it is relevant to mention that they were recently put on medication for a bladder infection. Yet, some of the drugs used to treat this problem have been implicated in triggering flare-ups in lupus patients. Since SLE can be induced by several drugs and possibly by certain infections, it is vital that a doctor be informed about these conditions.

Few people would consider talking about their vacations as part of their medical history, yet it can be invaluable information when dealing with SLE. For example, if a patient's symptoms worsen after a Mediterranean vacation, it may be an indication of photosensitivity. Since photosensitivity is a sign of SLE,

a physician must know if the patient has been exposed to the sun recently, even if just for a day.

An accurate account of a patient's gynecological history is mandatory. Letting a doctor know a recent change in menstrual status or whether a patient has currently or ever taken birth control pills or estrogen replacement therapy is important since there may be an endocrinal factor in the etiology of SLE. Also, a history of miscarriage may be relevant since certain antibodies found in some SLE patients can cause spontaneous abortion or stillbirth.

Step 3: THE PHYSICAL EXAMINATION

In addition to a complete yearly physical examination, which includes a check of blood pressure and weight as well as a review of all vital organs, a physician may also need to take extra care in looking for telltale signs of SLE and other related diseases.

Hair Loss: A physician will examine the scalp for signs of hair loss or scarring from a discoid rash.

Eye examination: A physician may do an examination of the eyes signs of cytoid bodies, evidence of blood vessel inflammation, which is related to CNS disease.

Ulcerations: A physician will check for any oral or nasal ulcers of which the patient may be unaware.

Lymph Nodes: Swelling in the lymph nodes can be sign of inflammation. Therefore, a physician will palpate areas around the patient's neck, above the collarbones, in the armpits, above the elbows, and in the groin.

Thyroid gland: A physician will check for enlargement of this gland, which may be a sign of an underactive thyroid. This condition is sometimes seen in lupus.

Skin: A physician should look closely at the patient's skin for active rashes or evidence of scarring from a discoid rash, particularly in the ears. Frequently, a patient may have had a discoid rash and might not have even known it or may have mistaken it for something else. The remnant of the rash is a telltale scar, which provides important information for the doctor.

Chest examination: A physician will listen with a stethoscope for evidence of pleuritis, inflammation of the lining around the lung, or pericarditis, inflammation of the lining around the heart. He will also check for fluid, another sign of inflammation.

Organ Enlargement: A physician will palpate the liver and spleen for evidence of swelling, a sign of inflammation.

Edema: A physician will check for edema or fluid in the lower legs. This could be a sign of kidney disease, which can be induced by SLE.

Joints: A physician will palpate the joints for signs of tenderness and swelling. This is particularly important in patients with lupus arthritis.

Abnormalities in fingers or toes: Discoloration (blueness) or other abnormalities of the fingers or toes can be a sign of SLE-related problems such as Raynaud's syndrome.

Neurologic exam: A physician will do a careful neurologic exam to make sure that the patient's sensation, reflexes, and muscle strength are normal. This could be very important because it may alert the physician to any problems involving the CNS.

Step 4: LABORATORY TESTS

In many cases, a physician will be able to reach a diagnosis on the basis of family history, personal medical history, and the physical examination. In certain instances, however, the doctor may still not be able to pinpoint the particular disease or disorder. In either case, the physician will probably call for other laboratory tests in addition to the ones which are normally performed. These other tests either verify a suspected diagnosis or allow the obtaining of more information. When SLE is suspected, the physician will usually order the following laboratory tests.

COMPLETE BLOOD COUNT (CBC): Blood cells can reveal a great deal about a patient's overall health. Usually, about half of all SLE patients have a low white blood cell count. Most will also have a low red blood cell count. Unfortunately, low red blood cell count is such a frequent sign of chronic illnesses that is has been called the anemia of chronic disease. A small

number of SLE-patients will develop hemolytic anemia in which they are producing antibodies against their own red blood cells. This also results in a low red blood cell count. Another 15 percent of SLE patients have thrombocytopenia, a lower than normal level of platelets. Any or all of these abnormalities in blood cells could be a sign of SLE.

BLOOD CHEMISTRY SCREEN: A blood chemistry screen tests for a variety chemicals and enzymes in the blood. However, when SLE is suspected, the physician is most interested in those tests which measure kidney function. These tests include measurements of creatinine, BUN (blood urea nitrogen), and serum albumin

URINALYSIS: The physician will look for protein in the urine or for red or white blood cells scattered or in clumps called casts, all of which are signs of inflammation of the kidney.

SEDIMENTATION RATE (ESR): This exam is a very nonspecific test which is used as a general screen to determine whether there is an inflammatory disease. People who have active inflammation will usually have an elevated ESR. However, it can also heightened by most infections and the presence of some tumors, and the occurrence of other connective tissue diseases.

ANA: This is a screening test for autoantibodies to cell nuclei in the blood. However, patients with many other related problems or those who are taking certain medications may also have a positive ANA. In addition, people

who have absolutely no symptoms may test positive for ANA. In this instance, the test results should be ignored until, or unless, any additional symptoms arise. A negative ANA test suggests that the patient may not have SLE. Less than 5 percent of all lupus patients do not test positive for ANA. Virtually all of these patients will show some other abnormal antibodies.

RHEUMATOID FACTOR (RF): If a patient has arthritic symptoms, the doctor may test for RF. About 75 percent of patients with rheumatoid arthritis test positive for RF. Only 20 percent of patients with lupus will test positive. Patients with lupus, who are RF positive, tend to have milder cases of lupus.

SEROLOGIC TEST FOR SYPHILIS: A false positive for this test is one of the immunologic criteria for establishing a diagnosis of lupus. Roughly 20 percent of SLE patients will test false-positive for syphilis.

LYME TITER: The symptoms of Lyme are similar to those of SLE. Therefore, it is important to rule out the possibility of Lyme disease before diagnosing a patient with SLE. This is particularly important if she has been in an area where Lyme is frequently encountered.

HIV TEST: Although they are very different illnesses, many of the manifestations of AIDS can be confused with those of SLE. Mouth ulcers, facial rashes, hair loss, swollen lymph nodes, low white blood cell counts, fever, and protein in the urine can all be signs of either illness. Patients who have been sexually active or who have other AIDS risk factors should be tested for HIV. Frequently, SLE patients will be put on immunosuppressive drugs, which is

exactly opposite of the treatment for HIV and could accelerate the undiagnosed or misdiagnosed AIDS patient's demise.

After this initial set of tests, a doctor may have sufficient information to warrant a diagnosis. However, in some cases, more highly specific tests may be necessary to rule out other connective tissue diseases. Even if a doctor is convinced that a patient has SLE, additional tests may be ordered so that a "serologic fingerprint" may be obtained at the time of diagnosis. From this additional blood data, a doctor can often predict complications that may arise later.

TEST FOR ANTI-DS (DOUBLE-STRANDED OR NATIVE) DNA ANTIBODIES: Many SLE patients produce antibodies to their own DNA or genetic material. Indeed, antibodies to DNA is one of the immunologic criteria for establishing SLE. The test for anti-ds DNA antibodies is positive in approximately 70 percent of all SLE patients (Dibner and Colman, 1994). It is rare for antibodies to ds DNA to be present in diseases other than lupus. They are more often found in SLE patients with active disease or kidney disease.

TEST FOR ANTI-SM (SMITH) ANTIBODIES: The antibody to this particular protein found in the cell nucleus is one of the immunologic criteria. This test is very specific for lupus.

ANTIBODIES TO RIBONUCLEIC PROTEIN: These antibodies are common to SLE and other related disorders. Often, women with nonspecific lupus-like symptoms who do not fulfill the criteria for SLE will have high levels of

antibodies to ribonucleic protein. These women may be diagnosed as having mixed connective tissue disease, overlap syndrome, or undifferentiated connective tissue disease and may or may not later develop SLE.

ANTIBODIES TO RO AND LA (ANTI-SSA/RO, ANTI-SSB/LA): These particular autoantibodies can be found in 30 to 40 percent of all SLE patients as well as in people with other autoimmune diseases (Dibner and Colman, 1994). Because these autoantibodies can cause complications during pregnancy, it is important for women of childbearing age to know if they test positive. They are most often positive in patients who have Sjogren's syndrome.

ANTIPHOSPHOLIPID ANTIBODIES: Antiphospholipid antibodies are directed against certain phospholipids, a family of fat molecules that are widely distributed in the body. Although many SLE patients have these antibodies, there are also many people with antiphospholipid antibodies who do not have SLE. Some may have clotting problems and others appear to be perfectly healthy. The two antiphospholipid antibodies which are most frequently associated with SLE are the lupus anticoagulant and the anticardiolipin antibodies. Women with either the lupus anticoagulant, or the anticardiolipin antibodies, or both, the so-called antiphospholid antibody syndrome, are at risk of developing clotting problems that could include heart attack, stroke, and deep venous thrombosis (leg clots). In addition, both SLE

and non-SLE women with antiphospholipid antibodies may be more prone to miscarry.

SERUM COMPLEMENT LEVELS: Complement is a family of proteins in the blood involved in fighting infection and inflammation. People with active SLE tend to have lower than normal complement levels. The combination of a low complement and a high level of antibodies to DNA may indicate a patient at greater risk of developing kidney disease. In some patients, complement levels are followed across time and may be used to predict flare-ups of lupus.

Step 5: COMPLICATIONS

There are times when even after a thorough examination and a battery of laboratory tests a doctor is not able to make a concrete diagnosis. A patient may be experiencing only one or two symptoms - fever and a rash, or Raynaud's syndrome and fatigue - that could suggest a variety of connective tissue diseases, including SLE. The test results may reveal some evidence of inflammation and autoimmune activity. However, based on the symptoms and the laboratory findings, it may be virtually impossible to identify the specific problem. In these cases, a doctor may say to his patient, "You have some kind of autoimmune disease, and we have to wait and see what happens to determine which disease it becomes." Obtaining a diagnosis of SLE is much different from reaching a diagnosis for many other ailments. For example, in the

case of cancer, the proof is in the biopsy. In most cases, a physician can render a definitive diagnosis of cancer based solely on laboratory tests. Unfortunately, this is not the case with SLE. A diagnosis of SLE is often a judgment call on the part of the physician. But an accurate, quick diagnosis of lupus, particularly SLE, is crucial since early intervention can often make the difference between a minor problem and a major emergency.

Many women with SLE have only mild symptoms, and although they may experience an occasional flare, most develop few serious medical problems. However, SLE can increase the odds of developing particular complications that are very serious, especially if they are not treated promptly. These include:

1.) Kidney disease

2.) Cardiopulmonary complications: Pericarditis, Myocarditis, Coronary artery disease, Valvular heart disease, and Pulmonary disease

3.) Neuropsychiatric disorders: Central nervous system disease and clinical depression

4.) Sjogren's syndrome

5.) Eye disorders

6.) Orthopedic complications

CHAPTER 3 DISEASES CONSIDERED: ADD

3.1 DESCRIPTION OF ADD

Numerous diagnostic labels have been given to children who show such symptoms as poor sustained attention, hyperactivity, impulsiveness, and sometimes learning disabilities with conduct problems. These labels generally reflect various historical concepts related either to the etiology of the disorder (Minimal brain damage syndrome, Minimal brain dysfunction, Developmental hyperactivity) or to what were considered its principal manifestations (Hyperactive impulse disorder, Hyperactive child syndrome, and more recently Attention Deficit Disorder with Hyperactivity). However, regardless of the label, the general category of attention deficit disorder is one of the most prevalent chronic behavioral disorders in children (Buttross, 1988). In the United States, the prevalence of ADD has been estimated from 2% to 20% (Shaywitz and Shaywitz, 1985). The range is due to both differences in the criteria used to classify a child as ADD and differences in study design. As is typical in childhood behavior disorders, males rather than females tend to be classified as ADD. The male to female ratio may be as high as 9:1 (Miller, Palkes, and Stewart, 1973). The problem of Attention Deficit Disorder is not exclusive to the United States. The disorder has been reported, with less frequency, in several Western countries as well as in some rapidly developing Third World countries. For example, in a population study on the Isle of Wright (Rutter et al, 1970), an

ADD prevalence rate of 100 per 100,000 was determined. However, this appears to be primarily due to differences in diagnostic practices (Sandberg, 1985).

3.2 ETIOLOGY OF ADD

The precise etiology of ADD is unknown although much research has been conducted. In the past, an innate or acquired organic pathology was frequently cited as the cause. For example, Still first described children who had a cluster of behavioral problems such as hyperactivity, learning difficulties, conduct disorders and poor attention. He assumed that the etiology was probably organic (e.g. inborn differences of temperament), but that environmental factors might also play a role (Still, 1902). In a 1934 study of post-encephalitic behavior disorders in children, characteristics of impulsiveness, antisocial behavior, and emotional instability were noted (Kahn and Cohen, 1934). Clinicians believed that the problem was primarily due to brain stem damage. At that time, special residential treatment centers were established to treat these children who had disruptive behavioral episodes following their contraction of encephalitis lethargica. It was noted that the behavioral problems could be improved through residential treatment but that a relapse occurred if the children were returned to maladjusted parents. It was implicitly recognized, even then, that "etiology" may be multiple, namely organic and environmental. However, identifiable organic factors for ADD appear to be

present in a rather small number of children (Shaywitz and Shaywitz, 1985). In instances where diseases of the central nervous system have occurred, retrospective studies have shown a small increase in a variety of behavioral disorders (Shaywitz, 1982).

Lead poisoning, at one time, was implicated in several cases of hyperactivity and attention deficit disorder (Rummo, 1979). Unfortunately, the validity of this finding is questionable since such studies may have been confounded by parental IQ levels and the quality of the child's living conditions (Ernhart, Landa, and Schell, 1981). Allergic reactions to certain types of foods, most notably additives and sugar, was thought to be factors for ADD-like behavior (Feingold, 1975). However, more careful studies seem to indicate that any such ADD-like behavior is short-term and thus, the effect is more pharmacological rather than immunological (Stare, Whelan, and Sheridan, 1990). The problem of determining causative dietary factors is further complicated, and confounded, by changes in family involvement and attitudes toward the child when a diet is instituted.

Familial, but not necessarily genetic, etiological factors have been the focus of attention in recent years. In a study of a large cohort of ADD children, it was found that there was an increased incidence of ADD in siblings of girls with ADD. The risk was heightened when one or both parents had a history of ADD (Pauls et al, 1983). Twin studies also demonstrate a higher concordance of hyperactivity in monozygotic versus dizygotic twins (Torgerson and Kringlen,

1978). Additionally, a study which compared adopted children whose biological parents were psychiatrically disturbed with adopted children of mentally normal parents found that the children of disturbed parents were more likely to have problems, particularly hyperactivity (Cunningham et al, 1975).

It has also been hypothesized that a hyperactive child is in a state of disordered arousal (Satterfield and Dawson, 1971). However, later studies have yielded contradictory results (Satterfield et al, 1979) which in turn casts doubt on hyperactivity as solely a dysfunction of arousal. Instead, ADD children may have a higher reward threshold than do normal children. This need for reward may manifest itself in inappropriate behavior (Haenlein and Caul, 1987).

A genetic flaw in the central nervous system, particularly in the dopamine subsystem, has been postulated as a factor in a child's development of ADD (Evans, Gualtieri, and Hicks, 1986). Other studies have implicated a CNS dysfunction in the frontal lobes (Lou, Henricksen, and Bruhn, 1984) and a decreased glucose mechanism in the prefrontal cortex (Zamekin et al, 1990). Regardless of the specific research hypothesis being tested, current etiological research has moved from a single causative factor to the interplay of multiple biological and environmental factors. Because of this, the cooperation of numerous experts, in the assessment of a given child, has become crucial.

3.3 USE OF DRUGS TO CONTROL SYMPTOMS

The discovery of the "paradoxical quieting effect" and the marked behavioral and school improvement of hyperactive children treated with Benzedrine (a mixture of dextro- and levoamphetamine) was important breakthrough (Bradley, 1937). It has been estimated that about 86% of hyperactive children will, at some time, be given medication to control their symptoms (Lambert et al, 1979). Additionally, about 75% of hyperactive children seem to respond favorably to medication, particularly CNS stimulants (Routh, 1983). In a recent placebo-controlled trial, adolescents with a childhood history of ADD who were given stimulants showed significant improvement in behavior, attention to tasks, vigilance and excitability, as noted by both parents and teachers (Klorman, 1988). However, this increased use of stimulants is controversial. By 1987, six percent of public elementary school children had been prescribed stimulants (Shaywitz and Shaywitz, 1988). Studies have shown a less favorable response to stimulants among preschoolers than among older children (Schleifer et al, 1975). In summary, stimulants seem to improve symptoms of attention span and increased motor activity, but the medication does not cure the condition and it is of short-term duration, only.

3.4 SYMPTOM CONTROL THROUGH BEHAVIOR MODIFICATION

Although drugs have been used quite frequently in quelling some of the more disruptive behaviors of children with ADD, behavioral therapy has not

been used as frequently. Indeed, in a recent national survey of family practitioners, it was noted that there was a serious under-use of systematic behavioral treatments in the primary care of ADD children (Wolraich et al, 1990). The behavioral modifications may be grouped into two major categories: positive reinforcement such as praise and tangible rewards and negative reinforcement such as time-out and verbal reprimand. Although negative reinforcement may be appropriate in specific instances, it is generally believed that positive reinforcement can be as effective in modifying a child's behavior without weakening their self-esteem (Lin-Dyken and Wolraich, 1992). Behavioral modification may actually help the child develop internally, rather than externally, imposed control which can result in excellent short-term benefits (Douglas et al, 1976). However, setting up and maintaining a behavioral program involves considerable time and skill (Copeland and Wolraich, 1987). Additionally, parents, teachers, and siblings must understand how their own attitudes influence and augment a child's behavior. Multiple-problem families, frequently characterized by parental drug abuse, depression, spouse/child abuse, and/or precarious finances, require extensive case-work and psychiatric intervention before the ADD child's problems may be considered.

3.5 OUTCOMES OF RESEARCH IN HYPERACTIVITY

If the above helped generate widespread research interest in the hyperactive syndrome (and in the past 5 years the number of publications is still increasing), the question remains as to whether the research has been beneficial. Robert Sprague, a key researcher in the field, wrote, "such a mass of contradictory and misleading literature confounds...". (Sprague, 1979). Ross and Ross (1982) in their revised textbook comment that intervention research in hyperactivity has too often been uncontrolled and short term, without assessing either long-term effect or generalization into natural settings. They also emphasized the difficulties of comparing results across studies which have used different methodologies and inclusion criteria and finally researchers demonstrating the same findings over and over again.

While these points are well made, the reader should bear in mind that research on the hyperactive child led the field of research in child psychopathology. We see the painstaking slowness in generating a solid body of empirical data as the growing pains of beginning research in a complex area. For example, much current research is focusing on "childhood depression." The researcher interested in this equally complex condition can learn both from the mistakes and from the resultant better grasp of crucial methodological issues which arose from research on hyperactivity. Certainly in the past 5 years new research findings concerning the hyperactive syndrome have led to some

interesting questions, not the least of which is the controversy over the existence of a syndrome of hyperactivity apart from that of conduct disorder.

The clinical picture has wide agreement among investigators and clinicians. Hyperactive children have a short attention span, high distractibility, and an inability to ignore extraneous stimuli while trying to attend to a task. They are impulsive in behavior and on cognitive tasks, they do not "stop, look, and listen," and they jump in where angels fear to tread. They speak out of turn, and impulsively interrupt adults. They have a hard time regulating their activity to conform with expected social norms, and may be actually overactive or inappropriately active. They tend to have poor frustration tolerance and are often poor at losing games, waiting in line, obeying rules of a game, etc. The main presenting symptoms vary according to the age of the child referred, and for this reason subsequent chapters are devoted to discussions of the syndrome at different ages. All these attributes are well summarized in DSM-III under the diagnosis ADD(H). The clinical picture is so well known that one is almost hesitant to describe it once again. What is less well known are the conceptual difficulties in calling these symptoms one syndrome and giving them the status of a diagnosis.

In a review article, David Shaffer and Lawrence Greenhill (1979) questioned the value of the concept of the hyperactive child syndrome. They felt that on the grounds of postdictive, concurrent, and predictive validity there was insufficient evidence for the presence of a syndrome. Postdictive validity

required that there be a common etiology, which would direct the clinician to the underlying psychopathology or neurophysiology. Concurrent validity required that the children who are diagnosed as hyperactive differ from other deviant children on grounds other than the presence of the defining symptoms. This does not mean that all hyperactive children must have identical symptoms, but rather that some generalizations should be able to be made about the clinical state by virtue of belonging to the diagnosis. Predictive validity would be present if in spite of diverse etiology, prediction could be made about the natural history, final outcome, and response to treatment.

In their perusal of the literature, Shaffer and Greenhill (1979) conclude that a diagnosis of the hyperactive child syndrome tells little about etiology and does not allow generalizations to be made about clinical state. Finally, after reviewing the available follow-up studies, they found that these indicated widely different outcomes, so that in their view the syndrome lacks also predictive validity. They concluded that there is little validity or clinical usefulness for the diagnostic concept of the hyperactive child syndrome.

With respect to postdictive validity, no one etiology has been demonstrated for the hyperactive syndrome. Various possible biological etiologies or at least correlates exist, which were summarized in an excellent review article by Rapoport et al (1978). They discussed the following:

1.) Prenatal and perinatal risk, referring to Knobloch and Pasamanick's findings and the results of the Kauai study, which indicated that

there was a group of children whose environment was not good enough to compensate for perinatal trauma to the brain. In these children, conditions such as the hyperactive syndrome were present. The collaborative project of the National Institute of Neurological Diseases and Strokes (NINDS) followed 50,000 pregnancies until the children were 7 years old. Hyperactivity was one of four factors at age 7 which could be predicted from prenatal variables.

2.) Some studies have shown that hyperactive children compared to normals have a greater number of soft neurological signs (Mikkelson, 1980). However, both the specificity of this finding for hyperactive children compared to other disturbed children and its significance are obscure.

3.) Rapoport and Quinn (1979) and Waldrop and Halverson (1971) reported the association of minor physical anomalies with children who were hyperactive.

4.) Review articles are now available which summarize the data related to underarousal of some hyperactive children.

5.) Toxic substances appear to be causal in some hyperactive children. For example, high levels of lead in the blood of some hyperactive children are improved by chelation therapy. In addition, Fetal Alcohol Syndrome has been demonstrated by Shaywitz et al 1980[a] to result sometimes in hyperactivity.

6.) Genetic factors may be causal.

7.) Biochemical abnormalities have been postulated to lead to the syndrome of hyperactivity. Much work is currently proceeding to clarify the issue. Various investigators have postulated from their findings that hyperactive children have deficiencies in dopamine transmission.

In addition to the above, a recent study from Sweden of 141 hyperactive children (selected from 4000 kindergarten children), who were evaluated two years later at age 7 and compared to 59 normal controls, indicated a remarkably strong correlation of hyperactivity with signs of cerebral dysfunction. Eighty-seven percent of the children who had pervasive hyperactivity also had signs of brain dysfunction).

One may conclude that biological correlates clearly exist, some of which are causal. However, as Rapoport et al (1978) pointed out, some of the correlates sometimes lack specificity for the hyperactive syndrome and may also be present in other disturbed children. Furthermore, as shown in the Kauai study, organic antecedents interact with psychosocial factors which may be stronger predictors (Werner and Smith, 1977). Many investigators now take an interactional view of causality and consider the hyperactive syndrome to be the final common path of various antecedent variables, which include both biological and psychosocial factors.

3.6 ADDITIONAL SYNDROMES

With respect to the hyperactive child syndrome, there are some analogies. Only a small percentage of hyperactive children have a single known organic pathology. The majority have varying degrees of biological (brain damage or dysfunction) and psychosocial antecedent variables. Recent findings indicate that the syndrome has concurrent validity. If a child is diagnosed to be pervasively hyperactive, he or she is more likely to have concomitant:

1.) Cognitive deficits (including lower IQ)

2.) Reading retardation

3.) More severe other psychiatric problems

4.) Neurodevelopmental difficulties (i.e., signs and symptoms of MBD)

5.) Symptoms of the syndrome which are likely to endure

Although there are some discrepancies in the findings of outcome, there appear to be similarity of the results from very widely different kinds of studies, all of which agree on some fundamental outcome issues, suggesting that there exists a fairly high predictive validity.

Michael Rutter (1982) has recently summarized in a masterful review article the various difficulties in making a diagnosis of the hyperactive syndrome in spite of the widely accepted behavioral symptoms. He concluded that the notion of a hyperactive syndrome begins to look rather illusionary. We will

discuss briefly some of the difficulties he referred to regarding the concept of hyperactivity as a distinct syndrome.

1.) Studies by Kenny et al (1971) and Lambert et al (1978) showed that there was relatively low agreement among parents, teachers, and clinicians as to which children were reported as hyperactive. This low level of agreement may have two quite different reasons. One possibility is that inter-observer reliability is indeed poor. That is, two people looking at the same time at the same child do not agree on whether the behavior is hyperactive. This has not been demonstrated in the literature. A second reason for the poor correlation of different defining systems is that a given child may be situationally hyperactive, that is, hyperactive either at home or at school or in the physician's office. When a child is hyperactive in all these situations, he or she is said to be "pervasively" hyperactive, as opposed to "situationally" hyperactive. The confusion between pervasive and situational hyperactivity has plagued the literature, and even the nomenclature of DSM-III. The latter suggests that when parents' reports do not agree with teachers' reports of hyperactivity, the latter should be given preference. Barkley has suggested that the disorder should be diagnosed only when it is "pervasive" and has drawn attention to the lack of clarity regarding this issue in the DSM-III diagnosis of ADD(H). It was felt when studies were initiated in the early 1960s that when hyperactive symptoms were specific to one situation there was a stronger possibility that the child was reacting to that situation, be it in the home or in the classroom.

2.) A second problem regarding the hyperactive syndrome mentioned by Rutter is the difference in prevalence of the hyperactive child syndrome between the United States and Britain. Figures in Britain used to be given as 1 in 1000 and as 5% in the United States. There are important new data on this apparent discrepancy, which previously was assumed to be due only to diagnostic criteria differences between the United States and Britain; namely that the British workers excluded hyperactive-aggressive children from the hyperactive child syndrome diagnosis and included them in the conduct disorder category. Now we know that this discrepancy was also confounded by confusing pervasively and situationally hyperactive children. Lambert et al (1978) found that 1.2% of 5000 children living in the East Bay area near San Francisco were hyperactive when diagnosed by the parents and the teacher and the physician. In an attempt to confirm this finding from the United States, Schachar and coworkers returned to the Isle of Wright in 1975-1976, 5 years after their initial studies, and once again sent questionnaires to teachers and parents of all 14- and 15-year old adolescents on the island (Schachar et al, 1981). Of approximately 2000 children, 500 were excluded, mostly because parents failed to return the questionnaire. The 25% who could not be followed represented a more deviant subgroup (lower socioeconomic status, more likely to be rated by teacher as disturbed, initially more hyperactive, and having lower scores on cognitive tests). Hence, the finding that 2% of the children who were contacted were pervasively hyperactive represents, if anything, an

understatement. We can conclude that when the issue of pervasive versus situational hyperactivity is addressed, prevalence figures are remarkably constant for the hyperactive syndrome in the United States and in Britain.

3.) Rutter also suggested that the poor agreement between different measures of hyperactivity - for example, the many mechanical devices available (actometer, watch, ballistographic cushion, photoelectric systems, etc.), direct observational methods in natural settings, and questionnaires -- muddies the definition of the syndrome. A mechanical device measures quantity of activity. Teachers' or parents' ratings on a questionnaire may measure quantity, but are more likely to measure mainly the type of non-task-oriented and annoying activity characteristic of hyperactive children. Our feeling is that good correlation between these two types of measurement would be highly unlikely, for they obviously measure different things.

4.) Until recently, few investigators could demonstrate by statistical techniques (e.g., factor analysis) a factor for hyperactivity. More recently, Shachar et al (1981) found that combining both parent and teach scales of the Rutter questionnaire at ages 10 and 15, resulted in a restricted factor of these items. These were "very restless," "squirmy," and "cannot settle to anything," which represented one dimension in the ratings of both sexes in pervasively hyperactive children. They called this factor the "hyperactivity factor." In addition, the empirically derived syndrome of Achenback include a narrow-band Hyperactivity Disorder (including attention deficit). Langhorne et

al (1980) have demonstrated that a factor of hyperactivity could be obtained if the ratings of a child were derived from one source, for example, the teacher or the parent.

While Langhorne has cautioned against a tendency to rely solely on factor-analytic studies in the issue of syndrome status for hyperactivity, the most recent study on this issue gave clear evidence of the existence of an independent factor of hyperactivity. Trites and laprade (1983) carried out factor-analytic studies on Conners teacher ratings of 9000 elementary-school children. They found a factor of hyperactivity which accounted for the greatest proportion of the variance. When these investigators looked at the overlap between the factors of conduct disorder and hyperactivity, they found a group of children who were hyperactive and not conduct disordered. These authors suggest that their findings provide evidence for an independent syndrome of hyperactivity in a sample of Canadian children.

5.) Finally, there is the as yet unsolved problem of the overlap with conduct disorders. Schachar et al's (1981) findings indicated that pervasively hyperactive children had a higher likelihood of conduct disorders, which were present in two-thirds of the pervasively hyperactive children and in one-half of the situationally hyperactive group ($p < 0..01$). This finding of the large overlap between hyperactive and aggressive (or conduct-problem) children has been found by virtually all workers, including systematic studies by Stewart et al (1981) in Iowa and by McGee, Williams, and Silva (1984) in Dunedan, New

Zealand. Whether or not there is anything to be gained by separating diagnostically conduct disorders without hyperactivity and hyperactivity with or without conduct disorders is not only a semantic issue. The issue rests on whether these conditions are distinct with respect to treatment and outcome.

The concerns of Shaffer, Greenhill, Rutter, and others regarding the existence of a distinct syndrome have been dealt with in detail. Empirical findings described as well as alternate explanations for the difficulties they have raised clearly lead, in the opinion of the authors, to the conclusion that a syndrome of hyperactivity exists. It is also clear that clinically most (but not all) children diagnosed as hyperactive have some degree of concurrent conduct disorder, at least at some stage of their development.
adulthood.

3.7 Diagnostic Criteria

There are several key clinical issues regarding diagnosis and assessment. The diagnosis of hyperactivity is not made on the basis of a single symptom. Indeed, there are no definitive tests and no unequivocal positive indicators. Instead, several symptoms, behavioral and (sometimes) cognitive difficulties, appear together in one child form the syndrome. This syndrome is usually present in some form from early childhood, although it may not be diagnosed until the child enters school. Hyperactivity and related symptoms may also occur along with other diagnoses such as childhood psychosis,

autism, cerebral palsy, and mental retardation. Most studies of hyperactive children tend to exclude children with the above other disorders as the primary diagnoses.

The following operational criteria are listed in DSM-III for ADD(H):

A.) Inattention (at least three of the following)

1.) Often fails to finish things he or she starts

2.) Often does not seem to listen

3.) Easily distracted

4.) Has difficulty concentrating on schoolwork or other tasks requiring sustained attention

5.) Has difficulty sticking to a play activity

B.) Hyperactivity (at least two of the following)

1.) Runs about or climbs on things excessively

2.) Has difficulty sitting still or fidgets excessively

3.) Has difficulty staying seated

4.) Moves about excessively during sleep

5.) Is always on the go or acts as if "driven by a motor"

C.) Impulsiveness (at least three of the following)

1.) Often acts before thinking

2.) Shifts excessively from one activity to another

3.) Has difficulty organizing work (this not due to cognitive

impairment)

4.) Needs a lot of supervision

5.) Frequently calls out in class

6.) Has difficulty awaiting turn in games or group situations

D.) Onset before the age of 7

E.) Duration of at least 6 months

F.) Not due to schizophrenia, affective disorder, or severe or profound mental retardation

Barkley (1982) has expressed the view held by many clinicians and researchers that the above DSM-III criteria represent an improvement over other classifications. However, he noted the lack of norms at different ages for determining abnormality of symptoms and the failure to clarify whether the condition is pervasive or situational. Others have commented on the degree of overlap between symptoms even across categories (McGee and Share, 1988).

An additional development of the concept of ADD(H) may be seen in DSM-IV. A diagnosis of Attention-Deficit/Hyperactivity Disorder may be done if either Situation 1 or Situation 2 occurs.

A.) Situation 1: Six (or more) of the following symptoms of inattention have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level.

1.) Often fails to give close attention to details or makes careless

mistakes in schoolwork, work, or other activities.

2.) Often has difficulty sustaining attention in tasks or play activities

3.) Often does not seem to listen when spoken to directly

4.) Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)

5.) Often has difficulty organizing tasks and activities

6.) Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)

7.) Often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools)

8.) Is often easily distracted by extraneous stimuli

9.) Is often forgetful in daily activities

Situation 2: Six (or more) of the following symptoms of hyperactivity-impulsiveness have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level.

Hyperactivity:

1.) Often fidgets with hands or feet or squirms in seat

2.) Often leaves seat in classroom or in other situations in which

remaining seated is expected.

3.) Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)

4.) Often has difficulty playing or engaging in leisure activities quietly

5.) Is often "on the go" or often acts as if "driven by a motor"

6.) Often talks excessively

Impulsiveness:

1.) Often blurts out answers before questions have been completed

2.) Often has difficulty awaiting turn

3.) Often interrupts or intrudes on others (e.g., butts into conversations or games)

B.) Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before age 7 years.

C.) Some impairment from the symptoms is present in two or more settings (e.g., at school/work and at home)

D.) There should be clear evidence of clinically significant impairment in social, academic, or occupational functioning.

E.) The symptoms do not occur exclusively during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder and are not better accounted for by another mental disorder (e.g., Mood Disorder, Anxiety Disorder, Dissociative Disorder, or a Personality Disorder).

A person may be considered to have "Attention-Deficit/Hyperactivity Disorder, Combined Type" if both Situations 1 and 2 occur for the past six months. A person has "Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Type" if Situation 1 occurred but not Situation 2 for the past six months. A person has "Attention-Deficit/Hyperactivity Disorder, Predominantly Hyperactive-Impulsive Type" if Situation 2 happened but Situation 1 did not occur for the past six months. A category for "Attention-Deficit/Hyperactivity Disorder Not Otherwise Specified" is for those disorders with prominent symptoms of inattention or hyperactivity-impulsiveness that do not meet criteria for Attention-Deficit/Hyperactivity Disorder.

3.8 Diagnostic Process

A comprehensive multidisciplinary assessment is required for diagnosis in order to formulate the optimal treatment plan, which must be directed to whatever deficits exist in the child, family, and school. The following types of evaluation are usually carried out.

1.) A history of the pregnancy, delivery, and the child's developmental milestones from infancy on. A parental history of hyperactivity, alcoholism, sociopathy, hysteria, may be looked for.

2.) Assessment of the child's behavioral aberrations; the specific symptoms present, their severity and frequency, the degree to which individual symptoms are situational; the duration of the problem.

3.) An educational assessment to determine if a specific learning disability is present and if so, its nature. This is a great importance for remedial educational measures.

4.) Assessment of the intrapsychic processes in the child, how he or she views himself or herself, family, peers, school; what personality strengths the child possesses.

5.) Assessment of the interactions of the child and family. Cause and effect are irrelevant at the point of diagnosis after years of interaction. Parents frequently require help to interact constructively, and their guilt and blaming of one another needs to be addressed.

6.) Assessment of the child's classroom. Is the educational environment conducive to learning? Sometimes specific remedial programs can be incorporated into the regular school curriculum. Based upon the experience of several psychologists, it was rare that a "special education class" was required. The relationship between the child and teacher may require

help, and the teacher can benefit from being brought into the treatment team as an important member, for assessment, diagnosis, and management.

7.) Assessment of the child's neurological status if there is any suspicion of a neurological lesion. Routine neurological examinations of hyperactive children are usually negative except for the presence of soft signs whose significance is not known. EEG's often show diffuse dysrhythmias which tend to disappear in adolescence. Again, the significance is not known.

In conclusion, hyperactivity in childhood, now termed ADD(H), has a long history of terminologies reflecting different theories of etiology or current thinking on key symptoms of the syndrome. The syndrome for various reasons has attracted a great deal of research, some of which has thrown doubt on the existence of a specific syndrome. There appears to be substantial evidence for the existence of a syndrome of hyperactivity. Various biological measures can be shown to correlate with the hyperactive syndrome, but these correlations are nonspecific and are overshadowed by psychosocial parameters. To make a diagnosis, a careful assessment of biological and psychosocial factors is required and is carried out usually by professionals of different disciplines.

CHAPTER 4 FLMCM

4.1 INTRODUCTION

In this chapter, a modification of the method called "fuzzy linguistic multi-criteria measure" (FLMCM), developed by Liou and Wang (1994) is presented. In the FLMCM method, the criteria ratings of symptoms/diagnostic elements and their corresponding importance weights are assessed through linguistic terms which can be described by fuzzy numbers. The criteria and weights are combined through a fuzzy weighted average. The resulting fuzzy number is translated back into linguistic terms. This translation allows the linguistic representation of the overall subjective medical assessment to be obtained.

For the purpose of completeness, the concepts of linguistic variables and fuzzy numbers are defined. Additionally, several fuzzy operations with α-cuts are presented. The definitions and notation which is used may be found in a variety of books, notably in Kaufmann and Gupta (1985).

Definition 4.1 (Linguistic variable): A linguistic variable is a variable whose values are words or sentences in a natural or artificial language.

For example, "height" may be a linguistic variable if its values are linguistic rather than numerical. The values could be, for example, "very tall", "tall", "medium", "short", and "very short". Since linguistic values are frequently too

nebulous, ill-defined, or complex to be characterized quantitatively, they can be represented by the approximate reasoning of fuzzy set theory. For the purpose of this paper, the symptom criteria and their importance weights are considered to be linguistic variables. The resulting combination of the criteria and weights, although calculated as a fuzzy number, will be translated back into linguistic terms.

Fuzzy set theory was introduced by Zadeh (1965) to deal with problems where subjective criteria were specified. A fuzzy number may be considered as a special fuzzy subset of real numbers. The concepts of a fuzzy number and its integral are defined in the following manner.

Definition 4.2 (Fuzzy number): A real fuzzy number A is a fuzzy subset of the real line with membership function f_A which satisfies the following conditions:

I.) f_A is a continuous function from $\Re$ to a closed interval [0,1].

ii.) $f_A(x) = 0$ for all $x \in (-\infty, a]$

iii.) f_A is strictly increasing on [a, b]

iv.) $f_A(x) = 1$ for all $x \in [b,c]$

v.) f_A is strictly decreasing on [c, d]

vi.) $f_A(x) = 0$ for all $x \in [d,\infty)$

where $a \le b \le c \le d \in \Re$. Unless otherwise specified, it is assumed that A is convex, normal and bounded (i.e. $-\infty < a , d < \infty$).

For notational convenience, the fuzzy number in the previous definition can be denoted by [a,b,c,d], and the membership function f_A of the fuzzy number A=[a,b,c,d] can be expressed as

$$f_A(x) = \begin{cases} f_A^L(x) & , a \le x \le b \\ 1 & , b \le x \le c \\ f_A^R(x) & , c \le x \le d \\ 0 & , \text{otherwise} \end{cases} \qquad (4.1.1)$$

where $f_A^L : [a, b] \to [0, 1]$ and $f_A^R : [c, d] \to [0,1]$.

From Definition 4.2, it is clear that $f_A^L(x)$, which is the left membership function of the fuzzy number A, is continuous and strictly increasing on [a, b], and $f_A^R(x)$, which is the right membership function of the fuzzy number A, is continuous and strictly decreasing on [c, d].

The inverse functions of f_A^L and f_A^R are denoted by g_A^L and g_A^R respectively. In the special case of a=b, then $f_A^L(x) = f_A^L(b) = 1$ and $g_A^L(y) = b$ for $y \in [0, 1]$. Similarly, if c=d then $f_A^R(x) = f_A^R(c) = 1$ and $g_A^R(y) = c$ for $y \in [0, 1]$.

Definition 4.3 (Integral value of A): Suppose A is a fuzzy number with the left membership function f_A^L and the right membership function f_A^R. Suppose that

g_A^L is the inverse function of f_A^L and g_A^R is the inverse function of f_A^R. Then the left integral value of A is defined as

$$I_L(A) = \int_0^1 g_A^L(y)dy \tag{4.1.2}$$

and the right integral value of A is defined as

$$I_R(A) = \int_0^1 g_A^R(y)dy. \tag{4.1.3}$$

Definition 4.3 (Total Integral Value): If A is a fuzzy number with membership function f_A, then the total integral value with the index of optimism k is

$$I_T^k(A) = k\, I_R(A) + (1-k)\, I_L(A) \tag{4.1.4}$$

where $I_R(A)$ and $I_L(A)$ are the right and left integral values of A respectively, and $k \in [0, 1]$.

The index of optimism k represents the degree of optimism of a decision maker. A larger k indicates a higher degree of optimism. More specifically, when k=0, the total integral value represents a pessimistic decision maker's viewpoint and is equal to the left integral value of A. Conversely, for an optimistic decision maker, i.e. k=1, the total integral value is equal to the right integral value. For a moderate decision maker, with k=0.5, the total integral value becomes the arithmetic average of the two quantities, namely

$$I_T^{0.5}(A) = 0.5\{I_R(A) + I_L(A)\}. \tag{4.1.5}$$

Definition 4.4 (Trapezoidal Fuzzy Number): Given $a > -\infty$ and $d < \infty$ when $b \neq c$ and f_A has two straight line segments in [a, b] and [c, d] then A is a trapezoidal fuzzy number, and is denoted by (a, b, c, d;1).

A triangular fuzzy number is a special case of a trapezoidal fuzzy number with b=c. In this case, it is denoted by (a,b,d;1). In this section, linguistic values are represented either by triangular or trapezoidal fuzzy numbers due to their ease in use and interpretation. However, in general, the membership functions need only adhere to the properties of fuzzy numbers. For convenience, some basic properties of fuzzy numbers are presented.

Definition 4.5 (α-cut of A): Suppose that A is a fuzzy number with membership function f_A. Then for every $\alpha \in [0, 1]$, the set $A_\alpha = \{x | f_A(x) \geq \alpha\}$ is called an α-cut of A. If $\alpha=0$, then $A_\alpha = \{x | f_A(x) > \alpha\} \cup [a, b]$ where a and b are the infimum and supremum of $A_\alpha = \{x | f_A(x) > \alpha\}$ respectively.

Since the membership function of a fuzzy number is continuous in $\Re$, the α-cut of fuzzy number A is a closed interval. This can be denoted by $A_\alpha = [a_1^\alpha , a_2^\alpha]$. Further, the addition and multiplication of fuzzy numbers are defined as follows.

Definition 4.6 (Addition of Fuzzy Numbers) : The sum of fuzzy numbers A and B is a fuzzy number, denoted by $A \oplus B$ with membership function

$$f_{A \oplus B}(z) = \max_{z=x+y}(\min[f_A(x), f_B(y)]) \qquad (4.1.6)$$

Proposition 4.1: The α-cut of $A \oplus B$ is $[a_1^\alpha + b_1^\alpha , a_2^\alpha + b_2^\alpha]$.

Definition 4.7 (Multiplication of Fuzzy Numbers): Suppose A and B are two nonnegative fuzzy numbers. The product of A and B is a fuzzy number, denoted by $A \otimes B$ with membership function $f_{A \otimes B}$ where

$$f_{A \otimes B}(z) = \max_{z=xy}(\min[f_A(x), f_B(y)]) \qquad (4.1.7)$$

Proposition 4.2: The α-cut of $A \oplus B$ is $[a_1^\alpha \, b_1^\alpha , a_2^\alpha \, b_2^\alpha]$.

Definition 4.8 (Multiplication of a fuzzy number by an ordinary number): The product of a fuzzy number and an ordinary number $k \in \Re^+$ is a fuzzy number, denoted by kA. The membership function is f_{kA} where $f_{kA}(z) = f_A(x)$, for $z=kx$.

Proposition 4.3: The α - cut of kA is $[ka_1^\alpha, ka_2^\alpha]$.

4.2 FLMCM ALGORITHM

The framework of the fuzzy linguistic multi-criteria measure method is as follows:

a.) Measure the subjective assessment of disease

b.) Select criteria for ascertaining that disease

c.) Assign criteria ratings and weights using linguistic terms (These are linguistic values of linguistic variables)

d.) Represent the linguistic ratings and weights as fuzzy numbers

e.) Aggregate these fuzzy numbers by finding the fuzzy weighted average

f.) Obtain an aggregated fuzzy number which represents the overall assessment of disease

g.) Translate the aggregated fuzzy number back to linguistic terms (The integral values and an optimism index used to rank fuzzy numbers is applied)

h.) Overall assessment of disease in linguistic terms is obtained.

Suppose there is a set of decision criteria C_1, C_2, ..., C_n which are utilized to represent different aspects of the disease assessment and to each criterion C_i, an importance weight W_i is assigned. The criteria are linguistic variables with linguistic values VL, L, M, H, and VH, where VL = Very Low, L=Low, M=Medium, H=High, and VH = Very High. For ease of application, these linguistic values are treated as fuzzy numbers with triangular membership functions. These membership functions, which have been determined

somewhat arbitrarily, may be given by the following formulae. The graphs for these function are given in Figure 1.

VL: (0,0,3;1) $f_C(x) = 1 - x/3,\ 0 \le x \le 3.$

L: (0, 3, 5;1) $$f_C(x) = \begin{cases} \frac{1}{3}x, & 0 \le x \le 3 \\ 0.5(5-x), & 3 \le x \le 5 \end{cases}$$

M: (2,5, 8; 1) $$f_C(x) = \begin{cases} \frac{1}{3}(x-2), 3 \le x \le 5 \\ \frac{1}{3}(8-x), 5 \le x \le 8 \end{cases}$$

H: (5,7,10;1) $$f_C(x) = \begin{cases} 0.5(x-5), 5 \le x \le 7 \\ \frac{1}{3}(10-x), 7 \le x \le 10 \end{cases}$$

VH: (7,10,10;1) $f_C(x) = (x-7)/3,\ 7 \le x \le 10.$

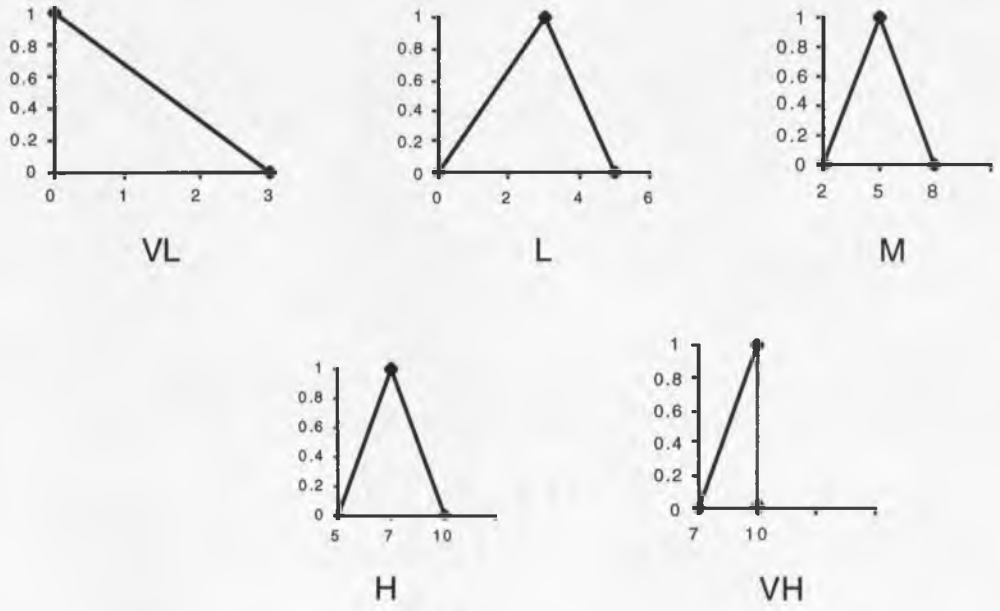

Figure 1: Membership functions of the criteria

Similarly, the importance weights are linguistic variables with linguistic values U, B.U & SI, SI, B.SL&M, M, B.M&SE, SE, B.SE&VSE, and VSE where U=Unimportant, B.U&SL=Between Unimportant and Slightly Important, SL =Slightly Important, B.SL&M=Between Slightly Important and Moderately Important, M=Moderately important, B.M&SE=Between Moderately Important and Seriously Important, SE=Seriously Important, B.SE&VSE=Between Seriously Important and Very Seriously Important, and VSE=Very Seriously Important. For ease of application, these linguistic values are treated as fuzzy numbers with triangular or trapezoidal membership functions. These membership functions, again derived as examples only, are as follows.

U: (0,0,2;1) $\quad f_W(x) = 0.5\,(2 - x), \quad 0 \le x \le 2$

B.U&SL: (0,0,2,4;1) $\quad f_W(x) = \begin{cases} 1, & 0 \le x \le 2 \\ \frac{1}{2}(4 - x), & 2 \le x \le 4 \end{cases}$

SL: (0,2, 4;1) $\quad f_W(x) = \begin{cases} \frac{1}{2}x, & 0 \le x \le 2 \\ \frac{1}{2}(4 - x), & 2 \le x \le 4 \end{cases}$

B.SL&M: (0,2,5,7;1) $\quad f_W(x) = \begin{cases} \frac{1}{2}x, & 0 \le x \le 2 \\ 1, & 2 \le x \le 5 \\ \frac{1}{2}(7 - x), & 5 \le x \le 7 \end{cases}$

M: (3,5,7;1) $\quad f_W(x) = \begin{cases} \frac{1}{2}(x - 3), & 3 \le x \le 5 \\ \frac{1}{2}(7 - x), & 5 \le x \le 7 \end{cases}$

B.M&SE: (3,5,8,10;1) $f_W(x) = \begin{cases} \frac{1}{2}(x-3), 3 \le x \le 5 \\ 1, \ 5 \le x \le 8 \\ \frac{1}{2}(10-x), 8 \le x \le 10 \end{cases}$

SE: (6,8,10;1) $f_W(x) = \begin{cases} \frac{1}{2}(x-6), 6 \le x \le 8 \\ \frac{1}{2}(10-x), 8 \le x \le 10 \end{cases}$

B.SE&VSE: (6,8,10,10;1) $f_W(x) = \begin{cases} \frac{1}{2}(x-6), 6 \le x \le 8 \\ 1, 8 \le x \le 10 \end{cases}$

VSE: (8,10,10;1) $f_W(x) = 0.5\,(x-8), \quad 8 \le x \le 10$

For each criterion C_i and its importance weight W_i, a linguistic rating value C^*_i and weighting W^*_i is assigned respectively, where $C^*_i \in S_C$ and $W^*_i \in S_W$ with i=1,2,...,n are fuzzy numbers, S_C = {VL,L,M,H,VH} and S_W = {U,B.U&SL, SL,B.SL&M,M,B.M&SE,SE,B.SE&VSE,VSE} are the sets of fuzzy numbers which represent the linguistic values. The C^*_i and W^*_i are then aggregated to get the final rating y*.

A fuzzy weighted average is used to combine the criteria ratings C^*_1, C^*_2, ..., C^*_n and their importance weights W^*_1, W^*_2, ..., W^*_n. This combination gives the weighted average y* which is the aggregation of different criteria C^*_i and their importance weights W^*_i. The weighted average is calculated by

$$y^* = f^*(C^*_1, C^*_2, ..., C^*_n, W^*_1, W^*_2, ..., W^*_n)$$

$$= \frac{W^*_1 \otimes C^*_1 \oplus \cdots \oplus W^*_n \otimes C^*_n}{W^*_1 \oplus \cdots \oplus W^*_n} \qquad (4.2.1)$$

4.3 FUZZY WEIGHTED AVERAGE

Calculation of the weighted average specified in Equation (4.2.1) may be a rather complicated procedure. As is customary with fuzzy numbers, however, interval arithmetic and α- cuts will be used. The following procedure streamlines a method of Liou and Wang by eliminating unnecessary index sets J, R_L, and R_U and by providing an easier iterative scheme.

1.) Divide the range of membership [0,1] into a finite number of values $\alpha_1, \alpha_2, ..., \alpha_m$ with $0 = \alpha_1 < \alpha_2 < ... < \alpha_{m-1} < \alpha_m = 1$. The degree of accuracy depends upon m, the number of α- cuts desired, which in turn depends upon the interpretation precision for the membership range.

2.) For each α_j, find the corresponding intervals $[a_i, b_i]$ and $[c_i, d_i]$ which are the α_j - cuts for C^*_i in x_i and W^*_i in W_i, i=1,2,...,n.

3.) Find the minimum and the maximum of

$$f(x_1, x_2, ..., x_n, w_1, w_2, ..., w_n) = \frac{w_1x_1 + \cdots + w_nx_n}{w_1 + \cdots + w_{n1}} \tag{4.3.1}$$

where $x_i=a_i$ or b_i, and $w_i=c_i$ or d_i, i=1,2,...,n. Define

$$f_L(w_1, w_2, ..., w_n) = f(a_1, a_2, ..., a_n, w_1, w_2, ..., w_n)$$

$$= \frac{w_1a_1 + \cdots + w_na_n}{w_1 + \cdots + w_{n1}} \tag{4.3.2}$$

$$f_U(w_1, w_2, ..., w_n) = f(b_1, b_2, ..., b_n, w_1, w_2, ..., w_n)$$

$$= \frac{w_1 b_1 + \cdots + w_n b_n}{w_1 + \cdots + w_{n1}} \tag{4.3.3}$$

$$f_L(w_1, w_2, ..., w_n | d_k) = f_L(w_1, ..., w_{k-1}, d_k, w_{k+1}, ..., w_n) \tag{4.3.4}$$

and

$$f_U(w_1, w_2, ..., w_n | d_k) = f_U(w_1, ..., w_{k-1}, d_k, w_{k+1}, ..., w_n). \tag{4.3.5}$$

To determine the previous minimum and maximum, the following computational steps are done.

a.) Let $L=f_L(c_1, c_2, ..., c_n)$ and $U=f_U(c_1, c_2, ..., c_n)$.

Let $I = \{I: a_i < L, i=1,2,...,n\}$ and $J=\{j: b_j > U, j=1,2,...,n\}$.

b.) If $I=\varnothing$ then L is the minimum of f_L and stop step (b)

Otherwise, $w_i = d_i$ for $i \in I$ and $w_i=c_i$ for $i \notin I$

b.1) Evaluate $L_i = f_L(w_1, w_2, ..., w_n | d_i)$ for $i \in I$

b.2) Let $L=L_m=\min_{i \in I} L_i$. Delete index m from set I.

b.3) If $I \neq \varnothing$, then repeat step (b).

Otherwise, stop step (b) and L is the minimum of f_L.

It has been shown that L is the minimum of $f(x_1, x_2, ..., x_n, w_1, w_2, ..., w_n)$ and the left end-point of the α_j - cut of y* is obtained (Liou and Wang, 1992).

c.) If $J=\varnothing$ then U is the maximum of f_U and stop step (c)

Otherwise, $w_i = d_i$ for $j \in J$ and $w_i=c_i$ for $j \notin J$

c.1) Evaluate $U_j = f_U(w_1, w_2, ..., w_n | d_j)$ for $j \in J$

c.2) Let $U = U_m = \max_{j \in J} U_j$. Delete index m from set J.

c.3) If $J \neq \varnothing$, then repeat step (c).

Otherwise, stop step (c) and U is the maximum of f_U.

It has been shown that U is the maximum of $f(x_1, x_2, ..., x_n, w_1, w_2, ..., w_n)$ and the right end-point of the α_j - cut of y* is obtained (Liou and Wang, 1992).

d.) [L, U] is the α - cut of y*. The α_j - cut of [L, U] is denoted by $[l_j, u_j]$.

4.) Repeat steps (b) and (c) for every α_j. From these α-cuts, an approximate membership function of y* is obtained.

The method for finding the α - cuts of y* is summarized in Figure 2.

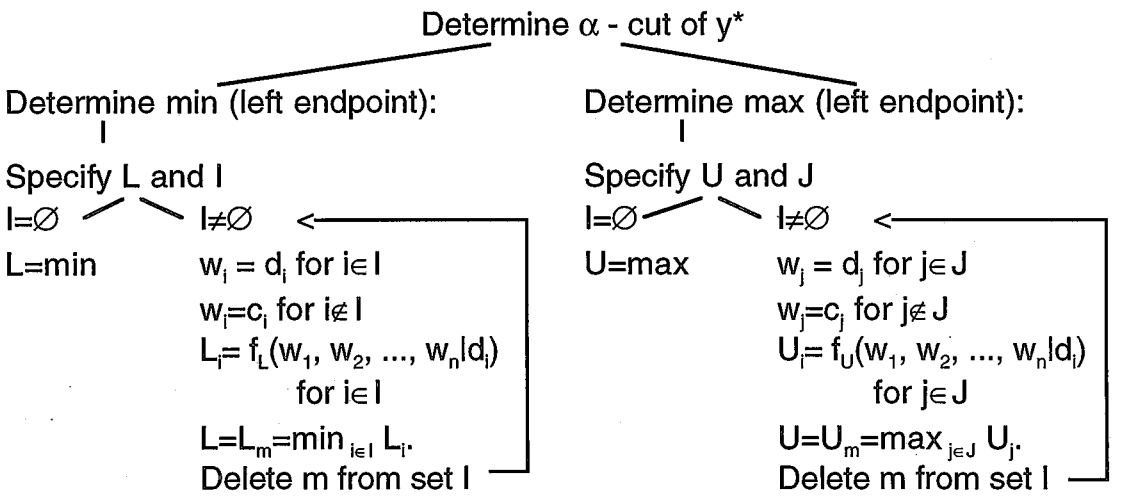

Figure 2: Flowchart for determination of an α - cut of y*

The aggregated rating of the disease assessment obtained by the fuzzy weighted average is a fuzzy number with an approximate membership function specified through the α-cuts. The fuzzy number may be readily translated into linguistic terms using its integral value and optimism index.

4.4 TRANSLATING FUZZY NUMBERS INTO LINGUISTIC TERMS

Translating a membership function back to linguistics is a rather sophisticated problem given that the desired fuzzy number is convex and normal. Several methods have been proposed (e.g. Schmucker (1985) and Eshragh and Mamdami (1979)). In this section, an optimism index method, proposed by Liou and Wang (1992), which ranks fuzzy numbers with integral value is applied.

Let d^*_i, i=1,2,...,n be fuzzy numbers with membership functions $f_{d^*i}(x)$, where x belongs to $\Re$, i=1,2,...,n. The definition of the left integral value $I_L(d^*_i)$ and the right integral value $I_R(d^*_i)$ are given by Definition 4.3.

An optimist would rank the d^*_i's using the $I_R(d^*_i)$ where the larger the $I_R(d^*_i)$, the higher the rank. On the contrary, a pessimist would rank the $d^*_{i's}$ by the $I_L(d^*_i)$. In general, $I_R(d^*_i)$ and $I_L(d^*_i)$ are combined through a convex combination with an index of optimism k, where $0 \le k \le 1$. A larger k value represents a higher degree of optimism. The total integral value of d^*_i is

$$I_T(d^*_i) = k\, I_R(d^*_i) + (1-k)\, I_L(d^*_i) \text{ where } 0 \le k \le 1. \qquad (4.4.1)$$

The concept of total integral value is then utilized to translate the aggregated measurement of disease assessment y* back to linguistic terms.

The criteria c^*_i may be chosen from the linguistic value set $S_C = \{VL,L,M,H,VH\}$. Let $S_D = \{d^*_1, ..., d^*_p\}$ where $d^*_i \in S_C$. Thus, the d^*_i are the rating criteria which were actually used in a given application. The total integral value $I_T(d^*_i)$ of d^*_i, i=1,2,...,p and $I_T(y^*)$ of y* can be found.

Without loss of generality, assume that $I_T(d^*_1) < I_T(d^*_2) < \ldots < I_T(d^*_p)$, $d^*_i \in S_D$ and i=1,2,...,p. Let $I_T(i) = I_T(d^*_1)$. Then there exists j such that $I_T(j) \leq I_T(y^*) \leq I_T(j+1)$. Let $M_0 = \min(| I_T(y^*) - I_T(j) |, | I_T(y^*) - I_T(j+1) |, |I_T(y^*) - 0.5[I_T(j) + I_T(j+1)]|)$.

Thus, the translation rules are:

1.) The linguistic disease assessment is d^*_j if $M_0 = | I_T(y^*) - I_T(j) |$

2.) The linguistic disease assessment is d^*_{j+1} if $M_0 = | I_T(y^*) - I_T(j+1) |$

3.) The linguistic disease assessment is between d^*_j and d^*_{j+1} if $M_0 = |I_T(y^*) - 0.5[I_T(j) + I_T(j+1)]|$.

For example, if d^*_j = M (Medium), d^*_{j+1} = H (High), then the disease assessment is "Medium" if $M_0 = | I_T(y^*) - I_T(j) |$; the disease assessment is High if $M_0 = | I_T(y^*) - I_T(j+1) |$ and the disease assessment is between Medium and High if $M_0 = |I_T(y^*) - 0.5[I_T(j) + I_T(j+1)]|$.

Since d^*_j , $d^*_j \in S_D$, is a fuzzy number with triangular membership function denoted by $(a_i, b_i, c_i;1)$, i=1,2,...,p, then from Definitions 4.1.2 - 4.1.3, the total integral value of d^*_j is

$$I_T(d^*) = 0.5[k\, c_i + b_i + (1-k)\, a_i],\ i=1,2,....,p. \qquad (4.4.2)$$

The α-cuts form an approximate membership function of y*. The points (l_i, α_i) and (u_i, α_i), i=1,2,...,m generate the approximate left membership function $f^L_{Y^*}$ and the right membership function $f^R_{Y^*}$ respectively. Hence, the points (α_i, l_i) and (α_i, u_i), i=1,2,...,m determine the approximate inverse function of $f^L_{Y^*}$ and $f^R_{Y^*}$ respectively. The necessary numerical integration, via Simpson's Rule, can be described as follows.

Divide the interval [0, 1] into n sub-intervals, where n is an even number, the length of each sub-interval h is equal to 1/n (i.e. h=1/n and m=n+1). Then the left integral value $I_L(y^*)$ and the right interval value $I_T(y^*)$ are

$$I_L(y^*) \approx h(l_1 + 4l_2 + 2l_3 + 4l_4 + 2l_5 + ... + 4l_n + l_{n+1})/3 \qquad (4.4.3)$$

$$I_U(y^*) \approx h(u_1 + 4u_2 + 2u_3 + 4u_4 + 2u_5 + ... + 4u_n + u_{n+1})/3 \qquad (4.4.4)$$

Thus, the total integral value of y* is

$$I_T(y^*) = k\, I_R(y^*) + b_i + (1-k)\, I_L(y^*) \qquad (4.4.5)$$

4.5 APPLICATION WITH SLE CASE DETERMINATION

The following is an example of a new application of the FLMCM algorithm. This application determines whether a given patient has SLE. Although the numbers which are used are fictitious, the appropriateness of the procedure will be demonstrated.

Characteristic	Weight	Severity for Patient
Malar Rash	Seriously Important (6,8,10)	Moderate (2,5,8)
Relative(s) with Lupus	Very Seriously Important (8,10,10)	Several (2,5,8)
Arthritis	Moderate (3,5,7)	Slight (0,3,5)
Fatigue	Slightly Important (0,2,4)	Severe (5,7,10)

Table 1: SLE criteria and weights

The first step in the procedure is to determine the α-cuts for y^* where

$$y^* = f^*(C^*_1, C^*_2, \ldots, C^*_n, W^*_1, W^*_2, \ldots, W^*_n)$$

$$= \frac{W_1^* \otimes C_1^* \oplus \cdots \oplus W_n^* \otimes C_n^*}{W_1^* \oplus \cdots \oplus W_n^*} \qquad (4.5.1)$$

For example, let α=1. Then, the α-cuts for the four given symptoms and their associated weights are given as follows.

Malar Rash:	[8,8] = 8	[5,5] = 5
Lupus Relative:	[10,10] = 10	[5,5] = 5
Arthritis:	[5,5] = 5	[3,3] = 3
Fatigue:	[2,2] = 2	[7,7] = 7

The evaluation of $f(C^*_1, C^*_2, \ldots, C^*_n, W^*_1, W^*_2, \ldots, W^*_n)$ reduces to ordinary arithmetic.

So $f(C^*_1, C^*_2, ..., C^*_n, W^*_1, W^*_2, ..., W^*_n)$

$= [8(5) + 10(5) + 5(3) + 2(7)]/[8 + 10 + 5 + 2] = 4.76$ (4. 5.2)

Similarly, the for α=0, the α-cuts for the four given symptoms and their associated weights are given as follows.

Malar Rash:	[6,10]	[2,8]
Lupus Relative:	[8,10]	[2,8]
Arthritis:	[3,7]	[0,5]
Fatigue:	[0,4]	[5,10]

The procedure for finding the approximation to y* at this α-cut must invoke the iterative scheme. Calculation of the lower endpoint (minimum) is given as follows.

Let the current minimum be

$L = [6(2) + 8(2) + 3(0) + 0(5)]/[6 + 8 + 3 + 0]$

$= 28/17 = 1.647$ (4.5.3)

Then, $I = \{i \mid a_i < L\} = \{3\}$. Thus, $L_3 = [6(2) + 8(2) + 7(0) + 5(0)]/[6 + 8 + 7 + 0]$ = 1.333. This improves (creates a lower value) the estimate for L. The new value for L is 1.333, and since $I = \varnothing$ for this step, the best estimate for L is 1.333.

Calculation of the upper endpoint (maximum) follows a similar procedure.

Let the current maximum be

$$U = [6(8) + 8(8) + 5(3) + 10(0)]/[6 + 8 + 3 + 0]$$
$$= 127/17 = 7.471 \qquad (4.5.4)$$

Then, $J = \{j \mid b_j > U\} = \{1,2,4\}$. Thus, three values must be tested to determine if an improvement in the maximum is obtained.

$$U_1 = [10(8) + 8(8) + 5(3) + 10(0)]/[10 + 8 + 3 + 0] = 7.571$$
$$U_2 = [6(8) + 10(8) + 5(3) + 10(0)]/[6 + 10 + 5 + 0] = 7.526 \qquad (4.5.5)$$
$$U_4 = [6(8) + 8(8) + 5(3) + 10(4)]/[6 + 8 + 3 + 4] = 7.952$$

Since U_4 improves the estimate (increases the maximum), then only two values are left to consider. Namely, $J = \{1, 2\}$. Calculations are repeated for the parameters which remain.

$$U_1 = [10(8) + 8(8) + 5(3) + 10(4)]/[10 + 8 + 3 + 4] = 7.96$$
$$U_2 = [6(8) + 10(8) + 5(3) + 10(4)]/[6 + 10 + 3 + 4] = 7.957 \qquad (4.5.6)$$

Again, the estimate is improved, U_1 is kept, and $J = \{2\}$. Improvement in the maximum is demonstrated with

$$U_2 = [10(8) + 10(8) + 5(3) + 10(4)]/[10 + 10 + 3 + 4] = 7.962. \qquad (4.5.7)$$

Since $J = \varnothing$ for this step, the upper endpoint of the α-cut is 7.962. For $\alpha = 0$, the interval is [1.333, 7.962].

This method of determining the approximated weighted average has a definite advantage over the typical method of fuzzy division. As can be seen in the following calculation, fuzzy division yields a much broader, and potentially less meaningful, interval.

Thus, the conservative approach to finding the fuzzy weighted average yields

$$\{[6,10][2,8] + \ldots + [0,4][5,10]\}/\{[6,10] + \ldots + [0,4]\}$$

$$= [28, 235] / [17, 31]$$

$$= [28/31, 235/17] = [0.903, 13.824] \qquad (4.5.8)$$

Although additional α-cuts may be obtained, it is sufficient for this example that the approximate membership function for y* is (1.333, 4.76, 7.962)

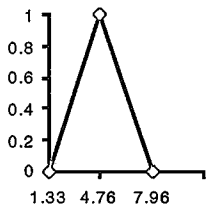

Figure 3: Approximate membership function for y*

To translate the fuzzy number into linguistic terms, the left and right membership functions of f and the corresponding inverse ones (g) are presented.

$$f_L(x) = (x-1.333)/3.427 \qquad g_L(y) = (3.427y + 1.333)$$

$$f_R(x) = (7.962 - x)/3.202 \qquad g_R(y) = (7.962 - 3.202y) \qquad (4.5.9)$$

Using the definition of a total integral, then

$$I_T(y^*) = 0.5\int_0^1(3.427y+1.333)dy + 0.5\int_0^1(7.962-3.202y)dy = 4.704 \qquad (4.5.10)$$

Since $I_T(d_1^*) = I_T(\text{Low}) = 2.75$ and $I_T(d_2^*) = I_T(\text{Moderate}) = 5$ then

$$M_0 = \min(|\, I_T(y^*) - I_T(d_1^*)\,|, |\, I_T(y^*) - I_T(d_2^*)\,|, |I_T(y^*) - 0.5[I_T(j) + I_T(j+1)]|)$$

$$= \min(1.954, 0.296, 0.829)$$

$$= 0.296 \qquad (4.5.11)$$

The minimum was associated with a moderate value. Hence, the linguistic translation of y* is that the patient has a moderate possibility of lupus.

CHAPTER 5 FUZZY ANALYSIS OF TREATMENT EFFECTIVENESS

5.1 INTRODUCTION

This chapter uses fuzzy set theory to distinguish the effectiveness of action of drugs in a group of patients. Since the criteria for effectiveness of a given drug is whether or not a particular symptom disappears over a given period of time, the question of long-term effectiveness is not considered. The decision regarding effectiveness is based on finding eigen-fuzzy sets associated with given fuzzy relations where the basic operation is a max-min composition. The theoretical model is applicable to both ADD and Lupus. Drugs or other treatment schemes may be taken by both sets of patients to influence their behavior.

Given the results of examination carried out on a group of patients with a set of symptoms, one can estimate the theoretical level of effectiveness of the drug used by the patients belonging to this group. The following fuzzy method provides a simple solution for finding the minimal and maximal level of recovery which, if found theoretically, may not change even during the extension of treatment. This method is based on the concept of eigen-fuzzy sets (Gerstenkorn and Rakus, 1994).

5.2 TREATMENT EFFECT ON SYMPTOMS

Let us assume that there are some characteristic symptoms in a sample of m observed patients. All the patients have the same symptoms, which in this case, are qualitative parameters. These symptoms should disappear entirely after the treatment if the drug is effective but persist when the drug is not effective enough. Denote the set of symptoms by $S = \{S_1,...,S_n\}$ where S_i is the ith symptom and S is a nonfuzzy set.

Estimation of the maximal level is possible using a fuzzy relation described by the sentence, "The action of the drug on the ith symptom is equal to or stronger than on the jth one, where i,j=1,2,...,n." Recall that the so-called relation R_1 is the set of pairs ($symptom_i$, $symptom_j$) for i,j=1,2,...,n and $\mu_{R1}(symptom_i, symptom_j)$ is the membership function of R_1 with [0,1] as the range indicating the degree to which the relation is true for the ith and jth symptoms. The type of membership function is taken either to be experimentally derived or assumed to be triangular/trapezoidal for mathematical convenience.

The influence of the tested drug or treatment on the symptoms must be compared for each pair of symptoms. Let a denote the number of patients examined and let b_{ij} denote the number of patients for whom the above description of R_1 constitutes the true sentence for $symptom_i$ and $symptom_j$. The membership function μ_{R1} is calculated according to

$$\mu_{R1}(S_i, S_j) = \frac{b_{ij}}{a},\ i, j = 1, 2, ..., n; i \neq j \qquad (5.2.1)$$

The following example illustrates how to estimate the membership function for two symptoms in a group of nine patients. Let "-" mean the lack of the symptom after treatment and "+" its constant presence; to find b, we must consider both configurations of these signs, i.e.

- -, the drug acts as strongly on S_i as on S_j

- +, the drug acts more strongly on S_i than on S_j . An example of these configurations is in Table 2.

Patient	S_i	S_j
P_1	-	-
P_2	-	+
P_3	-	+
P_4	+	+
P_5	-	-
P_6	+	-
P_7	+	+
P_8	+	+
P_9	+	+

Table 2: Treatment effectiveness

The membership function of the pairs (S_i, S_j) is 0.444 (i.e. 4 out of 9) and for (S_j, S_i) it is 0.333 (3 out of 9). Thus, the fuzzy relation R_1 can be written as a matrix:

$$R_1 = \begin{bmatrix} 0 & \mu_{R1}(S_1, S_2) & \cdots & \mu_{R1}(S_1, S_n) \\ \mu_{R1}(S_2, S_1) & 0 & \cdots & \mu_{R1}(S_2, S_n) \\ \vdots & & \ddots & \\ \mu_{R1}(S_n, S_1) & \mu_{R1}(S_n, S_2) & \cdots & 0 \end{bmatrix} \tag{5.2.2}$$

The diagonal elements of R_1 are zero by definition.

5.3 EIGEN-FUZZY SET

The next step in the process of determining drug effectiveness requires Gerstenkorn's and Rakus' notion of an eigen-fuzzy set W_1 which is associated with a fuzzy relation R_1. Their procedure is simplified to a one-step eigen-fuzzy method.

Definition 5.1 (Eigen-fuzzy set): Let W_1, a fuzzy set in the universe S, satisfy the fuzzy equation

$$W_1 \otimes R_1 = W_1 \tag{5.3.1}$$

This fuzzy set is called the eigen-fuzzy set of the previous fuzzy equation with the membership function

$$\mu_{W1}(S_j) = \max_{S_i \in S}[\min(\mu_{W1}(S_i), \mu_{R1}(S_i, S_j))], \; i, j = 1, 2, \ldots, n \tag{5.3.2}$$

and the sign $\otimes$ means the max-min composition of R_1 with W_1. The unknown membership function value of S_j for every S_j belonging to S is denoted by $\mu_{W1}(S_j)$.

In order to determine the fuzzy set W_1, let us consider a sequence of fuzzy sets:

1.) W^1, where the membership function value $\mu_{W1}(S_j)$ is

$$\mu_{W1}(S_j) = \max_{S_i \in S} \mu_{R1}(S_i, S_j) \text{ for all } S_j \text{ in } S \tag{5.3.3}$$

2.) $W^2, W^3, \ldots, W^n, W^{n+1}$ are defined by

$$W^2 = W^1 \otimes R_1 \tag{5.3.4}$$

$$W^3 = W^2 \otimes R_1 \tag{5.3.5}$$

...

$$W^{n+1} = W^n \otimes R_1 \tag{5.3.6}$$

According to the theorem in E. Sanchez (1979, p. 428), there exists an integer n less than or equal to the cardinality of W^n such that W^n is the greatest eigen-fuzzy set associated with R_1.

The following is a method for determining the solution W^n.

1.) We determine the set W^1.

2.) Set the index I=1.

3.) Find $W^{i+1} = W^i \otimes R_1$

4.) Finally, we must check whether $W^{i+1} = W^i$. In case this is true, W^{i+1} is the maximal eigen-fuzzy set. If W^{i+1} and W^i, we should take the index i=i+1 and go to step 3. The number of compositions of the set with the relation cannot be greater than n.

Fortunately, the relation R_1 "the drug acts equally strongly or more strongly on the ith symptom than on the jth one" has an eigen-fuzzy set W_1 which does not change after composition with R_1. This lack of change in W_1 leads to the conclusion that the membership of W_1 shows that the level of "the drug action on the considered symptoms is not stronger" and this permits the estimation of the maximal level to which the medicine can be effective. Moreover, we are able to accept this level as the optimal one, because W_1 is the maximal solution in the sense of the greatest membership function value.

Evaluation of the minimal level of drug action is related to another fuzzy relation R_2 given by "the action of the drug on the ith symptom is equal to or weaker than on the jth one, i,j=1,2,...,n." The proposed method of calculating the membership function of R_2 is similar to the previous procedure, but a different configuration of signs is used, i.e.

- -, the drug acts as strongly on S_i as on S_j

+ -, the drug acts more weakly on S_i (than on S_j)

Using the above-described algorithm it is easy to find an eigen-fuzzy set W_2 for the relation which is a solution of the equation

$$W_2 = W_2 \otimes R_2 \qquad (5.3.7)$$

Because W_2 does not change its membership function after composing with R_2, "the drug acts equally poorly or more weakly on the ith symptom than on the jth one", we can deduce that the membership function of the elements S_1, ..., S_n shows the minimal level of the medicine effectiveness on them, i.e. the level, "the drug action on the considered symptoms is not weaker." The range (min level - max level) for every $S_i \in S$ gives an indication about the efficiency of the tested drug.

5.4 APPLICATION WITH TREATMENT EFFECTIVENESS FOR ADD

The following is a new application of eigen-fuzzy sets. This application determines the relative effectiveness of treatments for children with Attention Deficit Disorder. Although the numbers which are used are fictitious, the appropriateness of the procedure will be demonstrated.

Suppose the efficacy of drugs versus counseling versus physical activities is to be assessed for the following four symptoms of ADD:

S_1: Often fails to finish things he/she starts

S_2: Often does not seem to listen

S_3: Easily distracted

S_4: Has difficulty concentrating on schoolwork or a play activity.

Let the following data be for the efficacy of the drug methylphenidate:

	S_1	S_2	S_1	S_3	S_1	S_4	S_2	S_3	S_2	S_4	S_3	S_4
P_1	-	-	-	-	-	-	+	+	+	+	-	-
P_2	-	+	+	-	+	+	-	-	+	-	-	-
P_3	-	+	+	-	+	+	+	-	+	-	-	-
P_4	+	+	-	-	+	+	+	+	+	-	-	-
P_5	-	-	-	-	+	+	-	+	-	-	-	-
P_6	+	-	-	-	+	+	-	+	-	-	-	-
P_7	+	+	+	+	+	+	+	-	+	+	-	-
P_8	+	+	+	+	+	+	-	-	+	+	-	-
P_9	+	+	+	+	+	+	+	+	+	+	+	+

Table 3: Efficacy of the drug methylphenidate

For purposes of illustration, let each row be replicated 10 times so as to generate data for 90 people for efficacy of drug treatment. Then, the upper levels of efficacy are:

$$R_{1U} = \text{“drug: methylphenidate”} = \begin{bmatrix} 0 & 0.444 & 0.444 & 0.111 \\ 0.333 & 0 & 0.444 & 0.222 \\ 0.666 & 0.444 & 0 & 0.888 \\ 0.111 & 0.555 & 0.888 & 0 \end{bmatrix}$$

$$W_{1U} = 0.666/S_1 + 0.555/S_2 + 0.888/S_3 + 0.888/S_4 \qquad (5.4.1)$$

Similarly, the lower levels of efficacy are:

$$R_{1L} = \text{“drug: methylphenidate”} = \begin{bmatrix} 0 & 0.333 & 0.666 & 0.111 \\ 0.444 & 0 & 0.444 & 0.555 \\ 0.444 & 0.444 & 0 & 0.888 \\ 0.111 & 0.222 & 0.888 & 0 \end{bmatrix}$$

$$W_{1U} = 0.111/S_1 + 0.222/S_2 + 0.444/S_3 + 0.111/S_4 \qquad (5.4.2)$$

Thus, the ranges of efficacy of methylphenidate on the previously mentioned symptoms are

S_1 11.1% - 66.6%

S_2 22.2% - 55.5%

S_3 44.4% - 88.8%

S_4 11.1% - 88.8%.

Similarly, without presenting the data, the following results may be obtained for the other treatment methods.

$$R_{2U} = \text{“counseling”} = \begin{bmatrix} 0 & 0.733 & 0.733 & 0.733 \\ 0.833 & 0 & 0.833 & 0.833 \\ 0.9 & 0.9 & 0 & 0.9 \\ 0.9 & 0.9 & 0.9 & 0 \end{bmatrix}$$

$$W_{2U} = 0.9/S_1 + 0.9/S_2 + 0.9/S_3 + 0.9/S_4 \text{ (upper level)} \qquad (5.4.3)$$

$$R_{2L} = \text{“counseling”} = \begin{bmatrix} 0 & 0.833 & 0.9 & 0.9 \\ 0.733 & 0 & 0.9 & 0.9 \\ 0.733 & 0.833 & 0 & 0.9 \\ 0.733 & 0.833 & 0.9 & 0 \end{bmatrix}$$

$$W_{2L} = 0.733/S_1 + 0.833/S_2 + 0.9/S_3 + 0.9/S_4 \text{ (lower level)} \qquad (5.4.4)$$

$$R_{3U} = \text{“physical activity: karate”} = \begin{bmatrix} 0 & 0.867 & 0.867 & 0.867 \\ 0.9 & 0 & 0.9 & 0.9 \\ 0.9 & 0.9 & 0 & 0.9 \\ 0.967 & 0.967 & 0.967 & 0 \end{bmatrix}$$

$$W_{3U} = 0.9/S_1 + 0.9/S_2 + 0.9/S_3 + 0.9/S_4 \text{ (upper level)} \qquad (5.4.5)$$

$$R_{3L} = \text{“physical activity: karate”} = \begin{bmatrix} 0 & 0.9 & 0.9 & 0.967 \\ 0.867 & 0 & 0.9 & 0.967 \\ 0.867 & 0.9 & 0 & 0.967 \\ 0.867 & 0.9 & 0.9 & 0 \end{bmatrix}$$

$$W_{3L} = 0.867/S_1 + 0.9/S_2 + 0.9/S_3 + 0.967/S_4 \text{ (lower level)} \qquad (5.4.6)$$

In summary, the effectiveness of the treatment regimens on four symptoms of ADD is given by:

Symptom	Drug	Counseling	Physical Activity
S_1	11.1-66.6	73.3-90.0	86.7-90.0
S_2	22.2-55.5	83.3-90.0	90.0
S_3	44.4-88.8	90.0	90.0
S_4	11.1-88.8	90.0	90.0 - 96.7

Table 4: Relative effectiveness of treatment regimens

Thus, in this hypothetical example, the therapy of physical activity completely alleviates the symptoms in more patients than any other therapy. Drugs appeared to lessen distractibility and increase concentration in at most 88 % of the patients. Counseling was moderately effective in improving all symptoms for a majority of children.

CHAPTER 6 COMBINING EXPERTS' OPINIONS

6.1 INTRODUCTION

This section presents a fuzzy set approach for combining experts' imprecise opinions. The procedure would, for example, allow the combination of opinions from psychologists, parents and teachers to evaluate a child for ADD. Similarly, physicians' diagnoses of a patient's potential for Lupus may be expressed as fuzzy numbers which reflect the confidence and uncertainty of their decisions. Specifically, the independent, fuzzy diagnoses or evaluations are combined by a fuzzy number approach called mixed linear extension. The combined result is a fuzzy number. Four essential properties of this combination are discussed, namely, *agreement preservation, order independence, possibility conservation and possibility interval preservation.* Defuzzication yields crisp results which coincide well with the actual observations representing the "true" values.

If several physicians are consulted sequentially and very different expert opinions are obtained, what is the result and when should the process be stopped? It seems that the more we consult, the greater the information and also the cost. Combining imprecise information to reduce overall uncertainty is a practical way to resolve this problem.

To combine opinions via traditional mathematics a weighted average or a probabilistic approach is used. However, an ordinary weighted average does

not preserve the original possibilities and a probabilistic approach requires a sufficient amount of statistical data, so that some type of distribution governing the process must be assumed. In medical diagnosis, there are often not enough data to assume a probability distribution or accept subjective probability assumptions. Thus, a fuzzy number approach seems to be appropriate to make a decision in such an uncertain environment.

The combining of different expert opinions, various diagnoses or evaluations, is an everyday problem in medical practice. It happens very often that different diagnoses are made from the same set of data. The fuzzy number approach provides a relatively simple mathematical method for combining physicians' diagnoses, with some advantages over traditional techniques.

6.2 CHARACTERIZATION OF PATIENT STATE

Let E_i denote Evaluator i, I=1,...,n. Let the group of m patients be evaluated by each E_i. The evaluations may be simplified to the following linguistic forms:

"Definite normal"	(N1), coded as 1
"Probable normal"	(N2), coded as 2
"Possible normal"	(N3), coded as 3
"Possible abnormal"	(A3), coded as 4
"Probable abnormal"	(A2), coded as 5

"Definite abnormal" (A1), coded as 6

Among m patients, there will be k patients that are Normal and m-k that are Abnormal. In some cases, the n diagnoses may be quite different. Indeed, the diagnoses may occasionally be incorrect due to evaluator error. Under such a fuzzy environment caused by a group of experts giving imprecise information, fuzzy numbers are used to express the confidence and uncertainty in the diagnoses.

Let the scale on the X axis be from 1 to 6 as above, i.e. 1=N1, ... 6=A1. Let the vertical axis scale be a confidence level from 0 to 1. For example, if a diagnosis is N2 (Probable Normal), then a triangular fuzzy number (TFN) (1,2,3) is used to model this diagnosis, with 100% confidence at point 2(=N2) and linear variations between N1 and N3, two neighboring points.

A diagnosis involving a "Probable" or "Possible" state is typically expressed as a TFN. However, if the diagnosis is "Definite" Normal/Abnormal, it is not considered to be as fuzzy as "Probable" or "Possible" would be. It is therefore modeled as a crisp number N1=(1,1,1) or A6=(6,6,6) for simplicity sake. Therefore, for each case, we have n fuzzy numbers corresponding to n diagnoses with their associated measures of imprecision.

6.3 PROPERTIES OF COMBINING OPINIONS

Various techniques for combining fuzzy numbers have been given in Bardossy et al (1992), together with a set of necessary or desirable properties. Upon examining the four main properties listed below, it is difficult to find combination methods that satisfy all of them at the same time.

1.) Agreement preservation: if $E_i = E_j \; \forall$ i, j, then $E = E_j$

This requires that if all evaluations E_i are the same, the result E should be the common one. This is a consistency requirement.

2.) Order independence: The result E does not depend on the order of individual judgments which are combined. This is also a consistency requirement.

3.) Possibility conservation: $\forall x, \exists i$ such that $u_{Ei}(x) > 0 \Rightarrow u_E(x) > 0$

where $u_E(x)$ is the membership function. This property means that if a value x was considered to be possible for at least one judgment, $u_{Ei}(x) > 0$, then it should remain possible for the combination, $u_E(x) > 0$. Since each diagnosis is considered to be reliable, this property is needed. It is clear that a simple average does not preserve all original possibilities.

4.) Possibility interval preservation: $\forall x, \exists i, j, x_i, x_j, u_{Ei}(x_i) > 0, u_{Ej}(x_j) > 0,$

$x_i \leq x \leq x_j \Rightarrow u_E(x) > 0.$

This property means that if a value is located between two numbers which are considered as possible judgments, then that value is also possible.

For example, if 2 and 4 are possible, 3 should also be possible. Note that property 4 implies property 3 but not vice versa. The property of possibility interval preservation appears to be contradictory to the traditional Bayesian approach.

6.4 MIXED LINEAR COMBINATION

The following fuzzy combination, mixed linear combination, created in Bardossy et al (1992) satisfies all of the above four properties. A convex set of weights a_i is assigned to the individual diagnosis E_i, then the combining rule for

$$a_i \geq 0 \qquad \sum_{i=1}^{4} a_i = 1 \qquad E_C(x) = \sum_{i=1}^{4} a_i E_i(x)$$

is then

$$u_E(x) = \min\{\sup[b_i\, u_{Ei}(t), u_{Ec}(t), t > x], \sup[b_i\, u_{Ei}(t), u_{Ec}(t), t < x]\} \text{ with } b_i > 0. \quad (6.4.1)$$

To illustrate the combination rule, suppose we have the following as an example. Let (Evaluator, Diagnosis) be: (E1,A2), (E2, N1), (E3, N3), (E4, A2).

Step 1: Model the diagnosis by fuzzy numbers.

For each triangular fuzzy number (a,b,c), the membership function is

$$u_{Ri}(x) = \begin{cases} \dfrac{x-a}{b-a}, \text{if } a \leq x \leq b \\ \dfrac{c-x}{c-b}, \text{if } b \leq x \leq c \end{cases} \quad (6.4.2)$$

denoted as (a,b,c). Thus, A2, N1 and N3 are expressed by (4,5,6), (1,1,1) and (2,3,4) respectively.

Step 2: Perform the first combination by convex weighting of TFN's, $u_C(x)$ also a TFN, is obtained. This TFN yields the group mean. Any conventional technique of weighting could be used here, such as equal weighting or weighting by previous performance. This step is a linear transformation, however the result does not satisfy properties 3 and 4. An equal weighting scheme is used in this section.

Step 3: Assign weights b_i to the membership functions while keeping $u_C(x)$. This is another linear transformation, but it is performed along the confidence direction. Equal or unequal weighting could be used according to the specific case and the information on hand.

Step 4: Calculate a second combination by the $u_R(x)$ min sup equation. This is a nonlinear transformation using max-min operation. Thus the combined result has been obtained from a mixed linear combination. It satisfies all the previous important properties.

The combined result is a fuzzy number, its membership function is piecewise linear and it is associated with different confidence or uncertainty levels. The combined result covers all original possibilities and get the highest confidence level at the position of the group mean. In our example, the membership function is

$$u_{c2}(x) = \begin{cases} 0.25, & 0 \le x \le 2.9 \\ 1.33(x-2.75), & 2.9 \le x \le 3.5 \\ 1.33(4.25-x), & 3.5 \le x \le 3.9 \\ 0.5, & 3.9 \le x \le 5 \\ 0.5(6-x), & 5 \le x \le 6 \end{cases} \qquad (6.4.3)$$

Pictorially, the previous membership function has the following appearance.

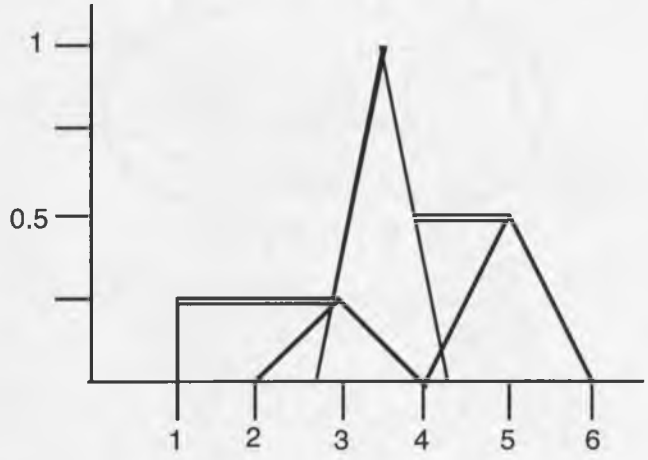

Figure 4: Combined opinions

If only crisp results, Normal or Abnormal, are required, defuzzification is necessary. One simple method is to compute the ratio of areas under the membership function of the combined result on the left and right side of the Normal/Abnormal threshold, which in this case could be set at 3.5. For example, let (Evaluator, Diagnosis) be (R1,A3), (R2, A1), (R3, A1), and (R4, N2) with the associated fuzzy numbers. Then, the ratio of right to left side areas, for the Normal/Abnormal threshold, is about 2.41; thus, our conclusion is "Abnormal." Consider now a fifth diagnosis, which might be located at one of the six possible positions, N1, N2, N3, A3, A2, A1. Assume this 5th diagnosis to

be "N1" which will have the largest negative impact on our current combined result. By the combination technique of "mixed linear extension", the resulting combination will have an area ratio of about 1.3, the result is still "Abnormal".

The membership function for this example is

$$u_{c2}(x) = \begin{cases} 0.25(x-1),\ 0 \le x \le 2 \\ 0.25,\ 2 \le x \le 4.5 \\ 2.5(x-4.4),\ 4.5 \le x \le 4.8 \\ 2.5(5.2-x),\ 4.8 \le x \le 5 \\ 0.5,\ 5 \le x \le 6 \end{cases} \qquad (6.4.4)$$

If a 5th possible diagnosis with maximum divergence did not change the present combined result, the other two possible diagnoses, N2 and N3, will not either. If the 5th diagnosis is either A3, A2, or A1, then the new result will obviously make the "center of gravity" move in the direction of "Abnormal" and further confirm our current combined result. Thus for this example we can stop; it is not necessary to consult with the 5th physician since the result will remain "Abnormal".

Zhang and Duckstein (1993) developed this technique and tested it on radiologists' readings for 45 patients. With the mixed linear extension technique, all 45 cases were tested and the results coincided very well with the "true" results (as determined by another method); the error rate was less than 7%. Among the 45 cases, only 3 cases did not agree with the true result. Those cases were really exceptional, since in each case two of the four diagnoses corresponded to physician error. The correct combined result could not be

gotten from the wrong diagnoses under such conditions. On the other hand, simply taking a "vote" to determine the combination would have worked in most of the cases except where there were ties. For this case, the advantage of the fuzzy technique becomes apparent since a decision is made not only on the basis of a vote (the mean) but also on the extent of the uncertainty.

The fuzzy number approach to combine expert imprecision opinions is natural and practical. The mixed linear extension method was tested on data of radiologists' diagnoses. The result is better than a traditional mathematical method of combining opinions from the view point of the properties and flexibility in handling the imprecise information; note that any crisp weighting technique may be used in this method.

The various diagnoses can be described by fuzzy numbers, and the combined result is a fuzzy number. Its membership function is piecewise linear and preserves all original possibilities and possibility intervals associated with different confidence levels. The defuzzification may be performed by computing areas under the membership function. The upper-right region above our confidence curve reflects the risk of this combined result.

Future work might involve calculating the probability of the fuzzy event "Normal" or "Abnormal", since a new diagnosis might impact the current combined result and the realization of this fuzzy event becomes uncertain. When the ratio of areas is about 1, this probability is a critical quantity in the diagnostic process.

6.5 APPLICATION WITH EXPERTS' OPINIONS IN ADD(H)

The following is an example of a new application of mixed linear combinations. This application determines whether given children have ADD(H). Although the numbers which are used are fictitious, the appropriateness of the procedure will be demonstrated. Suppose the opinions of four experts (two psychologists, a special education teacher, and the child's parent) are sought to determine the validity of a diagnosis of ADD for a child. Using another method, that of group consensus, the "True" status of the child is determined. The conclusions of the fuzzy method of combining experts' opinions are then compared. The data and results are given in Table 5.

Patient	Expert 1	Expert 2	Expert 3	Expert 4	True	Fuzzy
1	A1	A1	A1	A3	A	A
2	A2	N1	N3	A2	A	A
3	A3	N1	A1	N2	A	N
4	N3	N1	N3	N1	N	N
5	N2	N1	N2	N2	N	N
6	A1	A1	A1	A1	A	A
7	N2	N1	A1	N2	N	N
8	A2	A1	A1	A3	A	A
9	A1	A1	A1	A1	A	A
10	A2	A2	N1	N2	A	N
11	N3	N1	A2	N2	N	N
12	A3	N1	A3	N2	N	N
13	A1	A1	A1	A1	A	A
14	N3	N1	N2	N1	N	N
15	N3	N1	A3	A1	N	?
16	A2	N2	N2	N1	N	N
17	A1	A3	A1	A1	A	A
18	N2	N1	N3	N2	N	N
19	A3	N1	N2	A1	N	N
20	N2	N1	A2	A3	A	N

Table 5: Expert's opinions and combined opinion

As can be seen, the fuzzy method agrees quite closely (80%) with the "True" value. There were four exceptions (Patients #3, #10, #15, and #20) in the twenty cases examined. For patient #3 (A3, N1, A1, N2), the fuzzy method basically considered that Experts 2 and 3 "canceled each other" since one claimed "Definite Normal" and the other claimed "Definite Abnormal". Of the two remaining experts, A3 (Possibly Abnormal) carried less weight than a diagnosis of N2 (Probably Normal). Thus, the fuzzy combining of the experts' opinions resulted in an outcome of Normal. Similar explanations hold for the three other discrepancies. Patient #10 had two experts cancel each other, while of the remaining two, a diagnosis of "Definitely Normal" carried more weight than "Probably Abnormal". Patient #20 had a comparable situation except the two different diagnoses were "Definitely Normal" versus "Possibly Abnormal".

An even more diverse case occurred for Patient #15. Expert #2 claimed that the child was "Definitely Normal" whereas Expert #4 claimed "Definitely Abnormal". Experts #1 and #3 were more ambivalent with diagnoses of "Possibly Normal" and "Possibly Abnormal", respectively. Given the evenness of the split of opinion, the fuzzy method could not yield a Normal/Abnormal result. Note that the above results were obtained using equal weightings. If certain experts were more experienced, more knowledgeable, etc., then their opinions may be given a higher value.

CHAPTER 7 RULE-BASED AND DISTANCE-BASED APPROACHES

7.1 INTRODUCTION

In this chapter, two fuzzy approaches to medical decision making are discussed and applied. First, a fuzzy rule-based approach is used to define the state of a child at risk for ADD using an n-tuple. Medical experts may describe this vector state for patients in terms of linguistic categories. Fuzzy rules may be established on the basis of half the patient files and validated on the remaining files. The model reproduces the average answer at least as well as most experts. Second, a distance-based approach is used to categorize the state of a lupus patient. The norm, measurement and pathology are represented as fuzzy numbers. The state of a patient is described by an index synthesizing the distances measurement-norm, measurement-pathology. The model again may be calibrated on half of the study cases, and validated on the remaining cases. In a previous application by Duckstein et al (1993), this yielded excellent agreement with expert's judgment. Both approaches define patient state as a continuous variable, are robust, appear not to depend on the shape of membership function, can be used with dependent parameters and may easily be extended to other types of medical categorization.

The purpose of this chapter is to discuss two fuzzy approaches to medical decision making. The first one, which uses a fuzzy-rule based

technique, is applied to the categorization of potential ADD subjects. The second approach, based on the distances between fuzzy numbers representing normal/pathological values and the experimental observations, is applied to Lupus patients.

Either fuzzy logic approach includes:

1.) Definition of states and categories to be reproduced

2.) Definition of experimental data set and the corresponding membership functions

3.) Choice of a technique to categorize patients.

Fuzzy logic has been widely implemented (Kaufmann and Gupta, 1988; Bardossy and Duckstein, 1992), but only few medical applications to patient classification can be found. Yet, the experts' opinions are expressed in imprecise, linguistic terms, such as mild, average or severe distractibility and low, moderate or high lack of concentration. Additionally, the whole process of classification, given a patient's characteristics, is imprecise (Pedrycz et al, 1992). Indeed, if two experts give different opinions in the same case, it does not necessarily mean that one of them is right and the other wrong, but that the degree of imprecision is high.

The examples deal with conveying a precise description of patient state to the physician, as a decision aid. Although in medical practice, discrete categories are usually defined in linguistic terms, our description of patient state appears as a continuous index.

7.2 DEFINING PATIENT STATE

To define patient state in the ADD case, experts may construct the questionnaires with three possible answers (=linguistic categories coded 1,2,3) to each question:

1.) Often fails to finish things he/she starts: no (1), I do not know (2), yes (3)

2.) Often does not seem to listen: no (1), I do not know (2), yes (3)

3.) Easily distracted: no (1), I do not know (2), yes (3)

4.) Has difficulty concentrating on schoolwork or other tasks requiring sustained attention: no (1), I do not know (2), yes (3)

5.) Has difficulty sticking to a play activity: no (1), I do not know (2), yes (3).

These questions involve the criteria for Inattention. Similar questions may be formulated to ask about Hyperactivity and impulsiveness. Together, these three categories help form a diagnosis of ADD/ADHD.

In the case of Lupus, the physician may define four categories of patient state in the following linguistic terms: normal state, borderline state, clear-cut pathology, severe pathology.

In both cases, we wish to classify a given patient using an adequate fuzzy procedure. State categories and the initial set of experimental parameters have to be defined, in accordance with medical practice. The fuzzy set membership functions should then be assessed for each of these parameters in

each category. After considering various shapes of membership functions, in both cases, the simplest, namely triangular form, has been selected. With this information in hand, the initial set of parameters should be reduced to a small subset of representative and pertinent parameters.

In the ADD example, physicians may assign a patient state to a five-dimensional vector whose elements belong to the coded set {1,2,3}, for example (1,3,1,1,3) corresponding to "Does not often fail to finish things he/she starts", "Often does not seem to listen", "Is not easily distracted", "Does not have difficulty concentrating on schoolwork or other tasks", and "Has difficulty sticking to a play activity". Since this assignment is done into imprecise categories by means of "If (values of experimental parameters are...) then (state is ...) type of reasoning, a fuzzy-rule approach may be appropriate (Duckstein et al, 1992, Blinowska et al, 1992a).

In the Lupus example, the notion of distance appears naturally, because the physician must determine how far patient observations are from the norm, so as to be able to follow the patient state evolution. Accordingly, a concept of distance between fuzzy numbers has been applied to this case as in Blinoska et al (1992b).

Triangular membership functions are defined by the minimum, mean and maximum value of the corresponding parameter for each category, the peak being at the mean value. Only those parameters are retained whose membership functions exhibit both an important difference between categories

and a monotonic behavior, in other words parameters that have some discriminant power. Thus, parameters whose membership functions clump together, not surprisingly, do not have high discriminant power.

7.3 RULE-BASED DESCRIPTION

A randomly selected sample of patient files may be examined by experts in the field of ADD/ADHD. Suppose these experts, n=5, follow their regular practice of examining the complete file of a patient and making a decision. Each expert would give his evaluations independently, without the knowledge of other experts' answers, according to his interpretation of the meaning of the questions. The goal would be to develop a methodology that reproduces the average coded answer.

The data is split into two sets of patient files, say 50 each, a calibration set and a validation set. Let $A_i^*(j)$ be the average coded answer to the j-th question, $A_i(j,r)$ the model (r=0) and experts' (r=1,...,r') answers to the j-th question. In order to evaluate both the dispersion and the bias of the results, two criteria are used: for the dispersion, the sum of the squared differences $S^2(j,r)$ and for the bias, the sum of the differences D(j,r) are respectively

$$S^2(j,r) = \sum_{i=1}^{50} (A_i^*(j) - A_i(j,r))^2 \qquad (7.3.1)$$

$$D(j,r) = \sum_{i=1}^{50} (A_i^*(j) - A_i(j,r)) \qquad (7.3.2)$$

Using the calibration set, patients are evaluated for every question, according to the average opinion of the experts, rounded off to the next integer. Membership functions of binary parameters (such as onset before age 7 or parental antecedents) are defined by means of the two-tuple:

$$\mu(n,j,k) = (f_{yes}, f_{no})/\max(f_{yes},f_{no}) \tag{7.3.3}$$

where f_{yes} and f_{no} are respectively the frequencies of occurrence of "yes" and "no" answers to the question j concerning the parameter n within the k-th category. Fuzzy rules are then sought that reproduce the targets, which are the average coded answers to the five questions. Only a fuzzy rule "and", possibly with weights, appears to be needed. This rule may be constructed as follows. Let patient I be represented by membership function values $\mu_i(n,j,k)$ where n is an experimental parameter, k (k=1,2,3) is a category index and j (j=1,...,5) is the question. Then the overall index for category k of question j for patient I is defined as the product:

Overall category index = $OCI_i(j,k)$

$$= \prod_{n=1}^{N^*} \mu_i(n,j,k) \tag{7.3.4}$$

where N* is the number of parameters selected for question j.

The model answer $A_i(j,0)$ to the j-th question is calculated as

$$A_i(j,0) = \frac{\sum_{k=1}^{3} (k * OCI_i(j,k))}{\sum_{k=1}^{3} ((OCI_i(j,k))} \tag{7.3.5}$$

A priori sensitivity analysis is then performed in order to determine the combination of parameters that minimizes the sum of squared errors $S^2(j,r)$. The previous equation is applied to the patient files in the validation set. The results are compared to the average coded answers and to the individual experts' coded answers. $S^2(j,r)$ and $D(j,r)$ are then calculated. The fuzzy rule approach appears to be able to reach the target very closely. On the average, $S^2(j,0)$ and $D(j,0)$ are relatively small, as compared to $S^2(j,r)$ and $D(j,r)$ for $r=1,...,5$.

7.4 DISTANCE-BASED DESCRIPTION

A similar procedure may be followed with the Lupus patients. The calibration set will contain a certain number of suspected Lupus patients from one hospital, and the validation set, suspected Lupus patients from another hospital with similar characteristics to the first hospital. The measure of distance developed in Bardossy et al (1992), and used herein is as follows. Let P° and M° be two fuzzy numbers with respective triangular membership functions $\mu P^\circ(x)$ and $\mu M^\circ(x)$, where $\mu M^\circ(x)$ corresponds to the membership function of a measurement and $\mu P^\circ(x)$ corresponds to membership function of pathology. For a given ordinate value h, $x\ M^\circ_L(h)$ is the abscissa of the point on the increasing (left) branch of $\mu M^\circ(x)$ and $x\ M^\circ_R(h)$ is the abscissa of the point on the

right (decreasing) branch of $\mu M^{\circ}(x)$, with similar definitions for P°. The distance $D(M^{\circ},P^{\circ})$, a scalar quantity, is

$$D^2(M^{\circ},P^{\circ}) = \int_0^1 [(xP_L^{\circ}(h) - xM_L^{\circ}(h))^2 + (xP_R^{\circ}(h) - xM_R^{\circ}(h))^2] f(h)dh \qquad (7.4.1)$$

In this equation, f(h) is a weighting function selected to be non-decreasing with level of credibility h. The state of a patient is represented by an index synthesizing the distances between observations on the one hand and norm and pathology on the other hand.

Several distance measures have been proposed (Dubois and Prade, 1980; Kaufmann and Gupta, 1985, 1988; Diamond, 1986; Bardossy et al, 1992). Among several possibilities, the distance measure given in the previous equation was chosen to yield, for each experimental parameter n=1,...,I, the distance values $D^2(M^{\circ}_n, P^{\circ}_n)$ and $D^2(M^{\circ}_n, N^{\circ}_n)$. The difference in distance $[D^2(M^{\circ}_n, P^{\circ}_n) - D^2(M^{\circ}_n, N^{\circ}_n)]$ is then normalized so as to obtain a value equal to 1 at the peak abscissa x^* of $\mu N^{\circ}(x)$

Normalized distance=ND_n^2 =

$$[D^2(M^{\circ}_n, N^{\circ}_n) - D^2(M^{\circ}_n, P^{\circ}_n)]/[D^2(x^*, N^{\circ}_n) - D^2(x^*, P^{\circ}_n)] \qquad (7.4.2)$$

This normalization is necessary to account for different units of experimental parameters, which would lead to the assignment of arbitrary weights. The normalized fuzzy pathology index, NFPI, is then defined as

$$NFPI = \sum_{n=1}^{N} ND_n^2 \qquad (7.4.3)$$

The model would be been validated on the remaining cases. It appears that, in the authors case study (Duckstein et al, 1993), all manners of calculating the NFPI yielded satisfactory results. Because of this robustness the simplest approach of taking the measurement as crisp number and the weighting function f(h) in the distance measure as unity is quite sufficient. Note that this may not be the case in a more complex situation.

7.5 SUMMARY OF PROCEDURES

In the ADD example, the membership functions have been defined on an experimental basis. A triangular form has been selected because of its simplicity. If the size of the calibration set is limited, e.g. 50 patient files, then a more sophisticated membership function would not be appropriate Bardossy and Duckstein (1992). In some cases, a category may be defined by so few points that the experimental information would need to be completed by a subjective extension of the triangular membership function width. The definition of the triangle peak as a mean value appears to be a reasonable choice, but other choices could have been made. Given more data, a statistical procedure might be used to refine the definition of membership function (Civanlar and Trussel, 1986). Similarly, a statistical procedure might be developed for the frequency scheme used to incorporate the binary parameters.

The "and" fuzzy rule used in this section is defined in Bardossy and Disse (1992). Note that such rules can be applied even in the case of dependent parameters, which represents an important advantage as compared to a statistical approach (Blinowska et al, 1991).

The problem of eliciting, encoding and combining multiple experts' opinions is extremely difficult and complex (Heidel et al, 1992). The high dispersion values in answers to questions 2, and 3 do not necessarily reflect an imprecision of experts' opinions, but may be due to different interpretations of attitudes. In fact, one may wonder about the value of the analysis for questions 2 and 3, which results in both very high dispersion and strong bias. These two questions should be reformulated or well-agreed upon in a feedback procedure.

In the Lupus example, uncertainty, first in experimental observations, and then, in both norm and pathology for a given disease has been through a distance-based fuzzy number analysis. The model includes the selection of a distance measure and of a normalized fuzzy pathology index, NFPI, representing the differential distance of a patient from norm and pathology. This distance, which is a continuous variable, as is patient state itself, has been discretized in order to fit linguistic states used by the physician. Discretization usually corresponds to a loss of information. However, it should be demonstrated with actual data.

CHAPTER 8 RANKING

8.1 INTRODUCTION

Another use of fuzzy analysis in epidemiology is for ranking the importance of symptoms in the diagnostic process and the effectiveness of treatments. Actually, the problem of ranking objects in a particular order of importance has existed for a long time and it continues to cause difficulties in the present. Its significance should not be underestimated because given the inherently limited resources of time, money, and materiel, ordering allows a choice of which tasks are to be done first, and hence, lets work proceed more efficiently. Univariate problems, those where the objects are characterized by a single, ordinal measure, are trivial to solve. But by its very nature, the ranking of items frequently involves a large number of qualitative and quantitative variables as well as information and concepts which may not be clearly defined.

As an example, a consumer might prefer one brand of cereal over another brand based not only upon nutritional considerations, availability, and cost, but also according to the often nebulous standards of personal preference. In this instance, numerical data and emotion are combined to generate a choice. On the other hand, the ranking of players through a comparison of win-loss records in specific tournaments emphasizes quantitative factors in the ranking process. Thus, criteria which range from vague to detailed may be

assimilated in simplistic or elaborate ordering procedures with the ranking scheme as a desired end result.

8.2 ORDINARY RANKING

The literature of ranking objects and courses of action is wide-ranging and extensive. Indeed, the problem of ordering and its resolution in given situations has challenged numerous authors. The following papers were chosen based upon not only their relevance to the present research, but also to exemplify the diverse nature of the ranking problem.

An extension of one-dimensional ordering concepts into the multi-dimensional realm was proposed by Barnett (1976). He considered a restricted ordering of data, termed sub-ordering, in which several of the typically one variable, quantitative summary statistics are compared. Sub-ordering actually consists of four major types: marginal ordering, reduced (aggregate) ordering, partial ordering, and conditional (sequential) ordering. Marginal ordering yields a ranking only within a restricted, marginal sample. Reduced ordering takes the original multivariate observations and collapses them into a single quantity by some generalized metric. The use of partial ordering produces a partitioning of the data into groups similar to that of cluster analysis. Intra-group rankings are impossible, but inter-group orderings may be done. Lastly, conditional ordering extends the concept of marginal ordering by the requirement that the rankings be conditional on the results of another marginal sample. Barnett then

considered how these ordering types might be implemented in various multivariate statistical procedures.

A different approach was taken by Gibbons (1982) in her paper on ranking and selection procedures. In it, she examined the processes of choosing the best item or items among several, ranking the items according to a given characteristic, or finding an item which is better than a specified ideal. All of these procedures were accomplished while controlling for the probability of making a correct selection. The same ideas are exhibited in an article by Duong (1984) in the choice of the order of an autoregressive process in time series analysis. The question of choice is cast as a multiple decision procedure where a subset of good models is gained by considering the AIC, the Akaike Information Criterion, as well as the sampling variation and a priori information on the true order of the model. Ranking and selection procedures have also been used by Berger and Deely (1988) to order teams in the National Baseball League. This was done on the basis of not only recording the highest batting average for a player on a team but also through a Bayesian approach. In this, the actual batting averages for each player (i) are taken to be sample estimates of p_i, the true probability of getting a hit by the player where the distribution is assumed to be Binomial. A Bayesian model of exchangeability for the p_i is then used to obtain the posterior probabilities that the p_i is largest. This method may yield a different ranking of the teams than that gotten from an ordering of the batting averages since a high batting average does not

guarantee a high probability of being the best batter. Thus, the teams with the highest batting average may not be judged the best.

The ordering of patients based upon predicted mortality in an intensive care unit was considered by Lemeshow et al (1988). They used a multiple logistic regression model with variables: presence of coma or deep stupor at admission, emergency admission, cancer part of present problem, probable infection, cardiopulmonary resuscitation prior to admission, age, and systolic blood pressure at admission. The paper also compared the proficiency of this model (MPM) with results developed by Knaus et al (1981) and Le Gall et al (1984).

Kirkwood and Sarin (1985) developed an algorithm that orders a set of items based upon multivariate information about the items. The paper also obtained conditions which ascertain whether items can be totally ranked on the basis of the multivariate attributes. This algorithm will be extended in the present research. Similar procedures were also considered by Robert E. Shannon (1968). He first attempted to determine whether a group of experts agreed on comparative rankings of items by use of Kendall's coefficient of concordance. If there was significant agreement among the experts, Shannon then considered techniques by which a final ranking could be achieved. The ranking of the teams by a given expert was turned into a point system. Thus, a ranking of first would yield one point, a second ranking would have two points, and so forth. The points would then be summed for each team across experts to

produce a single numeric quantity for the team. Teams with lower sums would be considered best. The second assimilation technique was basically majority rule. If team A were preferred to team B by more experts, it would receive a better ranking.

This use of decision analysis is quite common in ranking literature. Gass (1983) looked at the use of operations research decision-aiding models in policy analysis and questioned whether they were appropriate in this context. White (1984) considered an ongoing decision process of selecting the best course of action when the preference criteria might change in the future. In connection with this, Hazen (1986) examined the ordering of alternatives when preference information is scarce. The difficulty of requiring that multiple objectives be optimized was examined by Hahn (1984). Korhonen, Moskowitz, and Wallenius (1986) developed a progressive algorithm which could suggest different courses of action based upon the successive introduction of decision alternatives.

The use of paired-comparisons has been developed by several authors to achieve rankings of various data sets. David (1987) suggested that the ordering of players, based upon an incomplete paired-comparison tournament with no more than one comparison per pair, be done in the following fashion. The ranking score for player C is "the total number of wins of players defeated by C minus losses of players to whom C lost, plus C's wins minus C's losses. A tied match counts as half a win plus half a loss." (p.432) In an expansion of this

and other techniques, Groeneveld (1990) considered several ranking methods of teams in the National Baseball League. The first was a simple ordering based upon the total number of games won by the teams. The second was a more complicated technique in which each team was assigned a score that consisted of two parts. Team A would receive a point for each victory and lose a point for each defeat, but it also would receive a point for each victory that a team previously defeated by Team A achieved and would lose a point for each defeat incurred by a team previously victorious over Team A. Such a procedure is an extension of methods by Kendall (1955) and Wei (1952). The third method generalized the technique by David. In it, team A receives an initial score based on the proportion of times it won over a given team minus the proportion of times it lost to the given team. The final score is created by summing over all of the teams in the league. Finally, Groeneveld considered the Bradley-Terry model which was developed in 1952 and which establishes rankings based upon maximum likelihood. Paired comparisons were also used by Joe (1990) to rank sixty-four chess masters. In his article, he cast the problem as an evaluation of asymmetric cumulative function at specified points. Covariate information as well as data on the peak and total length of the chess masters' careers were also considered. Lastly, the author looked at appropriate goodness-of-fit tests.

The ranking of items sometimes is of critical importance. During the Korean War, material such as cobalt, nickel, and chromium, which were vital to the war effort, were assigned indices apparently based on the amount of the substance in the reserves of allied nations. Stalker et al (1984) considered similar strategic substances and ranked them in twenty-one different ways. Among these ways were their importance in peace-time and war-time economies, the amount of stockpiled reserves in the United States, and the cost to refine the raw materials into usable goods. Additionally, a total ranking which was the sum of the twenty-one separate orderings and a ranking based upon an incorporation of such subjective weightings as availability, reliability of supply source, and the potential of a creation of a mineral cartel to control supplies were also specified.

Pfeffermann and Ben-Tuvia (1985) considered a method of ranking sections of roadways to determine which sections would be accorded priority in resurfacing. The ranking was based on the single criterion of expected reduction, after resurfacing, in the number of accidents caused by skidding on wet pavement. A tacit assumption was that resurfacing does not influence the number of skids on dry pavement, but merely reduces the wet pavement incidents to a fixed percentage of total accidents.

Agriculture has always been a domain where ranking was heavily used. A selection index which evaluates the potential success of breeding stock was considered by Hazel (1943). Similar measures were looked at by Henderson et

al (1959) and by Robinson (1986) who developed a scheme in which the genetic qualities of cattle were gained from a best linear unbiased prediction model. In addition to the ranking of animals, there also has been the rating of importance of agricultural lands. Smit and Kristjanson (1989) used the criteria of land quality, land scarcity, and the demand for products produced on the land as the measure of importance. Various types of land ranging from good land for all varieties of crops to land suitable only for the production of hay were evaluated. Such evaluations assessed the production of crops, spanning fruit to forage grains, based upon each criterion separately. Ratings for the land for each use were gained by pooling across criteria, and then the overall ranking of the land in agriculture was achieved by consolidating over all uses.

Another area which requires ranking to be used is in chemical and pollutant analysis. In particular, a determination of which laboratories provide the best analyses is of special importance. This topic was considered by Elder (1987). He looked at the laboratory ranking test as developed by Youden in 1963 with especial attention paid to factors such as between-laboratory variation which may influence the performance of the test. The test's fallibilities are also considered. Einerson and Pei (1988) outlined procedures to measure the accuracy and precision of analytical laboratories. The criteria used were precision, accuracy, quality assurance documents, ability to customize reports, turnaround time, and price. Rankings in each standard were produced for the laboratories, and then these rankings were weighted and summed to produce a

final ordering. Schaeffer and Janardan (1989) created a nonparametric statistical procedure which ranked laboratories based upon results from numerous analytes. The metric used was

$$x_{ij} = 100*abs(y_{ij} - y_{is})/r_i y_{is}$$

where y_{ij} is the value for the ith analyte in the jth laboratory, y_i, is the true value of the ith spike, and r_i is the relative error of replication. The x_{ij}'s are then ordered from smallest to largest for each i. These ranks are then standardized and transformed to produce a final index.

The environmental hazard of chemicals has been studied by several people. Halfon and Reggiani (1986) used seven criteria for thirty-four chemicals in a vectorial approach to partial ordering. Schaeffer et al (1988) developed a method which took the qualitative and quantitative data on the physical and chemical properties, toxicity, and potential use of the chemical and combined them into an index which provided a ranking. This procedure was similar to the MITRE/EPA technique for ranking the hazardous waste sites. Ordering of waste sites was also studied by Halfon (1989) who again used a vectorial approach to rank thirty-eight waste disposal sites in the Detroit, St. Clair, and St. Mary's river areas in Canada. For clarity of presentation, he used a Hasse diagram to display the results. Greathouse, Clements, and Morris (1989) considered the use of expert systems to help determine the criteria and decisions in cleaning up waste sites. Taylor, Dellinger, and Lee (1990) provided a method of ranking

hazardous organic waste incinerability and also gave practical causes for deviations from the theoretical ordering.

8.3 FUZZY RANKING

In the previous references, the data which helped produce the rankings were assumed to be known within measurement error. However, a vast amount of literature in the ranking problem has centered around the assumption that the data and criteria may be fuzzy. To produce rankings from fuzzy information, it is first necessary to be able to rank fuzzy numbers and fuzzy sets. Dubois and Prade (1983) considered a complete set of four indices, within the structure of Zadeh's possibility theory, to totally characterize the respective location of two fuzzy numbers. They indicated that this might be expanded into ranking N fuzzy numbers, and further, in the case of two numbers, knowledge of their mutual compatibilities could allow a recovery of the respective locations of the numbers. Bortolan and Degani (1985) examined the performances of several ranking indices. They found that in simple cases, the indices all produced similar rankings. In uncertain cases, the Dubois-Prade index, which merely described the relative dominances of the alternatives and then left the actual ranking to the decision-maker, appeared to be most applicable.

Chen (1985) proposed the use of maximizing and minimizing sets to achieve the ordering value of each fuzzy number. These values then determine the ordering of N fuzzy numbers. For the specific membership functions with a

triangular, trapezoidal, or two-sided drum-like shape, the ordering value was calculated. Ovchinnikov and Migdal (1987) developed a mathematical model where an induced fuzzy ordering was defined as the inverse image of the usual linear ordering on real numbers. The image was generated by a fuzzy correspondence between fuzzy sets and real numbers.

Delgado, Verdegay, and Vila (1988) created a method, based on the concept of comparison functions, which gave fuzzy order relations between fuzzy numbers. These functions define the concept of "greater than" or "less than" a fuzzy number to be a linguistic property which allows decision makers to treat such properties via internal and external personal factors. This subjective approach was furthered by Campos-Ibanez and Munoz (1989). They proposed an index which contained two parts. The first part yielded a function at a given level set which reflected the position of the fuzzy numbers on the real number line. The second part then combined these values through subjective weights to obtain the complete index.

Ranking of fuzzy numbers also appears in fuzzy linear programming problems as examined by Campos and Verdegay (1989). In such problems, coefficients in the constraint set and the right hand side of the set are fuzzy. Because of this, ranking of fuzzy numbers was performed and depending upon the ranking method selected, several different types of conventional linear programming resulted.

Shimura (1973) proposed a rank-ordering algorithm where the relationship between any pair of objects might be characterized by a fuzzy function. In particular, he indicated that such an algorithm would be useful when attempting to place objects into groups which lacked sharply defined boundaries. In a related procedure, Smets (1981) looked at the process of classifying patients into groups based upon medical diagnosis. However, the diagnostic groups were considered to be fuzzy sets and the strength of how likely a patient was to belong to a given group was specified by a belief function. Indeed, he characterized the medical diagnostic process as a procedure where the physician places a level of belief on the diagnosis conditioned on the manifestation of symptoms and other fuzzy data. The medical dilemma of fuzzy information also extends to classification of the toxicity of poisons which may be characterized according to species-dependent factors, exposure conditions, and toxicity indices. This problem was studied by Chen (1988) who proposed both a mathematical standard of fuzzy classification and a fuzzy matrix to represent the various toxicity ratings more clearly.

Similar problems of classification were considered by Vila and Delgado (1983). Their method is analogous to discriminant analysis but with the difference that the classes were fuzzy sets. Additionally, the of an item in a group was characterized by a possibility distribution. To achieve a final, optimal membership function, they used Sugeno's integral to obtain a Bayes-optimal

function with respect to a fuzzy measure. The fuzzy measure was induced from a normalized, conditional possibility distribution. Fuzzy hierarchical analysis, considered by Buckley (1985b), allows an expert to place a fuzzy ratio on the relative importance between two alternatives. For example, an expert might consider Alternative A more important than Alternative B in a ratio of between 3 to 1 and 5 to 1. Once pairwise comparisons of the alternatives and criteria are done to create fuzzy matrices, then the geometric mean method is used to produce fuzzy weights for each matrix. The weights are eventually combined into a single weight for each alternative which then allows a ranking of the alternatives to take place. Buckley indicated that the method may be extended to the case of multiple experts and to missing data.

Fuzzy sets may be present not only in the data and criteria but also may be used to provide weights for rankings. Lusk (1982) looked at a technique which used conditioned sets of fuzzy variables to yield weights for rankings. He contrasted the results to those obtained by the eigenvalue priority assignment model. Van Laarhoven and Pedrycz (1983) extended Saaty's priority theory to a choice of alternatives under conflicting decision criteria. Decision makers express their opinions on the relative importance of alternatives through triangular fuzzy membership functions. These provide fuzzy weights of the decision criteria as well as weights for the alternatives given a specific criterion. The weights are combined to achieve score for the alternatives from which a decision can be made.

Efstathiou and Tong (1982) looked at the ranking problem not through the usual avenue of mathematical fuzzy ordering and decision theory, but by using linguistic relations. They provided definitions to overcome ambiguity in transitivity and ordering and then gave an algorithm to produce fuzzy preference relations. Wagenknecht and Hartmann (1983) noted that in the numerical methods of polyoptimization, numerous efficient solutions are obtained. Their technique allowed the decision maker to use fuzzy information on the pairwise ordering between objectives so as to reduce the number of points and eventually arrive at an optimal conclusion. Chakraborty and Sarkar (1987) considered various types of ordering such as fuzzy quasi-order, fuzzy partial order, fuzzy weak ordering, and fuzzy linear ordering. They proved several theorems regarding these orderings and detailed several properties. Ovchinnikov (1989) generalized the Baas-Kwakernaak index which induces a fuzzy ordering, and he further showed that this ordering, placed on a particular type of fuzzy number, may yield a reflexive fuzzy order.

Tanino (1984) studied the basic use of fuzzy preference orderings in decision theory. Defined as fuzzy binary relations which satisfy reciprocity and max-min transitivity, fuzzy preferences were expanded to include the case where fuzziness was caused by differences in individual opinion within the group decision. This concept of multiple experts is taken further by Buckley (1984) where a set of experts have fuzzy sets specified for both given issues under a particular criterion and for the criteria themselves. These sets may be

combined through various methods to achieve one fuzzy set which produces a final ranking for a specified issue. Similar methods were considered by Buckley (1985a) in which experts may use fuzzy numbers rather than merely fuzzy sets to express their preference, and by Buckley (1989a) in which a fast, computationally simpler method is presented to again rank alternatives via experts' fuzzy numerical criteria. Buckley (1989b) also presented a method that not only considers a decision theoretic problem, but also looks at statistical tests applied to fuzzy data. For example, a nonparametric Wilcoxon test which requires that data be ranked was extended to cover fuzzy numbers under the given ranking scheme.

Ammar (1989) considered the general issue of determining the best decision given a fuzzy environment. He developed several new definitions of "best" in both a weak and strong sense. Additionally, the results were extended from continuous fuzzy sets to discrete ones. Ammar did not specify the actual decision, but rather conceded that a best decision based on fuzzy information is itself a fuzzy concept. Hirota and Pedrycz (1989) also pondered the dilemma of which ranking method was superior. Each method could generate a different ranking, not only different in the numerical value assigned to the preference relations but also perhaps in the ordering produced. They used subjective entropy to interpret the entire family of results.

CHAPTER 9 MODIFIED KIRKWOOD-SARIN RANKING PROCEDURES

9.1 KSORG.FOR and KSAUG.FOR

In its original, simplest form, the Kirkwood-Sarin method for ranking multiattribute alternatives utilizes dominance relations to pairwise order the alternatives. The following algorithm, developed by Kirkwood and Sarin (1985), formed the basis of the new program KSORG.FOR and part of the new program KSAUG.FOR.

Original Rank-Ordering Algorithm: Let A_1, A_2,..., A_N denote the N alternatives. To generate a partial ranking, there are four steps.

1) Identify pairwise rankings between alternatives. For each pair of alternatives, either one is preferable, or it is not be possible to rank them.

2) Prepare a pairwise ranking table. List the alternatives in the same order down the left side and across the top of the table. Enter a 1 for an element of the table if the row alternative is preferred to the column alternative; otherwise, enter a 0. Determine the total number of 1's in each column, and list it at the bottom of the column. This total is the number of alternatives that are known to be preferred to the alternative listed at the top of that column.

3) Prepare a rank-ordering table. Form five columns with the headings "Required Number of Alternatives," "Column Totals," "Alternatives with Column Totals," "Number of Alternatives with Column Totals," and "Cumulative Number of Alternatives with Column Totals.

a) Under "Required Number of Alternatives," enter the numbers 1, 2, ... , N.

b) Under "Column Totals," enter the numbers N-1, N-2, ... , 2, 1, 0 in successive rows.

c) Under "Alternatives with Column Totals," list all alternatives with a "Column Total" on the pairwise ranking table that is equal to the number in the second column of the rank-ordering table.

d) Under "Number of Alternatives with Column Totals," enter the number of alternatives listed in the third column. Note that the sum of all entries in the fourth column is N.

e) Under "Cumulative Number of Alternatives with Column Totals," enter the sum of the entries in the fourth column down to and including that row.

4) Generate rankings and groupings of alternatives. In the rank-ordering table, draw a line across the table immediately below each row where the entries in the first and fifth columns are equal. The sets of alternatives in the third column listed between successive pairs of lines are successively more preferable going down the table. Within each set, it is not possible to rank-order

the alternatives given only the preference information contained in the pairwise ranking table.

In the new program KSORG.FOR, after the number of observations, the number of variables, and the data are read from a prepared data file, the pairwise ranking table of the algorithm, which is called the Kirkwood-Sarin 1-0 matrix KS(.,.) in the program, is constructed. Assuming that a smaller data value is to be preferred to a larger value, the observations associated with alternative I are compared to alternative J, $I \neq J$. If all of the variable values for alternative I are less than or equal to the variable values for alternative J, then a value of 1 is returned for KS(I,J). Otherwise, a value of 0 is provided for KS(I,J). The column sums for KS(I,J) are then calculated and stored in COLSUM(J). Thus, the first two steps of the algorithm are completed. Next, we determine

1) the alternatives with specified column totals and store them in PRTORD(.),

2) the number of such alternatives and store them in CNTLVL(I,I), and

3) the cumulative number of such alternatives and store them in CNTLVL(I,2).

Finally, we generate the rankings of the alternatives and the groupings of alternatives for which intra-group rankings are not possible.

Throughout the algorithm and its subsequent implementation in KSORG.FOR, no provisions were made to cope with inconclusive rankings or with missing observations. Procedures to resolve these difficulties would thus

be highly useful and are implemented as options in KSAUG.FOR. However, even in KSAUG.FOR, the user has the choice to maintain the status quo that was established in the original Kirkwood-Sarin ranking program KSORG.FOR.

9.2 INCONCLUSIVE RANKINGS

There are several techniques by which we can resolve inconclusive rankings. Four such options may currently be invoked in KSAUG.FOR; the first three methods attempt to resolve the issue, while the fourth retains the inconclusive 0 value for KS(I,J) which was generated by KSORG.FOR. In order to allow more possibilities for the KSAUG.FOR user, site-specific and variable-specific weights can also be entered. These weights allow the user to "stack the deck" in favor of one symptom or criteria versus another or one variable versus another; of course, neutral weights of 1 are also permitted. Once the weights are chosen, one of the inconclusive ranking techniques is selected. Option 1 is a basic counting procedure, and it has the following format. The number of times that the weighted value for symptom/criteria I is greater than the weighted value for symptom/criteria J, across all variables, is determined and stored in CNTGT. Similarly, the number of times that the weighted value for symptom/criteria I is less than the weighted value for symptom/criteria J, across all variables, is calculated and stored in CNTLS. If CNTLS is greater than CNTGT, and hence symptom/criteria I is preferred across more variables than symptom/criteria J, then a value of 1 replaces the original inconclusive value of

0 in the KS(I,J) entry. While the mere counting of larger or smaller values may lose much of the information contained in some datasets, this option also provides a way to resolve inconclusive rankings for categorical, particularly "Yes" - "No", data.

The second technique to resolve inconclusive rankings requires the use of the variable weights. If the weighted value for symptom/criteria I is greater than the weighted value for symptom/criteria J when variable K is considered, then the associated weight for the variable K is added to a running total stored in SUMGT. Similarly, if the weighted value for symptom/criteria I is less than the weighted value for symptom/criteria J when variable K is considered, then the associated weight for variable K is added to a running total stored in SUMLS. If, after all variables are considered, SUMLS is greater than SUMGT, then symptom/criteria I is preferred to symptom/criteria J and KS(I,J) equals 1; otherwise, the 0 value for KS(I,J) is retained. The benefit of this technique is that more important variables highly influence the final outcome while less important variables are still considered but are not as essential.

The third method involves the use of weighted differences. Again we look at the weighted value for symptom/criteria I in relation to the weighted value for symptom/criteria J when variable K is considered. However, the values obtained for SUMGWD and for SUMLWD are sums of weighted differences, weighted by variable, between the weighted values for symptoms/criteria I and J. The variable SUMGWD contains those sums where the weighted

value for symptom/criteria I is greater than the weighted value for symptom/criteria J, and in a comparable fashion, the variable SUMLWD contains those sums where the weighted value for symptom/criteria I is less than the weighted value for symptom/criteria J. This procedure utilizes not only the weights associated with the symptoms/criteria and the variables, but it also takes into account the relative differences in magnitude of the data for a given variable. Because of this, care should be taken when using this option on categorical data. Additionally, this method is highly influenced by merely a few large differences, and thus, the data should be analyzed to make certain such influence is desired.

In addition to the options by which inconclusive rankings are resolved, KSAUG.FOR also provides three techniques by which missing observations are replaced. Option 1 replaces all missing observations in variable I by the weighted minimum value associated with variable I. Similarly, option 2 uses the weighted maximum value, and option 3 utilizes the weighted average value. The weights used are obtained from a multiplication of the weights associated with symptoms/criteria and variables when missing data is encountered.

9.3 KSAUGI.FOR

To make the augmented Kirkwood-Sarin ranking scheme easier to use, KSAUGI.FOR was created. Based on KSAUG.FOR, the new program takes advantage of the inherent flexibility of the interactive mode to provide choices to

a program user. Indeed, throughout the program, the KSAUGI.FOR user has numerous options for both the input and output of data. The input of information is separated into several blocks, and for each block, a decision must be made as to whether to provide the data from the terminal or from the prepared file INFO.DAT. Similar choices are made for the output. For each section of output, the user may choose to send it only to the terminal, only to the file RANKD.DAT, to both, or to neither. The exception to this is that a few of the program parameters are automatically written to RANKD.DAT to provide some record of the computer runs.

KSAUGI.FOR may be re-run efficiently so that the user may see more quickly the effect of changing some of the program parameters. Such parameters as the weights for symptoms/criteria and variables, the choice of the inconclusive ranking method, and the choice of the missing data resolution technique may all be altered.

The program begins by asking the user to provide the following basic information from either the terminal or the file INFO.DAT.

1) Number of symptoms/criteria
2) Number of variables
3) Choice of the inconclusive ranking method
4) Choice of the missing data method
5) Symbol used in the original dataset for a missing data value

6) Temporary numeric replacement value for a missing data observation. Of this information, only the choice of the inconclusive ranking method and the choice of the missing data technique may be altered later in KSAUGI.FOR.

Once the previous six items are entered, the weights must also be provided from either the terminal or the file INFO.DAT. These weights are specific numeric values associated with the sites and the variables in the cases of inconclusive rankings and missing data. The first set of weights are those for the variables. For each variable, the inconclusive ranking weight and the missing data weight are entered in that order. The weights need not be equal, for any given variable since they correspond to the different cases of

1) an inconclusive ranking: symptom/criteria I is preferred to symptom/criteria J for some variables and not in others, and

2) a missing data point: for symptom/criteria I and variable J, a data value was not recorded.

Next, the set of weights for the sites are entered from either the terminal or the file INFO.DAT. Just as in the situation for variables, the sites also have weights corresponding to inconclusive rankings and missing data values. The method by which the preliminary data matrix will be entered and the matrix itself are next considered. The matrix may include missing observations and is read in character format. This allows for greater flexibility since different datasets might use different symbols denoting missing data. By a specification of the symbol for missing data, the program user allows KSAUGI.FOR to locate

the missing observations and replace them temporarily with a user-specified numeric value. This value, since it alerts the program to the presence of a missing observation, must be different from all recorded data points. After the numeric value replaces the character symbol for the missing data, the all-numeric data matrix is submitted to the subroutine MISSNG. A user-specified technique resolves the missing observations, and the enhanced data matrix is now ready for the ranking scheme.

Just as in KSAUG.FOR, the Kirkwood-Sarin 1-0 matrix is formed, and the resolutions of any inconclusive rankings are done by the subroutine INCONC. After the output location of the Kirkwood-Sarin 1-0 matrix is determined, the 1-0 matrix is put through the Kirkwood-Sarin algorithm, and a partial ranking is attained. Since the program is designed to be re-run with alterations particularly in the weights, the user has the option during post-initial runs to output the rankings for all of the sites or merely for those symptoms/criteria for which symptom/criteria-weightings have changed. Additionally, if such an altered-weighting site is part of a grouping tied for a rank, then the program offers the possibility of outputting the entire grouping or just the specified site.

KSAUGI.FOR finishes by asking the user whether any change in weights, inconclusive ranking, or missing data method is desired. If no changes are wanted, then KSAUGI.FOR is exited. Otherwise, the method by which the new program parameters will be entered must be selected, and the retention or alteration of the missing data technique and the inconclusive ranking method

must be decided. Once this is done, the program provides the option for the user to review the current weights for the variables and the symptoms/criteria. If any of the weights are to be changed, the new values may be entered from either the terminal or the file INFO.DAT. The program then repeats the process of generating a partial ranking.

9.4 RESOLUTION OF MISSING OBSERVATIONS

One difficulty with epidemiological data is that it may be incomplete for many patients either through missing values or uncodable information. If conventional multivariate techniques of analysis such as cluster analysis and correspondence analysis are used, the sparseness of the dataset suggests that the missing data should be handled in a manner other than deletion of the patient from any further consideration. There are several procedures through which we may deal with the missing observations.

We may use the definitions given by Little and Rubin (1987) to classify the data into three groups. The data points are said to be MCAR, missing completely at random, if the fact that we have missing data is not related to the variables under consideration. In other words, the observed values of the variables are a random subsample of the sampled values. The data is MAR, missing at random, if the distribution of the mechanism which causes the missing data does not depend on the missing values of the variables. Finally, the data is termed OAR, observed at random, if the distribution of the

mechanism which causes the observed data does not depend on the observed values of the variables. We will formalize these intuitive definitions in our study of techniques to handle missing data.

There are three basic methods for dealing with partially missing data. The first is merely to discard any incompletely observed data units. While this is relatively simple to accomplish in practice, it may be very undesirable if the amount of missing data is substantial. Indeed, serious biases could prevent any accurate interpretation of the data. Especially in some epidemiological datasets, this method may sometimes result in a reduction from several hundred patients under consideration to a few dozen patients being used.

The second method consists of imputation-based techniques. Little and Rubin (1987) list three such procedures. They include hot deck imputation which requires that observed data units in a sample be substituted for the missing data units, mean imputation which puts the means of the observed data units in the place of the missing data, and regression imputation where predicted values, based upon a regression on the known variables, are used as estimates of the missing information. In order that accurate interpretations can result, care must be taken to differentiate between the imputed values and the observed values of the variables. To gain a better insight into the data, the dataset is first considered in its entirety, and then separated into smaller sets. These sub-datasets include patients which are grouped together based upon criteria such as geographic location, socio-economic status, and ethnic status.

The third general procedure for dealing with missing data falls under the general category of model-based methods. In these techniques, we define a model for the incompletely observed data units, and then we base inferences on the likelihood under that model. Maximum likelihood methods can be used to obtain estimates of the parameters in the model. This basic procedure has several advantages, including flexibility and the avoidance of ad hoc techniques since the assumptions of the model could be clearly defined and verified. One problem with employing this method on certain epidemiological datasets is the lack of a well-specified model for the data. Indeed, the dilemma is circular in nature. We wish to be able to rank symptoms/criteria based upon the fewest number of important variables as suggested in some type of model. However, the data may contain a substantial amount of missing information which mandates that we deal with it in some manner other than deletion of the patient from consideration. If the initial technique we choose is a model-based procedure, the difficulty is apparent. Thus, one course of action is to use several of the imputation-based procedures to alleviate in some degree the problem of missing data. Once this is done, a subset of the data is analyzed, and if it conforms to a given model, the entire dataset is used. Of course, great care must be employed in this degree of data snooping to guard against faulty conclusions.

One of the serious problems of dealing with missing data is to decide whether the mechanisms that resulted in the incomplete observations occurring

can be ignored. Incorrect assumptions that the missing data happened by chance may seriously damage an accurate interpretation of any statistical results. It may be the case that the mechanism is either known or under the control of the statistician. Such an example would be found in survey sampling. By the process of sample selection, some of the elements in a given population are not chosen. For these units, no information would be gathered and thus, we have generated missing data. However, if the elements are chosen based upon probability sampling, then the mechanism which leads to the missing observations is known to the statistician, and so it can be ignored. On the other hand, if the chosen elements in the population do not respond, this yields a missing data mechanism which may not be well understood and which cannot be ignored. For a univariate sample, the process which causes the missing data can be ignored if the data are MAR. Otherwise, for analyses which do not take this into account, the results can be biased.

There are three basic methods which can be used with multivariate data that are assumed to be MCAR. In general, the techniques are not valid for data that are only MAR. The first procedure is called complete-case analysis which restricts attention to those units where data on all desired variables are present. In effect, this procedure discards information on the incomplete units, and it can be quite costly if there is a large amount of missing data. Additionally, if the assumption of MCAR is not truly valid, then those elements retained for analysis can differ significantly from the elements discarded. The severity of the bias

depends upon the mechanism causing the missing data to occur. As a test, we may use the information which has been discarded to see if the retained data can be considered a random subsample of the original sample. If it is not the case, then the MCAR assumption is not valid.

A second procedure is the available-case methods which are particularly useful when univariate analyses of multivariate data are desired. In this technique, all information about a given variable is used whether or not this would include units that are missing data in other variables. As a necessity, the base on which the univariate statistics are calculated could change from variable to variable. According to simulation studies performed by Kim and Curry (1977), under the MCAR assumption and with data that is only slightly correlated, the available-case method dominates the complete-case technique. This situation reverses for data with high correlation as other studies such as Azen and Van Guilder (1981) have shown.

The final type of procedure involves techniques which somehow fill in the missing values in the data. A common method is to predict the value of a variable, which contains units that are missing, by a highly correlated variable which has observed data. Another procedure is to estimate the missing value by either the mean of the recorded values of the given variable or the mean which has been conditioned upon the variables recorded in the incomplete units. The former strategy is employed in a portion of the subroutine MISSNG which is in the KSAUGI.FOR program. The latter calculation may be performed by a

method proposed by Buck in 1960. If we assume that the variables under consideration are multivariate normally distributed with a particular mean and covariance matrix, then estimates of these parameters are obtained from the sample mean and covariance matrix based upon the completely recorded units. The parameter estimates are then used to obtain the linear regressions of the missing variables on those variables which are present, in a case by case procedure. Once this is accomplished, we may substitute the observed values of the variables into the regression to obtain the predicted values of the missing data in each case. Unfortunately, the three previous methods may require ad hoc and unorthodox adjustments to yield results which are satisfactory, and it can be quite difficult to determine which situations will allow the methods to work accurately and for which situations the methods will fail. Thus, although the methods are attractive due to relative ease of implementation, other procedures are also considered which may give more accurate results.

According to Little and Schluchter (1985), a systematic alternative method for dealing with multivariate datasets which have missing observations requires that a model be proposed for the data and for the missing data mechanism. Once this is done, then maximum likelihood can be used to obtain estimates of parameters. However, for epidemiological datasets, with their mixture of continuous and categorical data, we cannot easily use the traditional multivariate normal model for continuous data nor the Poisson/multinomial model for categorical variables. Instead, the Little and Schluchter procedure

which combines the previous two models into one can be employed. Under the assumption of the data being MAR, the technique produces maximum likelihood estimates for the parameters of the joint distribution of continuous and categorical variables using the EM algorithm. The estimates may then be used to generate replacement values for missing observations. Other additional applications of this procedure include logistic regression and discriminant analysis when some of the predictor variables are missing, and there are unclassified observations, linear regression where both continuous and categorical predictors are missing, and parametric cluster analysis with incomplete multivariate data.

In the EM algorithm which is used to generate the parameter estimates, initial estimates of the parameters must be given for the iteration procedure. These initial values may be gotten through one of the three basic procedures for incomplete multivariate data. If we use the complete-case technique, then consistent estimates of the parameters are obtained provided that the data are MCAR and sufficiently many complete observations exist. In other words, if K variables are being considered, then K+I complete observations are needed. If the available-case method is used, then some problems may be encountered in the first iteration of the procedure due to the estimated covariance matrix not being positive definite. The imputation-based techniques will generally produce workable, but inconsistent, estimates of the covariance matrix. Depending upon which variables are present, the EM algorithm can also

reduce to various special cases. If no categorical variables are present, then the algorithm becomes a multivariate normal procedure. On the other hand, if there are incomplete categorical variables present, but no continuous variables are included, the data may be arranged in a multiway contingency table, and the algorithm reduces to ML estimation for such a table.

In our discussion of previous models, the assumption that the data are MAR or MCAR is prevalent. Formally, the models could include an indicator variable R which reveals whether each component of the data, denoted Y, is present. The models treat R as a random variable, and thus, we can specify the joint distribution of R and Y as

$$f(Y,R|T,S) = f(Y|T)f(R|Y,S) \qquad (10.4.1)$$

with unknown index parameters T and S. This joint distribution is called the distribution for the missing data mechanism. If we separate the data into two groups, the observed values denoted 0 and the missing values denoted M, then the data are MAR if

$$f(R|O,M,S) = f(R|O,S). \qquad (10.4.2)$$

In this case, the missing data mechanism would be ignorable. However, in other situations, it is not accurate to ignore the mechanism. Indeed, we must differentiate between situations where the missing-data mechanism is nonignorable but known versus nonignorable but unknown. In the former case, the distribution of R given Y depends upon the missing values of Y but not on S, while in the latter case, the parameter S in unknown and R depends upon it.

These models are particularly prevalent in sampling surveys where nonresponse is considered to relate to values of Y despite adjustments of covariate information for nonrespondents and respondents.

Thus, the task of dealing with the presence of missing values in a dataset is important, and many procedures attempt to cope with the problem. Perhaps the easiest way is to merely ignore any units for which we do not have complete information. This can result in a drastic loss of information particularly if the number of missing data points is substantial. An alternative is to replace the missing data with some type of imputed value obtained from the variables for which we have complete information. Both of these procedures are easy to perform, but may lead to biased interpretations if the missing data differs significantly from the observed data. A third general procedure is to formulate a model for the data and use it to gain replacement values for the missing data. Depending upon the type of data, a continuous variable case, a categorical case, or a mixture of the two might be considered. But always underlying any of these procedures is some type of assumption about the mechanism which has caused the missing data. Whether the data are MAR or MCAR and the mechanism is ignorable or nonignorable will influence the validity of the final interpretations. In epidemiological datasets with their sometimes numerous missing observations and variety of variable types, the use of several of the missing data procedures appears essential for a complete statistical analysis.

9.5 APPLICATION TO LUPUS OR ADD

The following is an example of the new application of the author-created program KSAUGI.FOR. The application ranks a set of patients for the likelihood of having lupus, based upon the values of fourteen criteria. Although the numbers which are used are fictitious, the appropriateness of the procedure will be demonstrated.

Let the data for 27 patients be given in Appendix B. In the data matrix, the rows represent patients and the columns represent symptoms (variables). Assume that small numbers are to be preferred to large ones. The KSAUGI program will do a pairwise comparison, between patients, across symptoms. If an inconclusive ranking is generated, the "Counting" scheme will be used to resolve it. In this way, the appropriate 1-0 matrix is generated. After the intermediate steps in the program are completed, a relative ordering of patients for the likelihood of lupus is obtained.

Ordering (from most likely to have lupus to least likely)

1.) Level 1:
    15

2.) Level 2:
    5

3.) Level 3:
    3

4.) Level 4:
    1,9

5.) Level 6:
7,6,2,24,4,16

6.) Level 12:
19

7.) Level 13:
11,8,22,18,12,17,21

8.) Level 20:
14,23,26

9.) Level 23:
20

10.) Level 24:
27

11.) Level 25:
10,25

12.) Level 27
13

Thus, it appears that patient #15 has the greatest chance of having lupus, whereas patient #13 has the least. Some patients were grouped together based upon the close similarity of their characteristics for most of the variables under consideration.

CHAPTER 10 CONCLUSIONS AND FURTHER RESEARCH

Since it quantifies subjectivity and includes a person's strength of belief, fuzzy numbers are a natural way to help in the "characterization and distribution of disease frequency in human populations." This previous phrase is one of the definitions of epidemiology. In this dissertation, fuzzy analysis was used in the study of ADD and of Lupus. It seemed to adequately describe a process which a physician uses to diagnosis a disease.

Fuzzy numbers are not a panacea, but they appear to be appropriate when human judgment is involved on at least an ordinal scale. Opinion is actually quite prevalent in epidemiological data as may be seen in ascertainments of both exposure and disease. Since judgment is rarely a narrowly defined quantity, the ability to associate an answer with the degree of belief in that answer is important, and may yield information unobtainable using more traditional approaches.

No surprisingly, this more careful depiction of an opinion is meaningless if the judgment itself is flawed. Fuzzy numbers will not substitute for the lack of a meaningful opinion. However, they may better document the presence of unreliability in judgment. This unreliability might be shown through an overly wide ambiguity range or an overly extreme range at any given α-cut level. This

instability of opinion might not be apparent if attention is restricted to ordinary numbers and common data gathering procedures.

In assessment of opinion, one is not confined to the use of only fuzzy numbers or only ordinary numbers. Since a fuzzy number requires an ambiguity range as well as a "best guess", and hence, potentially a doubling of the questions to be answered, fuzzy numbers might be reserved for special instances where ambiguity in judgment is crucial. Thus, in practice, a questionnaire might have both fuzzy and crisp components. A pilot study could be used to generate the requisite opinion shape for the fuzzy components through careful determination of intermediate belief levels. Then, in the main study, all participants would be asked for their answers at only a few levels, thereby fixing the placement of opinion along the response axis. The fuzzy number type, determined from the pilot study, could then be imposed upon this skeleton outline. This scheme maintains the potential benefits of fuzzy numbers without placing an unnecessary burden on the respondents.

In the current research, fuzzy numbers were used successfully to depict the vaguely defined disease of lupus. Patient and physician judgments were incorporated through the extensively modified FLMCM algorithm so that an assessment of lupus risk was made. Fuzzy numbers also seemed more realistically to capture the subjectivity associated with assessments of Attention Deficit Disorder. This was particularly true when the relative effectiveness of three therapies for ADD were clearly presented via one-step eigen-fuzzy sets.

Mixed linear combination, which generates a fuzzy average of opinions, produced results that compared favorably with the "true" value, but with substantially less effort. This method may also provide a means whereby opinions are actually "trained" as evaluators attempt to get closed to an idealized standard. By exploring the sensitivity of the fuzzy average to its input values, a better understanding may be obtained as to the relative importance of diagnostic standards and criteria. Similarly, fuzzy rule-based and distance-based descriptive measures of patient status yielded theoretical results which could be implemented in hospital studies. Thus, these three methods, created by other researchers, were favorably used in both the study of lupus and ADD. Lastly, the flexibility of a new ranking program, originally created by the author to rank hazardous waste sites for clean-up, was demonstrated by applying it to rank patients for likelihood of lupus. The program, unlike the algorithm upon which it was based, attempted to resolve inconclusive rankings and missing data.

Although the appropriateness of fuzzy numbers has been assessed theoretically, the next area of research would be to apply it to real-world situations in the study of ADD and of Lupus. Additionally, expansion of the methodological concepts into the realm of logistic regression, an important tool in epidemiology, has already begun by the present author. More advanced fuzzy techniques will complement existing statistical methods when opinion ambiguity is important. Indeed, given the relevance of opinion and the inability

of more conventional methods to adequately characterize judgment uncertainty, fuzzy procedures may provide insight into previously hidden relationships in epidemiological data.

APPENDIX A - KSAUGI FORTRAN CODE

The computer code for the Fortran program KSAUGI.FOR is given in the following. KSORG.FOR differs from KSAUGI.FOR in that inconclusive rankings and missing observations are not dealt with. Since this program is basically a subroutine in KSAUGI.FOR, separate code for KSORG.FOR is not given.

```
      Character*1 B(50)
      Character*7 MISDAT, MISREP, PD(770,50)
      Integer CHANG(770), CNTLVL(770,2), CNTPRF, COLSUM(770)
      Integer COUNT,CUM,I,ICHEK,ICHVAR,INEW,IOALL,IOCON
      Integer IOMETH, IOMIS, IOMSST, IORUN, IOSYMP, IOVAR, ITMP
      Integer J,K,KS(770,770), MCNT(770), NCHINC, NCHMIS, NCOUNT
      Integer NKS, NSTLVL, NUMOBS, NUMRUN, NUMVAR, PRTORD(770)
      Integer REVERS, TMPCH(770)
      Real D(770,50), REPLAC, W, WMS(770), WMV(50), WS(770), WV(50)
      Real MARGIN
      Data B/50*' '/, ICHVAR/0/, replac/-1.0/,WMS/770*1.0/
      Data WMV/50*1.0/, WS/770*1.0/ WV/50*1.0/

C
C ***************************************************************************
C
C     KSAUGI.FOR:  Augmented Interactive Kirkwood-Sarin Partial Ranking
C           Jean E. Merilan          January 1996
C
C     Algorithm from Craig W. Kirkwood and Rakesh K. Sarin "Ranking with
C     Partial Information:  A Method and an Application," Operations Research,
C     Vol. 33, No. 1, January-February 1985, pp. 38-48.
C
C     This program implements the Kirkwood-Sarin partial ranking algorithm
C     and provides several options to help alleviate the effect of missing
C     observations and inconclusive rankings.
C
C ***************************************************************************
C
```

```
C     The following files may be used by the program.
C     INFO.DAT:  File which may contain the following information in the
C           specified order
C     1.)  Number of symptoms (1 to 770)
C     2.)  Number of variables (1 to 5)
C     3.)  Choice of inconclusive-ranking resolution technique (1 to 4)
C     4.)  Choice of significant difference margin
C     5.)  Choice of missing-data resolution technique (1 to 3)
C     6.)  Symbol for missing data in a given dataset
C     7.)  Temporary numeric replacement value for missing data (it must not
C           be the same as any data value which is present in the dataset).
C     8.)  Weights assigned to the variables if inconclusive rankings are
C           encountered
C     9.)  Weights assigned to the variables if missing data is encountered
C     10.)  Weights assigned to the symptoms if inconclusive rankings are
C           encountered
C     11.)  Weights assigned to the symptoms if missing data is encountered
C     12.)  Original data (in character format)
C     13.)  Information for additional runs of the program
C
C     NINFO.DAT:  Dataset which is written by the program and which contains
C           the original data with missing observations replaced by a specific
C           numeric value (preset to -1.0)
C     RANKD.DAT:  Dataset which may contain the following information.
C     1.)  Echo of number of symptoms
C     2.)  Echo of number of variables
C     3.)  Echo of choice of inconclusive-ranking resolution technique
C     4.)  Echo of choice of significant difference margin
C     5.)  Echo of choice of missing-data resolution technique
C     6.)  Echo of symbol for missing data
C     7.)  Echo of temporary numeric replacement value for missing data
C     8.)  Echo of initial weights for variables and symptoms
C     9.)  Data matrix with missing data resolved
C     10.)  Kirkwood-Sarin 1-0 matrix
C     11.)  Partial ordering of symptoms
C     12.)  Changes in program parameters and subsequent program runs
C
C ******************************************************************************
C
C     The program uses the following subroutines.
C     INCONC:  Subroutine which attempts to resolve inconclusive rankings
C     MISSNG:  Subroutine which generates replacement values for missing
C           observations
```

```
C
C ***************************************************************************
C
C     The following variables are used in the main program.
C
C     B(I): Vector of blanks (used to separate columns in NINFO.DAT)
C     CHANG(i): Vector of symptoms for which weights have been changes
C     CNTLVL(I,1): Counts the number of sites at level I (column sum equal
C           to I)
C     CNTLVL(I,2): Cumulative number of symptoms through level I (column
C           sum less than or equal to I)
C     CNTPRF: Counts the number of times that symptom I is preferred
C           (either equally or strictly) to symptom J across all variables.
C     COLSUM(I): Sum of Kirkwood-Sarin 1-0 matrix entries in column I
C     COUNT: Miscellaneous counting variable
C     CUM: Running cumulative number of symptoms with column sum less
C           than or equal to a given value
C     D(I,J): Data matrix with row designating symptom and column
C           designating variable
C     I: Do-loop variable
C     ICHEK: Flag denoting multiple symptoms in the same level as a
C           changed weight symptom
C     ICHVAR: Flag denoting change in weights for some variables
C     INEW: Flag denoting initial entrance into ordering scheme
C     IOALL: Choice of whether to output the multiple symptoms or just the
C           changed weight symptoms
C     IOCON: Choice of new inconclusive ranking technique
C     IOMETH: Choice of input/output method
C     IOMIS: Choice of new missing data method
C     IOMSST: Choice of revising current missing data weights for
C           symptoms; also, number of altered missing data weights for
C           symptoms
C     IORUN: Choice to make any changes in program parameters and then
C           re-run the program
C     IOSYMP: Choice of outputting all symptoms or just the changed weight
C           symptoms; also, choice of reviewing current inconclusive
C           ranking weights for symptoms, and the number of altered
C           inconclusive ranking weights for variables
C     IOVAR: Choice of reviewing weights for variables
C     ITMP: Counting variable associated with TMPCH(I)
C     J: Do-loop variable; also, the number of the variable/site associated
C           with a change in weights
C     K: Do-loop variable; also, a counting variable which allows TMPCH(I)
```

```
C            values to be written to empty spaces in CHANG(I)
C       KS(I,J): Kirkwood-Sarin 1-0 matrix
C       MARGIN: Amount by which the weighted value for one symptom must
C            differ from the weighted value for another symptom before the
C            difference is considered significant
C       MCNT(I): Number of symptoms with a missing observation for variable I
C       MISDAT: User-supplied symbol for missing data in a given dataset
C       MISREP: User-supplied temporary numeric replacement value for
C            missing data (in character format); this value must not be the same
C            as any data point which is present in a given dataset
C       NCHINC: Choice of inconclusive ranking method
C       NCHMIS: Choice of missing data method
C       NCOUNT: Last symptom number of a given level
C       NKS: New Kirkwood-Sarin value obtained from subroutine INCONC
C       NSTLVL: Number of symptoms within a given rank level
C       NUMOBS: Number of symptoms (observations)
C       NUMRUN: Number of times the program has been run in a particular
C            session
C       NUMVAR: Number of variables
C       PD(I,J): Preliminary data matrix (in character format)
C       PRTORD(I): Vector containing partially ordered symptoms
C       REPLAC: Temporary numeric replacement value for missing data; this
C            value is the real format version of MISREP
C       REVERS: Backward counter starting at (NUMOBS-1) and ending at 0
C       TMPCH(I): Temporary vector of changed weight symptoms
C       W: Value of altered weight
C       WMS(I): Weight assigned if data is missing for symptom I
C       WMV(J): Weight assigned if data is missing for variable J
C       WS(I): Weight assigned to symptom I if inconclusive rankings are
C            encountered (may be different from WMS(I))
C       WV(J): Weight assigned to variable J if inconclusive rankings are
C            encountered (may be different from WMV(J))
C
C ***************************************************************************
C
      Open (15,File='INFO.DAT',Status='UNKNOWN')
      Rewind (15)
      Open (10,File='NINFO.DAT',Carriagecontrol='LIST',
Status='UNKNOWN')
      Rewind (20)
      Open (25,File='RANKD.DAT',Status='UNKNOWN')
      Rewind (25)
      Open (30,File='ACRNK.DAT',Status="UNKNOWN')
```

```
      Rewind (30)

C
C     Determine the method by which the number of symptoms, number of
C     variables, choice of inconclusive ranking resolution technique, choice
C     of missing data resolution techniques, symbol for missing data, and
C     temporary numeric replacement value for missing data will be entered.
C

      Write (*,10) ' '
10    Format ('1',A)
      Write (*,*) 'The following information must be provided:'
      Write (*,*) '   Number of site'
      Write (*,*) '   Number of variables'
      Write (*,*) '   Choice of inconclusive ranking method'
      Write (*,*) '   Choice of significant difference margin'
      Write (*,*) '   Choice of missing data method'
      Write (*,*) '   Symbol for missing data'
      Write (*,*) '   Temporary numeric replacement value for missing data'
20    Write (*,*) ' '
      Write (*,*) 'Choose the method by which all of this information will'
      Write (*,*) 'be entered:'
      Write (*,*) '   Terminal                    ...     Enter 1'
      Write (*,*) '   File (INFO.DAT)             ...     Enter 2'
      Read (*,*) IOMETH
      If (IOMETH .ne. 1 .and. IOMETH .ne. 2) then
            Write (*,*) '    *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.'
      Endif

C
C     Read in number of symptoms, number of variables, choice of
C     inconclusive ranking resolution technique, choice of missing data
C     resolution technique, symbol for missing data, and temporary numeric
C     replacement value for missing data.  The information is echoed
C     to RANKD.DAT.
C

      If (IOMETH .eq. 1) then
            Write (*,30) ' '
30          Format ('1',A)
            Write (*,*) 'Input number of symptoms'
            Read (*,*) NUMOBS
```

```
            Write (*,*) 'Input number of variables'
            Read (*,*) NUMVAR
            Write (*,*) 'Input choice of inconclusive ranking method'
            Read (*,*) NCHINC
            Write (*,*) 'Input choice of significant difference margin'
            Read (*,*) MARGIN
            Write (*,*) 'Input choice of missing data method'
            Read (*,*) NCHMIS
            Write (*,*) 'Input symbol for missing data (enclosed within " ")'
            Read (*,*) MISDAT
            Write (*,*) 'Input temporary numeric replacement value for'
            Write (*,*) 'missing data (enclosed with " ")'
            Read (*,*) MISREP
      Else
            Read (15,*) NUMOBS,NUMVAR,NCHINC, MARGIN,NCHMIS,
            MISDAT, MISREP
      Endif

      Write (25,*) 'Number of symptoms: ', NUMOBS
      Write (25,*) 'Number of variables: ', NUMVAR
      Write (25,*) 'Choice of inconclusive ranking method: ', NCHINC
      Write (25,*) 'Choice of significant difference margin: ', MARGIN
      Write (25,*) 'Choice of missing data method: ', NCHMIS
      Write (25,*) 'Symbol for missing data: ', MISDAT
      Write (25,*) 'Numeric replacement value: ', MISREP
      Rewind (20)
      Read (20,*) REPLAC
      Rewind (20)
      Write (30,*) 'KSAUGI ranks for 100 symptoms'
      Write (30,*) '3'
      Write (30,*) 'Symptom number'
      Write (30,*) 'Rank'
      Write (30,*) 'Run'

C
C     Determine the method by which the weights associated with the
C     variables will be entered
C

      Write (*,40) ' '
40    Format ('1', A)
      Write (*,*) 'Weights associated with variables when any'
      Write (*,*) 'inconclusive rankings are encountered and weights'
```

```
      Write (*,*) 'associated with variables when any missing data;
      Write (*,*) 'is encountered must be provided.'
50    Write (*,*) ' '
      Write (*,*) 'Choose the method by which the information will'
      Write (*,*) 'be entered:'
      Write (*,*) '   Terminal              ...     Enter 1'
      Write (*,*) '   File (INFO.DAT)       ...     Enter 2'
      Write (*,*) '   Default (WTS=1)       ...     Enter 3'
      Read (*,*) IOMETH
      If (IOMETH .ne. 1 .and. IOMETH .ne. 2 .and. IOMETH .ne. 3) then
            Write (*,*) '          *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.'
            Go to 50
      Endif

C
C     Read in weights associated with variables when inconclusive rankings
C     are encountered and weights associated with variables when missing
C     data is encountered.  The information is echoed to RANKD.DAT.
C

      If (IOMETH .eq. 1) then
            Write (*,60)
60          Format ('1',A)
            Do 70 I = 1, NUMVAR
                  Write (*,*) 'Input inconclusive ranking weight for'
                  Write (*,*) 'variable', I
                  Read (*,*) WV(I)
                  Write (*,*) 'Input missing data weight for variable', I
                  Read (*,*) WMV(I)
70          Continue
      Else
            If (IOMETH .eq. 2) then
                  Read (15,*) (WV(J),WMV(J), J = 1,NUMVAR)
            Endif
      Endif
      Write (25,80) ' '
80    Format ('1', A)
      Write (25,*) 'Inconclusive ranking weights (variables)'
      Write (25,*) (WV(J), J = 1, NUMVAR)
      Write (25,*) ' '
      Write (25,*) 'Missing data weights (variables)'
      Write (25,*) 'WMV(J), U = 1, NUMVAR)
```

```
C
C     Determine the method by which the weights associated with symptoms
C     when inconclusive rankings are encountered and weights associated
C     with symptoms when missing data is encountered will be entered.
C
      Write (*,90) ' '
90    Format ('1', A)
      Write (*,*) 'Weights associated with symptoms when inconclusive'
      Write (*,*) 'rankings are encountered and weights associated'
      Write (*,*) 'with sites when missing data is encountered must'
      Write (*,*) 'be provided.'
100   Write (*,*) ' '
      Write (*,*) 'Choose the method by which the information will be entered'
      Write (*,*) '   Terminal                ...      Enter 1'
      Write (*,*) '   File (INFO.DAT)         ...      Enter 2'
      Write (*,*) '   Default (WTS = 1)       ...      Enter 3'
      Read (*,*) IOMETH
      If (IOMETH .ne. 1 .and. IOMETH .ne. 2 .and. IOMETH .ne. 3) then
            Write (*,*) '              ***WARNING*** '
            Write (*,*) 'Invalid Choice.  Try again.'
            Go to 100
      Endif

C
C     Read in weights associated with symptoms when inconclusive rankings
C     are encountered and weights associated with symptoms when missing
C     data is encountered.  The information is echoed to RANKD.DAT
C

      If (IOMETH .eq. 1) then
            Write (*,110) ' '
110         Format ('1', A)
            Do 120 I = 1, NUMOBS
                  Write (*,*) 'Input inconclusive ranking weight for symptom', I
                  Read (*,*) WS(I)
                  Write (*,*) 'Input missing data weight for symptom', I
                  Read (*,*) WMS(I)
120         Continue
      Else
            If (IOMETH .eq. 2) then
                  Read (15,*) (WS(J),WMS(J), J = 1,NUMOBS)
            Endif
```

```
      Endif
      Write (25,*) ' '
      Write (25,*) 'Inconclusive ranking weights (symptoms)'
      Write (25,*) (WS(J), J = 1, NUMOBS)
      Write (25,*) ' '
      Write (25,*) 'Missing data weights (symptoms)'
      Write (25,*) (WMS(J), J = 1,NUMOBS)

C
C     Determine the method by which the preliminary data matrix will be
C     entered.
C

      Write (*,130) ' '
130   Format ('1',A)
      Write (*,*) 'Preliminary data matrix, each entry of which must be'
      Write (*,*) 'enclosed within " ", must be provided.'
140   Write (*,*) ' '
      Write (*,*) 'Choose the method by which the information will be entered'
      Write (*,*) '   Terminal              ...     Enter 1'
      Write (*,*)    File (INFO.DAT)      ...     Enter 2'
      Read (*,*) IOMETH
      If (IOMETH .ne. 1 .and. IOMETH .ne. 2) then
            Write (*,*) '            *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.
            Go to 140
      Endif

C
C     Read in the preliminary data matrix (in character format)
C

      If (IOMETH .eq. 1) then
            Write (*,150) ' '
150         Format ('1', A)
            Do 160 I = 1, NUMOBS
                  Write(*,*) 'Input data for symptom', I
                  Do 170 J = 1,NUMVAR
                        Write (*,*) ' and variable', J
                        Read (*,*) PD(I,J)
170               Continue
160         Continue
      Else
```

```
            Do 180 I = 1, NUMOBS
                  Read (15,*) (PD(I,J), J = 1, NUMVAR)
180         Continue
      Endif
      NUMRUN=0
190   NUMRUN=NUMRUN + 1
      Write (*, 200) ' '
200   Format ('1',A)
      Write (*,*) 'Results for run', NUMRUN
      Write (25,210) ' '
210   Format ('1',A)
      Write (25,*) 'Results for run', NUMRUN

C
C     Replace missing data with a user-specified numeric value.
C
      Do 220 J = 1, NUMVAR
            MCNT(J) = 0
            Do 230 I = 1, NUMOBS
                  If (PD(I,J) .eq. MISDAT) then
                        PD(I,J) = MISREP
                        MCNT(J) = MCNT(J) + 1
                  Endif
230         Continue
220   Continue

C
C     Write altered data matrix to NINFO.DAT
C

      Do 240 I = 1, NUMOBS
            Write (20,*) (PD(I,J), B(J), J = 1, NUMVAR)
240   Continue
      Rewind (20)

C
C     Read data matrix with missing values preset to a user-specified value
C
      Do 250 I = 1, NUMOBS
            Read (20,*) (D(I,J), J = 1, NUMVAR)
250   Continue
      Rewind (20)
```

```
C
C     Replace missing values via the chosen missing data resolution
C     technique
C
      Do 260 J = 1, NUMVAR
            If (MCNT(J) .gt. 0) then
              Call MISSNG(NCHMIS,REPLAC,D,J,NUMOBS,WMS,WMV)
            Endif
260   Continue

C
C     Choose where to write the altered data matrix
C

      Write (*,270) ' '
270   Format ('0', A)
      Write (*,*) 'Select the output location for the data matrix with any'
      Write (*,*) 'missing data resolved.'
280   Write (*,*) ' '
      Write (*,*) 'Terminal only                                    ...    Enter 1'
      Write (*,*) 'File (RANKD.DAT) only                            ...    Enter 2'
      Write (*,*) 'Terminal and File (RANKD.DAT) both               ...    Enter 3'
      Write (*,*) 'Neither Terminal nor File (RANKD.DAT)            ...    Enter 4'
      Read (*,*) IOMETH
      If (IOMETH .ne. 1 .and. IOMETH .ne. 2 .and. IOMETH .ne. 3 .and.
            IOMETH .ne. 4) then
            Write (*,*) '          *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.'
            Go To 280
      Endif

C
C     Write the data matrix with any missing data resolved to the specified
C     location.
C

      If (IOMETH .eq. 1) then
            Write (*,290) ' '
290         Format ('1', A)
            Write (*,*) 'Data matrix with any missing data resolved'
            Do 300 I = 1, NUMOBS
                  Write (*,*) (D(I,J), J = 1, NUMVAR)
300         Continue
```

```
      Else
      If (IOMETH .eq. 2) then
            Write (25, 310)
310         Format ('0",A)
            Write (25,*) 'Data matrix with missing data resolved'
            Do 320 I = 1, NUMOBS
                  Write (25,*) (D(I,J), J = 1, NUMVAR)
320         Continue
      Else
      If (IOMETH .eq. 3) then
            Write (*,330) ' '
330         Format ('1', A)
            Write (*,*) 'Data matrix with missing data resolved'
            Do 340 I = 1, NUMOBS
                  Write (*,*) (D(I,J), J = 1, NUMVAR)
340         Continue
            Write (25, 350) ' '
350         Format ('0', A)
            Write (25,*) 'Data matrix with missing data resolved'
            Do 360 I = 1, NUMOBS
                  Write (25,*) (D(I,J), J = 1, NUMVAR)
360         Continue
      Endif
      Endif
      Endif

C
C     Fill in Kirkwood-Sarin 1-0 matrix
C

      Do 370 I = 1, NUMOBS
            Do 380 J = 1, NUMOBS
                  CNTPRF = 0
                  Do 390 K = 1, NUMVAR
                        If (D(I,K) .le. D(J,K) .and. I .ne. J) then
                              CNTPRF=CNTPRF+1
                        Endif
390                 Continue
                  If (CNTPRF .eq. NUMVAR) then
                        KS(I,J) = 1
                  Else
                        Call INCONC(NCHINC,D,I,J,NUMVAR,WS,WV,
                              MARGIN,NKS)
```

```
                        KS(I,J) = NKS
                    Endif
380             Continue
370     Continue

C
C       Determine where to write the Kirkwood-Sarin 1-0 matrix
C

        Write (*,400) ' '
400     Format ('0', A)
        Write (*,*) 'Select the output location for the Kirkwood-Sarin 1-0 matrix'
410     Write (*,*) ' '
        Write (*,*) 'Terminal only                                  ...     Enter 1'
        Write (*,*) 'File (RANKD.DAT) only                          ...     Enter 2'
        Write (*,*) 'Terminal and File (RANKD.DAT) both             ...     Enter 3'
        Write (*,*) 'Neither Terminal nor File (RANKD.DAT)          ...     Enter 4'
        Read (*,*) IOMETH
        If (IOMETH .ne. 1 .and. IOMETH .ne. 2 .and. IOMETH .ne. 3 .and.
            IOMETH .ne. 4) then
            Write (*,*) '           *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.'
        endif

C
C  Output Kirkwood-Sarin 1-0 matrix
C

        If (IOMETH .eq. 1) then
            Write (*,420) ' '
420         Format ('1', A)
            Write (*,*) 'Kirkwood-Sarin 1-0 matrix'
            Do 430 I = 1, NUMOBS
                Write (*,440) (KS(I,J), j = 1, NUMOBS)
440             Format ('0', 60(I1))
430         Continue
        Else
            If (IOMETH .eq. 2) then
                Write (25, 450) ' '
450             Format ('1', A)
                Write (25,*) 'Kirkwood-Sarin 1-0 Matrix'
                Do 460 I = 1, NUMOBS
                    Write (25, 470) (KS(I,J), J = 1, NUMOBS)
```

```
470                     Format (')', 60(I1))
460                 Continue
            Else
                 If (IOMETH .eq. 3) then
                     Write (*, 480) ' '
480                  Format ('1', A)
                     Write (*,*) 'Kirkwood-Sarin 1-0 Matrix'
                     Format ('1', A)
                     Write (25, *) 'Kirkwood-Sarin 1-0 Matrix'
                     Do 500 I = 1, NUMOBS
                       Write (*, 510) (KS(I,J), J = 1, NUMOBS)
510                    Format ('0', 60(I1))
                       Write (25, 520) (KS(I,J), J = 1, NUMOBS)
520                    Format ('0', 60(I1))
500                  Continue
                 Endif
            Endif
       Endif

C
C      Calculate sum for each Kirkwood-Sarin matrix column
C
       Do 530 J = 1, NUMOBS
            COLSUM(J) = 0
            Do 540 I = 1, NUMOBS
                 COLSUM(J) = COLSUM(J) + KS(I,J)
540         Continue
530    Continue
       Write (*,*) ' '
       Write (25,*) ' '

C
C      Determine the number of symptoms at a particular level and the
C      cumulative level totals
C

       CUM = 0
       COUNT = 0
       Do 550 I = 1, NUMOBS
            CNTLVL(I,1) = 0
            REVERS = NUMOBS-I
            Do 560 J = 1, NUMOBS
                 If (COLSUM(J) .eq. REVERS) then
```

```
                        COUNT = COUNT + 1
                        CNTLVL(I,1) = CNTLVL(I,1) + 1
                        PRTORD(COUNT) = J
                    Endif
560             Continue
                CUM=CUM + CNTLVL(I,1)
                CNTLVL(I,2) = CUM
550     Continue

C
C       For other than the first run of the program, determine whether all
C       of the symptoms are to be outputted or just those symptoms for which
C       symptom-weighting information has changed.
C

        If (NUMRUN .ne. 1) then
                Write (*,570) ' '
570             Format ('0', A)
                Write (*,*) 'For the partial ordering of symptoms, do you want'
                Write (*,*) 'all symptoms to be outputted or just those symptoms'
                Write (*,*) 'for which site-weighting values have changed.'
                Write (*,*) '  Note:  A change in variable-weighting values requires'
                Write (*,*) 'all symptoms to be outputted'
580             Write (*,*) ' '
                Write (*,*) 'Output all symptoms                              ... Enter 1'
                Write (*,*) 'Output changed weight symptoms only      ... Enter 2'
                Read (*,*) IOSYMP
                If (IOSYMP .ne. 1 .and. IOSYMP .ne. 2) then
                        Write (*,*) '           *** WARNING ***'
                        Write (*,*) 'Invalid choice.  Try again.'
                        Go to 580
                Endif
                J = 0
                If (IOSYMP .eq. 2) then
                        Do 590 I = 1, NUMOBS
                                IF (CHANG(I) .ne. 0) J = 1
590                     Continue
                        If (J .eq. 0) then
                                Write (*,*) 'No weights for symptoms were changed'
                                Write (*,*) 'for this run.  Option 2 for this case will'
                                Write (*,*) 'no ordering output.  Choose Option 1.'
                                Go to 580
                        Endif
```

```
                If (ICHVAR .eq. 1) then
                    Write (*,*) '          *** WARNING ***'
                    Write (*,*) 'Variable weights were changed.'
                    Write (*,*) 'Choose Option 1 instead'
                    Go to 580
                Endif
            Endif
        Endif

C
C       Determine the method by which information will be outputted
C

        COUNT = 1
        INEW = 1
        J = 1
        If (IOSYMP .eq. 1 .or. NUMRUN .eq. 1) then
            Write (*, 600) ' '
600         Format ('0', A)
            Write (*,*) "Select the output location for the partial ordering'
            Write (*,*) 'of the symptoms'
610         Write (*,*) ' '
            Write (*,*) 'Terminal only                                  ... Enter 1'
            Write (*,*) 'File (RANKD.DAT) only                          ... Enter 2'
            Write (*,*) 'Terminal and File (RANKD.DAT) both             ... Enter 3'
            Write (*,*) 'Neither Terminal nor File (RANKD.DAT)          ... Enter 4'
            Read (*,*) IOMETH
            If (IOMETH .ne. 1 .and. IOMETH .ne. 2 .and. IOMETH .ne. 3
                .and. IOMETH .ne. 4) then
                Write (*,*) '          *** WARNING ***'
                Write (*,*) 'Invalid choice.  Try again.'
                Go to 610
            Endif

C
C       Output partial ordering to terminal
C

        If (IOMETH .eq. 1) then
            Write (*,620) ' '
620         Format ('1', A)
            Write (*,*) 'Partial ordering of symptoms'
            Do 630 I = 1, NUMOBS
```

```
                    If (CNTLVL(I,2) .eq. I) then
                        NSTLVL = CNTLVL(I,2) - CNTLVL(J,2)
                        If (NSTLVL .eq. 0) NSTLVL = 1
                        If (INEW .eq. 1) NSTLVL = CNTLVL(I,2)
                        Write (*,640) '**** Level ', COUNT, '****'
640                     Format ('0', A, I3, A)
                        NCOUNT = COUNT + NSTLVL - 1
                        Write (*, 650) (PRTORD(J), J = COUNT, NCOUNT)
650                     Format (' ', I3)
                        COUNT = NCOUNT + 1
                        INEW = 0
                        J = I
                    Endif
630             Continue
        Else

C
C       Output partial ordering to RANKD.DAT
C

        If (IOMETH .eq. 2) then
            Write (25, 660) ' '
660         Format ('1', A)
            Write (25,*) 'Partial ordering of symptoms'
            Do 670 I = 1, NUMOBS
                    If (CNTLVL(I,2) .eq. I) then
                        NSTLVL = CNTLVL(I,2) - CNTLVL(J,2)
                        If (NSTLVL .eq. 0) NSTLVL = 1
                        If (INEW .eq. 1) NSTLVL = CNTLVL(*,2)
                        Write (25,680) '**** Level ', COUNT, '****'
680                     Format ('0', A, I3, A)
                        NCOUNT = COUNT + NSTLVL - 1
                        Write (25, 690) (PRTORD(J), J = COUNT, NCOUNT)
690                     Format (' ', I3)
                        COUNT = NCOUNT + 1
                        INEW = 0
                        J = I
                    Endif
670             Continue
        Else

C
C       Output partial ordering to terminal and RANKD.DAT
```

```
C
      If (IOMETH .eq. 3) then
            Write (*, 700) ' '
700         Format ('1', A)
            Write (*,*) 'Partial ordering of symptoms'
            Write (25, 710) ' '
710         Format ('1',A)
            Write (25,*) 'Partial ordering of sites'
            Do 720 I = 1, NUMOBS
                  If (CNTLVL(I,2) .eq. I) then
                        NSTLVL = CNTLVL(I,2) - CNTLVL(J,2)
                        If (INEW .eq. 1) NSTLVL = CNTLVL(I,2)
                        Write (*,730) '**** Level ', COUNT,' ****'
730                     Format ('0', A, I3, A)
                        Write (25, 740) '**** Level ', COUNT,' ****'
740                     Format ('0', A, I3, A)
                        NCOUNT = COUNT + NSTLVL - 1
                        Write (*, 750) (PRTORD(J), J = COUNT,NCOUNT)
750                     Format (' ', I3)
                        Write (25, 760) (PRTORD(J), J = COUNT,NCOUNT)
760                     Format (' ', I3)
                        Do 761 JJ = COUNT, NCOUNT
                          Write (30, 762) PRTORD(JJ), COUNT, NUMRUN
762                       Format (' ', I3, 1X, I3, 1X, I3)
761                     Continue
                        COUNT=NCOUNT + 1
                        INEW = 0
                        J = I
                  Endif
            Continue
      Endif
      Endif
      Endif
      Else

C
C     Select output location for partial ordering when the changed weight
C     symptom output option (Option 2) was chosen
C

      Write (*, 770) ' '
770   Format ('0', A)
      Write (*,*) 'Select the output location for the partial ordering of the'
```

```
      Write (*,*) 'symptoms'
780   Write (*,*) ' '
      Write (*,*) 'Terminal only                                    ... Enter 1'
      Write (*,*) 'File (RANKD.DAT)                                 ... Enter 2'
      Write (*,*) 'Terminal and File (RANKD.DAT)                    ... Enter 3'
      Write (*,*) 'Neither terminal nor file (RANKD.DAT)            ... Enter 4'
      Read (*,*) IOMETH
      If (IOMETH .ne. 1 .and. IOMETH .ne. 2 .and. IOMETH .ne. 3 .and.
          IOMETH .ne. 4) then
          Write (*,*) '          *** WARNING ***'
          Write (*,*) 'Invalid choice.  Try again.'
          Go to 780
      Endif

C
C     Output partial ordering to terminal with option of outputting multiple
C     symptoms in a specified level
C

      If (IOMETH .eq. 1) then
          Write (*,790) ' '
790       Format ('1', A)
          Write (*,*) 'Partial ordering output for specified symptoms'
          Do 800 I = 1, NUMOBS
              If (CNTLVL(I,2) .eq. I) then
                  NSTLVL = CNTLVL(I,2) - CNTLVL(J,2)
                  If (NSTLVL .eq. 0) NSTLVL = 1
                  If (INEW .eq. 1) NSTLVL = CNTLVL(I,2)
                  NCOUNT = COUNT + NSTLVL - 1
                  ICHEK = 0
                  Do 810 J = 1, NUMOBS
                  Do 820 K = COUNT, NCOUNT
                      If (CHANG(J) .eq. PRTORD(K)) then
                          ICHEK=1
                          Write (*,830) 'Level ',COUNT, 'Site',
                          PRTORD(K)
830                       Format ('0', A, I3, A, I3)
                      Endif
820               Continue
810           Continue
              If (ICHEK .eq. 1 .and. NSTLVL .gt. 1) then
                  Write (*,*) ' '
                  Write (*,*) 'Due to multiple symptoms in same level'
```

```
                    Write (*,*) 'as a specified symptom, do you want all'
                    Write (*,*) 'sites in that level to be outputted?'
840                 Write (*,*) ' '
                    Write (*,*) 'Yes              ...     Enter 1'
                    Write (*,*) 'No               ...     Enter 2'
                    Read (*,*) IOALL
                    If (IOALL ne. 1 .and. IOALL .ne. 2) then
                        Write (*,*) '          *** WARNING ***'
                        Write (*,*) 'Invalid choice.  Try again.'
                        Go to 840
                    Endif
                    If (IOALL .eq. 1) then
                      Write (*, 850) '*** Level ', COUNT, ' ***'
850                   Format ('0', A, I3, A)
                      Write (*, 860) (PRTORD(J), J = COUNT,NCOUNT)
860                   Format (' ', I3)
                    Endif
                Endif
                COUNT = NCOUNT + 1
                INEW = 0
                J = I
            Endif
800     Continue
        Else

C       Output partial ordering to RANKD.DAT with the option of outputting
C       multiple symptoms in a specified level
C

        If (IOMETH .eq. 2) then
            Write (25,870) ' '
870         Format ('1', A)
            Write (25,*) 'Partial ordering output for specified symptoms'
            Do 880 I = 1, NUMOBS
                If (CNTLVL(I,2) .eq. I) then
                    NSTLVL = CNTLVL(I,2) - CNTLVL(J,2)
                    If (NSTLVL .eq. 0) NSTLVL = 1
                    If (INEW .eq. 1) NSTLVL = CNTLVL(I,2)
                    NCOUNT = COUNT + NSTLVL - 1
                    ICHEK = 0
                    Do 890 J = 1, NUMOBS
                    Do 900 K = COUNT, NCOUNT
                        If (CHANG(J) .eq. PRTORD(K)) then
```

```
                                        ICHEK=1
                                        Write (25,910) 'Level ',COUNT, 'Site',
                                        PRTORD(K)
910                                     Format ('0', A, I3, A, I3)
                                Endif
900                         Continue
890                 Continue
                    If (ICHEK .eq. 1 .and. NSTLVL .gt. 1) then
                        Write (*,*) ' '
                        Write (*,*) 'Due to multiple symptoms in same level'
                        Write (*,*) 'as a specified symptom, do you want all'
                        Write (*,*) 'sites in that level to be outputted?'
920                     Write (*,*) ' '
                        Write (*,*) 'Yes                ...     Enter 1'
                        Write (*,*) 'No                 ...     Enter 2'
                        Read (*,*) IOALL
                        If (IOALL ne. 1 .and. IOALL .ne. 2) then
                            Write (*,*) '           *** WARNING ***'
                            Write (*,*) 'Invalid choice.  Try again.'
                            Go to 920
                        Endif
                        If (IOALL .eq. 1) then
                          Write (25, 930) '*** Level ', COUNT, ' ***'
930                       Format ('0', A, I3, A)
                          Write (25, 940) (PRTORD(J), J = COUNT,NCOUNT)
940                       Format (' ', I3)
                        Endif
                    Endif
                    COUNT = NCOUNT + 1
                    INEW = 0
                    J = I
            Endif
880     Continue
        Else

C       Output partial ordering to terminal and RANKD.DAT with the option
C       of outputting multiple symptoms in a specified level
C

        If (IOMETH .eq. 3) then
            Write (*,950) ' '
950         Format ('1', A)
            Write (*,*) 'Partial ordering output for specified symptoms'
```

```
            Write (25,960) ' '
960         Format ('1', A)
            Write (*,*) 'Partial ordering output for specified symptoms'
            Do 970 I = 1, NUMOBS
                  If (CNTLVL(I,2) .eq. I) then
                        NSTLVL = CNTLVL(I,2) - CNTLVL(J,2)
                        If (NSTLVL .eq. 0) NSTLVL = 1
                        If (INEW .eq. 1) NSTLVL = CNTLVL(I,2)
                        NCOUNT = COUNT + NSTLVL - 1
                        ICHEK = 0
                        Do 980 J = 1, NUMOBS
                        Do 990 K = COUNT, NCOUNT
                              If (CHANG(J) .eq. PRTORD(K)) then
                                    ICHEK=1
                                    Write (*,1000) 'Level ',COUNT, 'Site',
                                    PRTORD(K)
1000                                Format ('0', A, I3, A, I3)
                                    Write (25,1010) 'Level ',COUNT, 'Site',
                                    PRTORD(K)
1010                                Format ('0', A, I3, A, I3)
                              Endif
990                     Continue
980               Continue
                  If (ICHEK .eq. 1 .and. NSTLVL .gt. 1) then
                        Write (*,*) ' '
                        Write (*,*) 'Due to multiple symptoms in same level'
                        Write (*,*) 'as a specified symptom, do you want all'
                        Write (*,*) 'sites in that level to be outputted?'
1020                    Write (*,*) ' '
                        Write (*,*) 'Yes              ...     Enter 1'
                        Write (*,*) 'No               ...     Enter 2'
                        Read (*,*) IOALL
                        If (IOALL ne. 1 .and. IOALL .ne. 2) then
                              Write (*,*) '           *** WARNING ***'
                              Write (*,*) 'Invalid choice.  Try again.'
                              Go to 1020
                        Endif
                        If (IOALL .eq. 1) then
                          Write (*, 1030) '*** Level ', COUNT, ' ***'
1030                      Format ('0', A, I3, A)
                          Write (25, 1040) '*** Level ', COUNT, ' ***'
1040                      Format ('0', A, I3, A)
                          Write (*, 1050) (PRTORD(J), J=COUNT,NCOUNT)
```

```
1050                        Format (' ', I3)
                            Write (25, 1060) (PRTORD(J), J=COUNT,NCOUNT)
1050                        Format (' ', I3)
                          Endif
                    Endif
                    COUNT = NCOUNT + 1
                    INEW = 0
                    J = I
              Endif
970     Continue
        Else

C
C       Determine whether the program user wishes to change any weights
C       and re-run the program
C

        Write (*,1070) ' '
1070    Format ('0', A)
        Write (*,*) 'Do you want to change any weights, choice of inconclusive'
        Write (*,*) 'ranking method, choice of significant difference margin, '
        Write (*,*) 'and/or choice of missing data method and re-run program?'
1080    Write (*,*) ' '
        Write (*,*) 'Yes                    Enter 1'
        Write (*,*) 'No                     Enter 2'
        Read (*,*) IORUN
        If (IORUN .ne. 1 .and . IORUN .ne. 2) then
              Write (*,*) '          *** WARNING ***'
              Write (*,*) 'Invalid choice.  Try again.'
              Go to 1080
        Endif
        If (IORUN .eq. 1) then
              Do 1090 I = 1, NUMOBS
                    CHANG(I) = 0
                    TMPCH(I) = 0
1090          Continue
              ICHVAR = 0

C
C       Choose the method by which new program parameters are entered.
C

        Write (*,1100) ' '
```

```
1100  Format ('1', A)
      Write (25,1110) ' '
1110  Format ('1', A)
      Write (*,*) 'Note:  Input of new choice of inconclusive ranking,'
      Write (*,*) 'significant difference margin, and/or missing data method'
      Write (*,*) 'will be done and then input of any new weights will be'
      Write (*,*) 'given in the following fashion:'
      Write (*,*) '    1.)  Provide the number of new weights'
      Write (*,*) ' '
      Write (*,*)      2.)  Provide the associated number of the variable or'
      Write (*,*) 'symptom and then input the new weight'
1120  Write (*,*) ' '
      Write (*,*) 'Choose the method by which the new information will be'
      Write (*,*) 'provided:'
      Write (*,*) 'Terminal                    ...    Enter 1'
      Write (*,*) 'File (INFO.DAT)             ...    Enter 2'
      Read (*,*) IOMETH
      If (IOMETH .ne. 1 .and . IOMETH .ne. 2) then
            Write (*,*) '          *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.'
            Go to 1120
      Endif
      If (IOMETH .eq. 1) then
            Write (*, 1130) ' '
1130        Format ('1', A)

C
C     Choose the inconclusive ranking method
C

      Write (*,*) 'Select inconclusive ranking method: '
1140  Write (*,*) ' '
      Write (*,*) 'Retain current method                              ... Enter 0'
      Write (*,*) '    where the current method is ', NCHINC
      Write (*,*) 'Method 1 (Counting)                                ... Enter 1'
      Write (*,*) 'Method 2 (Sum of weights)                          ... Enter 2'
      Write (*,*) 'Method 3 (Weighted difference)                     ... Enter 3'
      Write (*,*) 'Method 4 (Maintain 0 value)                        ... Enter 4'
      Read (*,*) IOCON
      If (IOCON .ne. 0 .and. IOCON .ne. 1 .and. IOCON .ne. 2 .and. IOCON
            .ne.3 .and. IOCON .ne. 4) then
            Write (*,*) '          *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.'
```

```
            Go to 1140
        Endif
        If (IOCON .ne. 0) then
            NCHINC = IOCON
            Write (25, 1150) ' '
1150        Format ('1', A)
            Write (25, *) 'New inconclusive ranking method:', IOCON
        Endif
        Write (*,*) ' '
        Write (*,*) 'Input significant difference margin'
        Read (*,*) MARGIN
        Write (*,*) ' '

C
C       Choose missing data method
C

        Write (*,*) 'Select missing data method: '
1160    Write (*,*) ' '
        Write (*,*) 'Retain current method                    ... Enter 0'
        Write (*,*) '    where the current method is ', NCHMIS
        Write (*,*) 'Method 1 (Minimum)                       ... Enter 1'
        Write (*,*) 'Method 2 (Maximal)                       ... Enter 2'
        Write (*,*) 'Method 3 (Average)                       ... Enter 3'
        Read (*,*) IOMIS
        If (IOMIS .ne. 0 .and. IOMIS .ne. 1 .and. IOMIS .ne. 2 .and. IOMIS
            .ne.3) then
            Write (*,*) '          *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.'
            Go to 1160
        Endif
        If (IOMIS .ne. 0) then
            NCHMIS = IOMIS
            Write (25, 1170) ' '
1170        Format ('1', A)
            Write (25, *) 'New missing data method:', IOMIS

C
C       Option to review current weights for variables
C
        Write (*, 1180) ' '
1180    Format ('1', A)
        Write (*,*) 'Do you wish to review the current weights for the variables?'
```

```
1190  Write (*,*) ' '
      Write (*,*) 'Yes                    ...     Enter 1'
      Write (*,*) 'No                     ...     Enter 2'
      Read (*,*) IOVAR
      If (IOVAR .ne. 1 .and. IOVAR .ne. 2) then
            Write (*,*) '          *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.'
            Go to 1190
      Endif
      If (IOVAR .eq. 1) then
            Write (*,1200) ' '
1200        Format ('0', a)
            Write (*,*) Current variable and weight (Inconcl. case)'
            Do 1210 I = 1, NUMVAR
                  Write (*,*) I, WV(I)
1210        Continue
            Write (*,1220) ' '
1220        Format ('0', A)
            Write (*,*) 'Current variable and weight (Miss. case)'
            Do 1230 I = 1, NUMVAR
                  Write (*,*) I, WMV(I)
1230        Continue
      Endif
      Write (*,*) ' '
      Write (*,*) 'Enter the number of new weights for variables '
      Write (*,*) '(Inconclusive ranking case)'
      Read (*,*) IOVAR
      If (IOVAR .gt. 0) then
            ICHAR = 1

C
C     Input new weights for variables
C

      Write (25, *) 'Variable and new weight (Inconcl. case)'
      Do 1240 I = 1, IOVAR
            Write (*,*) 'Enter the associated number of the variable and'
            Write (*,*) 'then enter the new weight'
            Read (*,*) J,W
            WV(J) = W
            Write (25,*) J,W
1240  Continue
      Endif
```

```
      Write (*, 1250) ' '
1250  Format ('1', A)
      Write (*,*) 'Enter the number of new weights for variables'
      Write (*,*) '(Missing data case)'
      Read (*,*) IOVAR
      If (IOVAR .gt. 0) then
            ICHVAR = 1
            Write (25, *) 'Variable and new weight (Miss. Case)'
            Do 1260 I = 1, IOVAR
                  Write (*,*) 'Enter the associated number of the variable'
                  Write (*,*) 'and then enter the new weight'
                  Read (*,*) J, W
                  WMV(J) = W
                  Write (25,*) J, W
1260        Continue
      Endif

C
C     Option to review current weights for symptoms
C

      Write (*, 1270) ' '
1270  Format ('1', A)
      Write (*,*) 'Do you wish to review the current weights for the symptoms?'
1280  Write (*,*) ' '
      Write (*,*) 'Yes                    ...     Enter 1'
      Write (*,*) 'No                     ...     Enter 2'
      Read (*,*) IOSYMP
      If (IOSYMP .ne. 1 .and. IOSYMP .ne. 2) then
            Write (*,*) '          *** WARNING ***'
            Write (*,*) 'Invalid choice.  Try again.'
            Go to 1280
      Endif
      if (IOSYMP .eq. 1) then
            Write (*,1290) ' '
1290        Format ('0', A)
            Write (*,*) 'Current symptom and weight (Inconcl. Case)'
            Do 1300  I = 1, NUMOBS
                  Write (*,*) I, WS(I)
1300        Continue
            Write (*, 1310) ' '
1310        Format ('1',A)
            Write (*,*) 'Current symptom and weight (Miss. Case)'
```

```
                Do 1320 I = 1, NUMOBS
                        Write (*,*) I, WMS(I)
1320            Continue
        Endif
        Write (*,*) ' '
        Write (*,*) 'Enter the number of new weights for symptoms'
        Write (*,*) '(Inconclusive ranking case)'
        Read (*,*) IOSYMP
        If (IOSYMP .gt. 0) then

C
C       Input new weights for symptoms
C

                Write (25,*) 'Symptom and new weight (Inconcl. Case)'
                Do 1330 I = 1, IOSYMP
                        Write (*,*) 'Enter associated number of symptom and then'
                        Write (*,*) 'enter the new weight'
                        Read (*,*) J, W
                        WS(J) = W
                        Write (25,*) J, W
                        CHANG(I) = J
1330            Continue
        Endif
        Write (*,1340) ' '
1340    Format ('1',A)
        Write (*,*) 'Enter the number of new weights for symptoms'
        Write (*,*) '(Missing Data Case)'
        Read (*,*) IOMSST
        If (IOMSST .gt. 0) then
                Write (25,*) 'Symptom and new weight (Miss. Case)'
                Do 1350 I = 1, IOMSST
                        Write (*,*) 'Enter the associated number of the symptom'
                        Write (*,*) 'and then enter the new weight'
                        Read (*,*) J. W
                        WMS (J) = W
                        Write (25, *) J , W
                        TMPCH(I) = J
1350            Continue
        Endif

C
C       Determine which sites have had weights changed
```

```
C
      ITMP = 0
      If (TMPCH(1) .ne. 0) then
            Do 1360 I = 1, IOMSST
                  If (CHANG(1) .ne. 0) then
                        COUNT = 0
                        Do 1370 J = 1, IOSYMP
                              If (TMPCH(I) .ne. CHANG(J))
                                    COUNT=COUNT+1
1370                          Continue
                        If (COUNT .eq. IOSYMP) then
                              ITMP = ITMP + 1
                              K = IOSYMP + ITMP
                              CHANG (K) = TMPCH(I)
                        Endif
                  Endif
1360        Continue
      Endif
      Else

C
C     Input Inconclusive ranking method and missing data method
C     from INFO.DAT
C

      Write (25, 1380) ' '
1380  Format ('1', A)
      Read (15,*) IOCON
      If (IOCON .ne. 0) then
            NCHINC = IOCON
            Write (25,*) 'New inconclusive ranking method: ', IOCON
      Endif
      Read (15, *) IOMIS
      If (IOMIS .ne. 0) then
            NCHMIS = IOMIS
            Write (25,*) 'New missing data method:', IOMIS
      Endif
      Read (15,*) IOVAR
      If (IOVAR .gt. 0) then
            ICHVAR = 1

C
C     Input inconclusive ranking method and missing data method
```

```
C       from INFO.DAT
C

                Write (25,*) 'Variable and new weight (Inconcl. Case)'
                Do 1390 I = 1, IOVAR
                        Read (15,*) J, W
                        WV(J) = W
                        Write (25,*) J, W
1390            Continue
        Endif
        Read (15,*) IOVAR
        If (IOVAR .gt. 0) then
                ICHVAR = 1
                Write (25,*) 'Variable and new weight (Miss. Data Case)'
                Do 1400 I = 1, IOVAR
                        Read (15,*) J, W
                        WMV(J) = W
                        Write (25,*) J, W
1400            Continue
        Endif
        Read (15,*) IOSYMP
        If (IOSYMP .gt. 0) then
                Write (25,*) 'Symptom and new weight (Inconcl. Case)'

C
C       Input new weights for symptoms from INFO.DAT
C

        Do 1410 I = 1, IOSITE
                Read (15, *) J, W
                WS(J) = W
                Write (25,8) J, W
                CHANG(I) = J
1410    Continue
        Endif
        Read (15,*) IOMSST
        If (IOMSST .gt. 0) then
                Write (25,*) 'Symptom and new weight (Miss. Data Case)'
                Do 1420 I = 1, IOMSST
                        Read (15,*) J, W
                        WMS(J) = W
                        Write (25,*) J, W
                        TMPCH(I) = J
```

```
1420        Continue
        Endif

C
C       Determine which symptoms have had weights changed
C

        ITMP = 0
        If (TMPCH(1) .ne. 0) then
                Do 1430 I = 1, IOMSST
                        If (CHANG(I) .ne. 0) then
                                COUNT = 0
                                Do 1440 J = 1, IOSITE
                                        If (TMPCH(I) .ne. CHANG(J))
                                                COUNT=COUNT+1
1440                            Continue
                                If (COUNT .eq. IOSYMP) then
                                        ITMP = ITMP + 1
                                        K = IOSYMP + ITMP
                                        CHANG(K) = TMPCH(I)
                                Endif
                        Endif
1430            Continue
        Endif
        Endif
        Go to 190
        Endif

        Close (15)
        Close (20)
        Close (25)
        Stop
        End


        Subroutine INCONC (SELECT,DATAM,I,J,NVAR,SWT,VWT,MARGIN,
                CHKS)
        Integer I,J, NVAR,CNTLS, SELECT<CHKS,CNTGT,K
        Real DATAM(770,50),VWT(50), SWT(770),SUMLS,SUMGT,
                SUMLWD, SUMGWD

C
C ********************************************************************************
```

```
C
C     This subroutine attempts to resolve inconclusive rankings.  The
C     following inconclusive ranking resolution techniques are available.
C           1.)  Count the number of times that the weighted value for
C     symptom I is greater than the weighted value for symptom J (across
C     variables) and generate a value for CNTGT.  Count the number of
C     times that the weighted value for symptom I is less than the value for
C     CNTLS.  If CNTLS > CNTGT then the K-S value is 1.  Otherwise, the K-S
C     value is 0.
C           2.)  Calculate the sum of weights associated with variables when
C     the weighted value for symptom I is greater than the weighted value for
C     symptom J and generate a value for SUMGT.  Calculate the sum of
C     weights associated with variables when the weighted value for symptom I
C     is less than the weighted value for symptom J and generate a value for
C     SUMLT.  If SUMLS > SUMGT then the K-S generate a value for SUMLT.
C     If SUMLS > SUMGT then the K-S value is 1.  Otherwise, the K-S value
C     is 0.
C           3.)  Calculate the sum of weighted differences between values for
C     symptoms I and J when the weighted value for symptom I is greater than
C     the weighted value for symptom J (across variables) and generate a
C     value for SUMGWD.  Calculate the sum of weighted differences between
C     values for symptoms I and J when the weighted value for symptom I is
C     greater than the weighted value for symptom J (across variables) and
C     generate a value for SUMLWD.  If SUMLWD > SUMGWD then the K-S
C     value is 1.  Otherwise, the K-S value is 0.
C           4.)  Maintain the inconclusive ranking and return a K-S value of 0.
C
C     The following variables are used in this subroutine.
C     CHKS:  K-S value generated by subroutine (either 0 or 1)
C     CNTGT:  Counts number of times that the weighted value for symptom I
C           is greater than the weighted value for symptom J (across
C           variables)
C     CNTLS:  Counts number of times that the weighted value for symptom I
C           is less than the weighted value for symptom J (across variables)
C     DATAM:  Data matrix (supplied by the main program)
C     I,J:  Markers denoting the symptoms to be compared
C     K:  Do-Loop variable
C     MARGIN:  Amount by which the weighted value for one symptom must
C           differ from the weighted value for another symptom before the
C           difference is considered significant
C     NVAR:  Number of variables (supplied by main program)
C     SELECT:  Choice of inconclusive ranking resolution technique
C     SUMGT:  Sum of weights associated with variables when the weighted
```

```
C     SUMGT:  Sum of weights associated with variables when the weighted
C             value for symptom I is greater than the weighted value for
C             symptom J
C     SUMGWD:  Sum of weighted differences between values for symptoms I
C             and J when the weighted values for symptom I is greater than the
C             weighted value for symptom J (across variables)
C     SUMLG:  Sum of weights associated with variables when the weighted
C             value for symptom I is greater than the weighted value for
C             symptom J
C     SUMLWD:  Sum of weighted differences between values for symptoms
C             I and J when the weighted value for symptom I is less than the
C             weighed value for symptom J (across variables)
C     SWT:  Weights associated with symptoms (supplied by main program)
C     VWT:  Weights associated with variables (supplied by main program)
C
C ***************************************************************************
C

      CNTLS = 0
      CNTGT = 0
      SUMLS = 0.0
      SUMGT = 0.0
      SUMLWD = 0.0
      SUMGWD = 0.0

C
C     Utilize inconclusive ranking technique 1
C

      If (SELECT .eq. 1) then
            Do 10 K = 1, NVAR
                  If (SWT(I)*DATAM(I,K) - SWT(J)*DATAM(J,K) .lt.
                    -1.0*MARGIN) CNTLS = CNTLS+1
                  If (SWT(I)*DATAM(I,K) - SWT(J)*DATAM(J,K) .gt.
                    Margin) CNTGT = CNTGT+1
10          Continue
            If (CNTLS .gt. CNTGT) then
                  CHKS = 1
            Else
                  CHKS = 0
            Endif
      Endif
```

```
C
C     Utilize Inconclusive ranking technique 2
C

      If (SELECT .eq. 2) then
            Do 20 K = 1, NVAR
                  If (SWT(I)*DATAM(I,K) - SWT(J)*DATAM(J,K) .lt.
                   -1.0*MARGIN) then
                        SUMLS = SUMLS + VWT(K)
                  Endif
                  If (SWT(I)*DATAM(I,K) - SWT(J)*DATAM(J,K) .gt.
                   MARGIN) then
                        SUMGT = SUMGT + VWT(K)
                  Endif
20          Continue
            If (SUMLS .gt. SUMGT) then
                  CHKS = 1
            Else
                  CHKS = 0
            Endif
      Endif

C
C     Utilize inconclusive ranking technique 3
C

      If (SELECT .eq. 3) then
            Do 30 K = 1, NVAR
                  If (SWT(I)*DATAM(I,K) - SWT(J)*DATAM(J,K) .lt.
                   -1.0*MARGIN) then
                        SUMLWD=SUMLWD+VWT(K)*(SWT(J)*
                        DATAM(J,K)-SWT(I)*DATAM(I,K))
                  Endif
                  If (SWT(I)*DATMA(I,K) - SWT(J)*DATAM(J,K) .gt.
                   MARGIN) then
                        SUMGWD=SUMGWD+VWT(K)**(SWT(I)*
                        DATAM(I,K)-SWT(J)*DATAM(J,K))
                  Endif
30          Continue
            If (SUMLWD .gt. SUMGWD) then
                  CHKS = 1
            Else
                  CHKS = 0
```

```
            Endif
        Endif

C
C       Utilize inconclusive ranking technique 4
C

        If (SELECT .eq. 4) CHKS=0

        Return
        End


        Subroutine MISSNG (SELECT,REPLAC,DATAM,J,NOBS,SMWT,VMWT)
        Integer SELECT,I,J,NOBS,MSCNT
        Real DATAM(770,50),SMWT(770), VMWT(50),MISS,SUM,REPLAC

C
C ********************************************************************************
C
C       This subroutine generates values for missing observations.  The
C       following missing data resolution techniques are available:
C               1.)  Replace missing observation (in variable J) by the weighted
C       minimum value associated with variable J
C               2.)  Replace missing observation (in variable J) by the weighted
C       maximum value associated with variable J
C               3.)  Replace missing observation (in variable J) by weighted
C       average of entries associated with variable J
C
C       The following variables are used in this subroutine.
C       DATAM:  Data matrix (supplied by main program)
C       I:  Do-Loop variable
C       J:  Marker associated with variable under consideration
C       MISS:  Unweighted value of missing data replacement
C       MSCNT:  Counts number of symptoms with non-missing values for
C               the variable under consideration
C       NOBS:  Number of observations (supplied by main program)
C       REPLAC:  User-specified numeric value to temporarily replace
C               missing observations
C       SELECT:  Choice of missing data resolution technique
C       SMWT:  Weights associated with symptoms when missing data is
C               encountered
C       SUM:  Sum of observations with non-missing values for the variable
```

```
C             under consideration
C       VMWT:  Weights associated with variables when missing data is
C             encountered
C
C ***************************************************************************
C

      MSNT = 0
      SUM = 0.0

C
C     Utilize missing data resolution technique 1
C

      If (SELECT .eq. 1) then
            MISS = DATAM(1,J)
            Do 10 I = 1, NOBS
                  If (DATAM(I,J) .ne. REPLAC) then
                    If (DATAM(I,J) .le. MISS .or. MISS .eq. REPLAC) then
                        MISS=DATAM(I,J)
                    Endif
                  Endif
10          Continue
            Do 20 I = 1, NOBS
                  If (DATAM(I,J) .eq. REPLAC) then
                    DATAM(I,J) = MISS*SMWT(I)*VMWT(J)
                  Endif
20          Continue
      Endif

C
C     Utilize missing data resolution technique 2
C

      If (SELECT .eq. 2) then
            MISS = DATAM(1,J)
            Do 30 I = 1, NOBS
                  If (DATAM(I,J) .ne. REPLAC) then
                    IF (DATMA(I,J) .ge. MISS .or. MISS .eq. REPLAC) then
                        MISS = DATAM(I,J)
                    Endif
                  Endif
30          Continue
```

```
            Do 40 = 1, NOBS
                  If (DATAM(I,J) .eq. REPLAC) then
                    DATAM(I,J)=-MISS*SMWT(I)*VMWT(J)
                  Endif
40          Continue
      Endif

C
C     Utilize missing data resolution technique 3
C

      If (SELECT .eq. 3) then
            Do 50 I = 1, NOBS
                  If (DATAM(I,J) .ne. REPLAC) MSCNT=MSCNT+1
                  SUM=SUM+DATAM(I,J)
50          Continue
            If (MSCNT .eq. 0) then
                  MISS=REPLAC
                  Write (25,55) 'All values missing in variable ', J
55                Format (A, I3)
            Else
                  MISS = SUM/MSCNT
            Endif
            Do 60 I = 1, NOBS
                  IF (DATAM(I,J) .eq. REPLAC) then
                    DATAM(I,J) = MISS*SMWT(I)*VMWT(J)
                  Endif
60          Continue
      Endif

      Return
      End
```

APPENDIX B - DATA AND 1-0 MATRIX

Data:

4	2	152	86	100	30	6	132	76	50	18	108	18	6
22	9	74	155	83	22	8	34	40	14	14	30	20	19
51	12	60	68	97	30	23	46	48	41	31	134	42	55
15	1	66	27	48	15	4	57	31	28	12	89	10	14
213	39	204	150	159	69	18	126	111	24	60	168	51	57
25	11	31	40	50	15	14	29	29	20	12	86	25	24
14	3	90	52	56	25	4	88	49	36	17	97	10	10
11	8	12	36	30	7	9	10	13	5	0	26	17	29
16	46	108	63	38	33	5	134	23	25	21	119	16	27
1	1	11	25	27	6	9	8	2	21	4	4	0	13
7	10	21	16	34	47	8	27	7	31	16	4	8	22
0	3	50	17	41	0	28	32	47	9	12	0	0	58
0	10	4	10	17	15	18	8	5	21	3	17	0	10
0	4	14	79	43	4	11	8	1	36	5	7	1	12
85	264	305	226	167	164	46	295	121	171	114	370	66	72
9	13	34	45	54	7	19	22	5	37	10	14	3	23
8	4	11	17	32	2	14	22	0	7	5	9	5	27
1	10	20	12	30	14	8	59	0	15	6	28	3	16
10	20	19	26	42	28	9	59	60	7	16	5	2	23
0	4	8	32	29	0	4	35	22	1	5	4	3	34
2	15	16	31	28	21	5	43	38	3	0	7	5	17
3	7	34	41	27	15	8	83	30	2	7	25	2	23
7	4	16	63	12	10	6	35	59	0	2	5	3	27
0	21	78	59	18	21	9	144	21	14	16	11	2	22
2	3	9	26	19	0	1	234	6	1	2	3	3	22
2	21	11	16	25	28	7	38	22	3	8	4	1	17
0	7	10	28	28	0	3	27	10	4	4	2	1	31

1-0 Matrix (using "Counting" to resolve inconclusive rankings)

0, 0, 1, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
1, 0, 1, 0, 1, 0, 0, 0, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
1, 1, 1, 0, 1, 1, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
1, 0, 1, 0, 1, 0, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
1, 0, 1, 0, 1, 0, 0, 0, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 0, 1, 0, 0, 1, 0, 0, 1, 1, 0, 1, 1, 0, 0, 0, 0, 1, 0, 0, 0
0, 0, 1, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1, 0, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1
1, 1, 1, 1, 1, 1, 1, 0, 1, 0, 0, 0, 0, 0, 1, 1, 0, 0, 1, 0, 0, 0, 0, 1, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 0, 1, 0, 0, 0, 0, 0, 1, 1, 1, 0, 0, 1, 0, 0, 0, 1, 1, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1, 1, 1
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 0, 0, 0, 1, 1, 0, 1, 1, 0, 1, 1, 1, 1, 0, 1, 0
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 0, 1, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1, 0, 0, 1, 1, 0, 1, 1, 0, 0, 1, 0, 1, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 0, 1, 0, 1, 0, 0, 0, 1, 1, 0, 0, 1, 0, 0, 1, 0, 1, 0, 0, 0
1, 0, 1, 0, 1, 1, 1, 0, 1, 0, 0, 0, 0, 0, 1, 1, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1, 0, 1, 1, 1, 1, 1, 1, 0, 1, 1, 1, 1, 0, 1, 0
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 0, 0, 0, 1, 1, 1, 0, 1, 0, 0, 1, 0, 1, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 0, 0, 0, 1, 1, 0, 0, 1, 0, 0, 0, 0, 1, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 0, 0, 0, 1, 1, 1, 1, 1, 0, 1, 1, 0, 1, 0, 0, 0
1, 1, 1, 0, 1, 1, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1, 0, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1, 0, 0, 1, 1, 1, 0, 1, 0, 1, 1, 0, 1, 0, 0, 0
1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 1, 0, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 1, 0

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