A STUDY OF RISK FACTORS FOR LOWER EXTREMITY AMPUTATION AMONG MEMBERS OF THE SIOUX NATION WITH TYPE 2 DIABETES MELLITUS

By

Christine Motley Burd

A Thesis
Submitted to the Faculty of Graduate Studies
in Partial Fulfillment of the Requirements
for the Degree of

Doctor of Philosophy

Department of Community Health Sciences
Faculty of Medicine
University of Manitoba
Winnipeg, Manitoba

ISBN 0-612-13004-5

Name Burd, Christine Motley

Dissertation Abstracts International is arranged by broad, general subject categories. Please select the one subject which most nearly describes the content of your dissertation. Enter the corresponding four-digit code in the spaces provided.

Public Health
SUBJECT TERM

0573
SUBJECT CODE

U·M·I

Subject Categories

THE HUMANITIES AND SOCIAL SCIENCES

COMMUNICATIONS AND THE ARTS
Architecture 0729
Art History 0377
Cinema 0900
Dance 0378
Fine Arts 0357
Information Science 0723
Journalism 0391
Library Science 0399
Mass Communications 0708
Music 0413
Speech Communication 0459
Theater 0465

EDUCATION
General 0515
Administration 0514
Adult and Continuing 0516
Agricultural 0517
Art 0273
Bilingual and Multicultural 0282
Business 0688
Community College 0275
Curriculum and Instruction 0727
Early Childhood 0518
Elementary 0524
Finance 0277
Guidance and Counseling 0519
Health 0680
Higher 0745
History of 0520
Home Economics 0278
Industrial 0521
Language and Literature 0279
Mathematics 0280
Music 0522
Philosophy of 0998
Physical 0523
Psychology 0525
Reading 0535
Religious 0527
Sciences 0714
Secondary 0533
Social Sciences 0534
Sociology of 0340
Special 0529
Teacher Training 0530
Technology 0710
Tests and Measurements 0288
Vocational 0747

LANGUAGE, LITERATURE AND LINGUISTICS
Language
- General 0679
- Ancient 0289
- Linguistics 0290
- Modern 0291

Literature
- General 0401
- Classical 0294
- Comparative 0295
- Medieval 0297
- Modern 0298
- African 0316
- American 0591
- Asian 0305
- Canadian (English) 0352
- Canadian (French) 0355
- English 0593
- Germanic 0311
- Latin American 0312
- Middle Eastern 0315
- Romance 0313
- Slavic and East European 0314

PHILOSOPHY, RELIGION AND THEOLOGY
Philosophy 0422
Religion
- General 0318
- Biblical Studies 0321
- Clergy 0319
- History of 0320
- Philosophy of 0322

Theology 0469

SOCIAL SCIENCES
American Studies 0323
Anthropology
- Archaeology 0324
- Cultural 0326
- Physical 0327

Business Administration
- General 0310
- Accounting 0272
- Banking 0770
- Management 0454
- Marketing 0338

Canadian Studies 0385
Economics
- General 0501
- Agricultural 0503
- Commerce-Business 0505
- Finance 0508
- History 0509
- Labor 0510
- Theory 0511

Folklore 0358
Geography 0366
Gerontology 0351
History
- General 0578
- Ancient 0579
- Medieval 0581
- Modern 0582
- Black 0328
- African 0331
- Asia, Australia and Oceania 0332
- Canadian 0334
- European 0335
- Latin American 0336
- Middle Eastern 0333
- United States 0337

History of Science 0585
Law 0398
Political Science
- General 0615
- International Law and Relations 0616
- Public Administration 0617

Recreation 0814
Social Work 0452
Sociology
- General 0626
- Criminology and Penology ... 0627
- Demography 0938
- Ethnic and Racial Studies 0631
- Individual and Family Studies 0628
- Industrial and Labor Relations 0629
- Public and Social Welfare 0630
- Social Structure and Development 0700
- Theory and Methods 0344

Transportation 0709
Urban and Regional Planning 0999
Women's Studies 0453

THE SCIENCES AND ENGINEERING

BIOLOGICAL SCIENCES
Agriculture
- General 0473
- Agronomy 0285
- Animal Culture and Nutrition 0475
- Animal Pathology 0476
- Food Science and Technology 0359
- Forestry and Wildlife 0478
- Plant Culture 0479
- Plant Pathology 0480
- Plant Physiology 0817
- Range Management 0777
- Wood Technology 0746

Biology
- General 0306
- Anatomy 0287
- Biostatistics 0308
- Botany 0309
- Cell 0379
- Ecology 0329
- Entomology 0353
- Genetics 0369
- Limnology 0793
- Microbiology 0410
- Molecular 0307
- Neuroscience 0317
- Oceanography 0416
- Physiology 0433
- Radiation 0821
- Veterinary Science 0778
- Zoology 0472

Biophysics
- General 0786
- Medical 0760

EARTH SCIENCES
Biogeochemistry 0425
Geochemistry 0996
Geodesy 0370
Geology 0372
Geophysics 0373
Hydrology 0388
Mineralogy 0411
Paleobotany 0345
Paleoecology 0426
Paleontology 0418
Paleozoology 0985
Palynology 0427
Physical Geography 0368
Physical Oceanography 0415

HEALTH AND ENVIRONMENTAL SCIENCES
Environmental Sciences 0768
Health Sciences
- General 0566
- Audiology 0300
- Chemotherapy 0992
- Dentistry 0567
- Education 0350
- Hospital Management 0769
- Human Development 0758
- Immunology 0982
- Medicine and Surgery 0564
- Mental Health 0347
- Nursing 0569
- Nutrition 0570
- Obstetrics and Gynecology .. 0380
- Occupational Health and Therapy 0354
- Ophthalmology 0381
- Pathology 0571
- Pharmacology 0419
- Pharmacy 0572
- Physical Therapy 0382
- Public Health 0573
- Radiology 0574
- Recreation 0575
- Speech Pathology 0460
- Toxicology 0383

Home Economics 0386

PHYSICAL SCIENCES
Pure Sciences
Chemistry
- General 0485
- Agricultural 0749
- Analytical 0486
- Biochemistry 0487
- Inorganic 0488
- Nuclear 0738
- Organic 0490
- Pharmaceutical 0491
- Physical 0494
- Polymer 0495
- Radiation 0754

Mathematics 0405
Physics
- General 0605
- Acoustics 0986
- Astronomy and Astrophysics 0606
- Atmospheric Science 0608
- Atomic 0748
- Electronics and Electricity 0607
- Elementary Particles and High Energy 0798
- Fluid and Plasma 0759
- Molecular 0609
- Nuclear 0610
- Optics 0752
- Radiation 0756
- Solid State 0611

Statistics 0463

Applied Sciences
Applied Mechanics 0346
Computer Science 0984
Engineering
- General 0537
- Aerospace 0538
- Agricultural 0539
- Automotive 0540
- Biomedical 0541
- Chemical 0542
- Civil 0543
- Electronics and Electrical 0544
- Heat and Thermodynamics ... 0348
- Hydraulic 0545
- Industrial 0546
- Marine 0547
- Materials Science 0794
- Mechanical 0548
- Metallurgy 0743
- Mining 0551
- Nuclear 0552
- Packaging 0549
- Petroleum 0765
- Sanitary and Municipal 0554
- System Science 0790

Geotechnology 0428
Operations Research 0796
Plastics Technology 0795
Textile Technology 0994

PSYCHOLOGY
General 0621
Behavioral 0384
Clinical 0622
Developmental 0620
Experimental 0623
Industrial 0624
Personality 0625
Physiological 0989
Psychobiology 0349
Psychometrics 0632
Social 0451

A STUDY OF RISK FACTORS FOR LOWER EXTREMITY AMPUTATION AMONG MEMBERS OF THE SIOUX NATION WITH TYPE 2 DIABETES MELLITUS

BY

CHRISTINE MOTLEY BURD

A Thesis submitted to the Faculty of Graduate Studies of the University of Manitoba in partial fulfillment of the requirements of the degree of

DOCTOR OF PHILOSOPHY

TABLE OF CONTENTS

LIST OF TABLES

Table

LIST OF FIGURES

Figure

ACKNOWLEDGEMENTS

This thesis has been accomplished with the assistance and generous support of a number of significant individuals. I would like to express my appreciation and thank those who have been instrumental in bringing the thesis to completion:

To Wakan Tanka, Whose presence I have sensed along every path of my life's journey, including this one.

To my chairperson, Dr. Joseph Kaufert, for his direction, teaching, support, and advisement throughout my doctoral education, and for the generous spirit in which he made these contributions. I am greatly appreciative of the time and investment he has made in facilitating the development of scholarship in my work, and of the rigorous, yet approachable manner in which he has mentored me through this project.

To Dr. T. Kue Young, whose sharing of his expertise in epidemiology over the course of three semesters, gave me the interest and the "tools" to effectively undertake this research, and whose continued involvement on my committee has added substantially to its successful outcome.

To other members of the thesis committee: Dr. Michael Moffatt and Dr. Cameron Mustard, whose direction, comments, and thought-provoking questions regarding this thesis project have been essential throughout its development; and also to Dr. Lorna

Guse, whose willingness to serve on the committee and provide her insight and comments on this project has been greatly appreciated.

To Dr. David Fish, who was willing to advise and assist me in successfully planning my graduate education in Manitoba as an international student.

To the other faculty in the Department of Community Health Sciences, particularly Dr. Linda Garro, Dr. John O'Neil, and Evelyn Shapiro, whose collective influence enhanced my ability to appreciate the larger contexts in which this study was embedded, greatly enriching my research experience; and to Dr. Thomas Hassard, whose patient and good-natured approach to the teaching of Biostatistics made it possible for me to undertake the process of data analysis in this project.

To Camille Guennette, who has been a pivotal source of information regarding many of the logistical facets of being a graduate student in Community Health Sciences. Her prompt, professional, and friendly response to my numerous inquiries has been extremely helpful throughout my program of study.

To Dr. Ruggles Stahn, who was the Diabetes Control Officer for the Aberdeen Area Indian Health Service until his untimely death last winter. Without Dr. Stahn, the completion of this project would not have been possible. I am indebted to him for his provision of surveillance data from the Diabetes Control Program, his assistance in recruiting research assistants, his facilitation of access to the Service Units and medical records, his prompt responses to any questions I had in planning and carrying out data collection, and his time in meeting with me for planning and consultation a number of times throughout the project.

To Dr. Thomas Welty, Medical Epidemiologist for the Aberdeen Area Indian Health Service, for his support of the study, assistance in helping me to network with the personnel critical to this study, and facilitation of access to the Service Units.

To the personnel of the Indian Health Service who made it possible to do this study, especially to: the Medical Records staff at Fort Yates, Wagner, Crow Creek, and Pine Ridge who were extraordinarily helpful in the accessing of charts; the Service Unit Directors who provided space to allow the study to be completed on-site; and Karen Froelich, the Diabetes Coordinator at Fort Totten who assisted me in accessing records for both the pilot study for this project and the actual data collection.

To the following physicians, who were willing to be assigned as research assistants on this project during their medical school training, and who worked so conscientiously on gathering data: Dr. Christine Horowitz, Dr. Robert Oberstein, Dr. Robert Malanuk, Dr. Jay Goldberg, and Dr. Christie Tammel.

To Dr. Mary Wright who so generously gave of her time to assist with the coordination of data collection at several of the Service Unit sites, and to edit the thesis manuscript.

To Dean Lois Merrill of the University of North Dakota College of Nursing, whose ongoing support for my professional goals made it possible to continue the pursuit of the doctoral degree while maintaining my professional career. I will always be grateful for her subtle, but effective manner of providing direction.

To the Nursing Professionalism and Practice Department of the University of North Dakota College of Nursing, and especially to the Department Chair, Dr. Helen Melland, whose unflagging support allowed me to continue my studies without disruption.

To Dr. LaVonne Russell, whose willingness to assume my duties at the University of North Dakota College of Nursing this semester, has allowed me to finish the thesis.

To Dr. Susan Henly, Statistical Consultant for the University of North Dakota College of Nursing, who was willing to consult with me on statistical questions throughout data analysis, and whose frequent direction to "just keep writing" was sound advice. I am grateful to her for her interest in my work and for her friendship.

To Dr. Henry Slotnik, Statistician for the University of Norht Dakota School of Medicine, who assisted me in the initial planning of the logistic regression analyses and cross-validation techniques.

To my parents, who instilled in me an appreciation of learning, and the belief that obstacles to the attainment of an education should, and could be, overcome.

To Marsha Berg who has been both kind and indispensable in assisting with the care of my family while I travelled, and without whom completion of this doctoral work would not have been feasible.

To Ollie Hillman, who graciously provided me with food, lodging, and friendship in her home during my frequent trips to Winnipeg.

To my extended family and friends who have been supportive throughout the process of doing this thesis, particularly to my sister Joan, and to Colleen and Randy

Wilson whose ongoing encouragement and optimism has meant more than they may ever realize.

To my children, Greg, John, Charles, and Mary Kathryn, who have been supportive and accepting of the educational goals of their parents, despite their youthful inability to fully understand them. My hope is that they will enjoy learning throughout their lifetimes as well.

And finally, to my husband, Larry Burd, who has shared literally every facet of this endeavor, and who has been the source of continuous and unrivaled support, encouragement, and good humor that has been the sustaining force in completion of this thesis work.

ABSTRACT

A Study of Risk Factors for Lower Extremity Amputation

Among Members of the Sioux Nation with Type 2 Diabetes Mellitus

Type 2 Diabetes Mellitus and its complications are epidemic among Native American tribes in the United States. Risk factors for lower extremity amputation (LEA) related to Type 2 diabetes has not been studied in Northern Plains tribes. Medical records of 144 Sioux tribal members who had undergone lower extremity amputation (LEA) related to Type 2 diabetes mellitus between 1984-1993 were matched to 288 controls for age and gender.

The Causal Pathways to LEA model (Bild, et. al., 1989) provided a framework for: (a) selecting variables from the records, (b) comparing odds ratios and means between cases and controls, and (c) creating stepwise logistic regression models. Odds ratios (with 95% confidence limits) and t-values were generated to compare cases to controls on selected variables. Initial logistic regression equations yielded expected risk factors of neuropathy, peripheral vascular disease, and previous history of lower extremity lesions.

Deletion of these three variables from the regression equation yielded the following predictors for LEA: (a) longer duration of diabetes (p=0.0000), (b) positive history of insulin therapy (p=0.0001), (c) hyperglycemia above 273 mg/dl (p=0.0294), and (e) diminished WT/HT ratio (p=0.0507). The results of the logistic regression models were

highly reflective of the univariate analyses. Gender based generation of odds ratios, mean comparisons, and logistic regression models suggested that gender specific risks may exist for males versus females.

Systematic clinical assessment of risk factors for LEA, accompanied by intensified foot care education, could enhance the prevention of foot lesions that lead to LEA. Further research needs to include a focus on gender and sociocultural influences in the understanding of Type 2 diabetes mellitus and its complications in rural reserve communities.

(This study was supported by grant number 1R03 HS07478-01 from the Agency for Health Care Policy and Research, United States Department of Health and Human Services.)

CHAPTER I

INTRODUCTION

Health problems within the aboriginal population in the United States are increasingly associated with chronic disease, and the overall health of aboriginal people in the United States remains poorer than that of the general population (Nutting, et. al., 1990; Indian Health Service, 1988; Office of Technology Assessment, 1986; Secretary's Task Force on Minority Health, U.S. Department of Health and Human Services, 1986). A recent two year study of the American Indians living in eight upper Midwest and Northwest states concluded that their health status "remains disgracefully below the norm" as compared to the U.S. all races health status data (American Indian Health Care Association of St. Paul, MN, 1993, p.23).

A trend towards an increasing incidence of chronic disease is expected to continue, since the group over 60 years of age is the most rapidly increasing among the Native American population (Heath, et.al., 1993). In particular, diabetes mellitus is a major contributor to the poor health status of Native Americans, and is almost universally of the non-insulin-dependent type (NIDDM or Type 2) (Gohdes, 1986; Knowler, et. al., 1990). In the 1987 Survey of American Indians and Alaskan Natives (SAIAN) (as part of the National Medical Expenditure Survey), diabetes mellitus was cited as the only distinct

disease entity in which a significantly higher prevalence was found in the Native population as compared to the general U.S. population.

Based on the estimated "Service Population" of 1.1 million, that is, the number of Native people who were eligible for services from the U.S. Indian Health Service (IHS), the 1986-1988 age-adjusted diabetes mortality rate for American Indians and Alaska Natives was 26.4/100,000. This rate was 2.7 times, or 169% higher than the U.S., all races rate (Indian Health Service, 1990; Indian Health Service, 1992).

Problem Statement

Although the risk of demise from diabetic ketoacidosis and infection has declined significantly, complications resulting from microvascular and macrovascular atherosclerotic changes are associated with 70% of deaths in people with diabetes. These complications include myocardial infarction, cerebrovascular accident, uremia, and gangrene leading to amputation (Brunner & Suddarth, 1988, p.922), which exacerbate human suffering through the potentiation of disability. Blindness, renal failure, paralysis, neuropathies, and amputations limit normal activities, and consequently the ability to maintain employment and independent living (National Diabetes Data Group, 1984; Rhoades, et.al., 1987).

Given the environmental context of rural reserve settings, the complication of lower extremity amputation (LEA) is of particular salience in the Native American population. The increasing prevalence of LEA in rural Native communities, related to an epidemic of Type 2 diabetes, demands the initiation of interventions specifically targeted

to the prevention of impairment and disability associated with chronic disease. Knowledge of the risk factors that predispose the diabetic person to LEA is essential to the task of prevention.

Although it is a priority of the Indian Health Service to prevent diabetes, diabetic complications, and accompanying disabilities, research literature specifically addressed to the identification of risk factors for LEA in Native communities is extremely limited. Literature related to the study of risk factors for LEA among tribes in the Northern Plains of the United States is non-existent.

Purpose

The purpose of this study was to strengthen the scientific basis for prevention of LEA among American Indians in the Northern Plains of the United States. Specifically, the study was conducted to identify risk factors that are associated with the development of LEA among members of the Sioux Nation with Type 2 diabetes mellitus. The configuration of a profile of risk factors associated with LEA will assist in the early identification of diabetic persons at risk, and in the modification of those risk factors that are amenable to change.

It is assumed that an interaction of variables contribute to the development of gangrene and amputation among American Indians with Type 2 diabetes mellitus. Therefore, the development of prevention strategies to reduce the incidence of diabetes-related LEA among members of Native American tribes requires the study of multiple risk factors for amputation. The Causal Pathways to LEA model (CPLEA) (Bild, et.al., 1989)

was utilized to identify variables that were investigated in this study. The CPLEA model is reflective of the literature pertaining to risk factors for LEA, and includes the variable of foot care as a mediating factor in the development of LEA.

A case-control design was utilized to allow the use of existing medical records to explore risk factors associated with diabetes-related LEA among members of the Sioux Nation, and to compare this data to that of Sioux people who also have Type 2 diabetes mellitus, but who have not had an LEA.

Long-term Objective

Data from this retrospective study serves as a foundation for future research in the area of diabetes-related LEA in North American Native peoples including: (a) prospectively designed study of risk factors for LEA, (b) clinically based studies focused on preventive strategies for LEA, and (c) the qualitative study of sociocultural factors that impact the lived experience of chronic disease and accompanying disability in reserve settings.

CHAPTER II

REVIEW OF THE LITERATURE RELATED TO NIDDM

The literature review which served as background for this study included the following topics related to Native Americans and Type 2 diabetes mellitus: (a) mortality rates, (b) prevalence, (c) risk factors associated with the development of Type 2 diabetes mellitus, (d) cultural influences in understanding diabetes within Native communities, and (e) studies specific to LEA as sequelae of Type 2 diabetes in this same population. The following literature review addresses each of these areas in the above sequence.

Morbidity / Mortality

Although the cause specific mortality rate related to NIDDM is increased in American Indian people, the diversity among different tribes is significant and must be taken into consideration in the analysis of reported rates. For example, it is important that there be a recognition of the range seen between the age-adjusted mortality rate of 93.4/100,000 due to NIDDM in the Tucson region when compared to 10.4/100,000 found in the Alaska region; the rates of the other ten IHS regions then fall between these two (Aberdeen Area Diabetes Control Program, 1986).

Cause specific mortality related to NIDDM among Native people, was the fifth leading cause of death among people aged 45 and older for the period from 1986 to 1988.

This yielded a cause specific mortality ratio of 3.4 in the group aged 45 to 64 years and a ratio of 2.1 in the 65 years and older group when compared to the U.S. all races rates in these same age groups (Indian Health Service, 1992). In the Aberdeen Area of Indian Health Service (AAIHS), diabetes was listed as the seventh leading cause of death for Fiscal Year 1985-1987 (Appendix A). However, interpretation of these figures requires caution, as they may underestimate the actual rates of diabetes related deaths.

Relatively less attention has been given to the enumeration of the probability of death among diagnosed cases of NIDDM. The proportionate mortality ratio, which is calculated by dividing the number of deaths assigned to a disease in a certain year (numerator) by the total deaths in the population in the same year (denominator) would be a useful indicator of mortality in the Native population. This ratio would clarify the overall role of NIDDM as a cause specific category of mortality.

For example, the same grouping of mortality data in people aged 45 and older also included "diseases of the heart", "cerebrovascular diseases", and "nephritis, nephrotic syndrome, and nephrosis" in the leading ten causes of death. Given the associations of these types of diseases with NIDDM, it is certainly likely that diabetes exerts a more far-reaching impact on the health of Native people than is evident from the available aggregate mortality statistics.

Similarly, according to an internal IHS document, Summary of Leading Causes for All Outpatient Visits: IHS Direct and Contract Facilities (1988), diabetes was cited as a specific cause of hospitalization in only 447 of 10,915 hospital separations among those aged 65 and older. The information that circulatory system diseases accounted for 2102

hospital separations in this same group seems somewhat incongruous with the data that indicates that among all age groups, NIDDM was second only to otitis media and upper respiratory infections as the leading specific condition treated in the outpatient setting by Indian Health Service in Fiscal Year 1990.

Along the same lines, it is difficult to determine the extent of disability which is known to be associated with NIDDM. Little direct information is available regarding the prevalence and incidence of disability among the Native population (National Institute of Handicapped Research, 1987). At this point in time "no state, federal, private, or tribal agency has an adequate information base" on the special population of Natives with disabilities (Toubbeh, 1985, p.4).

The 1987 National Medical Expenditure Survey (NMES) deliberately included a Survey of American Indians and Alaska Natives (SAIAN) living on or near reservations (Taylor & Johnson, 1991). The government publications that have been generated from this data, and which are available from the United States Department of Health and Human Services, do not yet include the report of disability that is condition specific, although this data was collected (Agency for Health Care Policy and Research, 1991).

In terms of health care service delivery, among all adults served in the outpatient setting by the Indian Health Service, Type 2 diabetes was the leading specific condition accounting for 273,827 clinical impressions in Fiscal Year 1990 (Indian Health Service, 1990; Indian Health Service, 1992). Non-insulin-dependent diabetes was also among the 10 leading causes of hospitalization (Rhoades, et.al., 1987; Indian Health Service, 1992).

Therefore, it may be useful to speculate about the role of diabetes in the pathologies of the vascular system that require hospitalization, beyond specific diagnoses of diabetes.

Prevalence of NIDDM in Native Americans

In this section, studies of prevalence of NIDDM among Native Americans are reviewed (Table 1). In 1940, the noted diabetologist, Elliot Joslin, had been able to identify only four cases of diabetes among the Navajo people of Arizona in the southwestern United States (in Gavin & Davidson, 1992). This provides a baseline prevalence rate to compare to the 11.6% NIDDM prevalence rate found in the period 1988-1989 among 768 Natives who responded to the Behavioral Risk Factor Surveillance System Study (Muneta, et. al., 1993) and also to compare to the 23.4% NIDDM prevalence rate reported for the Aberdeen Area of IHS in 1984 among Natives aged 45 to 64 (Brosseau, 1989).

Within the context of the 1987 NMES, the results of the SAIAN reported a 12.2% age-adjusted prevalence of NIDDM among the Native population in the United States. Age adjustment allowed for a comparison of rates after differences among the Native population have been removed to make them comparable to the general U.S. all races population. Adjustment for gender was not necessary since consistent difference in NIDDM rates had not been found in earlier studies (United States Department of Health and Human Services, 1991).

The review by West (1974) was definitive in elucidating the increasing prevalence of NIDDM among Native populations in the "new world". In fact, the rate of NIDDM

Table 1

PREVALENCE OF NIDDM IN NATIVE AMERICANS

Author & Year	Topic Area	Group Studied	Reported Findings
Brouseau (1993)	Prevalence	"Three Affiliated Tribes" (Hidatsa, Mandan, Arikara) in North Dakota	32.8% prevalence rate in 1988, an increase of 40% since 1975
Brosseau (1989)	Prevalence	Native Americans in Aberdeen Area of IHS	23.4% prevalence rate among 45 to 64 year old group
Freeman, et.al. (1989)	Prevalence	10 reservations in states of Washington and Idaho in 1987	7.1% total prevalence rate, 13% to 35.9% prevalence rate among adults 65 years of age and older within 9 of the reservation areas, 4.5% prevalence rate among the Quinalt only. Prevalence rates differed among culture areas.
Knowler, et.al. (1990)	Incidence	Pima 1965 through 1989	Incidence rate of 704/40433 person-years of follow-up
Knowler, et.al. (1978)	Prevalence	Pima	approaching 50% among adults 35 years of age and older
Muneta, et.al. (1993)	Prevalence	768 Native Americans responding to Behavioral Risk Factor Surveillance System Study	11.6% prevalence rate between 1988-1989

Author & Year	Topic Area	Group Studied	Reported Findings
National Diabetes Data Group in Sievers and Fisher (1984)	Prevalence	Native tribes throughout the United States	greater than 20% prevalence rate in 18 tribes located predominantly in the South and Southwest U.S. (other than the Pima) among adults 35 years of age and older
Schraer, et.al. (1988)	Prevalence	Alaska Natives	1.57% age-adjusted overall prevalence rate: 0.88% among the Inuit, 2.7% among the Aleuts, 2.2% among American Indians
Stahn, et.al. (1993)	Prevalence	Winnebago, Omaha, Sioux	Prevalence was 8.8 the U.S. rate among the Winnebago and Omaha, but 3.7 times the U.S. rate among the Sioux
U.S. Department of Health and Human Services (1991)	Prevalence	SAIAN within the 1987 NMES of U.S. Native American Population	12.2% age-adjusted prevalence rate
West (1974)	Prevalence	Native populations in the "new world"	dramatic increase of NIDDM in this last half of the 20th century compared to essential absence of the disease in the first half of the century

has climbed dramatically in the last half of this century (West, 1974; Gohdes, 1986; Knowler, et.al., 1990; Brosseau, et. al., 1979; Rate, et.al., 1983; Freeman, et.al., 1989; Schraer, et.al., 1988). Much of the work regarding the prevalence, incidence, risk factors, complications, and pathogenesis of diabetes among Native people in the United States has been done on a longitudinal basis since 1965 with the Pima tribes in the southwest (Bennett, et. al., 1971; Ingelfinger, et.al., 1976; Knowler, et.al., 1978; Lillioja, et.al., 1988; Nelson, et.al., 1988; Nelson, et.al., 1988a; Kunzelman, et.al., 1989; Nelson, et.al., 1989; Kriska, et. al., 1990; Nelson, et.al., 1990; Knowler, et.al., 1990).

A publication of the National Institutes of Health, Diabetes in America (1984) was a summary of diabetes data compiled by the National Diabetes Data Group (NDDG). The chapter devoted to diabetes in North American Indians stated that in addition to the Pima, there are 18 other tribes with reported prevalence rates of 20 % or more among adults 35 years of age and older (Sievers & Fisher, 1984). Of these 18 tribes (excepting the Oklahoma tribes and the Seneca of New York) all are located in Southern and Southwestern regions of the United States.

Notably, this national document did not include any data for Northern Plains, nor Alaskan, tribes. Given the available data within the IHS, the likely interpretation of this limitation in the NDDG report is not that there is nothing remarkable about the prevalence of NIDDM in the Northern Plains tribes, but rather that there has been a dearth of systematic study and published reporting on these groups until more recently. Consequently, the review of the literature is limited by the lack of regional data.

Prevalence of NIDDM among the Pima tribe has been reported as approaching 50% in the adult population who are over 35 years of age (Knowler, et.al, 1978). From the beginning of the study of the Pima in 1965 through mid-year 1989, the incidence rate (the number of new cases of disease divided by the population at risk for the disease in the same period) was reported as 704/40433 person-years of follow-up (Knowler, et. al., 1990). It has even been suggested that if current trends continue, "lifetime risk in the Pima may be approaching 100 %" for the development of NIDDM (in Weiss, et.al., 1989, p.284).

Freeman and his associates (1989) studied the prevalence of diabetes among Native people living on or near 10 reservations in the states of Washington and Idaho in 1987. Utilizing both IHS data and each health care facility's register to identify all diabetic patients on each reservation, Freeman, et. al. reported that the age/sex adjusted prevalence rate was significantly higher in each of these 10 reservation communities as compared to the U.S. general population prevalence (based on National Health Interview Survey data of 1979, 1981, and 1980 Census data).

In their study, the total prevalence rate (from data on the 10 reserves) was reported as 7.1% in contrast to the U.S. general population rate of 2.4%. However, the reported prevalence rates in the 65 and older age group ranged from 13% to 35.9% among nine of the tribes, with one tribe (Quinalt) having a rate of 4.5%. This data understates the true magnitude of the problem since cause specific mortality due to NIDDM will have eliminated an important percentage of Native people from the study

population by age 65. Another finding was that rates among the three anthropologically described "culture areas" represented by the tribes in the study, differed significantly.

A study done by Schraer, et. al. (1988) utilized IHS data bases to determine prevalence rates of NIDDM among Alaska Natives. They found that overall, this group had an age-adjusted prevalence of only 1.57%. This is considerably lower than rates reported for other tribal populations or for the U.S. general population. Of particular interest in this study, it was reported that differences in prevalence rates were found even within the Alaskan Native group: 0.88% among the Inuit, 2.7% among the Aleuts, and 2.2% among Indians.

Also utilizing IHS data, Stahn, et. al. (1993) reported that the prevalence rate of NIDDM among the Plains dwelling Winnebago and Omaha tribes was 8.8 times the U.S. rate, but the rate among the Sioux, also Plains tribes, was 3.7 times the U.S. rate. Again, the importance of acknowledging the diversity among Native groups is recognized, particularly in terms of the need to assess socio-cultural and genetic influences on disease.

Risk Factors for NIDDM in Native Americans

The variability in prevalence of NIDDM across Native tribes, even among those residing in contiguous reserves, suggests that there are multiple interacting influences on the development of NIDDM in Native peoples. Freeman, et. al. (1989) recommended that three explanations in particular be more fully investigated: (a) genetic influences (Table 2), (b) obesity (Table 3), and (c) sociocultural change (Table 4). The framework for this area of the paper includes a discussion of the first two areas, genetics and obesity, which then is

Table 2

GENETIC INFLUENCES IN NIDDM

Author & Year	Topic Area	Group Studied	Reported Findings
Barnett, et. al. (1981)	Genetic linkage	200 monozygotic twins	90% concordance rate among 21 twins with NIDDM
Brosseau, et.al. (1979)	Blood quantum in American Indians	"Three Affiliated Tribes" in North Dakota	22.3% prevalence rate among people 35 years of age and older who were full quantum natives but 4.1% among those less than one-half quantum
Chiu, et.al. (1992)	Genetic markers	275 unrelated Black males	genetic marker on the glucokinase gene increased odds ratio of having NIDDM to 2.85, as compared to men without the marker
Knowler, et.al. (1990)	NIDDM in offspring	Pima	NIDDM most often found in offspring of two diabetic parents who had NIDDM before age 45
Prochazka, et.al. (1993)	NIDDM in siblings	Pima	suggested the action of insulin is genetically determined by a gene on chromosome 4q
Schraer, et.al. (1988)	Blood quantum in American Indians	564 diabetic Natives	61% of diabetics were full quantum natives

related to the underlying pathophysiologic mechanism of insulin resistance. This section of the paper concludes with a discussion of the "thrifty gene" hypothesis, in which the risk factors of genetic influences and obesity are expressed within the context of social and cultural change.

Genetic Influences in NIDDM.

Non-insulin-dependent diabetes mellitus has long been thought to have a strong genetic component, and predisposition for NIDDM through a simple dominant mechanism is strongly supported (Teisberg, 1993). Barnett, et. al. (1981) in a study of 200 pairs of monozygotic twins, reported a 90 % concordance rate among the 21 twins with NIDDM.

There have been several significant breakthroughs in basic genetic research, such as the cloning of the human insulin gene (in Gavin & Davidson, 1992), identification of three alleles of the insulin-receptor gene (Raboudi, et. al., 1989), and the finding of a defect in the glucokinase gene that appears related to Maturity Onset of Diabetes in the Young (MODY) (Vionnet, et. al., 1992). Schumacher, et. al. (1992) reported evidence for a major gene locus for impaired insulin action in relatives of people with NIDDM. However, specifics of the pattern of inheritance continue to be studied (Thomas, et. al., 1994).

Supporting the influence of a genetic component among Native populations, Schraer, et. al. (1988) reported in their study of 564 diabetic subjects that 61% were identified as "full quantum" Natives, that is, people whose genealogy includes exclusively aboriginal ancestry. In a 1975 audit of IHS data by Brosseau, et. al. (1979), a NIDDM

prevalence rate of 22.3% was found among people over age 35 who were identified as having full quantum inheritance in the Three Affiliated Tribes (Mandan, Arickara, and Hidatsa) in North Dakota. In comparison, the prevalence rate was 4.1% among those persons who were less than one-half quantum.

In a follow-up study in 1988, Brosseau (1993) reported that the number of persons diagnosed as having NIDDM had increased by more than 40%, to a prevalence rate of 32.8%, despite no significant change in the size of the population of the Three Affiliated Tribes served at the IHS clinic. He also reported that although the number of full quantum Natives has been steadily decreasing, 90% of known diabetic patients are more than one-half quantum, that is, more than one-half of the total proportion of genetic inheritance is aboriginal. The prevalence ratio of women to men with NIDDM in Brousseau's study also increased from 1.2 to 1.9 between 1979 and 1988. It is unknown if this is due to a higher prevalence of older women, or if an interaction between age and gender would explain this finding.

Studies of the Pima have reported NIDDM as occurring most often in offspring whose parents both developed diabetes before age 45. Furthermore, this risk was associated not only with the development of NIDDM, but with an early onset, that is, prior to age 45. However, the rate among older persons was also reported to occur with "appreciable frequencies" in persons with two non-diabetic parents (Knowler, et. al., 1990).

More recently, the study of genetic markers has promised a potentially productive avenue of research in the etiology of NIDDM. A study of 275 unrelated Black males

(Chiu, et. al., 1992) reported the presence of a genetic marker on the glucokinase gene that increased the odds ratio of having NIDDM to 2.85 as compared to men without the genetic marker. Among Native Americans, Prochazka, et. al. (1993) have reported the results of a study of siblings in the Pima population which suggested the action of insulin is genetically determined by a gene on chromosome 4q.

It does appear evident that genetic influences play a significant role both in setting a threshold for NIDDM and in its actual development. However, other factors known to increase risk, particularly obesity, are presented in the next section.

Obesity as a Risk Factor for NIDDM.

Obesity has been identified as an important risk factor for the development of Type II diabetes in many populations, including the Native American (West, 1974; Gavin & Davidson, 1992; Shaten, et. al., 1993; Cowie, et. al., 1993; Freeman, Hosey, Diehr, & Gohdes, 1989; Schraer, Lanier, Boydo, Gohdes, & Murphy, 1988; Brousseau, Eelkema, Crawford, & Abe, 1979). Although obesity has not been adequately studied across tribes (Nutting, et.al., 1990), it has been cited as the primary influence in the development of Type 2 diabetes among Native Americans (West, 1974). A more thorough discussion is presented below of the thrifty gene hypothesis (p. 21), which proposed that the prevalence of obesity among Native peoples results from a genetic adaptation which maximizes fat storage (Wendorf & Goldfine, 1991).

Joslin described a study of height and weight in 1,000 diabetic subjects in 1921 and stated that 75% fell above the standard weight taken from life insurance tables (in Barett-

Table 3

OBESITY AS A RISK FACTOR FOR NIDDM

Author & Year	Topic Area	Group Studied	Reported Findings
Brosseau (1993)	Obesity	Three Affiliated Tribes in 1988	30% of women with NIDDM weighed more than 200 pounds; 43% of men with NIDDM weighed more than 220 pounds
Cowie (1993)	Obesity	Second NHANES (1976-1980)	Suggested an interaction of obesity with race and gender
DeFronzo and Ferrannini (1991)	Insulin Resistance	review of studies	Obesity markedly increases insulin resistance; insulin sensitivity is reduced up to 30-40% in persons who are 35-40% over ideal body weight
Joslin (1921) (in Barett-Connor, 1989)	Obesity	1000 diabetic subjects	75% fell above the standard weight in actuarial tables
Kriska, et.al. (1993)	Activity	1054 Pima men and women	Reported inverse relationship of activity to glucose intolerance, obesity, and centralized fat distribution
Lillioja, et.al. (1993)	Insulin Resistance	200 Pima followed prospectively for an average 5.3 years	Best predictor of future NIDDM was decreased glucose uptake at mean plasma insulin concentrations of 130 uU per milliliter during euglycemia

Author & Year	Topic Area	Group Studied	Reported Findings
Muneta, et.al. (1993)	Obesity	Native Americans and Whites in the Behavioral Risk Factor Surveillance System data for 1988-1989	34.4% prevalence of obesity in Natives as compared to 23.9% prevalence in whites
West (1974;1978)	Obesity	Native Americans in the United States	suggested obesity as primary risk factor for NIDDM, and is of relatively recent origin in Native Americans

Connor, 1989). West (1978) suggested that obesity was a primary environmental risk factor for NIDDM, and is of relatively recent origin: "Diabetes was also rare prior to 1940 ... but has recently become common in these Oklahoma tribes. They were formerly lean and are now fat" (West, 1974, p.841).

A comparison of obesity between Natives (n=768) and Whites (n=121,986) in a study of the Behavioral Risk Factor Surveillance System data for 1988-1989, found the overall prevalence of obesity to be 34.4% and 23.9% respectively (Muneta, et. al., 1993). When stratified into diabetic and non-diabetic groups, the prevalence of obesity significantly increased in both Native and White groups with diabetes. Brosseau's 1988 study of the "Three Affiliated Tribes" (1993) supported the connection between obesity and NIDDM through his findings that 30% of 140 women with NIDDM weighed more than 200 pounds, and 43% of 72 men weighed more than 220 pounds. Unfortunately, a relative ratio of weight to height measurements, such as would be afforded by use of the body mass index (BMI), a weight to height index (Wt/Ht), or a waist to hip ratio (W/H) was not available from this report.

Although not specific to the Native population, differences in the relationship between obesity and NIDDM, related to race and sex were found in the Second National Health and Nutrition Examination Survey (NHANES) conducted between 1976 and 1980 (Cowie, 1993). At ideal body weights (100% desirable weight), the odds ratio between Blacks and Whites for diabetes was 1.0. However, as the percentage of desirable weight increased over 100%, the odds ratios increased in a non-linear fashion. For example, the odds ratio between Blacks and Whites at 125% of desirable weight was 1.5, and at 150%

was 1.7. The effect of obesity on the risk of NIDDM was greatest in Black women, with an odds ratio of 7.0 at 150% of desirable weight.

Although it has been suggested that a "threshold effect" of obesity on NIDDM risk exists, that is, "that insulin sensitivity in subjects with normal glucose tolerance is impaired at a critical level of obesity", the NHANES results suggest that the risk for NIDDM involves an interaction of obesity with other factors such as race and gender (Cowie, 1993, p.727). In the twin study by Barnett, et. al. (1981) referred to above, there was a lack of concordance for obesity in the 21 twins who were highly concordant for NIDDM. It has been proposed that "obesity promotes diabetes in the genetically susceptible, but is neither a necessary nor sufficient cause of NIDDM" (Barrett-Connor, 1989,p.175). Also, the question remains to be studied more thoroughly as to the existence of a genetic basis for obesity as well as for NIDDM (Barrett-Connor, 1989, p. 175).

Obesity as a risk factor for NIDDM has also been found to be mediated by the pattern of body fat distribution and physical activity. Upper-body, centralized distribution of fat has been found to be more common in persons with NIDDM than in non-diabetic males and females (in Young, 1990; Bjorntorp, 1988; Haffner, et. al., 1990; Ohlson, et.al., 1985). Physical activity has been reported as significant in the epidemiology of NIDDM, although methodological problems have made "activity" difficult to standardize for measurement (Zimmet, 1991).

Recently, the impact of physical activity as a mediator for the influence of obesity on NIDDM in the Pima tribe was studied by Kriska, et. al. (1993). Obesity (BMI) was studied in relationship to glucose tolerance, level of physical activity (Metabolic cost of

activity), and fat distribution (Waist to hip ratio) in 1054 Pima subjects. Overall, men were found to be more physically active than women, and physical activity also was found to be inversely related to glucose intolerance, obesity, and centralized fat distribution. Obesity as an increasingly prevalent problem among Native peoples will require continued study to determine its role as a risk factor (genetics and/or environmental interaction), and to implement appropriate interventions for its role in prevention and treatment.

Obesity as Mechanism for Insulin Resistance.

It is generally accepted that the pathogenesis of NIDDM involves both pancreatic beta-cell failure as well as insulin resistance at the cellular level (Gavin & Davidson, 1992). It is still unknown exactly how insulin acts to facilitate the uptake of glucose into cells. However, ongoing basic research of glucose transporter systems (of which 5 have thus far been discovered) has determined that when insulin binds to a cell, it greatly facilitates the movement of intracellular glucose transporters to the cell membrane, and increases the absorption of glucose into the cell, where it is then utilized for energy production (Lienhard, et. al., 1992).

One of the earliest pathological mechanisms of NIDDM is the decreased ability of muscle, fat, or liver cells to respond to elevated blood insulin levels. Initially, the pancreas responds to the insulin resistance by the hypersecretion of insulin. Eventually, however, the beta cells of the pancreas lose their ability to secrete enough insulin to counteract the resistance, eventually yielding a persistent hyperglycemic state, accentuated by hepatic

glucose output (DeFronzo & Ferrannini, 1991; Dineen, et. al., 1992; Lienhard, et. al., 1992).

Obesity has been shown in a number of studies to markedly increase insulin resistance, primarily in muscle, with insulin sensitivity being reduced by up to 30-40% in persons who are 35-40% over ideal body weight (in DeFronzo & Ferrannini, 1991). The obese state is suspected to increase insulin resistance by the enlargement of muscle cell, thereby reducing access of insulin to its site of action (Lillioja, et. al., 1987).

Obesity can also induce insulin resistance in the absence of NIDDM; however, in the non-diabetic person, the pancreatic response is usually able to compensate adequately for the increased demand for insulin without deterioration into glucose intolerance. On the other hand, in persons with a genetic predisposition for insulin resistance, "the *B*-cell response is less than perfect, and glucose intolerance ensues" (DeFronzo & Ferrannini, 1991, p.175).

Obesity and insulin resistance were reported to be major independent risk factors for the development of NIDDM among the Pima. Of 200 subjects who were followed prospectively for an average of 5.3 years, 38 subjects developed NIDDM. Diabetes was most likely to develop in the more obese subjects (obesity was measured by waist to thigh circumference ratios) and in subjects with higher fasting insulin concentrations. However, the best single predictor of future NIDDM in this study was decreased glucose uptake at mean plasma insulin concentrations of 130uU per milliliter during euglycemia (euglycemic clamp technique) (Lillioja, et. al., 1993).

Conditions such as diabetes, hypertension, and obesity can be considered both as risk factors for vascular disease, and as diseases in their own right (Young, 1990). Hypertension and diabetes frequently occur together (Weidman, 1989; Christlieb, Krolweski, Warram, & Soeldner, 1985; Trost, Weidman, Beretta-Piccoli,1985; Houston, 1989) and increase morbidity, mortality, and generalized atherosclerosis when they co-exist (Fuller, 1985). "Syndrome X" has been described by Reaven (1988) as a combination of increased very low density liprotein levels (VLDL), decreased high density lipoprotein levels (HDL), glucose intolerance, hypertension, and insulin resistance.

A longitudinal study of 600 diabetic patients carried out in West Germany found elevated serum triglycerides and elevated systolic blood pressure were the most significant risk factors for major vascular complications (Janka & Dirschedl, 1985). It has been argued that elevated plasma insulin levels increase production of very-low-density-lipoproteins, leading to hypertriglyceridemia (DeFronzo & Ferrannini, 1991; Ginsberg, 1991).

It has been suggested that elevated levels of circulating insulin as a response to insulin resistance, complicated by obesity, may play an important role in the development of atherosclerotic lesions in Type II diabetes (Stolar, 1988; DeFronzo & Ferrannini, 1991). Hyperinsulinemia may be the common link in an interactive relationship among hypertension, diabetes, and obesity (Christleib, et. al., 1985; Reaven, 1991).

Based on the proposed role of hyperinsulinemia and insulin resistance in atherogenesis (Genuth, 1990; Donahue & Orchard, 1992), it has also been suggested that perhaps even therapeutically prescribed insulin for hyperglycemia may increase

macrovascular complications (Stolar, 1988). High dosages of insulin, combined with weight gain which facilitates insulin resistance may possibly exacerbate macrovascular complications. Therefore, the benefit of intensive insulin therapy in preventing microvascular lesions has been questioned in terms of the possible risk of macrovascular disease (Lasker, 1993), although the biologic plausibility of this has been challenged (Jarrett, 1992).

The genetic predisposition and the development of obesity in Native groups has not occurred in a "vacuum", detached from the sociocultural experience of Native people. It is proposed here that another elemental criteria exists for the severity of the clinical expression of NIDDM among Native groups, that of the sociocultural environment. The following section explores the intersection of obesity and genetic influences with the historical moment in which NIDDM has achieved epidemic proportions.

Thrifty Gene Hypothesis / Acculturation in NIDDM.

The term "coca-colonization" (Zimmet, 1991) has been coined to implicate the massive changes in social, economic, and cultural conditions in the creation of epidemics of NIDDM in many areas of the developing world. International studies have suggested that cross-cultural transitions from subsistence farming and hunting to a westernized existence has become a significant etiologic factor in the development of diabetes among a number of migrant populations (Stern, 1991).

In 1962, Neel was the first to suggest the "thrifty gene" hypothesis to explain the rising prevalence of NIDDM in Native populations in the United States (in Wendorf,

Table 4

THRIFTY GENE HYPOTHESIS/ACCULTURATION AS RISK FACTOR FOR NIDDM

Author & Year	Topic Area	Group Studied	Reported Findings
Ritenbaugh and Goodby (1989)	Acculturative factors	Native populations in the U.S.	suggested that Pima more acculturated than Navajo, and consequently have highest prevalence of NIDDM
Szathmary (1986; 1989)	Acculturative factors	Dogrib of the Canadian Northwest Territories	NIDDM is rare, cultural transition has only recently begun, yet insulin response to glucose challenge is elevated; suggested that NIDDM related to transition from protein to carbohydrate diet; hypothesized that NIDDM will become prevalent in Dogrib as acculturation proceeds
Wendorf and Goldfine (1991)	Thrifty gene	Native populations in the U.S.	suggested thrifty genotype may be related to mechanism of insulin resistance in muscle, allowing energy storage in fat or liver during times of abundance
Wendorf (1989)	Acculturative factors	Native populations in the U.S.	suggested that Native diet now is high in fat and sugars, and low in fiber and complex carbohydrates; imposed sedentary lifestyle has disrupted usual subsistence patterns

Author & Year	Topic Area	Group Studied	Reported Findings
Wiedman (1989)	Acculturative factors	Cherokee	suggested major "technoeconomic change" between 1936 and 1946 correlated with epidemic development of NIDDM

1989). Neel proposed that biological adaptations occurred within hunter-gatherer groups over thousands of years which promoted the efficient storage of energy in the body. In times of "feast", the body adapted to store layers of fat so as to be able to survive times of "famine" by drawing on this stored source of energy. Wendorf and Goldfine (1991) have further proposed that the thrifty genotype in NIDDM may be related to the mechanism of insulin resistance in muscle, which would effectively buffer hypoglycemia in the fasting state, yet would allow energy storage in fat or liver in times of abundance.

However, as Native groups have rapidly acculturated, their diets have approximated the "average" U.S. diet which is high in fat and simple sugars, and low in fiber and complex carbohydrates (Wendorf, 1989). In addition, a sedentary lifestyle has resulted from the imposed disruption of usual subsistence patterns.

Under the "thrifty gene" hypothesis, the continuous availability of food that now exists (albeit in the form of government commodities in remote reserve areas) has pre-empted the "famine" portion of the hypothetical equation. This has resulted in the continued ability among Native populations to store fat without a concomitant demand for its expenditure, an ability that is complicated by the loss of traditional occupational activities. As Weiss (1989) described the situation: "Relative to their energy demands, Amerindians are currently too efficient at metabolic food storage" (p.287).

However, Ritenbaugh & Goodby (1989) have suggested that NIDDM is not inevitable among Native groups, but is related to the degree of acculturation. They stated that the Navajo have the lowest prevalence of obesity and diabetes among the Southwest tribes, yet retain a tradition of scattered housing in a remote, rural reservation which

demands high energy expending tasks, such as splitting wood, hauling water, herding, small-scale farming, and weaving. In contrast, they cite the Pima tribe as an example of the "most acculturated Indians" (p.232), who as cited above, have the highest reported prevalence of NIDDM in the world.

The acculturation-NIDDM connection was traced by Wiedman (1989) among the Cherokee culture of the United States. Prior to 1940, diabetes was unknown in this tribe, yet was of epidemic proportions by the 1960's. A major "technoeconomic" change occurred between 1936 and 1946 when the Cherokee moved out of their mountain homes to live closer to newly built roads, and the increasing use of automotive transportation diminished their usual patterns of walking long distances. The Cherokee farming economy was surrendered for a cash economy, resulting in a significant decrease in their consumption of corn as a major foodstuff, and an increase in the use of refined foods. In addition, their adaptation to technologies, such as gas and electric stoves, led to the frying of foods in fat. By 1977, their mortality rate due to diabetes was reported as 26.23/100,000.

In support of the influence of acculturation in developing risk for NIDDM, another study among the Pima has been reported. This study investigated the association between obesity and traditional lifestyles among people of Pima ancestry and found that obesity was significantly less prevalent among those living in a remote mountain setting in northwestern Mexico than among those living in Arizona in the United States. The less acculturated group was also found to have significantly lower serum cholesterol levels than the Arizona Pima (Ravussin, Valencia, Esparza, Bennett, & Schulz, 1994).

Szathmary's work (1986; 1989) holds promise in elucidating the specific effects of cultural transition on the development of NIDDM among the Native Dogrib of the Canadian Northwest Territories. The Dogrib are in a relatively early phase of modern contact and transition to a sedentary lifestyle, and diabetes has been extremely rare among them (the first clinical case was diagnosed in 1981). Yet they exhibit elevated insulin levels in response to glucose challenge as compared to White populations.

Szathmary's work has also explored the possibility that NIDDM among Native people may result from a transition from protein to carbohydrate as a primary food source. This possibility was based on the premise that carbohydrate food sources would have been extremely scarce among hunter-gatherers of the extreme North, and they subsequently adapted to efficiently extract energy from protein rather than glucose. The inability to metabolically process glucose as a primary food source, combined with an increasing availability of glucose sources through acculturation, hypothetically results in increased rates of diabetes.

Continued longitudinal study of the Dogrib will afford a unique opportunity to identify factors that influence glucose tolerance in an ongoing, prospective fashion, rather than trying to retrospectively determine the etiology of NIDDM in Native populations in which social and environmental changes have already occurred.

Cultural Influences in Understanding NIDDM

The cultural context in which NIDDM is embedded was not the focus of the present study. However, it is essential to recognize the influence of this dimension on the

experience of having, and living with, this chronic disease. Illness implies experiences of meaning and interpretation, and social relations (Good, 1977; 1980), while the experience of illness, itself, is shaped by sociocultural forces (Kleinman, 1978; 1988).

In a contemporary Anishinaabe community in Canada, Garro utilized Kleinman's explanatory model framework as one of two interview formats for data collection in her study of lay people's understanding of diabetes (1995). Among the respondents, a shared perception of diabetes was as a "white man's sickness". "White man's sickness" is understood as including those diseases that were unknown among the Native community prior to European contact. The understanding of diabetes as the "white man's fault" (p.41) is significant in terms of cultural perceptions of etiology, appropriate treatment, and perceived ability to control or cure it.

Utilizing a narrative reconstruction approach, Lang (1985; 1989) also studied the understanding of Type 2 diabetes mellitus among the Dakota in the Devils Lake/Fort Totten reserve area (included in this study). In Lang's work, a theme of "white man's sickness", strikingly similar to that described in Garro's work, was found. The perception that diabetes was not a part of past Dakota experience, and that it has been imposed from the "outside" was an evident theme throughout the Dakota narratives.

Significantly, respondents in both Garro's and Lang's studies identified the interruption of traditional Native foodways as a primary etiologic component of NIDDM in their communities. For example, one respondent stated: "In the old days, Indians ate nothing but wild food. Nobody ever was sick" (Garro, p.41). There were also references to the belief that Native people who did not use store bought foods were healthier (Lang,

1989). This component of the cultural model for diabetes seems to demonstrate an almost intuitive lay knowledge of the premise on which the "thrifty gene" hypothesis is based.

Although there were consistent themes that emerged from the studies, there was also a diversity among respondents in Garro's and in Lang's studies. Despite shared cultural understandings of illness, variation also exists among individual members of a culture in terms of how much they are informed by the cultural model (Garro, 1988). For example, one etiologic theme voiced within the Dakota study was the stress of contemporary life: "For me, I think it is the stress from living all bunched together in these new housing projects that I think keeps my sugar up" (Lang, 1989, p.318). In contrast, another respondent stated: "I used to drink a lot when I was younger...The drinking might have brought it on" (Lang, 1989, p.315).

Among the Anishinaabe, a theme of unpredictability and a lack of control over the prevalence of diabetes emerged. This may hold great portent for the prevention and treatment of diabetes, if in fact it is thought of as a capricious disease that is impossible to control. The perceived ubiquitous nature of diabetes may negatively influence attempts to control it, particularly as its prevalence has increased to epidemic proportions in Native communities.

Of the tribes of the Southwest U.S., it has been said: "one of the things we find very frustrating about developing a prevention program is the fatalistic attitude among tribal members, even the young children. Diabetes is so prevalent and pervasive that the attitude is one of passive acceptance of the disease" (Joe, 1988). In order to stem the current epidemic of NIDDM among American Indians, it is essential that continued

study be focused on the sociocultural dimensions of this chronic disease and its complications.

Lower Extremity Amputation Related to NIDDM

An understanding of the prevalence and etiology of NIDDM in the Native American population provides a basis for the study of LEA, a disabling complication of NIDDM. The remainder of the Review of the Literature is targeted to LEA according to the following outline: (a) policy issues for the prevention of LEA, (b) presentation of a conceptual framework utilizing the Causal Pathways to LEA model (Bild, et.al., 1989), (c) discussion of risk factors for development of vascular disease, neuropathy, and infection leading to amputation, and (d) review of studies specific to LEA among Native Americans.

Policy Issues in Prevention of LEA.

The rate of LEA in the general diabetic population resulting from vascular compromise and/or infection, has been reported at more than 40 times the rate of those without diabetes (Connell, Shaw, & Will, 1991). The reduction of the rate of LEA among diabetics, from the 1988 rate of 8.2/1000 to 4.9/1000 by the turn of the century, has been targeted by the United States Public Health Service as a national health objective in the Healthy People 2000 National Health Promotion and Disease Prevention Objectives (U.S. Department of Health and Human Services, 1991).

It has also been recognized that the number of diabetic-related amputations significantly stresses the limited resources of the Indian Health Service (Zwemer, 1990). Given the specter of finite resources, and the impoverished socioeconomic conditions that exist in reservation areas (Office of Technology Assessment, 1986), prevention of LEA's among American Indian people becomes imperative to improve health and contain costs. Logically, early identification of those persons at increased risk for LEA is needed in order to take measures to prevent foot ulcers and infection (Connell, Shaw, & Will, 1989).

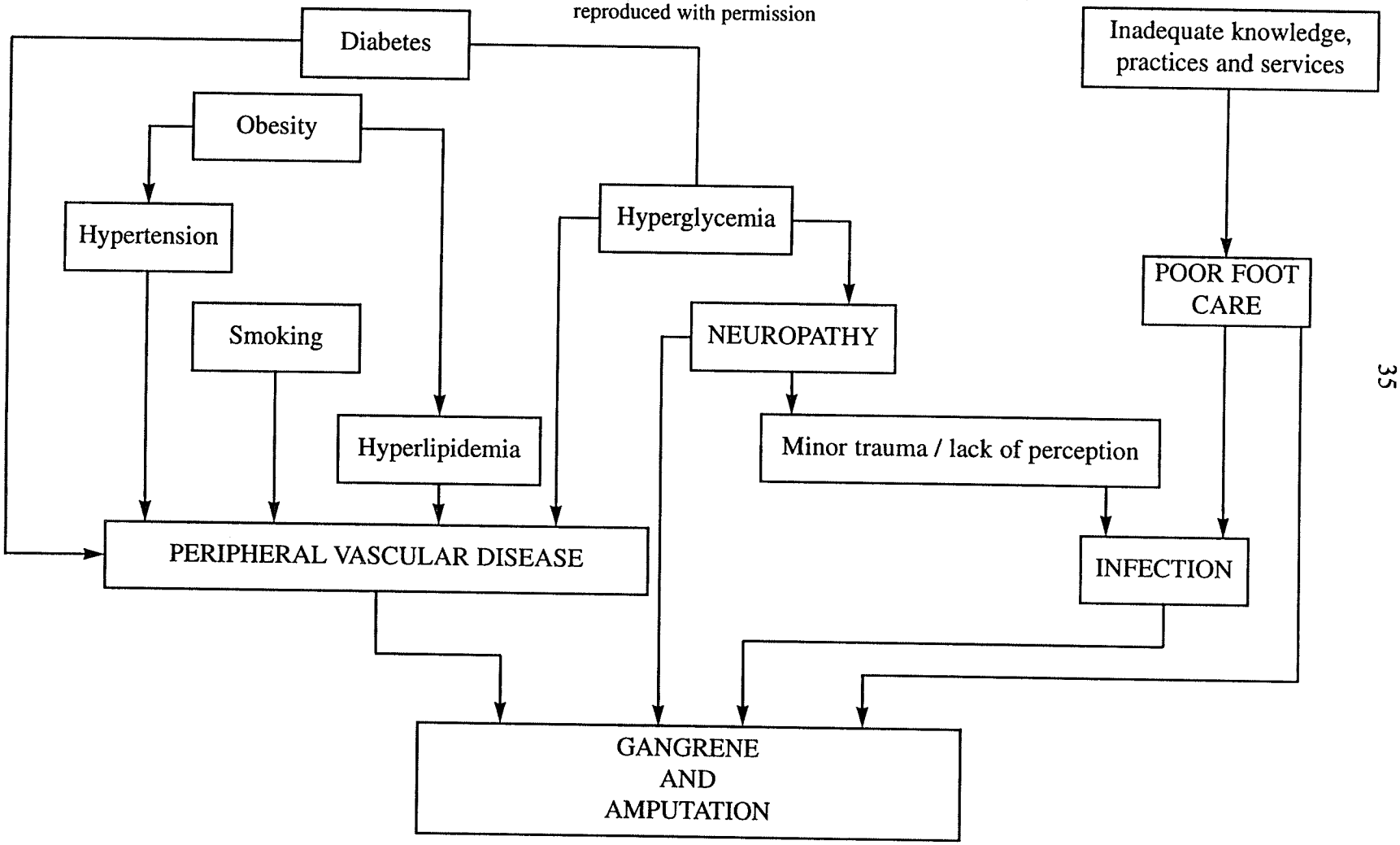
Causal Pathways to LEA.

The Causal Pathways to LEA model proposed by Bild, Selby, Sinnock, Browner, Braveman, & Showstack (1989) was utilized as the conceptual framework for this investigation of risk factors in the etiology of LEA (Figure 1). The model proposes parallel and interactive pathways among factors which contribute to peripheral vascular disease, neuropathy, and infection in persons with diabetes, culminating in the risk for gangrene and amputation.

Risk Factors for LEA.

Smoking and duration of diabetes have been cited as risk factors for impaired arterial blood flow to the extremities (Kannel & McGee, 1985; Palumbo & Melton, 1985). Peripheral vascular disease is thought to be a significant complication of diabetes that may lead to LEA, however, it has not been consistently defined in studies (Rate, et. al., 1983).

Figure 1
Causal Pathway to LEA
(Bild, Selby, Sinnock, Browner, Braveman, & Showstack, 1989)
reproduced with permission



There has also been a lack of a standard definition for peripheral neuropathy; however, it is recognized as a common complication in Type II diabetes (Bild, et. al., 1989), affecting up to 50 per cent of people with long-term diabetes (Pirart, 1978). As a precursor to the development of foot ulcers, neuropathy may be the most significant contributor (Boulton, et. al. 1986). Hyperglycemia is now thought to be the major risk factor for the development of neuropathy and microvascular disease (Greene, Lattimer, & Sima, 1988; Harati, 1987; Janka, Standl, & Mehnert, 1980). An association has been found between LEA and blood glucose concentrations in a multi-national study of diabetes by the World Health Organization (West, et. al., 1983).

Infection is frequently found in lower extremity ulcers, often becoming the precipitating indication for amputation in the diabetic person (Pecoraro, et. al., 1990). Neuropathy may not only predispose to unrecognized traumatic injury, but may also influence structural and functional changes in feet. This often results in the breakdown of soft tissue, particularly under the metatarsal heads, with subsequent infection and gangrene (Leichter, Schaeffer, & O'Brian, 1991; Elkeles & Wolfe, 1991). The presence of edema has also been identified as a precipitating risk factor for the development of gangrene (Lithner & Tornblom, 1984).

Foot Care.

The "aetiopathogenic factors of foot problems in diabetes" have been described by Young, et.al. (1993, p.110) as "multifactorial" with sensorimotor and autonomic neuropathy, and peripheral vascular disease as two of the main contributors. These

authors have also described other risk factors for LEA including retinopathy, nephropathy, history of previous foot problems, and the use of smoking and alcohol. The 1991-1992 Clinical Practice Recommendations of the American Diabetes Association also has stated that those at high risk for foot lesions have one or more of the following conditions: (a) neuropathy, (b) vascular disease, (c) structural deformities, (d) abnormal gait, (e) skin or nail deformities, and/or (f) history of previous ulcers or infections (1992).

Neuropathically induced decreases in sensation, in conjunction with atherosclerotic changes associated with Type II diabetes, constitute a powerful combination in predisposing the diabetic to infection, gangrene, and amputation. In contrast to the control of metabolic pathways that may prove elusive to prevention strategies at this point in time, improved foot care has been demonstrated as effective in reducing amputations and preventing diabetic foot lesions. Reductions in amputation rates have been reported as high as 85 per cent through intensive foot care training and education (Assal, et. al., 1985; Chantelau, Kushner, & Spraul, 1989).

Despite the gains to be made with improved foot care, however, it has not always been given the clinical priority it deserves. One study found that routine foot examinations were done only 12.3 per cent of the time in a diabetic clinic (Bailey, Yu, & Rayfield, 1985). Another study reported that clinicians were more likely to prescribe preventive foot care behaviors if they were aware of a prior history of a foot ulcer. However, awareness of neuropathy and/or peripheral vascular disease, without a previous history of a foot lesion, did not increase clinicians' attention to preventive foot care strategies (Del Aguila, Reiber, & Koepsell, 1994).

In contrast, Litzelman, et. al. (1993) reported the results of a blinded, randomized, controlled trial of a twelve month foot care education and assessment program including both patients and health care providers. The patients who received the foot care intervention were significantly less likely to have serious foot lesions ($p=0.05$), and the physicians who participated in the intervention of specific assessment guidelines were more likely to examine people's feet and make podiatric referrals ($p=0.04$).

Lack of knowledge regarding diabetes care among patients was found to be significantly related to the development of foot lesions in a case-control study by Delbridge, et. al. (1983), while the implementation of improved foot care programs has been reported to reduce the rate of LEA by 44% to 85% (Bild, et.al., 1989). A "Meeting Report" of the Fifth Malvern Diabetic Foot Conference held in May of 1994 discussed several foot care programs that have been initiated in several European countries (Shaw, Bileikyte, Connor, & Boulton, 1995).

A large-scale program has been undertaken in Germany to educate 2000 general practitioners on diabetic issues, and specifically on foot care. They in turn, are holding education sessions in their own practices. Patients who have gone through the education sessions have been reported to have lost weight and have improved knowledge of foot care. In a Dutch diabetic clinic, since a foot care clinic was established, a "significant fall" in the amputation rate has been demonstrated. An interesting variable was identified in the experience of a British foot care education program. Despite improving their knowledge of foot care, the patients did not see themselves as "vulnerable" to foot problems, and

therefore were not inclined to make lifestyle or behavioral changes based on the knowledge.

In terms of cost-effectiveness, an economic analysis done in Sweden comparing the cost of amputation to primary healing management found that the treatment of people with diabetic foot ulcers through the use of a multidisciplinary team was far less costly when compared to the cost of surgical amputation. The study also reported that the costs for clinic visits to the members of the foot care team, the use of antibiotics, and orthopedic appliances were quite low in comparison to costs associated with amputation (Apelqvist, et.al., 1994).

Wooldridge and Moreno (1994) recently analyzed Medicare payments made over a three year demonstration study of prescriptions for therapeutic shoes for diabetic patients in three states in the U.S. They concluded from the demonstration that the inclusion of coverage for therapeutic shoes for people with diabetic foot disease would not increase total Medicare costs. Appropriate footwear is an example of a logical but highly effective intervention for the prevention and treatment of diabetic foot complications (American Diabetes Association, 1992; Gavin, et.al., 1993; Skolnik, 1992; Farrell & Miner, 1988).

In the Causal Pathways to LEA model, the conscientious implementation of foot care programming appears to be a most accessible and logical target for the prevention of gangrene and amputation.

LEA in Native Americans

A review of research most directly related to purposes of this study is presented in this section. A limited literature exists on the incidence, prevalence, and risk factors associated with diabetes-related LEA among Native Americans. Weiss and associates stated that a "Medline search of literature since 1975 did not locate a single reference which was coded for the combination of 'American Indian, Foot and Diabetes Mellitus'" (Weiss, Ulbrecht, Cavanaugh, & Buchanan, 1989, p.292). A review of the studies that are available is presented here (Table 5).

Gohdes (1986) noted that 76 per cent of all LEA's performed in Indian Health Service hospitals during Fiscal Year 1983 were on diabetic patients. Ninety-five per cent of LEA's among 84 members of the Pima tribe in the Southwestern United States were attributed to NIDDM (Nelson, et. al., 1988).

Among the Sioux tribes in North and South Dakota, and Nebraska, the age-adjusted incidence rate for LEA has been reported to be 1.5 times higher than the U.S. general population. Also, 84 per cent of LEA's among the Sioux in 1988 were in diabetic persons, a proportion that was 1.8 times higher than the general U.S. population rate (Stahn, Gohdes, & Valway, 1993). This compares with Most and Sinnocks' definitive study of LEA across six states, where 45 per cent of LEA's were attributed to diabetes in their 1978 study of hospital discharges (1983).

There were two published works found specific to risk factors for LEA in an American Indian population. In a longitudinal study of the Pima, the rate of LEA was found to increase with duration of Type II diabetes and was also associated with

Table 5

LEA IN NATIVE AMERICANS

Author & Year	Topic Area	Group Studied	Reported Finding
Bild (unpublished study done 1982-1983)	Risk factors for LEA among Native Americans	18 Eastern Cherokee with LEA, 36 without LEA	Risk factors included: age over 40, positive smoking history, toe ulcer, previous LEA, hypertension, retinopathy, poor glycemic control
Gohdes (1986)	Prevalence of LEA/NIDDM	Diabetes-related LEA within all IHS hospitals in 1983	76% of all LEA related to NIDDM
Lee, et.al. (1993)	Incidence and risk factors for LEA among Native Americans	Longitudinal study of Oklahoma Natives	18.0/1000 person years incidence rate of first-time LEA; males had incidence rate twice that of females; risk factors included: retinopathy and duration of NIDDM; Male-specific risk factors included: fasting plasma glucose, insulin use, systolic blood pressure; Female-specific risk factors included: cholesterol, diastolic blood pressure
Nelson, et.al. (1988)	Prevalence of LEA/NIDDM	84 Pima undergoing LEA	95% of all LEA related to NIDDM

Author & Year	Topic Area	Group Studied	Reported Finding
Nelson, et. al. (1988)	Risk factors for LEA among Native Americans	Longitudinal study of the Pima	Risk factors included: duration of NIDDM, hyperglycemia, medial arterial calcification, retinopathy, nephropathy, impaired toe vibration-perception threshold, absence of patellar tendon reflexes
Stahn, et.al. (1993)	Prevalence of LEA/NIDDM	Sioux in ND, SD, NE undergoing LEA in 1988	84% of all LEA were among people with NIDDM; 1.8 times higher than the general U.S. population rate of LEA related to diabetes

hyperglycemia, medial arterial calcification, retinopathy, nephropathy, impaired toe vibration-perception threshold, and absence of patellar tendon reflexes (Nelson, et. al., 1988). However, besides deriving from a culture group distinct from the Plains tribes, the Southwestern Native Americans have been reported to have a low prevalence of smoking (Sievers & Fisher, 1984). Smoking was not cited as a risk factor in the Pima study of LEA, but smoking rates have been reported to be considerably higher among the Plains Indians (Hrabovsky, Welty, & Coulehan, 1989) and may have a greater influence in the pathway to LEA in this group.

The second published report of risk factors for LEA in a Native American population was a longitudinal study of Oklahoma Indians (Lee, et al., 1993). The incidence rate of first-time LEA in this population was found to be 18.0/1000 person-years, with the incidence rate among males twice that of females. Retinopathy and duration of diabetes were reported as being significant risk factors for LEA for both males and females; however, there were also differences in risk factors found between males and females. Fasting plasma glucose, insulin use, and systolic blood pressure were significant risk factors among men, while for women, cholesterol and diastolic blood pressure were found to be significant risk factors.

An unpublished case-control study of LEA among the Eastern Cherokee was done in 1982-1983 in which a chart review was combined with an interview survey design (Bild, unpublished study). Eighteen cases of LEA were matched to 2 controls each for age, sex, and duration of diabetes. The risk profile for LEA that emerged included: (a) age over 40,

(b) smoking history, (c) toe ulcer, (d) previous amputation, (e) hypertension, (f) retinopathy, and (g) poor glycemic control.

Summary

In contrast to LEA's that occur among non-diabetic persons, LEA's in the diabetic person most probably result from interaction among a number of contributory factors rather than from a singular cause (Pecoraro, Reiber, & Burgess, 1990; Steffes and Mauer, 1991). However, there is a dearth of the epidemiologic evidence needed to develop sound prevention strategies for LEA at this time (Stern, 1991). Therefore, "definition and quantitation of the major independent risk factors for amputation and description of their common interactions must precede the implementation of strategies for prevention of lower-extremity amputation in diabetes" (Pecoraro, Reiber, & Burgess, 1990, p. 513.).

This case-control study was undertaken to contribute to the "definition and quantitation" of those factors predisposing members of the Sioux Nation with Type II diabetes to LEA. Results from this study will be used to design prospective studies and clinical studies, and eventually will contribute to the prevention of LEA and its associated disability among Native Americans.

CHAPTER III

METHODOLOGY

In this section of the report, the methodologic approach to the collection and analysis of data undertaken in this study is presented.

Research Questions / Hypotheses

The general research question addressed in this study was: What factors are associated with increased risk of LEA among diabetic members of a Plains dwelling American Indian tribe?

Five hypotheses for study were proposed based upon identified risk factors for LEA found in the review of the literature, with particular reference to variables in the Causal Pathways to LEA model (Bild, et. al., 1989):

(a) There will be a decreased risk of LEA among diabetics who do not smoke than among those who do smoke;

(b) There will be an increased risk of LEA among diabetics who are/have been treated with insulin than those who have not been treated with insulin;

(c) There will be a decreased risk of LEA among diabetics who have had foot examinations recorded on a regular basis;

(d) There will be a decreased risk of LEA among diabetics who maintain glycemic control;

(e) There will be an increased risk of LEA with increased Weight to Height ratios (Wt/Ht).

Design

A study of existing medical records, utilizing a retrospective case-control design, was conducted to explore relationships between the presence of identified variables and the status of having a LEA (case) or not having a LEA (control). The controls were matched to the cases for sex and for age within 5 years (Figure 2).

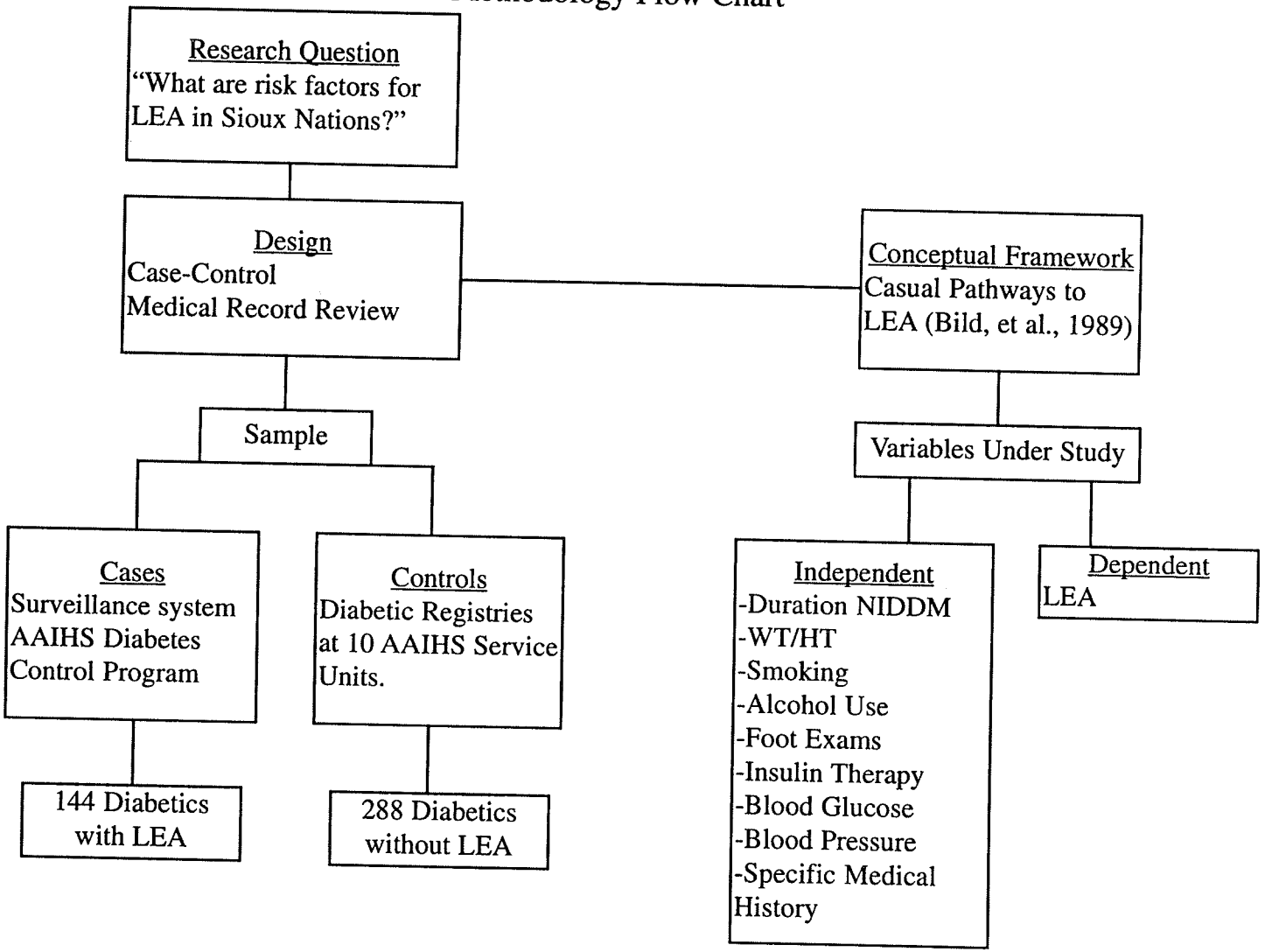
Several advantages of the case-control method include that it: (a) is suited for the study of rare diseases or those with long latency, (b) is relatively inexpensive, (c) can utilize existing records, and (d) allows for the study of multiple potential causes of a disease (Schlesselman, 1982).

Description of the Diabetic Population

The Indian Health Service (within the United States Public Health Service) is regionalized into 12 geographic areas; these areas are further subdivided into 134 Service Units. The Service Unit facilities are predominantly located in rural locations, within the 33 reservation states of the United States.

In the Aberdeen Area of the Indian Health Service (AAIHS), the utilization of health services is profoundly influenced by epidemic rates of NIDDM. Dr. Ruggles

Figure 2
Methodology Flow Chart



Stahn, the Diabetes Control Officer for the AAIHS Diabetes Control Program generously served as a consultant at the time of this study, and provided the following prevalence and incidence information for the AAIHS, including the graphs and audit forms in Appendices A through F.

Prevalence of diabetes in the AAIHS is 105/1000 as compared to 25/1000 in the general United States population (Appendix B), and the AAIHS diabetes death rate continues to be 4 to 5 times higher than that of the general U.S. population (Office of Technology Assessment, 1986; Aberdeen Area Indian Health Service, Diabetes Control Program, 1991). The 1984 hospital discharge rate for diabetes was 60/10,000 population in the AAIHS as compared to a rate of 25.3/10,000 in the U.S., all races population (Office of Technology Assessment, 1986).

The Service Unit population of the AAIHS is approximately 85,000 with almost 5,000 persons diagnosed with NIDDM (Aberdeen Area Indian Health Service, Diabetes Control Program, 1991). The prevalence of diabetes among American Indian adults in the Aberdeen Area, over the age of 45, averages 30 per cent (Indian Health Service, 1990; Aberdeen Area Indian Health Service, Diabetes Control Program, 1991). Approximately 70 per cent of recorded LEA's in the AAIHS in 1988 were performed on persons between the ages of 45 and 70 years.

The 1982-1987 incidence rate of LEA ranged among American Indians and Alaskan Natives between 24.1/1000 diabetic persons (Pima) and 7.4/1000 diabetic persons (Navajo) (Appendix C). During Fiscal Year 1987 to 1989, the average incidence rate of LEA in the AAIHS was 87/10,000 diabetic persons as compared to the incidence rate in

the general United States population of 59.7/10,000 diabetic persons (Appendix D). The AAIHS rate of LEA can be further delineated as 69.3/10,000 diabetic persons for women and 124.2/10,000 diabetic persons for men. These figures compare to the rate of LEA among the general diabetic population in the United States of 54.3/10,000 diabetic women and 77.3/10,000 diabetic men (Aberdeen Area Indian Health Service, Diabetes Control Program, 1991) (Appendix E).

The Sioux Nation comprises most of the population in the AAIHS, and dwells predominantly in the Northern Plains states of North and South Dakota. Ten of the 15 Service Units in the AAIHS serve predominantly Sioux populations. The 1987-1988 prevalence rate of Type II diabetes mellitus among the Sioux tribes in North and South Dakota and Nebraska was 3.7 times the U.S. all population rate.

Enrolled members of the Sioux Nation residing in the AAIHS, who have been diagnosed with Type 2 diabetes mellitus served as the target population for this study. As of May, 1991, the number of LEA's currently on record among Sioux people living in this area was 281, 142 of which had been performed on females, and 139 performed on males (AAIHS, 1991). However, this figure reflects the number of amputations and not the number of persons with amputations, since there are people who have had multiple progressive amputations.

Case Definition.

For this study, the definition of cases was as follows:

> All medical records of members of the Sioux Nation who: reside in the Aberdeen Area of Indian Health Service, are older than 20 years of age, have Type 2 diabetes mellitus, and have undergone a non-traumatic LEA between 1984 and 1993. For those who have had multiple amputations, data was collected surrounding the first LEA event only, yielding a total of 144 cases for this study.

Control Definition.

For purposes of this study, the definition of controls was as follows:

> Medical records of members of the Sioux Nation, who: reside in the Aberdeen Area of Indian Health Service, who also have Type 2 diabetes, but who have not undergone LEA. Controls were matched for sex, and also for age within 5 years. For this study, 288 controls were randomly selected.

Sources of Data

In the U.S., where the majority of health care is provided within a privatized context of provider/consumer markets, the IHS health care delivery system is unique with regard to its Federal oversight, as well as to its derivation from the historical treaty status of the Service Population with the U.S. Federal Government. Consequently, the IHS

medical records system is also unique in that multiple IHS systems track all in-patient and out-patient information which is then aggregated by regional area, ICD-9 code, and tabulated by fiscal year. Therefore, in the literature, this data base has been extensively cited in population-based studies of health issues among Native people.

At each of the Service Units within the AAIHS, diabetes records are audited quarterly, with new cases of the disease and associated complications being reported to the Diabetes Control Program Officer, a physician epidemiologist based in Rapid City, South Dakota. (Examples of the audit and reporting forms that were being used at the time of this study are in Appendices F and G). The Diabetes Control Program Officer also makes routine on-site visits throughout the year, to oversee collection of diabetes data. A diabetic coordinator is identified at each Service Unit; however, selected Service Units also have been designated as Diabetes Control Program (DCP) sites and have additional personnel assigned specifically to the DCP. In this study, only the Fort Totten Service Unit in North Dakota was a designated DCP site.

Separate registries of all people with diagnosed diabetes are kept at each Service Unit, while the DCP Officer, Dr. Ruggles Stahn, in Rapid City keeps additional registries of all diabetic complications as well. In this study, the DCP Officer forwarded the list of cases (diabetic persons with LEA) drawn from the centralized, computerized list of all known members of the Sioux tribe within the AAIHS who have undergone LEA(s) related to Type 2 diabetes mellitus. This list is continually updated through the surveillance system at each Service Unit in the AAIHS.

Controls (diabetic persons without LEA) were drawn from the computerized registries of diabetic persons which are kept at each of the Service Units within the Aberdeen Area. Individual medical records are maintained on each person who accesses health care through the Service Unit. The diabetic registry list at each of the ten Service Units in this study was stratified for age and gender. Two controls were then randomly drawn for each identified case.

Data Collection was begun in October of 1992 and completed in August of 1993. Over ten thousand miles were logged across the states of North and South Dakota in travelling to Service Unit sites for data collection. The number of days spent at any given Service Unit ranged from one to fourteen, depending on the number of charts to be reviewed, and the logistics of retrieving older records. Each individual medical record was accessed directly at each Service Unit site, and was reviewed on site by the investigator, sometimes with the assistance of research assistants trained specifically for data collection in this study.

Specification of Variables

The independent variables chosen for study were derived largely from the causal pathways model described by Bild and Associates (1989). Data related to gender, age, and duration of diabetes were also identified as variables in the study. The eventual benefit envisioned from this study is an enhanced ability to prevent diabetes-related LEA through early identification of risk factors. Therefore, this study focused on the collection of data that was proximal to the date of the precipitating lesion (**PL**) leading to LEA,

rather than data surrounding the LEA itself. In this way, the study may contribute to an earlier interruption of the Causal Pathways to LEA.

Independent Variables

The independent variables specified for this study included:

(a) gender (male or female)

(b) duration of diabetes (years since first diagnosed)

(c) WT/HT index (pounds/inches)

(d) smoking history ("yes" for either previously or presently smoking; "no" for never smoking; "unknown" if not addressed at all in the available medical record

(e) alcohol use history ("yes" for past or present diagnosis of alcoholism, "heavy" use of alcohol; "no" for never using alcohol, "occasional" use; and "unknown" if not addressed at all in the available medical record)

(f) frequency of foot exams (number of foot exams by health care provider in the one year prior to the discovery of the PL leading to LEA)

(g) history of insulin therapy as part of a treatment regimen for NIDDM ("yes" if previous or present prescriptions for insulin therapy in the medical record; "no" if no medical prescription for insulin therapy noted in the record)

(h) laboratory measures of blood glucose (mean blood glucose in mg/dl)

(i) clinical measures of blood pressure (systolic and diastolic in mmHg)

(j) presence or absence of a history of specified medical conditions ("yes" if previous or current medical diagnosis is indicated in the medical record; "no" if no medical diagnosis is indicated from the available record).

Medical Conditions Included in the Study

The medical conditions identified for inclusion in this study were: (a) hypertension, (b) angina, (c) claudication, (d) end-stage renal disease (dialysis), (e) myocardial infarction (MI), (f) congestive heart failure (CHF), (g) stroke (cerebrovascular accident [CVA] or transient ischemic attack [TIA]), (h) lower extremity ulcer or infection (other than the PL), and (i) neuropathy.

These medical conditions were defined as present if they were made by medical diagnosis, and if they existed at any point prior to the development of a PL that led to LEA. Medical conditions that were diagnosed after the PL date in the case record were not included in this study. As was assumed before the collection of data, many of the cases and controls had multiple co-existing medical conditions in addition to diabetes.

Dependent Variable.

The dependent variable in this study was categorical and dichotomous in nature, defined as either the presence or absence of LEA. Lower extremity amputation was defined as the surgical removal of any portion of the lower extremities, including toes, related to the diagnosis of Type 2 diabetes mellitus.

Because it was noted in the surveillance system at Rapid City that approximately half the people with LEA had proceeded to have subsequent LEA's, the definition was further limited to the first time LEA. All data, therefore, was collected relative to this point in time, that is, the first LEA.

The surveillance system of the DCP also indicated that a smaller percentage of LEA's are related to traumatic injuries. Amputations resulting from traumatic injuries were not included in the definition of the dependent variable.

Data Collection Tool

The data retrieval form used to record the data from medical charts at ten Indian Health Service Units was constructed to primarily capture the variables in the Causal Pathway model. The investigator was provided by AAIHS with a copy of the unpublished study of LEA among the Eastern Cherokee, conducted by Diane Bild. The investigator had discussed the Cherokee study, and the data retrieval form used in that study with Dr. Bild (personal telephone communication, 1991). Portions of the data retrieval form used in the Eastern Cherokee study were then integrated into the data collection form for this study of the Sioux.

At the proposal stage for this study, the Agency for Health Care Policy and Research had also suggested that the investigator discuss this LEA study with Dr. Jennifer Mayfield, a primary investigator for an AHCPR funded study of LEA within the IHS in New Mexico. Information regarding variables of interest in the respective studies was exchanged, and the final data collection form was developed.

A Pilot Study was conducted at Fort Totten to trial the data collection form, and revisions were made prior to the beginning of the study. Revisions included deletion of variables that were not going to be available from the AAIHS medical records, for example, routine description of the presence or absence of foot deformities. The format of the form was changed to contain fewer pages after an actual data collection at the first Service Unit site.

Reliability of Data Collection

The investigator travelled to nine of the ten Service Units to conduct and oversee data collection. A total of four medical students and one podiatry resident served as research assistants at various times at six of the Service Units during the data collection phase. The medical students and podiatry resident were affiliated with the AAIHS Diabetes Control Program on clinical rotations through their respective universities. In addition, Mary Wright, Ph.D. served as a methodological consultant and also assisted in data collection at two Service Units.

All research assistants were trained exclusively by the investigator. The investigator was physically present, personally monitoring the extraction of the chart data throughout the entire data collection phase. Questions regarding uncertainties in the medical record were decided upon by the investigator. Only at the Rosebud Service Unit did two research assistants collect data independently, but only after the investigator had trained and completed data collection with these research assistants at a previous data collection site.

Protection of Human Subjects

This study of existing medical records is considered exempt under the Department of Health and Human Services regulations regarding the study of human subjects. Individual contact with subjects was not a part of the case-control design. Data extracted from medical chart information has been treated confidentially and anonymously.

No identifiers were used that could be linked to individual subjects. Data is available only to the investigator and to the Diabetes Control Program Officer for the AAIHS. Results from the study are being reported in aggregate for all 10 Service Units combined, although upon request, each Service Unit may have the data from its specific site analyzed.

Institutional Review Board approval was obtained from both the University of Manitoba (UM) and the University of North Dakota (UND) prior to data collection. Permission to access data was also sought and received from the Research Committee of the AAIHS and the 10 Service Unit Directors. A letter of introduction from AAIHS officials was sent to the Service Unit Directors, Clinical Directors, and Medical Records Directors at each of the Service Units prior to the commencement of data collection. A letter of support for this study was also sought and received from the Aberdeen Area Tribal Chairmen's Health Board. Additionally, the investigator and all research assistants on the study were required to sign volunteer agreements that included a strict confidentiality clause relating to their work with the IHS (Appendix H).

Methodological Problems

A number of methodological problems were faced in this investigation of risk factors for LEA which are addressed in this section.

Ascertainment of Cases.

The AAIHS DCP has the most complete record of existing LEA's within its area. However, it is possible that persons who access health care through non-contract facilities or whose health care costs are covered by alternative payment systems, such as Medicare or private insurance, may have been missed. When such cases are identified, the AAIHS Diabetes Control Program (DCP) is notified and the registry is updated.

Constant surveillance for new cases of LEA and other diabetic complications is routinely maintained. The investigator established contact with Community Health Nurses at each Service Unit site in order to check if any new cases had been found, and also kept in regular contact with the AAIHS Diabetes Control Program Officer prior to going to each new data collection site.

All known cases at each Service Unit at the time of the data collection were included. In one situation, a chart that was selected as a control was found to be a previously unidentified LEA case. In three situations, the case record contained so little information that it was not usable for this study. One case record had been sent to Colorado for permanent storage, and was deleted from the study because it was not feasible to drive the 600 miles that would have been necessary to return to that data collection site when the chart was sent.

Matching of Controls.

In eight situations it became necessary to obtain controls with birthdates that were not within five years of the case birthdates. This was a particular problem with the exceptionally old or exceptionally young cases. In these situations, controls were selected that most closely matched the case birthdates.

At one Service Unit, retrieval of older records was inordinately complicated. Of the total of 17 cases, it was only possible to find two appropriate controls for 13 of them after 36 man hours of intensive searching for records in storage on site. In consultation with the AAIHS Diabetes Control Program Officer, it was decided to draw the missing controls for the other 4 cases from the closest Service Unit, which was approximately 130 miles away, in a similarly remote reservation area. Otherwise, with the generous cooperation of the medical records department personnel at each of the Service Units, controls were able to be obtained at each site.

Records as the Data Source.

Because the research questions were answered through data acquired from medical records, a number of observations were made about this data source. Records from other health care facilities were not consistently forwarded, and were often not available in the IHS records. Records of hospitalizations outside of the IHS that were forwarded usually consisted of a one to two page discharge summary that was helpful, but necessarily brief.

Lack of hospital discharge summaries seemed especially prevalent in the case of male veterans who had access to the Veterans Administration (VA) hospitals for health

problems. Although there were record entries that would indicate that a person had been transferred, referred, or had just returned from a VA setting, it was rare that records of any type were available from these hospitalization episodes. It was difficult, therefore, to accurately determine the health care services that veterans were accessing.

Besides veterans, the pattern of health care use was also difficult to ascertain in those over 65 years of age. Under the Medicare Program in the United States, people over the age of 65 years are able to access health care at any hospital or clinic, and a secondary analysis of data from the 1987 SAIAN report has suggested that the use of the IHS system seems to decline after the age of 65 (Ludtke & Pan, 1994).

Because people over the age of 65 years are not soley dependent upon the IHS system for paid health care services, it is unknown how often those over age 65 in this study may have received care elsewhere. As an example, one record in the study indicated that the person had received care at a combination of 5 IHS and private clinics, but records from all of these sites were not available. It was also noted that even when people were seen at different clinics within the AAIHS, records were not always forwarded within the system.

Another variable in terms of medical records was a lack of consistency in the management of medical records departments. At the majority of the Service Units, a very clear mechanism for retrieval of old charts was in place, and the investigator was assisted in accessing the multiple volumes of individual patient records, a number of which went back as far as 30 to 40 years. However, at two of the ten Service Units, access to

complete records proved to be difficult, and at one became impossible (see above section on "Matching Controls").

The format of the clinical entry forms on the charts also created an unwanted element of variability. Until the 1990 implementation of a new computerized charting form that organizes clinical visits into a standard format, the older form yielded inconsistent information. Narrative assessments were mixed with vital signs and lab reports, and were dependent on the style of individual practitioners. In some cases, a consistent style was developed by an individual practitioner, so the progress of a person could be tracked easily. However, frequent changes in physicians providing care at the different Service Units hindered any reliable approach to reviewing the narrative information in the records.

Missing Data for Specific Variables.

The charts of all but one of the identified cases of LEA between 1984 and 1993 were available to the investigator at each of the Service Units, however, there were gaps within records (both cases and controls). It is acknowledged as a limitation of this study that information in the medical records may not be complete.

From the review of the records, it was evident that this population of diabetic persons frequently received care not only from IHS providers, but from non-IHS providers from whom there were no records. It was also evident that people commonly travelled to other states for extended periods of time, and it is reasonable to assume that

they probably accessed care in other health care settings. For obvious reasons of feasibility, data collection was confined to the available records at each Service Unit.

A pilot study at Fort Totten prior to the start of data collection had been indicative of potential problems in collecting data for certain variables, particularly those of "height", "smoking", and "alcohol abuse". Although all the pilot records had contained Hgb A_1C reports, it was not possible to collect Hgb A_1C levels from the vast majority of medical records at the other Service Units. A problem was also found in the records of blood glucose levels, the resolution of which will be discussed below.

Although not specific to the research questions for this study, it was also noted throughout the data collection that variables that were outside the scope of this study, yet pertinent to the topic were routinely missing, for example, laboratory values for cholesterol and triglycerides.

Height.

Height measurements, essential for the calculation of a weight/height index, were found to not be recorded consistently. Of 432 records, heights were missing on 17. Heights were not measured on a regular basis, and it often became necessary to go through older records at length in order to retrieve a height. A new form for charting in the IHS medical records in the AAIHS had been introduced in 1990. These forms are organized to provide special spaces for vital signs, including heights. Hopefully, retrieval of height data will not be as cumbersome in future studies.

The absence of height information in 17 records posed a problem for the calculation of the WT/HT index, and particularly for the logistic regression analysis. In consultation with Dr. Henry Slotnik, statistician for the University of North Dakota School of Medicine, it was decided to impute the missing heights through a multiple regression equation utilizing weight, age, and gender to calculate a value for each of the missing heights. In this way, these records were able to be retained in the logistic regression models and the predictive power of the equation was maximized.

Smoking.

Smoking history was missing in 37 records, and in those in which it was mentioned, very few clinical entries indicated duration of the smoking history. The smoking variable had to primarily be collected from History and Physical forms that were associated with hospital admissions at a date closest to the PL date. Consequently, smoking was collected and entered as a dichotomous categorical variable, that is, as a "yes" or "no".

It is questionable how thoroughly smoking history was explored during the course of a History and Physical Examination associated with hospitalizations. It would seem that a record of smoking behavior would be more informative if collected within the context of the usual care setting, that is, during clinic visits for follow-up care for NIDDM. In terms of the known long-standing associations of smoking with many health problems, it was curious to see the extent of missing data related to this variable. It seems particularly odd that the availability of smoking data was so limited given that an increased

smoking prevalence has been identified as a problem among Plains Indians (Hrabovsky, Welty, Coulehan, 1989).

A chi-square analysis was done to look for differences between cases and controls as to the presence or absence of smoking information on the medical chart. It was found that there was no significant difference between the groups, that is, there did not seem to be a systematic bias as to the presence or absence of smoking information on the record related to the status of case or control (chi-square 0.24, 1 df, $p<0.627$). The results of the smoking analysis on the available data will be discussed below.

Alcohol Use.

Alcohol use as a variable was missing in 52 of the medical records. Retrieval of this variable was conducted in a fashion similar to the smoking variable, that is, often from History and Physical forms associated with hospitalizations. The clinical entries that were made on the medical record outside of the History and Physical forms were sometimes addressed to an immediate situation, such as "ETOH on breath", or simply stated a diagnosis of alcoholism. Again, a chi-square analysis demonstrated no systematic bias between the case and control groups in terms of the frequency of missing data for alcohol use (chi-square 0.01, 1 df, $p<0.916$).

As with the smoking variable, the known associations of alcohol use with many health problems, including motor vehicle injuries, made it seem unusual that this variable was not systematically recorded.

Blood Glucose.

Totally unexpected was the finding that the majority of blood glucose laboratory reports did not specify whether they had been drawn as a fasting or a random specimen. In this study, a total of 1604 individual blood glucose values were collected from clinical laboratory reports. Of these, only 129 values were definitively labelled as "fasting" among the case laboratory reports (8.0%), while 275 were specifically labelled as fasting among the control laboratory reports (17.1%). Random blood glucose values were labelled specifically for 52 values (3.2%) among the cases, and for 94 among the controls (5.9%).

In essence, it is unknown whether the glucose values were fasting or random for approximately two-thirds of the blood glucose values found in the medical records. In some situations it was possible to determine from a clinical entry whether a specimen had been fasting or random, but this was not routinely helpful.

To attempt to address this problem, it was decided to obtain four blood glucose measures from each medical record, and to create a mean glucose score for each individual in the study. It was suggested that although this was not a perfect resolution of this problem, a mean score would result in a more stable reflection of actual glucose status than would a single value.

In order to retain the pertinence of the blood glucose measurement to the development of the PL, a 3 year limit prior to the PL date was set on the period of time during which a blood glucose result had to have been reported. Not all medical records had 4 blood glucose values that met this criterion. However, 82% of the mean glucose scores were able to be created from 4 glucose values that met this criterion, and a total of

92.7% of the mean glucose scores were based on at least 3 or 4 blood glucose reports that were at least a month apart, and were within the three year period prior to the respective PL dates.

Duration of Diabetes.

The variable of "duration of diabetes" can only be estimated through documentation of the age at diagnosis. The diabetic condition very probably had been ongoing for indeterminable periods of time before diagnosis was made in any given person.

Reliability of Clinical Entries.

Medical Diagnosis.

It cannot be known if diagnostic criteria used for medical diagnoses such as "diabetes", "neuropathy" and "peripheral vascular disease" were consistently applied, especially since diagnoses were seen to have been made by a number of different physicians not only between Service Units, but within each of the individual medical records as well. It was clear from the record review, that people not only had physician providers outside of IHS, but that the usual mode of service delivery is by multiple providers within the IHS system.

However, for the purposes of this study, the physician statement of a medical diagnosis was assumed as evidence that a condition existed. Conversely, the absence of the mention of a medical diagnosis was assumed as meaning that the entity did not exist in

an individual's medical history, although this is not known to be a truly valid assumption. It was also assumed that a lack of recognition of a medical condition would not be systematically confined to either the case group or to the control group.

Foot Examination.

In terms of documentation of foot examination, it is possible that during clinic visits physical examination of the diabetic patient may have routinely included the feet, but may not have been specifically recorded. Unrecorded assessments, however, were obviously not available as data. In addition, clinical measures, such as blood pressures which are known to be subject to observer error, were assumed to be accurate and to not be systematically biased by virtue of case or control status.

Adherence to Medical Regimen.

Data related to insulin therapy cannot be assured as reliable. A label of "non-compliance" was frequently seen in the medical records of both cases and controls. It is difficult to know how closely people did or did not follow medical regimen instructions for diet, oral agent, or insulin therapies. Although the following of the medical regimen was not a variable that was systematically studied, at the last data collection site, a record was kept of how many charts had entries that indicated that the patient had not been following the medical regimen that was expected of him/her. Of 89 medical records accessed, 48 (54%) had entries that specifically noted "non-compliance".

The following excerpts, though isolated from the total medical record, are examples of the types of problems that seemed to commonly arise with following the medical regimen:

- "failed all DM clinics";
- "failed to keep appointment";
- "has not refilled medications, should have been out of insulin 3 weeks ago";
- "out of medications early, probably sharing";
- "Poor Compliance";
- "prognosis is poor secondary to his non-compliance";
- "has been on OA's (oral agents) because of non-reliability or non-compliance with using insulin".

At one Service Unit, a rubber stamp was used to leave "DKNA" in large red letters on the medical records to indicate that someone "did not keep appointment". Similarly, at another Service Unit, a rubber stamp left "FAILED APPOINTMENT" in red letters as a record entry. In contrast, there was a dearth of information indicating that follow-up was attempted, or that the reason for the "non-compliance" was sought. Occasionally, entries were seen that attempted to link a reason with the "non-compliant" behavior:

- "non-compliance due to ETOHism";
- "did not take her medication because she was worrying too much";
- "...at times he is too busy to take his insulin.

  Patient warned of consequences of lack of control";

- "Has not taken insulin for 2 days, no syringes";
- "came from jail, drinking since Friday, missed insulin".

Although a reason was cited, an element of judgment seems to reside within each of the above entries, linking the patient's "faulty" behavior to the non-compliance.

Because it was not possible to know with certainty, or to control for the patterns of any given person in adhering to the medical regimen, for purposes of this study a prescription for insulin therapy as part of the ongoing medical regimen was considered as "yes" for insulin use. No evidence of insulin prescription was indicated as "no" in the data analysis.

Beyond posing a problem of reliability for collection of data for the insulin variable, the effects of labelling people with diabetes as "non-compliant" needs to be questioned and studied further. This is important in terms of the influence of the label in biasing subsequent health care providers who provide services for the patient, especially since frequent changes in health care providers were seen in individual records. The sense of fragmentation in the provider-patient relationship communicated throughout the record review is elaborated upon further in the next chapter, within the description of the health care system (p. 70).

Limitation of the Design

As in any retrospectively conducted study, the opportunity to determine causal relationships is weaker than in an experimentally designed study where direct operationalization and manipulation of variables is possible. However, the use of the case-

control design will afford a stronger ability to suggest causal influences of the independent variables on LEA than would otherwise be possible.

The use of chart data does not allow for access to pertinent information related to LEA that may be acquired through interviews and surveys. Also, the more intangible influences of socio-cultural/socio-economic factors on the experience of LEA in a culturally distinct, and economically depressed, rural region cannot be systematically addressed through the design of this study, and will require future research.

CHAPTER IV

THE SETTING

Bronfenbrenner's ecological theory of human development (1979) recognized the impact of a given context upon the human experience:

> The ecology of human development involves the scientific study of the progressive, mutual accommodation between an active, growing human being and the changing properties of the immediate settings in which the developing person lives, as this process is affected by relations between these settings, and by the larger contexts in which the settings are embedded (p.21).

A description of the setting of the study is presented here in an effort to frame the broader contexts in which the phenomena of diabetes and LEA take place. Although many contextual issues are necessarily present in any given setting in which a study is conducted, the following were selected as areas pertinent to this study: (a) geographic realities in reserve settings, (b) population density in reserve settings, (c) demographics of the Native population served by IHS, (d) characteristics of health care service delivery in the IHS, (e) ideologic perspectives of health, and (f) socioeconomic forces.

Geographic Realities of the Setting

The IHS Service Units included in this study provide health services to Sioux tribal members who live on reserves located in remote, rural areas. The exception to this was the inclusion of the Rapid City hospital and clinic which is an urban-based facility housed among a large complex of AAIHS administrative offices. The recognition of the geographic reality of the setting of the study is important to understanding the challenges in the delivery of health care services to this population.

The early prevention of diabetes-related LEA through recognition of risk factors takes on an added dimension of importance when viewed within the context of an environment where routine and/or specialized medical care may be up to 75 miles from one's home community. The 1987 Survey of American Indians and Alaska Natives (SAIAN) reported that those in this population who identified an IHS facility as their usual source of care were nearly twice as likely to travel over 30 minutes to reach it than those who used other sources of health care (Beauregard, Cunningham, & Cornelius, 1991).

Table 6 presents the individual land mass encompassed by each of the reserve areas included in this study, yielding a total of 8483 square miles. Individual reserves in the study ranged from 57 square miles (Yankton Sioux reserve) to 2,782 square miles (Pine Ridge reserve). Few roads are available, allowing limited access to many parts of the reserves. During data collection, it was not uncommon to see dirt or gravel roads that were posted with signs that the road was not maintained.

Travels on remote roads while commuting daily to and from the Service Units during data collection (frequently up to 200 miles per day), yielded an appreciation of the

Table 6

Land Areas and Population Base
of Reserve Communities*

Reserve	Square Miles	Square Kilometers	Population of American Indians	Population Per Square Mile
Devils lake (Dakota)	83.18	(133.92)	2,676	32.2
Cheyenne River	2,181.1	(3511.57)	5,100	2.3
Crow Creek	196.0	(315.56)	1,531	7.8
Lower Brule	203.4	(327.47)	994	4.9
Pine Ridge	2,781.9	(4478.86)	11,182	4.0
Standing Rock	1,323.8	2131.32)	4,870	3.6
Sisseton	164.9	(265.49)	2,821	17.1
Rosebud	1,491.5	2401.31)	8,043	5.4
Yankton	57.1	(91.93)	1,994	35.0

*Rapid City deleted since it is an urban-based setting

natural beauty of the reserve areas, but also of the complexity of delivering health care services in such locations. It would seem that effective community based services would require a fleet of 4 wheel drive vehicles, as well as enough personnel to allow for the travel time required to make even one or two home visits in a day.

In fact, a concern heard from Community Health Representatives (CHR's) was that their responsibilities have been reduced to that of providing transportation. The need to utilize most of their time in the transportation of people to health care facilities was expressed several times as a source of frustration. Transportation duties did not leave time to make home visits and do other tasks for which they have been trained.

Topographic features such as hilly terrain, few and narrow roads, and a total absence of street lighting, could be easily recognized as contributors to motor vehicle injuries as a leading cause of death on reserves (Indian Health Service, 1992). The investigator's experience during data collection of coming upon a pedestrian-vehicle accident approximately 45 miles from the Pine Ridge hospital, vividly depicted the reality of the limited resources for emergency care. Although the pedestrian was not severely injured, it was clear that outcomes for injuries are critically dependent on local resources at hand.

In this case, the accident occurred along the "main" road to the Pine Ridge village, next to a very small community (approximately three rows of housing). It appeared that this community had access to an ambulance, as there was an ambulance on the scene and it was evident that the accident had just happened. It was also surmised that the ambulance

crew were volunteers from the immediate area, as they knew the victim and the onlookers and they were not dressed in paramedic uniforms.

During previous trips to Rapid City, the investigator had shared housing quarters at the "Lakota Lodge" with people from outlying areas of South Dakota who were in training programs to become Emergency Medical Technicians. These were often young people who, in spite of limited resources and educational backgrounds, strived to become "certified" to provide volunteer services to their communities. The experience of actually seeing such community members involved in providing hands-on emergency services in a remote location, reinforced the importance and necessity of community involvement in the provision of health services in rural reserves.

Population Density

In addition to the variation in land mass among the reserves, the population specifically identified as American Indian also varies on each reserve, from 994 at Lower Brule to 11,182 at Pine Ridge (Reddy, 1993). The sparse population density in the Aberdeen Area of IHS is captured in Table 6.

The most densely populated reserves were the Yankton (35 people per square mile), Dakota (32.2 people per square mile), and Sisseton (17.1 per square mile). It is of interest to note, that these were also the reserves that had the three smallest land areas. The Yankton and Sisseton clinics were also located in small towns in South Dakota, rather than directly on reserve land. At the other end of the spectrum, the Cheyenne River Sioux reserve is least populated in terms of the available land mass, with 2.3 people per square

mile. The vastness of the terrain, combined with the sparse population density, conveyed a sense of isolation and detachment that metaphorically could describe the lived reality of Northern Plains Natives as set apart from the mainstream American landscape.

Population Served by the IHS

Of the more than 1.5 million Native Americans in the United States, 96% are American Indians, while the remaining 4% is composed of people of Inuit and Aleut origin (Sievers & Fisher, 1984). Of the total Native American population, nearly 1.2 million are within the "service population" of the Indian Health Service (IHS), that is, those who are eligible for federally funded health care services by virtue of their aboriginal status and residence within the geographic regions for which IHS is responsible (Indian Health Service, 1992).

The ratio of males to females (49.038 to 50.962) in the total service population of IHS is comparable to that of the U.S. all races ratio (48.747 to 51.253), however, in terms of age, the two populations differ significantly (IHS, 1992). Among the IHS Service population, 33% of the people are younger than 15 years of age as compared to 22% in the U.S. all races population; this disparity is further emphasized in the comparison of the 28.9/1000 birth rate of the Native population to the 15.7/1000 birth rate of the U.S. all races population in 1987.

At the other end of the age spectrum, 6% of Native people are older than 64 years compared to 13% in U.S. all races group (Indian Health Service, 1992). However, the age group older than 60 years is the fastest growing age group in the Native American

population (Heath, et. al., 1993). A looming need to expand the usual base of health care services in the IHS to meet the needs of this group was exemplified in a poignant quote taken from a referral form on the medical record of a 78 year old woman with a fractured leg. This was a note to the CHR Office in response to the referral of this woman to the Public Health Nursing Office on a rural reserve:

> "Lack of time prevents us from seeing this patient, Maternal and Child health takes most of our time".

Health Care System

In addition to the rural setting, a unique feature of this study was also its setting within the context of Indian Health Service. The IHS is the Federal agency within the U.S. Department of Health and Human Services which has been charged with serving the health needs of people within recognized tribes. This section of the report discusses aspects of the IHS system as both the primary provider of health care in reserve settings, and as the data source for this study.

IHS Mandate.

The Indian Health Care Improvement Act of 1976 clarified the Federal responsibility for the health of aboriginal peoples in the United States stating:

> The Congress hereby declares that it is the policy of the Nation, in fulfillment of its special responsibilities and legal obligation to the American Indian People, to meet the national goal of providing the highest possible

health status to Indians and to provide existing Indian health services with all resources necessary to effect that policy (Office of Technology Assessment, 1986).

According to all crude health indicators, improvement has occurred steadily in most of the Indian Health Service Areas (IHS) (Rhoades, et. al., 1987; Windom, 1988). For example, the life expectancy at birth for Native Americans has increased from 60.0 years (between 1949 and 1954) to 71.5 years (between 1987-1989). In comparison, the 1988 life expectancy for the United States general population, all races was 74.9 years (Heath, et.al., 1993).

Access to Health Care Services.

A secondary analysis of the 1987 NMES SAIAN revealed that 91.1% of the Native American population have a usual source of health care, with the IHS being reported as the provider in 68.42% of the cases. This analysis included data from both urban and reserve survey participants (Ludtke & Pan, 1994); the percentage claiming IHS as their primary provider may have been higher if data only from the reserve participants were cited.

There are twelve IHS Areas throughout the United States where health care services are provided for American Indian people through an array of health care facilities including: IHS Hospitals, IHS operated Health Centers, Tribally operated Health Centers, and Environmental Health Field Offices. Although there is a segment of the Native population that is urban-based, the circumstances under which they live and access health

care is not directly comparable to those experienced by native people who reside in reserve areas served by IHS. A total of 48 hospitals and 452 outpatient facilities are operated by the IHS and/or the tribes, however, only 34 clinic and community service centers are specifically operated for Native people living in urban locations (IHS, 1992).

Consequently, this study was addressed to the Service Population of Native people who reside in reserve settings. The Service Units in this study were located in North and South Dakota only. The urban-based Rapid City Service Unit, which is attached to a constellation of program and administrative offices for the AAIHS in western South Dakota, is not seen on this map. Of the ten Service Units visited during this study, six had IHS Hospital facilities in addition to outpatient clinic services. The other four had Health Centers which include outpatient services only.

Table 7 and the the map in Appendix I note each of the AAIHS Service Units in this study. Of three Service Units that did not have their own IHS hospital, community hospitals were within 13 miles of one, and within 45 miles of two others. The fourth IHS Health Center was a brand new facility that had recently closed its IHS Hospital. However, it was located directly within the town of Wagner where a community hospital was available.

When hospital services are not available in a given Service Unit, or when the type of care needed is not possible at an IHS hospital, IHS utilizes and maintains "Contract" agreements with other hospital facilities, and payment is then routed through the IHS to these Contract facilities.

Table 7

Type of Health Care Facilities Available at Each Service Unit

Service Unit	State	Type of Facility at Service Unit	Approximate Distance to Nearest Hospital for Service Unit with Health Centers Only
Fort Totten	ND	IHS Health Center	13 miles
Fort Yates	ND	IHS Hospital	--
Sisseton	SD	IHS Hospital	--
Eagle Butte	SD	IHS Hospital	--
Fort Thompson	SD	IHS Health Center	45 miles
Lower Brule	SD	IHS Health Center	40 miles
Wagner	SD	IHS Health Center	Community Hospital in Wagner
Rosebud	SD	IHS Hospital	--
Pine Ridge	SD	IHS Hospital	--
Rapid City	SD	IHS Hospital	--

Discontinuity in Health Care

Frequent changes in physician signatures within each individual medical record were noted, suggesting fragmentation in the follow-up and management of diabetes. On occasion, the name of a health care professional was seen over the course of many years in clinical entries on a medical record, but these long-term providers were almost universally Physician Assistant or Nurse Practitioner providers.

There was one exception to this scenario at the Fort Totten clinic which serves the Dakota Sioux. At the time of this study, this Service Unit had been a designated site for a funded Diabetes Control Program (DCP) for approximately 10 years, and has had the same physician seeing patients for the monthly "Diabetic Clinic" throughout this entire time. The Registered Dietician assigned to the Fort Totten DCP had also worked there since the inception of the program, making this an unusual setting.

Although all of the other Service Units in this study also have a special day set aside for "Diabetic Clinic" each month, they are not designated sites for the DCP, and therefore, are serviced by available professionals on staff in any given month. However, despite the advantage of having permanently designated Diabetic Clinic staff, the 1987-1989 incidence rate of LEA in the AAIHS was higher at Fort Totten as compared to most of the other Service Units in North and South Dakota where this study was conducted (Appendix D).

From anecdotal observation of the medical records, it was concluded that attracting and keeping physicians in the IHS is a difficult proposition. Given the bureaucracy of the Federal government, the lack of adequate resources both within the

IHS and reserve communities, the isolation of rural settings, and the lack of routine preparation during medical education for practice in different sociocultural settings, it is not surprising that maintaining continuity of care through physician providers is problematic in reserve settings. Resolution of this problem is a priority for IHS (Bernie Long, personal communication).

Fragmentation was seen to be an issue in the delivery of pharmacy services also. It was noted that a significant number of people received pharmacy refills of prescription medications for which there was no recent clinical visit. It appeared that in some of these cases, people were going to private practice clinics in communities bordering the reserves, and then were filling their prescriptions through the IHS at no cost. In other cases, sporadic clinical visits were often incongruent with large number of pharmacy refills, and the medical record would reveal emphatic entries from pharmacists stating: "No more refills until seen in the clinic!".

The investigator noted at one Service Unit that one of the pharmacists had been working in the same setting for nearly a decade and had extended his practice to include an ongoing research project of anti-hypertensive medications. However, in another scenario, the investigator had seen a pharmacist at the Fort Thompson Service Unit (Crow Creek), who was then seen again during data collection at 3 other Service Units in South Dakota within a few months time. A lack of physician continuity, coupled with frequent changes in the personnel overseeing the dispensation of medications, bespeaks a system of care that perhaps is adequate for treating acute problems, such as otitis media, but inadequate for the ongoing treatment and management of chronic diseases.

Ideologic Perspectives of Health

The medical literature is relatively extant regarding descriptions of the epidemic prevalence of diabetes among Native people; however, broader contexts of health and societal structures are rarely addressed. A Marxist perspective would question the ability to make improvements in health without changes in the broader social order (Waitzkin, 1978). It is argued here, that the discussion of health issues among Native Americans must take place within broader social and political economic parameters. Otherwise, "social relations contributing to illness ... are in danger of being medicalized and privatized rather than politicized and collectivized" (Scheper-Hughes, 1990, p.192).

It can be argued that a privatized view regarding the genesis of illness is already entrenched in the health care system responsible for Native services through its apparent endorsement of the lifestyle hypothesis, and frequent documentation of "non-compliance". Although it is recognized that Native health is linked to social structures such as education and employment, it was nonetheless stated in an article entitled "The Indian Burden of Illness and Future Health Interventions" (authored by Indian Health Service officials) that Native people need to "use seat belts regularly and control drinking", and to stop smoking (Rhoades, et.al., 1987).

Such a statement may be expected from the "most influential proponent of the lifestyle hypothesis", that is, the United States Department of Health and Human Services, of which IHS is a part (Tesh, 1981, p.375, 379). This approach to illness, as a result of personal failure, provides a bitter political irony, that is, the dominant society which has

systematically destroyed and withheld the social and economic determinants of health from indigenous people, now considers itself "burdened" by their illness.

Unfortunately, the victim-blaming approach represents a typical political attitude that Native people are in need of colonial leadership (LaDuke & Churchill, 1985), and invites simplistic technological and technocratic solutions to extremely complex matters of illness. In reality, illness is "as much a social as a biological product" (Singer, et.al., 1990, p.182). It is therefore imperative that conditions of unsafe housing, plumbing, and heating, poor roads, inadequate nutritional resources, and deculturation stress (Brod, 1975) be figured into the equation of health.

It is also argued here that health professionals are not aware of their complicity in perpetuating political-economic structures. Waitzkin (1978) conceded that "medicine's ideologic features in no way diminish the efforts of individuals who use currently accepted methods in their clinical work and research" (p.270). What also needs to be conceded is that health professionals are products of their own cultural, social, and political environs, and for centuries their education has been grounded in the biological balance of the Cartesian equation. As Engel (1977) suggested, biomedicine has become both the basis for the scientific study of disease, as well as the western cultural perspective or "folk model" about disease.

Socioeconomic Forces

The current status of the health of Native peoples cannot be divorced from three centuries of colonial encroachment upon Native societies. It is difficult to grasp the

pervasiveness of the effects that have permeated the sociocultural and economic structures of aboriginal people since the arrival of Europeans in North America. Despite retaining sovereign status, Native community organization has sustained major disruption through forced relocation, and the destruction of subsistence economies through the wresting of lands accomplished "legally" by federal legislation, as well as by cooptation and expropriation of land and resources by business entities. Native American tribes have lost approximately 97% of their original land base (LaDuke & Churchill, 1985).

A subculture of poverty is created within the larger culture of capitalism when a community's wealth has been diverted into the hands of a few (Lewis, 1970), and in the Native context, into the hands of outsiders. Poverty has, in fact, entrapped many Native tribes. On the two largest reserves included in this study, Pine Ridge and Rosebud, the 1990 unemployment rates were 32.7% and 29.5% respectively (Reddy, 1993), alarming figures in a nation where unemployment rates of over 5% are apt to be considered intolerable by the general populace.

Native American tribes can be characterized politically as within the realm of the "Fourth World", that is, nations who have become colonized within their own sovereign boundaries (O'Neil, 1986). The rapidity with which the interruption of lifeways can lead to the compromised survival of a subsistence based economy was exposed in Shkilnyk's (1985) study of the Objibwa community in Grassy Narrows, who suffered relocation, then mercury contamination of their waterways.

It is difficult to appreciate the magnitude of the impact of an analogous experience on numerous tribal nations, begun simultaneously in the late nineteenth century during the

creation of reserves in the United States. The experience of the Navajo Nation is perhaps a poignant illustration of the rapid deconstruction of lifeways that many Native tribes have undergone in the United States. Among the Navajo, only 4.3% of working age people were described as self-sufficient in 1978, as compared to a 100 % rate of self-sufficiency in 1920 (LaDuke & Churchill, 1985).

Summary

Excepting the Fort Totten experience, it was observed that diabetes, an alarmingly prevalent and chronic disease, was treated much the same as episodic health problems. Perhaps in the past, when acute diseases were the primary causes of morbidity and mortality, it may not have been as important to establish a relationship with a health care provider.

However, if people with diabetes are seen predominantly within an episodic framework, it is inherently problematic to adequately address the parameters of Type 2 diabetes related to its chronicity. The increase in the demographic concentration of older Native Americans, accompanied by a concurrent rise in the incidence of chronic disease, would seem to demand that continuity issues in health care delivery be seriously addressed in this system.

The prominence of the biomedical paradigm appears to assure the continuation of the existing structure of the IHS, as well as the assignment of responsibility for health to individuals rather than societies. The unfortunate outcome is that the effectiveness of clinical intervention for people living with diabetes is seriously hampered. Therefore, it is

argued here that the acquisition of knowledge that spans geographic, demographic, cultural, political, economic, and societal parameters cannot be relegated to the realm of merely "interesting" information. Although attention to the larger contexts of Type 2 diabetes mellitus will not provide a panacea for the elimination and/or control of the diabetes among Native peoples, such knowledge will need to be included in any real attempt to successfully impact the epidemic prevalence of this disease and its complications in Native people.

CHAPTER V

DATA ANALYSIS

The data analysis for this case-control study is described in this section of the report. Following the collection of data from medical records located at each of ten Service Units within the AAIHS, the entire data set was coded and entered into Epi Info, Version 5.0 (Dean, Dean, Burton, & Dicker, 1990), and then imported to NCSS, Version 5.03 (Hintze, 1991). The statistical package "Epi Info" was utilized for a number of descriptive and analytic functions in the data analysis, while the "NCSS" software program was utilized for logistic regression techniques.

Odds Ratios

The 5 specific hypotheses were tested for the level of risk of LEA associated respectively with: smoking, insulin therapy, frequency of foot examinations, level of glycemic control, and Wt/Ht ratio.

Odds ratios were calculated utilizing 2 x 2 contingency tables. The Mantel-Haenszel Chi-square test statistic was then computed to test significance of associations at the .05 level. Confidence limits were established for each independent variable at the 95 per cent level.

Power Analysis

To determine the ability of the odds ratios to detect differences between "exposed" and "unexposed" groups utilizing the proposed sample, power indices were calculated. The power indices were determined on the basis of: (a) 120 cases; (b) using 1 and then 2 controls per case; (c) alpha levels (two-sided) of .05; (d) a minimum odds ratio of 2.0; and (e) a probability of exposure of 0.4 among the controls. It was determined that the utilization of 120 cases with two controls per case, would allow a power of .80 to be attained.

In the actual study presented here, the use of the 144 identified cases that met the case definition, along with 288 controls, fell above the curve for the statistical power necessary to detect differences between the two groups.

Comparison of Means

The Epi-Info program was utilized to calculate means between continuous variables. In this program, F-ratios are reported for two group tests, but the significance is interpreted as it is for the t-test (Dean, et.al., 1990). Also, the Kruskal-Wallis test statistic was generated by the Epi-Info program for testing means that demonstrated unequal variances. Significance was set for this study at the 0.05 level.

Logistic Regression

The logistic regression model has become the statistical model of choice in modern public health research involving a dichotomous dependent variable and a number of

independent variables, both categorical and continuous. The technique allows the estimation of coefficients and probabilities that an outcome will occur (Hosmer, Taber, Lemeshow, 1991). In this type of regression, a logistic transformation is utilized to "transform the sigmoidal risk/exposure curve into a much simpler linear relationship...the logistic regression model predicts the log odds of disease" (Hassard, unpublished manuscript, p.85).

It has been recommended that minimizing the number of variables in the logistic regression model will stabilize the model numerically, and will make it more easily generalized. Inclusion of irrelevant variables can lead to "overfitting" of the model and numerically unstable estimates (Hosmer and Lemeshow, 1989).

Decisions regarding the independent variables that were entered into the multiple logistic regression equation were informed by the interpretation of the odds ratios and resultant Chi-square tests. However, the choice of regression variables predominantly relied upon a judgment of clinical relevancy with reference to the Causal Pathways to LEA model. Maximum likelihood estimation, with corresponding confidence limits, was utilized to estimate the logistic model parameters (Hassard, unpublished manuscript).

Assessment of Fit

The appropriateness of a model is determined by how well it fits the observed data (Hosmer, Taber, Lemeshow, 1991). Validation of the regression model is particularly important when used to predict outcomes for future subjects (Hosmer & Lemeshow, 1989, p.171). This is pertinent to the results of this study which hopefully will be utilized

for designing further research and prevention programs. As is described in the Results section (p.106), a cross-validation of the logistic regression model was undertaken. In a sense, cross-validation provides a method to determine the "specificity and sensitivity" of the regression model to predict LEA (Dr. Henry Slotnik, personal communication).

Limitations of the Logistic Regression Model

Any regression model is only reflective of those variables that have been entered into the equation. Results that may appear strongly predictive of LEA need to be evaluated in light of the possiblity that LEA could be more strongly associated with other variables if they were known and studied. It is also necessary to evaluate the biologic plausibility of the regression coefficients (Hosmer & Lemeshow, 1989). The investigator has attempted to minimize this possibility as much as possible through a thorough review of the literature related to diabetes in Native Americans and to those variables that comprise the Causal Pathway to LEA model.

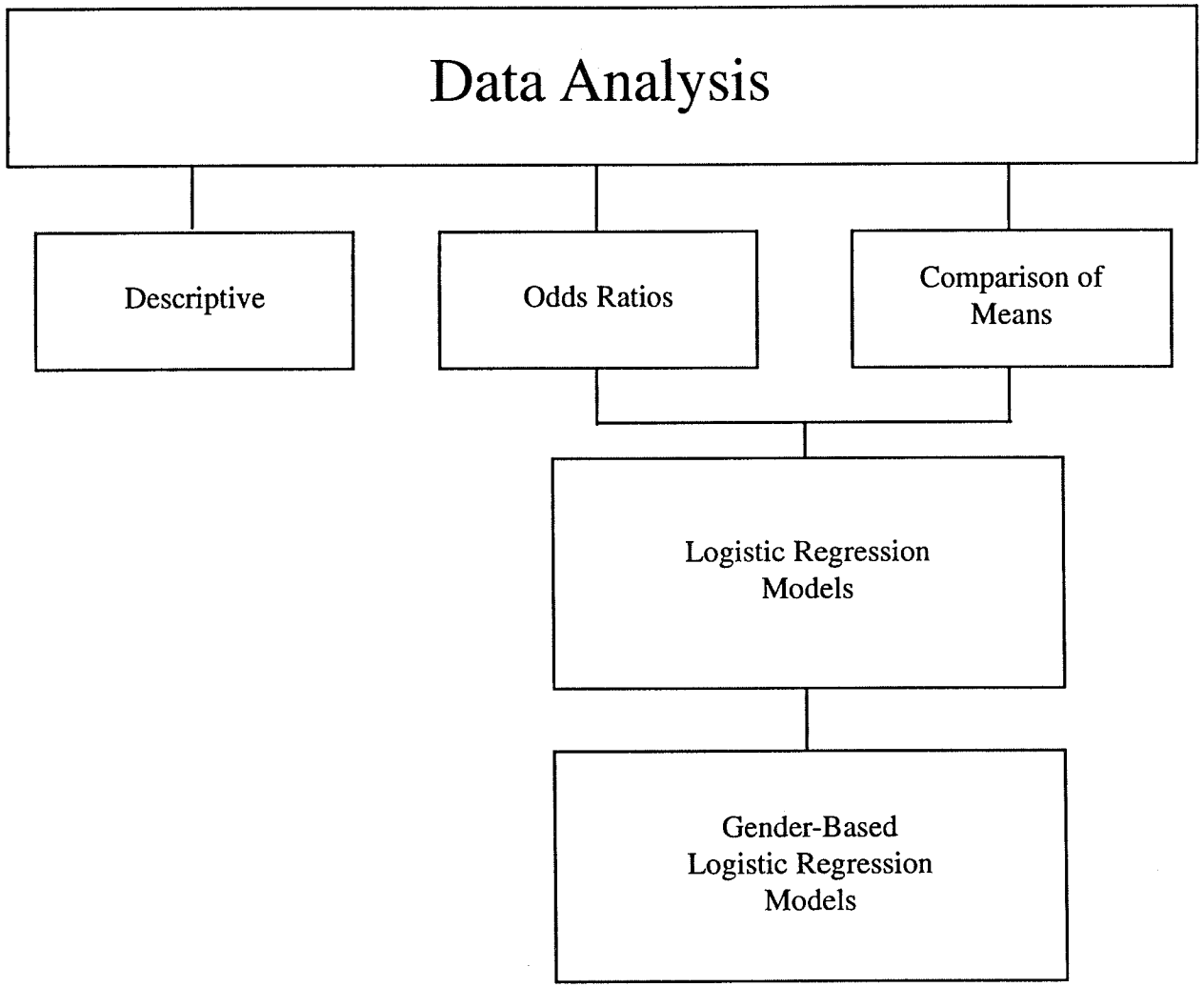
CHAPTER VI

RESULTS AND DISCUSSION

In this portion of the report, the statistical findings from the study will be reported and discussed as related to risk factors for LEA. The Epi Info program was utilized to generate the following analyses: (a) descriptive statistics, (b) odds ratios with 95% confidence limits for selected potential risk factors, and (c) Mantel-Haenszel Chi-square values to test the significance of the odds ratio results. The NCSS program was utilized to carry out multivariate logistic regression analyses, utilizing the stepwise option. The logistic regression techniques were utilized for the generation and testing of models predictive for the development of LEA as a complication of Type II diabetes mellitus in the Sioux Nation.

The Results and Discussion are addressed in the following order: (a) descriptive findings, (b) results of odds ratios, (c) identification of risk factors that emerged from the logistic regression modelling, and (d) consideration of gender influences in the identification of risk factors for LEA (Figure 3).

Figure 3
Data Analysis



Descriptive Analysis

Service Units Included in the Study.

All cases and controls for this study were drawn from ten Service Units in the Aberdeen Area of Indian Health Service which serve a predominantly Sioux population. The percentage of cases derived from each of the Service Units is presented in Table 8.

Age/Gender/Duration.

The total sample for this study consisted of 432 medical records, 144 of which met the case definition of people with Type II diabetes who had undergone a non-traumatic LEA within the time frame of 1984-1993. The other 288 records were of people with Type II diabetes who served as controls for the identified cases. The cases and controls were matched for sex and age within five years. A total of 174 males and 257 females were included in the study. The mean ages for cases and controls by gender are presented in Table 9. The mean age of the cases in this study was 58.39 years (standard deviation 12.87 years). Although there was no significant difference in age between cases and controls due to the matching procedure, a difference in age between male cases and female cases was found, with males being significantly younger than females. The mean age of the male cases was 54.2 years as compared to the mean age of the female cases of 61.0 years ($p<0.003$) (Table 10).

Another significant difference between the sexes was found in the duration of diabetes, that is, the time between diagnosis of Type II diabetes mellitus and the date of onset of the precipitating lesion (PL) that led to amputation. In addition to being

Table 8

Percentage of LEA Cases at Each Service Unit

Service Unit	Number of Cases	Percent of All Cases (N=144)
Fort Totten	9	6.3%
Fort Yates	19	13.2%
Fort Thompson	22	15.3%
Lower Brule	1	0.7%
Crow Creek	12	8.3%
Sisseton/Wahpeton	7	4.9%
Eagle Butte	17	11.8%
Pine Ridge	30	20.8%
*Rapid City	11	7.6%
Rosebud	16	11.1%

*Urban-based service unit

Table 9

Ages of LEA Cases and Controls by Gender

	Cases			Controls		
	Total	Male	Female	Total	Male	Female
n	144	58	86	287*	116	171
Mean (years)	58.39	54.52	61.0	58.02	54.13	60.66
Range (years)	32-92	32-83	35-92	26-86	26-86	35-84
Standard Deviation (years)	12.87	12.26	12.69	12.54	12.88	11.61

* Age was not available for one control

Table 10

Comparison of Age by Gender in Cases of LEA

	Mean Age (years)	F-value*	P value
Male (n=58)	54.52	9.298	<0.0031
Female (n=86)	61.0		

*Epi-Info program reports F-values rather than t-value. Significance is interpreted as for results of t-test. (Dean, et al., 1989)

significantly younger at the time of amputation, the males who had undergone LEA had also been diagnosed with Type II diabetes for a significantly shorter period of time. The mean number of years between the diagnosis of NIDDM and the onset of the PL was 11.9 years for males versus 14.8 years for females ($p<0.011$).

This finding may be clinically useful in recognizing that males with diabetes are prone to the development of this serious complication at a younger age, despite having been diagnosed with diabetes for significantly shorter periods of time than females. Treatment and clinical management could be directed to the prevention of LEA among males who do not fit the expected risk profile of increased age and longer duration of diabetes.

Type of LEA.

The definition for LEA in this study was a first-time amputation. Overall, a toe was most frequently the site of amputation (49.3%), while multiple toes amputated at the same surgery accounted for 9.7% of the LEA's. Below the knee (BK) amputations were carried out in 25% of the cases, above the knee (AK) in 8.3% of the cases, and bilateral amputations in 4.2% (Table 11). Amputations were done on a right lower extremity in 54.2% of the cases and on a left lower extremity in 41.5%.

Circumstances Associated with Development of the PL.

Each of the case records was examined for historical evidence of the circumstances surrounding the development of the PL that eventually led to the necessity for an LEA.

Table 11

Location of LEA

Location	n	Percent
Toe	71	49.3
Multiple Toes	14	9.7
Below Knee	36	25.0
Above Knee	12	8.3
Combination	6	4.1
Unknown	5	3.5

Cellulitis, osteomyelitis, and gangrene were cited either alone, or in combination as preceding the LEA in 63.2% of the cases. In the remaining 36.8%, these clinical conditions were not specifically documented.

The presence of a non-healing ulcer was most often recorded (33.1%), and was mentioned in association with another circumstance in 14% of the cases. A variety of circumstances surrounding the development of the precipitating lesion (PL) were documented (Table 12). However, evidence of the cause of the initial lesion or the formation of an ulcer was not consistently available in many of the medical records. In 53 of the cases (36.8%), no information as to the development of the PL was available.

The mean time measured between the clinical documentation of the PL and the actual LEA was 14.1 weeks, with a range of 1-163 weeks. However, in nearly half of the cases (45.9%), the time period between the first recorded presence of the PL and the subsequent LEA was four weeks or less. Additionally, in 40 (27.8%) of the cases, the LEA followed the clinical identification of the PL within one week or less (Table 13). Therefore, the median value of 6 weeks may be a more meaningful value than the mean for understanding the close proximity of the PL dates to the LEA dates.

In contrast, it should be noted that in one unusual case, there was an unique situation where the initial event of a motor vehicle accident caused an ongoing and longstanding tibial osteomyelitis of nearly fourteen years duration prior to the LEA.

Although the evidence surrounding the development of a lesion was not consistently recorded in the medical records, the categories constructed in Table 12 demonstrate the variety of circumstances that present serious risks to the person with

Table 12
Circumstances Related to The Development of the Precipitating Lesion Prior to LEA

Circumstance	Frequency in total number of cases	Percent *	Frequency in male cases	Frequency in female cases
Shoe Trauma	6	4.2%	1	5
Puncture	7	4.9%	4	3
Cut/Laceration	6	4.2%	3	3
Ingrown Toenail	5	3.5%	1	4
Blunt Trauma	11	7.7%	3	8
Thermal Injury-Heat	3	2.1%	2	1
Thermal Injury-Cold	4	2.8%	3	1
Fungal Infection	3	2.1%	1	2
Vascular Occlusion	4	2.8%	3	1
Lower Extremity Fracture	5	3.5%	1	4
Callous	9	6.3%	2	7
Non-Healing Ulcer	47	33.1%	16	31
Unknown	53	36.8%	19	34

*Greater than 100%: Includes where non-healing ulcer was recorded in conjunction with another circumstance

Table 13

Time Period (in weeks) Between Clinical Documentation of the PL and The Actual LEA Date

Range 1-163 weeks

*Median = 6 weeks

Number of Weeks	Frequency	Percent
1	40	27.8%
2-4	26	18.1%
5-20	44	30.5%
21-52	16	11.1%
>52	10	6.9%
Unknown	8	5.5%

*Based on available data

diabetes just in the course of daily living, for example, in situations as mundane as wearing a new pair of shoes. Anecdotal entries were informative where they were available, and in fact may be of tremendous assistance in developing pertinent educational programming for the prevention of LEA.

A description of several situations may serve to provide an appreciation of the interplay of circumstances which transpire in the course of daily living, yet which threaten serious injury to the person with diabetes. In one case, a fall led to abrasions to a woman's lower extremities. The lesions became infected and gangrenous, necessitating a BK amputation within a month's time. Additionally, the fall was related to a right hemiparesis from a CVA the woman had sustained only seven years after being diagnosed with diabetes.

In another scenario, a woman merely dropped a songbook on her foot during a church service. However, the injury induced a cellulitis and led to an amputation of a toe within two and a half weeks. This woman also had diabetic nephropathy that required dialysis. Another woman, who also had nephropathy, had also undergone toe amputation as a result of a similar injury. In this case, a frozen chicken was dropped on her foot. It may be possible that the mechanism of peripheral neuropathy was a contributing risk factor for these injuries, that is, the ability to hold onto objects was impaired by the same underlying mechanism that impairs sensation in the lower extremities.

In another record entry, a man presented at a clinic setting having no knowledge of a nail which was embedded in the plantar surface of his foot. Another man sustained a thermal injury when he stepped on hot coals in a Sweat Lodge ceremony. In yet another

case, a woman had a tack in her shoe of which she was unaware due to neuropathy and associated PVD. Within three weeks, she had undergone an amputation of the foot, and within seven weeks of the injury by the tack had undergone a BK amputation.

All of the above scenarios may be explained as sharing underlying mechanisms of neuropathy and vascular compromise associated with diabetes. In each case, a loss of sensation can be linked to the initial injury. The rapid progression of relatively minor lesions to loss of a toe or limb likely was facilitated by diminished circulation, and a decreased ability for healing, thereby creating a medium for infection. Even with medical care and the surgical removal of infection (gangrene), vascular compromise cannot always be compensated, as seen in the situation where initial amputation of a foot led to a BK amputation a month later. Though but a few, these cases succinctly portray the serious potential for injury that is clearly present in real life scenarios for the person with diabetes.

Odds Ratios for Categorical Variables.

The resulting odds ratios derived from the comparison of cases and controls on the categorical variables are included in Table 14, accompanied by their respective 95% confidence limits and Chi-Square values. Selected variables will be discussed immediately below.

Smoking.

Although smoking history was highly prevalent in the entire sample (60.6%), there was no statistical difference in either past or current smoking history between cases and

Table 14

Odds Ratios* Comparing LEA Cases and Controls on Selected Categorical Variables

Variable Positive Past History	Total N*	OR	95% Confidence Limits	Mantel-Haenszel Chi-Sqare	p-values
Smoking	(n=395)	0.94	0.59 - 1.50	0.08	NS
Alcohol Use	(n=380)	1.28	0.81 - 2.01	1.26	NS
Insulin Therapy	(n=430)	4.60	2.81 - 7.57	44.74	$p < .0000$
Oral Agent Therapy	(n=429)	0.79	0.48 - 1.33	0.89	NS
Hypertension	(n=431)	1.21	0.79 - 1.85	0.84	NS
Angina	(n=431)	1.83	1.16 - 2.88	7.80	$p < .005$
Myocardial Infarction	(n=431)	1.55	0.88 - 2.75	2.65	NS
Congestive Heart Failure	(n=432)	3.20	1.92 - 5.34	23.75	$p < .0000$
CVA/TIA	(n=431)	2.58	1.26 - 5.31	8.24	$p < .004$
PVD	(n=432)	15.71	7.30 - 34.69	83.01	$p < .0000$
Retinopathy	(n=432)	4.97	3.06 - 8.09	51.41	$p < .0000$
Lower Extremity Lesions	(n=432)	4.14	2.64 - 6.51	45.56	$p < .0000$
Claudication	(n=430)	2.33	0.89 - 6.16	3.74	NS
Neuropathy	(n=431)	10.00	6.05 - 16.60	105.12	$p < .0000$

*Odds ratios refer to the risk of LEA among individuals with a positive history compared to those without such a history.

controls. Smoking has been documented as a risk factor for the development of insulin resistance and macrovascular disease which predispose the diabetic limb to amputation (Attvall, Fowelin, Lager, Van Schenck, & Smith, 1993; Most & Sinnock, 1983; Kannel & McGee, 1985; Palumbo, 1984). However, a case-control study reported by Reiber, Pecoraro, and Koepsell (1992) had also found that smoking was not a statistically significant risk factor for LEA.

Based solely on the evidence from this study, it does not seem valid to minimize the threat posed by smoking in the Causal Pathways to LEA. It may be possible that a shared risk exists for both cases and controls of the interaction of diabetes and smoking in the development of macrovascular complications of diabetes, including peripheral vascular and cardiovascular diseases (Mulhauser, 1994; Welty, 1994; Acton, Rith-Najarian, & Gohdes, 1993; Young, 1990; Delbridge, Appleberg, & Reeve, 1983).

In this study, peripheral vascular disease (PVD) (which will be discussed with the results of the logistic modelling) was a powerful predictor for LEA. Since smoking is so highly prevalent, it may be justifiable to hypothesize that the development of PVD is related to this prevalence, and thus impacts the prevalence of LEA.

The prevalence of smoking across this sample is of interest. The overall prevalence of 60.6% (cases and controls combined) possibly could account for the inability of smoking history to be a predictor, since controls were as likely to smoke as cases.

This finding is in sharp contrast to the Pima study where smoking also did not emerge as a risk factor for LEA, but which was explained by the low prevalence of

smoking, where only 0.5% to 1.2% of 1110 subjects reported smoking more than one pack of cigarettes a day.

Prevalence rates of smoking have previously been reported among the Plains Indians as exceeding 50% (Welty & Coulehan, 1994). It is possible that the prevalence rate may have been even higher in the Sioux sample, had the medical records consistently contained the information on smoking history.

However, an alternative view of the lack of a significant difference between cases and controls on the basis of smoking needs to be considered. In this study, smoking history was not available at all for 8.6% of the sample. Additionally, of the 395 charts that did contain smoking history, only half (48.15%) contained information regarding the duration of smoking. Despite the limitations in the data, a comparison of mean "duration of smoking" in years was done on the data that was available from these records. No significant difference was found between cases and controls on duration of smoking.

Given the evident flaws in the lack of a systematic collection of smoking history during clinical encounters, it is entirely possible that the data base was simply not reliable enough to sustain a meaningful analysis. The smoking data in the medical records was similarly unattainable from both the case and control records, and as stated above, less than 50% of the records indicated the "duration of smoking". Therefore, it may have not been supportable to even attempt an analysis without the availability of better quality data.

Also, the presence or absence of smoking was primarily extracted from History and Physical examinations (H&P) related to hospitalizations, a situation which normally involves a limited encounter with a physician who is often not the usual health care

provider for an individual patient. Given the acute nature of hospitalization episodes, the accurate collection of smoking data may also not be a priority at the time of the H&P, further questioning the reliability of the data that was collected on smoking history for this study.

One final alternative explanation for the outcome of the smoking data analysis may be that smoking patterns are different in the Native culture as compared to those in the general population. Perhaps a number of those who stated that they smoke, use tobacco primarily in the context of ritual, rather than in an abusive fashion, since tobacco use has traditionally been part of sacred ceremony among the Sioux (Powers, 1977).

Since no solid conclusion can be drawn from the smoking data available in this study, intensive investigation of this link in the Causal Pathways to LEA would be a recommended area for further study in this population. This recommendation would necessarily need to be accompanied by implementation of a policy of systematic documentation of smoking history and patterns of tobacco use throughout the clinical settings of the AAIHS. At this time, given the known scientific evidence regarding the negative relationship of smoking to negative health outcomes, the investigation of effective smoking prevention and intervention modalities would seem to be of additional benefit in this population.

Alcohol.

There was no statistically significant difference in alcohol use history between cases and controls. Alcohol use was unambiguously documented in 29.3% of the entire sample in direct terms of "history of alcoholism" or "alcohol abuse". In another 17.8% of the sample alcoholism or alcohol abuse was not explicitly stated, but some extent of alcohol use was inferred in entries such as "quit in 1981" when referring to alcohol history on a History and Physical form. Chart entries that stated that alcohol was used "little" or "rarely" were not entered as positive for alcohol use.

As with the smoking data, despite the lack of a significant difference between cases and controls, it would appear that the prevalence of alcohol use may be of significance. However, important questions remain regarding the reliability of the data base for this variable. From the perspective of reliability, the poor quality of data that was available for the documentation of alcoholism, and the absence of data regarding actual patterns of alcohol use in terms of duration and quantity, does not allow a conclusion regarding the influence of alcohol in the progression to LEA.

Despite the questions related to reliability, it may be conjectured that alcohol use contributes to neuropathy, a major predictor for LEA found in this study. Alcohol has long been known to be implicated in the etiology of neuropathy, and thus may contribute to LEA through its exacerbation. Tattersall & Allison (1994) did not find alcohol to be a significant risk factor for peripheral neuropathy, however, they had studied newly diagnosed diabetic patients, so duration could have exerted a confounding influence on

this finding. In contrast, Young, Veves, & Boulton (1993) did identify alcohol as a risk factor for LEA.

Even if alcohol were not a direct influence along the Causal Pathways to LEA, it may indirectly exacerbate the loss of sensory perception that is needed to be vigilant against injury when diabetic neuropathy exists. Anecdotally, such a danger was poignantly demonstrated in one of the medical records where a bilateral LEA was preceded by a person's ingestion of alcohol and falling asleep in a poorly heated house, resulting in frostbite.

This scenario is also illustrative of the complexity of addressing problems of Native Americans living with diabetes in rural reserve settings. In this situation, the neuropathic risk is seen compounded by the reality of the reservation setting where a wood stove provided the only source of heat in this particular home during the winter months.

Medical History Variables.

In addition to the smoking and alcohol variables, data related to the presence or absence of specific medical diagnoses on the medical record were also compared between cases and controls. Odds ratios, with associated confidence limits and Chi-square values for these variables are also presented in Table 14. Very few data were missing among these variable entries since the lack of a medical diagnosis was judged as the absence of an entity; however, it cannot be known if standard criteria were followed by every physician making medical diagnoses.

Macrovascular Conditions.

Among medical conditions which were noted as either "present" or "absent" prior to the PL date, the following were found to demonstrate statistically significant odds ratios between diabetic cases that were positive for the condition and controls who were not positive: (a) angina, (b) congestive heart failure, (c) cerebrovascular accident (CVA) or transient ischemic attack (TIA), and (d) peripheral vascular disease (PVD). Given the known associations between macrovascular complications and diabetes (Janka, Standl, & Mehnert, 1980; West, 1983; Palumbo, 1984; Young, 1990; Ginsberg, 1991), these findings would be expected. Although an indirect result of atherogenesis, congestive heart failure is most probably associated with edema which interferes with perfusion of the lower extremities and compromises the integrity of the skin.

A history of myocardial infarction had a non-significant odds ratio of 1.55, despite the significance level for angina. Claudication also was not found significant, and was only specifically diagnosed in 21 of the 432 charts, the lowest prevalence of any of the medical conditions on which data was collected. This would appear to be a rather low prevalence of a lower extremity vascular condition among a population at risk for LEA. This seems especially unusual given the odds ratio for PVD of 15.71, an underlying basis for claudication.

An odds ratio of 1.21 for history of hypertension was also found to be non-significant between cases and controls. However, as with the smoking and alcohol variables, the 50.23% prevalence of a history of hypertension across the sample would seem in itself to be an important finding, especially in terms of the rising incidence of

cardiovascular disease in the Aberdeen Area of Indian Health Service (Welty, 1994). However, it should be noted, that the mean systolic and diastolic blood pressures collected from the records were within normal range for both cases and controls.

Microvascular Conditions.

Two highly significant findings in this study appear to underline the microvascular component of the pathophysiology of diabetic complications, including LEA: (a) all of the 28 medical records in which dialysis was documented were case records (constituting 19.4% of the case sample), and (b) the odds ratio for retinopathy was 4.97 (95% confidence limits 3.06-8.09).

Although retinopathy is not in the direct causal pathway to LEA, it has been cited as strongly associated with LEA in several studies (Nelson, et.al., 1988; Reiber, et. al., 1992; Walters, Gatling, Mullee, & Hill, 1992; Lee, et.al., 1993; Gavin, Stess, & Goldstone, 1993; Tattersall & Allison, 1994). In fact, based on a Centers for Disease Control study of LEA in the Cherokee, a foot assessment program was begun in the Retinopathy Clinic at Cherokee, NC to screen for foot problems among the patients presenting for diabetic eye exams (Farrell & Kingsley, 1988). The presence of retinopathy, and associated visual impairment, also has the potential of interfering with the self-assessment skills that are needed in foot care activities (Young, et.al., 1993).

Triopathy.

Nephropathy and neuropathy have also been associated with LEA in other Native American populations (Lee, et.al., 1993; Nelson, et.al., 1988). In the present study, neuropathy was a highly predictive finding in the comparison of cases to controls, with an odds ratio of 15.71 (95% confidence limits 7.30-34.69). The shared underlying pathophysiology of nephropathy, retinopathy, and neuropathy is suspected as being microvascular in nature (Siperstein, 1988; Greene, 1988). The interrelatedness of these variables, therefore, may be useful as interrelated markers of risk that can alert clinicians to the potential for LEA.

The application of this information in a clinical setting may lead to measures such as the earlier provision of intensive foot care education and monitoring in someone diagnosed with retinopathy or persistent proteinuria, even if no immediate problem with a neuropathic foot is presented. Waiting until a problem does arise with a neuropathic foot lesion, delaying implementation of appropriate foot care, greatly increases risk for LEA. The history of the presence of a lower extremity lesion at any point in time prior to, but not including, the development of the PL, yielded an odds ratio between cases and controls of 4.14 (95% confidence limits 2.64-6.51).

Comparison of Means for Continuous Variables

Variables in the study which were of a continuous nature (interval-ratio level data) included: (a) Weight/Height ratio (pounds/inches), (b) number of foot exams recorded within a year preceding the PL, (c) systolic blood pressure (mm Hg), (d) diastolic blood

pressure (mm Hg), (e) blood glucose values (mg/dl), and (f) duration of diabetes (years since diagnosis). The comparison of means as obtained from the Epi Info analysis is presented in Table 15, including the Kruskal-Wallis statistic for non-normal distributions.

The difference in the means of each of these variables was found to be significant between cases and controls; however, not all were in the predicted direction.
Only the hypotheses relating LEA to blood pressure, and blood glucose were supported in the expected direction, that is, cases having higher mean measures than controls. However, the difference between the case and control mean blood pressures was only 2 mm Hg for both the systolic and diastolic measures, which would not be clinically relevant.

In contrast, despite the significant difference in the blood glucose levels, the mean of 220.7 mg/dl for the control group would be considered quite elevated from a clinical perspective. The role of hyperglycemia has been implicated in the Diabetes Control and Complications Trial (DCCT) as the major cause of microvascular disease, contributing to the mechanism underlying neuropathy, retinopathy, and renal disease (Diabetes Control and Complications Trial Research Group, 1993). Therefore, although the blood glucose levels for controls were lower than the cases, it would appear that those in the control group remain at risk for a variety of diabetic complications.

Table 15

Comparison of Means for LEA Cases and Controls on Continuous Variables

Variable	Case n	Case mean	Case SD	Control n	Control mean	Control SD	t-value * F-ratio Kruskal-Wallis	p<
Wt/Ht ratio** (pounds/inches)	134	2.687	(0.5785)	280	2.896	(0.5204)	3.678 t-value	0.002
Foot Exams within year	135	3.437	(2.924)	287	2.213	(2.924)	12.266 Kruskal-Wallis	0.0004
Systolic BP (mm Hg)	144	135.368	(15.381)	287	133.512	(15.381)	1.316 Kruskal-Wallis	0.0251
Diastolic BP (mm Hg)	143	76.056	(9.301)	287	78.338	(8.606)	6.386 F-ratio	0.0114
Blood Glucose (mg/dl)	143	242.734	(6.768)	287	220.731	(67.828)	-2.6298 t-value	0.0085
Duration Diabetes (years)	143	13.643	(6.768)	287	8.244	(6.546)	63.478 F-ratio	0.0000

*t-values from NCSS program
F-ratios from Epi-Info program
Kruskal-Wallis from Epi-Info program
**pounds/inches

WT/HT Ratio.

Another unexpected finding in this study was a relationship between LEA and WT/HT ratio which was the inverse of what had been predicted. The results demonstrated a significant difference in WT/HT between cases and controls, but the mean WT/HT of the control group was greater than that of the case group. Increased body mass index is a known risk factor for Type II diabetes mellitus (Lillioja, 1987; Young, 1990, 1993; Muneta, Newman, Wetterall, & Stevenson, 1993; Shaten, Smith, Kuller, & Neaton, 1993).

Perhaps an assumption that a risk factor for a disease was also a risk factor for a complication of that disease was unfounded. However, it is more likely that WT/HT is associated with another risk factor for LEA, such as the loss of body mass that occurs with aging. In support of this speculation, an Italian study of Type 2 diabetes in a population of 1,947 elderly people found a higher prevalence of diabetes among older people with a "low degree of obesity" (Pagano, Bargero, Vuolo, & Bruno, 1993).

It is also possible that a lower body mass may be associated with other serious illness such as end-stage renal disease. In support of this speculation, the 28 people who had a positive history for hemodialysis constituted 19.4% of the population of cases. The relationship of body mass to LEA remains an area that invites further investigation.

Duration of Diabetes.

Another unexpected finding among the comparison of means was the shorter time that males were diagnosed with NIDDM as compared to females. Duration has frequently been documented as a risk factor for LEA (Walters, et.al., 1992; Connell, et.al., 1991; Nelson, et.al., 1988; Young, McIntyre, Dooley, & Rodriguez, 1985). There is an inherent logic to the significance of duration as a variable associated with LEA, in that people would be expected to have more difficulty with diabetic complications the longer they have had diabetes.

The finding that male cases had a shorter mean duration of Type 2 diabetes mellitus than females suggests that males may be more susceptible to this complication of diabetes. Alternatively, it is possible that males have different patterns of seeking health care, and consequently are diagnosed later in the evolution of the disease. In fact, among the cases of LEA in this study were those in which the lower extremity was amputated in the same year that the diagnosis of diabetes had been made.

Related to the situation in which diabetes remains undiagnosed for a period of time, Gregory, Tattersall, & Allison (1994) reported a case-control study of 68 newly diagnosed diabetic patients, who presented with peripheral neuropathy at the time of diagnosis. Among this group it was reported that 20 of them also had retinopathy at the time of diagnosis, and 10 of the 20 retinopathies were sight-threatening. Given this information and the above finding of a shorter mean duration of diabetes among males in the present study of LEA, it may be important to recognize that diagnosis dates can be misleading in terms of the actual duration of Type 2 diabetes. It is also possible that

duration between males and females differs in relation to patterns of care for foot lesions, such as seeking early intervention or in actively pursuing follow-up care for lower extremity lesions.

Life circumstances may also be significantly different between males and females who undergo LEA. Reiber, et.al. (1992) reported that variables of "social connectedness", such as marital status, contact with friends and relatives, membership in church and/or other community groups were found to have odds ratios for LEA that ranged from 2.0 to 3.8, with significant confidence limits. Related to this finding, Murdock and Schwartz (1978) had reported that family structure was important to the access and provision of health care services to elderly Native Americans in the reservation setting.

This realm of study would certainly represent an abrupt change of venue from the realm of physiologic risk factors that are usually investigated for prediction of LEA. Nonetheless, "social connectedness" may prove a productive avenue of inquiry in the prevention of LEA, particularly if in the future, these variables were studied within the social and cultural context of Native American peoples.

Foot Exams.

Foot exams were done more frequently among the cases in this study than in the control group. It had been hypothesized that more frequent foot examination would lead to earlier detection of foot problems, earlier intervention for lesions and infections, and fewer LEA's. Instead, what the study findings suggested was an increased concern for the

foot as it neared serious compromise, rather than being a focus of preventive concerns. Although not collected systematically during the study, record entries about foot care education were virtually non-existent. In contrast, it was observed that dietary notations and references were ubiquitous in the medical records.

It also needs to be noted that the foot exam data for a large portion of the sample was extracted from the "Diabetic Flow Sheet" that was on each person's chart. The extent of the description for the foot examination many times was a check mark or an "ok" in the box on the flow sheet that had been delegated for indicating that a foot exam had been done at a visit to diabetic clinic. The criteria for placing the checkmark, or the actual thoroughness of the exam was not evident, however, and may have been subject to variation with each examiner.

It is of concern that 45.9% of the LEA's in this study took place within 4 weeks of a clinical notation of the PL, and that podiatric referral appeared to be made very infrequently. This would suggest that either people with diabetes are not knowledgeable about the serious potential of LEA, or that examinations are not routine and/or thorough. It also points out an opportunity to improve foot care through the development of a referral network that routinely includes podiatry.

A policy for the prevention of LEA that systematically incorporates the Causal Pathways model could prove quite useful in forcing an integration of the knowledge of physiologic risk factors with the more pragmatic aspects of diabetic education and clinical management in the care of diabetic feet. A team approach has been recommended as an integral component of successful foot programming including physicians, podiatrists,

nurses, and physical therapists (Acton, Rith-Najarian, & Gohdes, 1993; Gavin, Stess, & Goldstone, 1993; Apelqvist, Ragnarson-Tennvall, Persson, & Larsson, 1994).

Logistic Regression Modelling

As cited above, significance was established for a number of categorical and continuous variables in the development of clinical conditions leading to lower extremity amputation. The clinical application of this information for prevention purposes may be difficult, however, given the unlikely event that any of the study variables would occur as isolated risk factors in a true clinical situation. In order to establish the most likely risk factors for LEA in this population, while untangling the effects of multiple simultaneous influences, a stepwise logistic regression approach was selected to develop a prediction model (Hassard, unpublished manuscript).

Steps in Creating the Logistic Regression Equations.

The purpose of the logistic regression modelling process was to create an equation that would identify risk factors that would be useful in the prediction of LEA. It was also desired to validate the variables in the logistic regression equation, therefore, the modelling process included a cross-validation technique. The analysis originally proceeded in five steps: (**a**) utilization of the entire data set to generate a regression equation based on the entire number of cases and controls, (**b**) separation of the entire sample through random selection of the cases and their respective controls into two groups (Group I and Group II), (**c**) generation of two logistic regression models, one from

each of the randomly selected groups, and (**d**) a test of each of the models generated from the two randomly selected groups, that is, the model created from Group I data was used to predict LEA outcome in Group II; conversely, the model created from Group II data was used to predict LEA outcome in Group I.

Choice of Variables.

It was decided to utilize the results of the odds ratios and comparisons of means and to utilize the CPLEA framework in choosing the variables to be entered into the stepwise logistic regression equation. As previously stated, the CPLEA model offers an integrated view of the interrelationship of known biomedical risk factors in the creation of pathophysiologic conditions necessitating LEA.

Decisions Regarding Blood Glucose, Smoking, Alcohol.

There were difficulties with interpreting the contribution of the blood glucose variable in the initial regression equations, due to the extremely small unit of the mg/dl measure. Therefore, before including blood glucose levels into the final modelling equations, it was decided to convert the mean blood glucose measurements (mg/dl) into incremental categorical variables, based on quartiles of the blood glucose measurements. The blood glucose variable was divided into: **Quartile I** (90 mg/dl to 172 mg/dl), **Quartile II** (173 mg/dl to 218 mg/dl), **Quartile III** (219 mg/dl to 271 mg/dl), and **Quartile IV** (greater than 272 mg/dl).

It was also decided not to include the smoking and alcohol variables in the regression equation for three reasons. First, the odds ratios between cases and controls for both of these variables had been non-significant. Secondly, the missing data for these variables resulted in the elimination of entire rows of data (both cases and controls) from the regression equation, thus diminishing the power of the analysis. Third, the data itself is suspect in terms of reliability as was discussed in Chapter III.

In order to determine that the decision to leave the smoking and alcohol variables out of the regression equation was justifiable (and was not a decision to ignore potentially significant predictors), a number of preliminary models were run which included them. Neither smoking nor alcohol were significant predictors of LEA in any of these equations, therefore, the analysis proceeded without their inclusion.

Entire Data Set Model.

Eleven variables that were largely reflective of the CPLEA model were entered into the equation for the entire sample of cases and controls (case n=141; control n=281): (a) number of foot exams done by health providers within the year preceding the PL date ("poor foot care") (**Foot Exams**), (b) history of peripheral vascular disease ("peripheral vascular disease") (**PVD**), (c) history of neuropathy ("neuropathy") (**NP**), (d) history of previous lower extremity conditions that occurred prior to the development of the PL, including cellulitis, infection, and/or ulcers ("infection") (**LELESION**), (e) WT/HT ratio ("obesity") (**WT/HT**), and (f) blood glucose quartiles ("hyperglycemia") (**Quart I, Quart**

II, Quart III, Quart IV), (g) history of insulin therapy (**INSLN**), and (h) duration of diabetes in years since it was first diagnosed (**Year Diag**).

The results of this equation are seen in Table 16. The most significant predictors in the entire sample of cases and controls were: **NP**, **PVD**, and **LELESION**. The duration variable and the insulin variable approached significance with probability levels of 0.0561 and 0.0566 respectively.

Model Generated in Group I.

After random selection of the cases (with their respective controls) into two groups, a stepwise logistic regression model was entered for Group I, utilizing the same eleven variables as were used in the entire data set above. The results of this equation are presented in Table 17. The significant variables that emerged from the stepwise procedure were quite similar to those found for the entire data set of cases and controls: **NP**, **PVD**, **LELESION**, and **INSLN**.

Model Generated in Group II.

The identical process of selecting variables for the stepwise logistic regression equation was applied to the second group (Group II) that had been created through random selection. The prediction model resulting from this second group was similar to the previous models in that **NP**, **PVD**, and **LELESION** emerged as significant predictors.

Table 16

Results of Stepwise Logistic Regression Equation* for All Cases (N=133) and Controls (n=279)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-2.962632	0.3228942	84.19	0.0000
NP	1.449169	0.2911529	24.77	0.0000
PVD	2.47334	0.4346175	32.39	0.0000
LELESION	0.8196923	0.2814235	8.48	0.0036
INSLN	0.600266	0.3148824	3.63	0.0566
Year Diag	0.04179102	0.02187505	3.65	0.0561
Quart IV	0.4574507	0.2986177	2.35	0.1255

Model Chi-square = 168.66
df = 6
p < 0.0000

* Variables Entered For Tables 16, 17 and18
- Years Diagnosed
- Foot Exams
- PVD
- NP
- LELESION
- INSLN
- WT/HT
- Quart I Glucose
- Quart II Glucose
- Quart III Glucose
- Quart IV Glucose

Table 17

Results of Stepwise Logistic Regression Equation for

Group I (Cases n = 61) (Controls n = 135)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-2.037563	1.344047	2.30	0.1295
NP	2.00953	0.4538552	19.60	0.0000
PVD	3.15065	0.7435909	17.95	0.0000
INSLN	1.887399	0.5679805	11.04	0.0009
LELESION	1.05663	0.4463841	5.60	0.0179
WT/HT	-0.6216481	0.4314143	2.08	0.1496

Model Chi-square = 107.09; df = 5; $p < 0.0000$

However, in contrast, **Foot Exam** and **Year Diag** also emerged as significant variables, while **INSLN** did not appear at all in the Group II model (Table 18).

Cross-validations of Group I to Group II Models.

The model which was created from Group I data was then entered as the prediction equation for Group II. This was also run as a stepwise logistic regression. Three variables (**NP**, **PVD**, **LELESION**) maintained their significance as predictors in Group II, but **INSLN** did not appear in the final model. The model from Group I successfully classified 76.56% of the cases and controls that were in Group II (Table 19).

The model which was created from Group II data was then entered as the prediction equation for Group I. The variables that retained significance in this equation were: **NP**, **PVD**, **LELESION**, and **Year Diag**. Although similar to the Group I model, this Group II model demonstrated better prediction ability by correctly classifying 84.88% of the cases and controls that were in Group I (Table 20).

Preliminary Recommendation of a Model.

As can be seen, all three models generated from the data were quite similar. However, the question was posed as to which may actually be the most useful model in predicting LEA in the population under study. When cross-validation techniques suggest multiple models capable of prediction in future situations, the models need to be evaluated according to the best summary of the data, interpretability, and parsimony

Table 18

Results of Stepwise Logistic Regression Equation for

Group II (Cases n = 65) (Controls n = 141)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-2.5174	0.4211055	35.74	0.0000
NP	1.396346	0.4311618	10.49	0.0012
PVD	2.368223	0.5865872	16.30	0.0001
LELESION	0.9320467	0.3932923	5.62	0.0178
Foot Exam	-0.1521239	0.07086245	4.61	0.0318
Year Diag	0.05978103	0.02920263	4.19	0.0406
Quart IV	0.6542178	0.4200296	2.43	0.1193

Model Chi-square = 72.12; df = 6; $p < 0.0000$

Table 19
Results of Cross-Validation of Group I Model in Group II
(Cases n = 67) (Controls n = 142)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-1.980978	0.2858008	48.04	0.0000
NP	1.526848	0.3679932	17.22	0.0000
PVD	2.181716	0.5596225	15.20	0.0001
LELESION	0.8078566	0.3572935	5.11	0.0238

Model Chi-square = 61.22; df = 3; $p < 0.0000$; % Correctly Classified = 76.56

Table 20
Results of Cross-Validation of Group II Model in Group I
(Cases n = 64) (Controls n = 141)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-3.262812	0.4696176	48.27	0.0000
NP	2.028888	0.4340049	21.85	0.0000
PVD	2.882698	0.6697265	18.53	0.0000
Year Diag	0.08467893	0.03147418	7.24	0.0071
LELESION	0.910956	0.4286766	4.52	0.0336

Model Chi-square = 101.04; df = 4; $p < 0.0000$; % Correctly Classified = 84.88

(Henly, Klebe, & Cudeck, 1989). In support of parsimony, Hassard has also suggested that the simplest model that best predicts or "fits" the data at the most stringent level of significance, is the most useful. This is particularly so if it is also clinically relevant.

Based on the decision to utilize all the available data from the entire sample in order to maximize the predictive power of the regression equation, the three variable model of **NP**, **PVD**, and **LELESION** may be chosen as the "best" model of prediction for LEA in this population of Native Americans. This model is succinct, significant, and also basically reflective of the models found in Group I and Group II.

However, an alternative view of this model needs to be considered. It may be much more useful from a clinical perspective to look beyond the most obvious risk factors for LEA. The identification of NP, PVD, and LELESION as risk factors does not contribute to the expansion of new knowledge related to the etiology of LEA, since these risk factors have long been established as being associated with LEA, as seen in the Review of the Literature. The model also is lacking in terms of its clinical relevance for prevention of LEA. Although it is imperative that timely diagnoses of NP, PVD, and LELESIONS be made in order to heighten an awareness of the potential for LEA, directly intervening in the metabolic processes that are responsible for their development is not feasible.

Alternative Modelling.

In order to search for other useful predictors of LEA, it was decided that NP, PVD, and LELESION would be deleted from the logistic model equation, thus allowing other variables to emerge. In other words, if NP, PVD, and LELESION are known risk factors, it does seem redundant to maintain them as the primary variables of interest in the equation. As an alternative, the identical sequence of stepwise logistic regression modelling was again carried out, but this time PVD, NP, and LELESION were not included in the equations. In addition, systolic and diastolic blood pressures were also entered to reflect another component of the CPLEA framework. The results of these models are seen in Tables 21 through 25.

Entire Data Set Model.

When NP, PVD, and LELESION were deleted from the equation, the most significant variables that emerged through this new approach to the entire data set were: **Year Diag**, **INSLN**, **Quart IV Glucose**, and **WT/HT** (Table 21).

Model Generated in Group I.

When NP, PVD, and LELESION were deleted from the equation in Group I, the following variables emerged as significant: **INSLN**, **Year Diag**, **Foot Exam**, and **Quart II Glucose** (Table 22).

Table 21

Results of Stepwise Logistic Regression Equation* for

All Cases (n = 133) and Controls (n = 279)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-1.175571	0.7150888	2.70	0.1002
Year Diag	0.07718089	0.01844052	17.52	0.0000
INSLN	1.043553	0.2702132	14.91	0.0001
Quart IV	0.5641879	0.2590675	4.74	0.0294
WT/HT	-0.4395431	0.2249279	3.82	0.0507

Model Chi-square = 74.48
df = 4
p < 0.0000

Variables Entered For Tables 21, 22, 23, 29, and 30:
- Years Diagnosed
- Foot Exams
- Systolic BP
- Diastolic BP
- Insulin
- WT/HT
- Quartile I Glucose
- Quartile II Glucose
- Quartile III Glucose
- Quartile IV Glucose

* Note: NP, PVD, and LELESION deleted

Table 22
Results of Stepwise Logistic Regression Equation* for Group I
(Cases n = 61) (Controls n = 135)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-1.315448	1.148456	1.31	0.2520
INSLN	1.391395	0.4759804	8.55	0.0035
Year Diag	0.07254351	0.03107716	5.45	0.0196
Foot Exam	0.1431772	0.05125277	7.80	0.0052
Quart II	-1.184096	0.4793471	6.10	0.0135
WT/HT	-0.4988063	0.3528265	2.00	0.1574

Model Chi-square = 53.13; df = 5; $p < 0.0000$ * Note: NP, PVD, and LELESION deleted

Table 23
Results of Stepwise Logistic Regression Equation* for Group II
(Cases n = 65) (Controls n = 141)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-2.01198	0.3240881	38.54	0.0000
Year Diag	0.08187101	0.02342385	12.22	0.0005
INSLN	0.6266975	0.348708	3.23	0.0723

Model Chi-square = 25.11; df = 2; $p < 0.0000$ * Note: NP, PVD, and LELESION deleted

Model Generated in Group II.

When NP, PVD, and LELESION were deleted from the equation in Group II, only one variable emerged as statistically significant in this randomly selected half of the data set: **Year Diag** (Table 23).

Cross-validations of Group I to Group II.

The percentage of cases versus controls that were classified correctly by the Group I Model in Group II was 69.86%, with only **Year Diag** and **INSLN** retaining significance in the equation (Table 24). In contrast, the Group II Model correctly classified 72.15% ofthe cases and controls in Group I, retaining both **Year Diag** and **INSLN** in the equation (Table 25).

Recommended Model from this Study.

The removal of PVD, NP, and LELESION from the logistic regression equations allowed for the clear emergence of other variables useful in the prediction of LEA. In the full data set, the variables **Year Diag, INSLN, Quart IV Glucose**, and **WT/HT** all became significant in the regression model. In the Group I data set, **Year Diag, INSLN, Foot Exam**, and **Quart II** became significant, somewhat reflective of the full data set results. In the Group II data set, only **Year Diag** maintained significance. From all three models, it can be seen that the number of years that a person has been diagnosed with NIDDM is most highly predictive of their development of complications that lead to LEA.

Table 24
Results of Cross-Validation of Group I Model* in Group II
Data (Cases n = 67) (Controls n = 142)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-0.7826107	0.9503967	0.68	0.4102
Year Diag	0.07387014	0.02425086	9.28	0.0023
INSLN	0.7046484	0.3507246	4.04	0.0445
WT/HT	-0.408251	0.3088211	1.75	0.1864
Quart II	-0.2280063	0.3802123	0.36	0.5487

Model Chi-square = 28.82; df = 4; $p < 0.0000$; % Correctly Classified = 69.86 *Note: NP, PVD, LELESION deleted

Table 25
Results of Cross-Validation of Group II Model in Group I
Data (Cases n = 69) (Controls n = 142)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-2.751172	0.4214233	42.62	0.0000
Year Diag	0.08023611	0.0273831	8.59	0.0034
INSLN	1.620766	0.4494571	13.00	0.0003

Model Chi-square = 47.15; df = 2; $p < 0.0000$; % Correctly Classified = 72.15 * Note: NP, PVD, LELESION deleted

Since the purpose of this study was the identification of risk factors for LEA, with the accompanying objective of the utilization of the findings to prevent LEA, the model generated from the entire data set from all cases and controls is proposed as the recommended model from this study (Table 21). Besides having the most predictive power statistically by its inclusion of all available data from cases and controls, it is also argued that this model would be more clinically relevant in that it identifies variables that are potentially amenable to some sort of clinical intervention, particularly that of blood glucose level.

Discussion of Recommended Model.

The variable **Year Diag** is not directly manipulable in the clinical setting. However, this variable may prove important in terms of diagnosing NIDDM as early as possible. In the comparison of mean duration of diagnosis in years between males and females, it was found that males had a significantly shorter duration of NIDDM. Despite their having NIDDM for a longer period of time, this may be interpreted in a positive light, if it is proposed that women are able to at least forestall the onset of complications leading to LEA. Implications for early diagnosis and treatment of NIDDM are inherent in this finding, although further study is needed to validate this hypothesis.

The variable **INSLN** is manipulable, however, the mechanism by which it predicts LEA is not clear. Therefore, manipulating insulin therapy for purposes of preventing LEA is not yet justifiable, especially since it is an established pharmacological treatment for control of hyperglycemia. It is possible that **INSLN** is reflective of duration, in that a

person with progressive NIDDM will eventually require exogenous insulin to control rising blood glucose levels. In this way, the **INSLN** variable may also be a marker for severity of disease, in that it is prescribed when hyperglycemia cannot be controlled in any other way.

However, it is also possible that the therapeutic use of insulin, like many other pharmacologic interventions, has untoward long-term side-effects that contribute to diabetic complications. Further research in the basic sciences, as well as in epidemiology, is clearly indicated to define this connection between insulin therapy and LEA.

Only **Quart IV** can be directly targeted for clinical prevention strategies in the arena of dietary and exercise programming. It is not a surprising finding that the highest range of blood glucose levels contributes to LEA, particularly with the known association between hyperglycemia and microvascular disease. An added benefit of this finding may be to impart an increased confidence on the part of health care providers in the clinical instruction of patients when telling them that it is beneficial to keep their blood glucose levels as low as possible, even if they cannot achieve euglycemia.

The clinical implementation of exercise and weight loss programming could induce the more efficient use of glucose, while at the same time reduce the need for high dosages of insulin, possibly contributing to a reduction in both microvascular and macrovascular complications. The model that was generated in Group I (Table 22) would seem to support this instruction, as well. In Group I, **Quart II** was significant as a negative predictor for LEA. That is, keeping blood glucose levels between 172 mg/dl and 218 mg/dl seemed to confer a "protective" effect against the development of LEA. It is

curious as to why **Quart I** did not emerge as the predictor rather than **Quart II**, since it would be expected that an even lower blood glucose level would be even more "protective" against the development of microvascular conditions leading to LEA. However, given the mean blood glucose of 220.73 mg/dl in the control group (case mean blood glucose = 242.73 mg/dl), this finding is understandable.

The negative relationship found between **WT/HT** ratio and LEA requires an explanation different from assuming that people with increased body mass will have decreased odds of having an LEA. As discussed previously in this Chapter (under the interpretation of the Odds Ratios, p.101), it would appear that those who are older, more frail, and who have had a longer duration of NIDDM, have also been subjected to other chronic diseases and complications of NIDDM, such as renal failure.

The loss of weight would be expected with the progression of aging and other health problems, thereby explaining the decrease in the WT/HT ratio. In other words, the negative relationship between WT/HT ratio and LEA should be interpreted more as a reflection of overall health status of people who undergo amputation, rather than as a predictor for amputation.

Therefore, the recommended prediction equation derived from the full data set (all cases and controls) in this study, is reported in Table 26:

$$\mathbf{Ln\ y = -1.175571 + 0.07718089\ X_1 + 1.043553\ X_2 + 0.5641879\ X_3 - 0.4395431\ X_4}$$

where:

$\mathbf{X_1}$ = Years since the diagnosis of NIDDM was first made

$\mathbf{X_2}$ = Positive history of insulin therapy

Table 26

Final Recommended Prediction Model* for

LEA for all Cases (n = 133) and Controls (n = 279)

with Estimated Odds Ratios and 95% Confidence Limits

$$\text{Ln } y = -1.175571 + 0.07718089\ X_1 + 1.043553\ X_2 + 0.5641879\ X_3 - 0.4395431\ X_4 \quad **$$

Model Parameter	Estimated Odds Ratio	Chi-square of Parameter	95% Confidence Limits	P value
Year Diag	1.08	17.52	1.042 to 1.120	0.0000
INSLN	2.84	14.91	1.671 to 4.821	0.0001
Quart IV	1.76	4.74	1.058 to 2.921	0.0294
WT/HT	0.64	3.82	0.415 to 1.001	0.0507

* Based on Results of Model in Table 21 deleting NP, PVD, LELESION

** X_1 = Year Diag
X_2 = INSLN
X_3 = Quart IV
X_4 = WT/HT

X_3 = Highest quartile of blood glucose level

X_4 = Weight to Height ratio (pounds/inches)

Gender Based Analysis

Although the above model is recommended when looking at the diabetic population as a whole, lingering questions remain that arose from the incidental findings of the odds ratio differences between males and females. Based on the significant differences in age and duration between males and females, it was decided to look for other significant differences also based on gender.

Odds Ratios Comparing Male and Female Cases.

Odds ratios for categorical variables between male and female cases only are presented in Table 27. As can be seen from the table, there were a number of gender specific differences that were significant between male and female cases. Males were far more likely to have a smoking and alcohol use history than females (O.R. 4.40 and 6.77 respectively). However, males were significantly less likely to have a positive medical history for the following variables: insulin therapy, angina, CHF, and CVA/TIA.

The difference in the smoking and alcohol use variables is of interest. As stated before, the medical record did not reliably demonstrate the systematic collection of these variables in the clinical setting. A question arises then: Do men, in fact, use tobacco and alcohol more often? Or, because of social and cultural influences, are men asked more frequently if they use tobacco and alcohol? Only a change in policy that would implement

Table 27

Odds Ratios* Comparing Male to Female Cases Only

On Selected Categorical Variables

Variable (Positive History)	Total N	OR	95% Confidence LiImits	Montel-Haenszel Chi-Square	P-Value
Smoking	133	4.40	1.78-11.19	12.81	0.00034
Alcohol Use	127	6.77	2.69-17.49	21.40	0.00000
Insulin Therapy	142	0.36	0.14-0.88	6.20	0.01278
Hypertension	144	0.56	0.27-1.15	2.90	NS
Angina	144	0.33	0.15-0.74	8.83	0.00296
Myocardial Infarction	143	0.78	0.30-1.97	0.34	NS
Congestive Heart Failure	144	0.25	0.10-0.60	12.11	0.00050
CVA/TIA	143	0.30	0.07-0.99	4.69	0.03030
PVD	144	0.53	0.24-1.15	3.04	NS
Retinopathy	144	0.91	0.44-1.88	0.07	NS
Neuropathy	144	0.53	0.25-1.11	3.37	NS
Lower Extremity Lesions	144	0.73	0.35-1.56	0.76	NS

* Odds ratios refer to the odds of having a positive medical history among males as compared to females having the history

the routine elicitation and documentation of this information from all patients could assist in answering this question with any certainty.

The difference in insulin therapy may be explained by the difference also seen in the duration variable. That is, it may be that women were followed and treated for NIDDM for longer periods of time, hence they were more likely to be on insulin therapy than men. It may be that more men would have been on insulin therapy if they had been treated for NIDDM for longer periods of time before LEA, or perhaps that men do not want to be "put on the needle" (as the investigator heard insulin therapy described by one Native American with diabetes). It cannot be stated with certainty why the difference exists for insulin use. However, it would seem important to investigate the health care access patterns of men and women overall, and of those with NIDDM.

Differences between males and females for angina, CHF, and CVA/TIA may be explored in two directions. One plausible explanation may be that the significant difference in age between males and females (with women being an average of 6.48 years older than the men in this study) may account for the increased risk for these vascular diseases. As an alternative, but yet unfounded explanation, it may be interesting to question the role of insulin therapy in atherogenesis. Although this area has not yet been studied comprehensively, if, in fact, women use insulin therapy more often than men, it may be that they become more at risk for macrovascular diseases over time.

Depending on the outcome of future research investigating insulin's potential role in the development of macrovascular disease, the clinical management of NIDDM in the future may need to strike a balance between the control of hyperglycemia and its

accompanying microvascular lesions, and the avoidance of macrovascular complications that could be related to insulin therapy.

Comparison of Means between Male and Female Cases.

An analysis of the continuous variables to study differences between male and female cases in presented in **Table 28**. There were no significant differences between males and females on most of these variables, other than the previously stated differences in age and duration of diabetes. Although there was a statistically significant difference seen between mean diastolic blood pressures, the mean pressures for each group (males = 79.62 mm Hg; females = 73.65 mm Hg) were well within what would be considered a normal range for diastolic pressure in adults.

Logistic Regression Equations for Males and Females.

The results of the odds ratios and comparison of means between male and female cases indicate the probable existence of distinct, gender based predictors for LEA among men and women with diabetes. Although it was recognized that instability in the regression equation may result from diminishing the sample size considerably, especially in the group of males (male n=164; female n=248), it was nonetheless decided to split the total data set into two groups again, this time by gender. The identical logistic regression equation that was entered for the full sample (with the deletion of NP, PVD, and LELESION) was then entered for each gender group. The resulting stepwise logistic

Table 28

Comparison of Means Between Male and Female Cases Only
on Selected Continuous Variables

Variable	Males N	Males Mean (SD)	Females N	Females Mean (SD)	t-value	p-value
WT/HT Ratio (pounds/inches)	53	2.758016 (0.47464)	81	2.64195 (0.636042)	1.207067	0.2296
Age (years)	58	54.51724 (12.25782)	86	61 (12.68069)	-3.049242	0.0027
Duration (years diagnosed)	58	11.93103 (6.802637)	86	14.63953 (6.684332)	-2.367894	0.0192
Foot Exams (Exams within year)	57	2.964912 (4.048655)	85	3.470588 (4.951162)	-0.6405336	0.5229
Blood Glucose (mg/dL	58	253.3914 (100.5246)	85	235.4612 (77.82689)	1.144382	0.2551
Systolic BP (nnHg)	58	134.4655 (17.7529)	86	135.9767 (18.79673)	-0.4837852	0.6293
Diastolic BP (nnHg)	58	79.62069 (9.002587)	86	73.65116 (8.756534)	3.967147	0.0001

regression model and equation for males is seen in Tables 29 and 31. The model and equation for females is seen in Tables 30 and 32.

As can be seen from these tables, two different models did emerge when based on gender. The only significant variable that is shared by both males and females is **Year Diag**, that is, duration of diabetes since diagnosis. Otherwise, for males, the other significant predictors for LEA were **Quart II** and **Foot Exam**.

For males, there appears to be less risk of having an LEA if blood glucose is maintained within the 172 mg/dl to 218 mg/dl range. It is also possible that the variable of Foot Exam may be indicative of patterns of access and utilization of health care services by males, an area that has already been mentioned as being important for further investigation.

The model that emerged for females was similar to the model for the entire sample of cases and controls, although the WT/HT and Quart IV variables did not achieve significance in the exclusively female model ($p=0.0813$ and $p=0.1044$ respectively). However, as in the combined (male and female) model for all cases and controls (Table 21), significant predictors of LEA for females included **Year Diag** and **INSLN**. The significance of these two variables was not surprising, especially given the results of the odds ratios and comparison of means for female cases as compared to male cases (Tables 27 and 28).

Table 29
Results of Stepwise Logistic Regression Equation for
Males Only (Cases n = 53) (Controls n = 111)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-0.2882753	1.272566	0.05	0.8208
Year Diag	0.1438333	0.03163286	20.67	0.0000
Quart II	-1.169319	0.5183313	5.09	0.0241
Foot Exam	0.1522512	0.06309312	5.82	0.0158
WT/HT	-0.6237512	0.4199652	2.21	0.1375

Model Chi-square = 41.57; df = 4; $p < 0.0000$

Table 30
Results of Stepwise Logistic Regression Equation for
Females Only (Cases n = 80) (Controls n = 168)

Variable	Beta Estimate	Standard Error Estimate	Chi-Square	Probability
Intercept	-1.419229	0.8943795	2.52	0.1126
INSLN	1.518596	0.4011869	14.33	0.0002
Year Diag	0.06119454	0.02363697	6.70	0.0096
WT/HT	-0.4827713	0.2769704	3.04	0.0813
Quart IV	0.5493995	0.3383393	2.64	0.1044

Model Chi-square = 47.70; df = 4; $p < 0.0000$

Table 31

Prediction Equation for Males Based on

Available Data in This Study

$$\text{Ln } y = -0.2882753 + 0.1438333\ X_1 - 1.69319\ X_2 + 0.1522512\ X_3\ *$$

Model Parameter	Estimated Odds Ratio	Chi-square of Parameter	95% Confidence Limits	P value
Intercept				
Year Diag	1.15	20.67	0.082 to 0.206	0.0000
Quart II	0.31	5.09	0.112 to 0.858	0.0241
Foot Exam	1.16	5.82	1.029 to 1.318	0.0158
WT/HT	0.54	2.21	0.235 to 1.221	0.1375

* X_1 = Year Diag
X_2 = Quart II
X_3 = Foot Exam

Table 32

Prediction Equation for Females Based on

Available Data in This Study

$$\text{Ln } y = -1.419229 + 1.518596\ X_1 + 0.06119454\ X_2 \quad *$$

Model Parameter	Estimated Odds Ratio	Chi-square of Parameter	95% Confidence Limits	P value
Intercept				
INSLN	4.57	14.33	2.080 to 10.023	0.0002
Year Diag	1.06	6.70	1.015 to 1.113	0.0096
WT/HT	0.62	3.04	0.359 to 1.062	0.0813
Quart IV	1.73	2.64	0.892 to 3.362	0.1044

* $\mathbf{X_1}$ = INSLN
$\mathbf{X_2}$ = Year Diag

Summary

It would appear that caution needs to be exercised in the recommendation of one model for the prediction of LEA in both males and females. Although the number of years that a person has been diagnosed with NIDDM is shared as a highly significant predictor for LEA, the specific roles of insulin therapy, blood glucose control, and frequency of foot examination may need to be considered with reference to gender specific influences.

It is not possible to state that the equations seen in Table 31 and Table 32 are definitive models for the prediction of LEA among Northern Plains male and female Natives. However, it would be important to tailor group-specific strategies for the effective prevention of LEA; therefore, further research in the area of diabetes-related LEA in Native Americans would benefit from the inclusion of a focus on the variable of gender differences.

In conclusion, it would be clinically prudent to utilize knowledge from several models in the prevention of LEA. It is recommended here that the CPLEA framework be incorporated into clinical practice as the basis for risk assessment LEA. It is further concluded that the estimated odds ratios from the logistic regression equations in Tables 26, 31, and 32 would prove clinically useful if incorporated into the development of a risk profile for LEA among Northern Plains Natives with NIDDM.

CHAPTER VII

RECOMMENDATIONS FOR FUTURE STUDY

Many risk factors appear to threaten the lower extremities of Sioux people with Type 2 diabetes. Although risk factors such as history of PVD, NP, LELESION, and INSLN use have been identified in this study as most predictive of LEA, the specific pathophysiologic mechanisms and interactions of these risk factors remain to be discovered (Thomas, 1992; Dyck, 1992). At this point in time, the state of the science does not lend itself to the interruption of the metabolic pathways of diabetes.

However, it is possible to implement the knowledge that is already known in identifying those most at risk for the development of foot lesions. It is also possible to interrupt the pathway to amputation through the one pathway that is amenable to manipulation, that is, through increased foot care education and improved foot care services for people with diabetes.

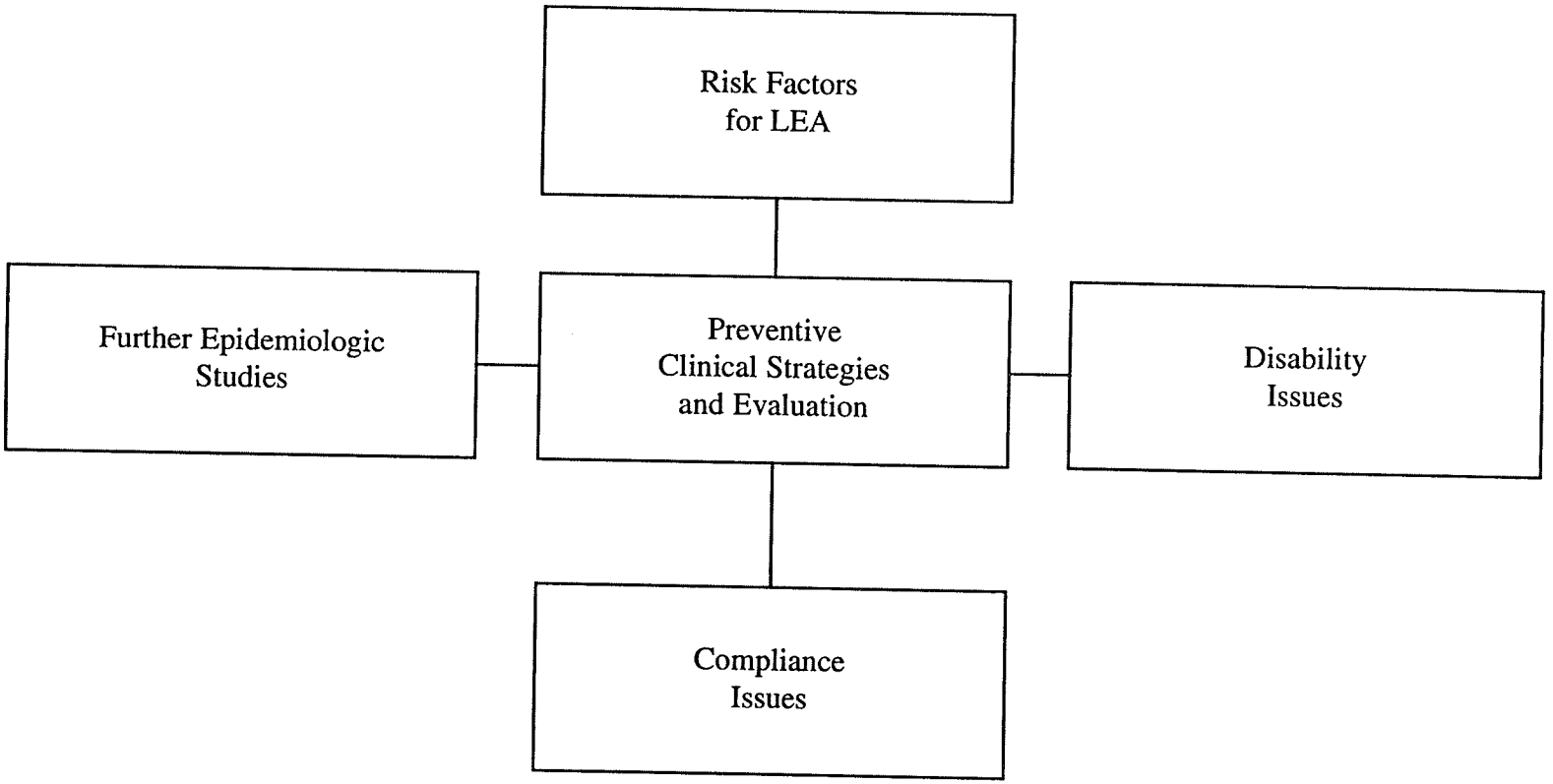
Towards this end, it is recommended that further research in the prevention of LEA needs to include both epidemiologic investigation and implementation of clinical prevention strategies. It is also recommended that culturally specific educational approaches be implemented in the teaching of diabetic foot care to health care providers, and to people living with Type 2 diabetes. Research of outcomes evaluating such interventions are also needed.

Prospective studies of outcomes related to relatively uncomplicated but effective assessments of risk are also essential. For example, use of the Semmes-Weinstein 5.07 monofilament has been shown to effectively and non-invasively screen for those at risk for LEA in a primary care setting, at the Red Lake Reservation in the Bemidji Area of IHS (Rith-Najarian, Stolusky, & Gohdes, 1992; Rith-Najarian, Stolusky, Mayfield, & Gohdes, 1993).

It is also recommended that the most effective utilization of the knowledge gained from this study would fall into two related categories: (a) a heightened awareness of the potential for the severity of lower extremity problems among Native people with NIDDM, and (b) a heightened awareness of the potential for the prevention of these problems. "Foot problems still remain one of the most common reasons for hospital admission amongst diabetic patients. Conversely, diabetic foot problems are potentially the most preventable long-term complication of diabetes" (Young, Veves, & Boulton, 1993).

In this final section of the report, four categories of recommendations for further study are presented. First, recommendations for study that derive from an epidemiologic viewpoint are offered. Second, recommendations from a clinical prevention/intervention perspective are proposed. Third, the systematic study of "non-compliance" as a clinical issue is suggested. Finally, this section is concluded with brief recommendations for future study of disability, not previously addressed in this study, yet inexorably linked to the experience of having an LEA (Figure 4).

Figure 4
Recommended Areas for Continued
Study of LEA



Epidemiologic Studies

Eight research questions that arose during the course of this study related to the epidemiology of LEA include the following:

A. What is the prevalence of LEA within family units?

At one Service Unit, it was discovered that one male case of LEA was related to another case in his immediate family, his mother. At another Service Unit, it was found that identical twin brothers met the case definition, and had LEA's within three years of one another. The woman mentioned previously in the section on explanatory models, indicated she had three family members who had undergone LEA. It is known that NIDDM has a genetic component, however, possible familial linkages to diabetic complications would be important to explore. A compilation of family history data could be approached from both retrospective and prospective perspectives.

B. Is the presence of proteinuria eventually related to an outcome of LEA?

There were 28 records of people who had been on dialysis for renal failure, all of whom were cases in this study versus controls. It may be possible that there were people on renal dialysis who met the control definition, but who were not selected during the random selection of controls from the diabetes registries. It may be useful to investigate associations of proteinuria as an early marker of renal failure, as well as its ability to predict LEA.

Studies to address this question could be designed either retrospectively or prospectively dependent on the resources available to carry them out.

C. What is the relationship between the length of time since a diagnosis of specific medical conditions and the date of an LEA?

The variables studied as possible risk factors in this study were entered categorically as "present or absent". It would be more informative to know the length of time that someone had a medical condition, in addition to its presence or absence. A difficulty with using a retrospective design to collect this data would be the lack of control over systematic assessment for medical conditions, for example, the use of Doppler technology, radiography, or arteriography in the evaluation of peripheral vascular disease. Unless the assessment could be controlled for through a change in the existing clinical practice in IHS, a prospective design, with established assessment protocols specific to the study would be necessary.

D. What is the incidence of repeat LEA and the survival rate of people with LEA?

In defining cases in this study, data surrounding only the first time LEA was collected. It would be of interest to return to the medical records of the cases, and to extract and analyze additional information about the prevalence and patterns of repeat LEA and mortality. Another case-control study could then be done to compare risk factors of people who do go on to have repeat LEA to those who do not. Survival

analysis techniques would then be applied to the data to generate survival curves for people who have had a single versus repeated LEA surgeries.

E. How many of the controls in this study eventually require an LEA?

A prospectively designed study of the charts that were used as controls for this study could be done to determine what percentage of people in the control group undergo LEA in the future. Those controls in this study who do go on for an LEA could then serve as cases, and their previous data could be utilized as control data. Having the ability to have cases also serve as their own controls would seem to strengthen the ability of the retrospective design to identify risk factors for LEA.

This approach, though inviting, is not feasible from the data set in the possession of the investigator at this time. To honor the protocol for protection of human subjects that was approved by the Institutional Review Boards, no identifiers were permanently recorded of the patient numbers on the control charts.

F. Is there a difference between males and females in the age that diabetes is actually acquired?

The finding that males had a shorter mean duration of diagnosed diabetes prior to LEA, and also had a younger mean age at the time of LEA should be investigated further. The duration of diabetes does not validly indicate the onset of the disease, since diagnosis may occur at any point along the disease trajectory. Therefore, it is unknown if males

were more frequently undiagnosed while actually having an ongoing active disease process, or if the process of diabetes is more virulent in males.

A prospectively designed program of periodic screening for diabetes in the Sioux population, as has been done in the Pima for three decades, may resolve the question regarding the accuracy of duration as a variable, as well as the question of differences in age of onset between males and females.

G. What are the patterns of health care services utilization in males as compared to females?

This question is related to F, in that it may be hypothesized that women access health care services more often and thus would be more likely to be diagnosed with diabetes earlier in the disease process. It would follow that women would have more frequent medical treatment for a diabetic condition, and thereby would forestall the time of onset of complications.

H. What is the relationship of insulin therapy to LEA?

The logistic regression models that were run without the self-evident variables of PVD, NP, and LELESION very clearly indicated that insulin therapy was a significant predictor for LEA in this study. However, this variable was entered into the equation in a categorical fashion, so the clinical significance of this variable is still in question in terms of the nature of its relationship to LEA.

An inordinate amount of time was directed to the collection of data regarding the type of insulin and the length of time people had been on insulin. However, the frequency of gaps in the medical record, and the inability to know the patterns that people actually utilized in taking prescribed insulin, provided the basis for the decision to not include duration of insulin therapy in this analysis.

A longitudinal prospective design that included an interview schedule with subjects as to their actual dosages of insulin would be extremely informative. Data related to actual dosages and duration of insulin therapy would be helpful to investigate a dose-response link to LEA, versus the possibility that insulin is simply a marker for duration or for severity of the disease. The drawback to this design would be the number of years that may be necessary to obtain the data from a longitudinal perspective.

A more feasible alternative strategy may be to retrospectively collect the insulin prescription data from physician entries in the medical record, and then to correlate them with pharmacy entries rendered in the filling of prescriptions. As a criteria for inclusion in the study, an interview component may still be necessary to determine health care access patterns, that is, the filling of prescriptions elsewhere during the time period of the study, or accessing different health care providers outside of the IHS.

Summary.

Overall, the effective use of retrospective and prospective case-control designs could be highly advantageous at this point in time in the study of NIDDM among Native populations. The data bases in the IHS are essentially the only population based clinical

health records in the United States at the present time. Unfortunately, these records have only been computerized within the past few years, so studies that would require going back more than a few years may be rather time consuming in attempting to find variables of interest.

Given that caveat, however, studies that are retrospective to only a few years since the new system was installed, could be done rather efficiently, and future studies could be more realistically planned and efficiently executed using the new computerized system. Prevalence studies and accompanying case-control studies could logically and feasibly be carried out on the smaller populations of individual tribes, and could be used to tailor the identification of risk factors and odds ratios to specific tribal groups.

Clinical Prevention

Based on the overall findings from the study, two general hypotheses are proposed for the immediate address of LEA in the clinical arena of AAIHS:

A. **An initiative to establish a clinically based program, to be implemented by health care providers in the examination and care of the diabetic foot,will be related to a decrease in the incidence of diabetic-related LEA in the AAIHS.**

Two descriptive findings were indicative of the serious potential for LEA in this population of Sioux Natives: (a) in 27.8% of the cases, the precipitating lesion (PL) was first recorded in the clinic record within one week of the LEA and (b) 45.9% of all

diabetic related surgical amputations took place within 4 weeks of the first clinical notation of the PL. In more than a third of the cases, documentation of a PL was not stated anywhere in the clinical record.

In most cases, the PL could be traced to a particular date and cause, such as a non-healing ulcer, but the specific circumstances that initiated the lesion were very rarely recorded. As a result, in many situations it was not known if an acute or chronic situation led to the LEA. A related source of concern was that foot exams were seen to cluster around the time of identification of a lower extremity problem, not in a preventive pattern.

The diabetic flow sheet that contains a check-off box for foot exams to be done at each routine clinic visit for all patients was inconsistently used. When it was used for routine visits, a check mark may have been placed in the box, but no corresponding description of the foot (deformities, conditions of the skin and nails, presence of callouses) was available. Thorough description of foot conditions written in a clinical entry were almost universally in the context of an existing foot lesion.

No single clinical intervention would seem capable of preventing LEA. However, a consistently carried out set of clinical protocols as part of a concerted foot care program may make an impact. Such a program would target the following:

(a) thorough examination and recording of diabetic feet as part of every clinic visit, and recording of the examination on a revised Diabetic Flow Sheet that includes space for description of deformities, condition of skin, and lesions;

(b) aggressive follow-up and treatment of foot lesions, including minor injuries;

(c) thorough historical interview regarding the nature and circumstances of injuries that surround the development of a PL;

(d) referral to, and increased availability of podiatric services within AAIHS;

(e) routine bi-annual standardized assessment of peripheral vascular disease and neuropathy, as part of an overall plan of care for people with diabetes, utilizing non-invasive vascular techniques and Semmes-Weinstein filament assessment;

(f) systematic assessment and recording of tobacco use patterns;

(g) increased utilization of non-physician providers (Physician Assistants, Nurse Practitioners, Public Health Nurses, Dieticians, Community Health Representatives) in doing follow-up assessments and educational programs for people with diabetes;

(h) cost-assessment studies comparing the short and long-term costs of standardized foot care programming to the costs of surgical LEA;

(i) formative and summative evaluation of these strategies for determination of those that are most effective and that should be implemented with the IHS.

It is realized that an invalid assumption may be implicit in these recommendations, that is, that established protocols can compensate for the lack of continuity of professional providers delivering care. However, it will not be within the scope of future study for this investigator to determine how to stem the health manpower problems in the IHS.

B. An educational program related to the examination and care of the diabetic foot, and targeted to American Indians with diabetes and to their communities, will be related to a decreased incidence of diabetes-related LEA in AAIHS.

Throughout the review of the medical records, entries related to education for the routine care of feet were not seen. In contrast, entries related to dietary instruction were seen very often. It was difficult to know from the medical record over what period of time people had a lesion before they presented to the clinic for care. Perhaps as importantly, it is not known why the decision to seek medical treatment was made. It also is not known if people with diabetes were aware that the situation had serious potential to lead to an LEA at the time of their initial presentation to the clinic.

Although it is not proposed that providing foot care instruction to people as an isolated intervention will translate to lower incidence of LEA, it certainly seems remiss for professionals to not actively share such information as part of an integrated plan of diabetic care. Steps to be taken towards implementation of foot care education programming for people with diabetes include the following:

(a) development of brief, easily accessed instructions for foot care in brochure form, followed by distribution of brochures in clinic and community settings: food stores, Bureau of Indian Affairs buildings, schools, congregational meal sites for senior citizens, and churches. The investigator has begun implementation of this strategy. Brochures have been developed under a grant from the Administration on Aging

and 1750 of them have been distributed to the Service Units in the study, and to the Tribal Health Directors for each of the reserve communities;

(b) community presentations related to care of feet for people with diabetes and their family members;

(c) bi-annual instruction in foot care in the clinic setting in culturally appropriate terms;

(d) incorporation of foot care instruction into an overall program of diabetic education, rather than as an isolated intervention;

(e) assignment of overall diabetic instruction, including foot care, to dieticians in the IHS, since these professionals are already heavily utilized for other diabetic instructions

(f) instruction to people with diabetes to ask to have their feet checked each time they come to the clinic by the health care provider;

(g) application for funding to establish a "shoe bank" in the community from which people could choose and receive new shoes that fit well and are comfortable.

Compliance Issues.

Continued follow-up care is essential for people with NIDDM due both to its chronic nature, as well as its associated complications. However, a problem surrounding issues of patient compliance with medical regimens was identified incidental to the process of reviewing medical records. The problem of "non-compliance" was seen to be clearly labelled, yet was not as clearly addressed in terms of resolution.

The label of "non-compliance", coupled with the apparent fragmentation in the delivery of care by multiple providers may lead to two undesirable outcomes: (a) an increase in the number of diabetic complications, and (b) a negative impact on the delivery of care for individual patients by IHS providers who view people in terms of this label. Therefore, it is recommended that a study of people's understanding of NIDDM and their reasons for non-adherence to medical regimens be instituted.

The future planning of clinical intervention and prevention strategies could draw upon this information in order to adapt medical regimens to the lived reality experienced by people with diabetes in rural reserve communities. The investigation of people's understanding of NIDDM, including their treatment decisions, could be based upon an application of Kleinman's Explanatory Model. The use of explanatory models has been advocated by Kleinman (1978;1988) as an approach to explaining illness at both individual and contextual levels of meaning.

Explanatory models serve to define and organize symptoms, etiologies, sick role behaviors, and types and goals of treatment. The components of the model include explanations of disease etiology, onset of symptoms, pathophysiology, course of sickness, and treatment (Kleinman, 1978).

It is proposed that health care providers' understanding of patients' explanatory models of NIDDM would serve to illuminate the understanding of NIDDM as held by the people who live with this disease, and foster respect for their decision-making concerning its treatment. It is further proposed that such understanding on the part of health care providers would serve to stimulate cooperation between providers and patients. A

supportive and collaborative approach to the management of diabetes may help to ensure continued follow-up for NIDDM, and may result in new definitions of "compliance", as well as improved clinical outcomes.

A study to incorporate the use of explanatory models into clinical practice would be conducted in three phases. **Phase I** would include the following activities to:

(a) identify 25 volunteer subjects who have been identified "at risk" for LEA based upon standardized clinical evaluations.

(b) conduct and record open-ended interviews with each subject regarding their understanding of NIDDM and its relationship to LEA. The interviews would utilize the components of the explanatory model as the topics in the interview schedule: etiology, symptoms, pathophysiology, course of sickness, and treatment.

(c) analyze interview data, using a content analysis method to organize findings into categories within each topic area of the explanatory model.

Phase II would include the following activities:

(a) utilization of results from Phase I to develop an education program for a group of health care providers in understanding the broader context of NIDDM in reserve communities, particularly as it relates to individual's decisions to continue ongoing treatment;

(b) training the group of health care providers in using an Explanatory Model approach in their clinical work with people with NIDDM.

Phase III would then proceed with an experimental study of the effectiveness of the use of an explanatory model approach in reducing labels of "non-compliance", and in

reducing the severity of lower extremity problems. Phase III would include the following activities:

(a) consistent utilization of the explanatory model approach by the trained providers over a two year period with their patients who are at risk for LEA;

(b) maintenance of the usual mode of clinical encounter by an alternate group of providers with their patients at risk for LEA;

(c) comparison of the frequency and definition of "non-compliance" as attached to the patients in each group after the two year period as documented from the medical record, and from interviews with the health care providers.

(d) comparison of the actual following of medical regimen activities by the two groups of patients will be made, as recorded in the medical record and through interviews with patients at risk for LEA.

(e) comparison of lower extremity problems and other diabetic complications in the two patient groups, as documented in the medical record.

Disability Issues

Up to this point, the recommendations have been targeted to the etiology and prevention of LEA, and issues of compliance in managing the chronic aspects of NIDDM. However, there are important questions remaining as to the impact of LEA in terms of disability and its meaning within the context of reserve communities. These questions were not the focus of this study, and consequently were not addressed. Yet, it is argued that addressing the actual disability imposed by LEA is co-requisite to a thorough

understanding of this complication of diabetes. Given the growing population of older Natives with chronic disease, and specifically with complications of NIDDM, disability issues will necessarily demand a position of prominence on the research agenda in Native American health.

It is proposed that the study of disability associated with LEA be incorporated as an integral part of a comprehensive research program in the study of diabetes-related LEA among American Indians living in reserve settings. It is recommended that research in disability begin through study of three areas:

(a) systematic description of disability in terms of functional assessment among those who have undergone a diabetes-related LEA;

(b) description of the actual patterns of follow-up care by people who have had LEA;

(c) systematic assessment of the availability of rehabilitative and long-term care services within the geographic boundaries of the AAIHS;

(d) description of the lived experience of handicap related to LEA in reserve settings.

This recommendation would necessarily require a combination of both quantitative and qualitative methodologies. It is suggested here, that such a study would be best approached by the utilization of standardized tools for assessment of ADL's and disability, and a narrative reconstruction approach for the description of handicap.

Summary

The planning and implementation of the above recommendations would seem appropriate to the tasks of studying the etiology, prevention, and experience of NIDDM

related LEA among the Sioux in the AAIHS. It is recommended here that epidemiologic and preventive strategies be instituted in as timely a manner as possible, then evaluated in an ongoing process to determine their effectiveness.

Planned interventions for the prevention of LEA need to be made pertinent to the population at hand. Data related to factors that influence "compliance" need to be incorporated into clinical strategies in order to maximize people's ability to manage chronic disease.

Although not the focus of the present study, attention to the dimension of disability and its relationship to NIDDM and LEA is an important area for future study. By combining epidemiologic and preventive approaches with an understanding of disability outcomes and services, the fuller spectrum of issues surrounding diabetes-induced LEA will be illuminated. Eventually, this knowledge may be used to decrease the incidence of this complication, and to mediate its disabling effects.

CHAPTER VIII

CONCLUSION

Type 2 diabetes mellitus is of epidemic proportions among the Native American population in the United States, hence, the incidence of diabetic complications is also increased. There has been little published research regarding the complication of lower extremity amputation within the Native population generally, and none that is specific to risk factors for LEA in the Northern Plains tribes. The purpose of this study was to identify risk factors for diabetes-related LEA in the Sioux Nation, a Native American population residing in the Northern Plains of the United States.

The case-control design for collection and comparison of data from medical records was utilized to collect information from 144 cases and 288 age and gender-matched controls. The data were analyzed through comparisons of odds ratios and means, and through the generation of logistic regression models. Models were created for the entire data set of cases and controls, and cross-validation techniques were applied to assist in the evaluation of predictors. Gender-stratified analyses were also conducted on the data, based on results from the odds ratios and comparisons of means.

Overall, several risk factors emerged that may provide direction in identifying people at risk for LEA in this population: duration of diabetes, history of insulin therapy,

and level of glycemic control. A significant finding of decreased WT/HT ratio associated with LEA suggests the presence of debilitation, related to chronic disease.

In addition, there seems to be indication for future studies of risk factors that are gender-specific, related to such variables as frequency of foot examination, level of glycemic control, and prescription of insulin therapy. It is suggested that patterns of health care access be studied as a common link among these gender differences.

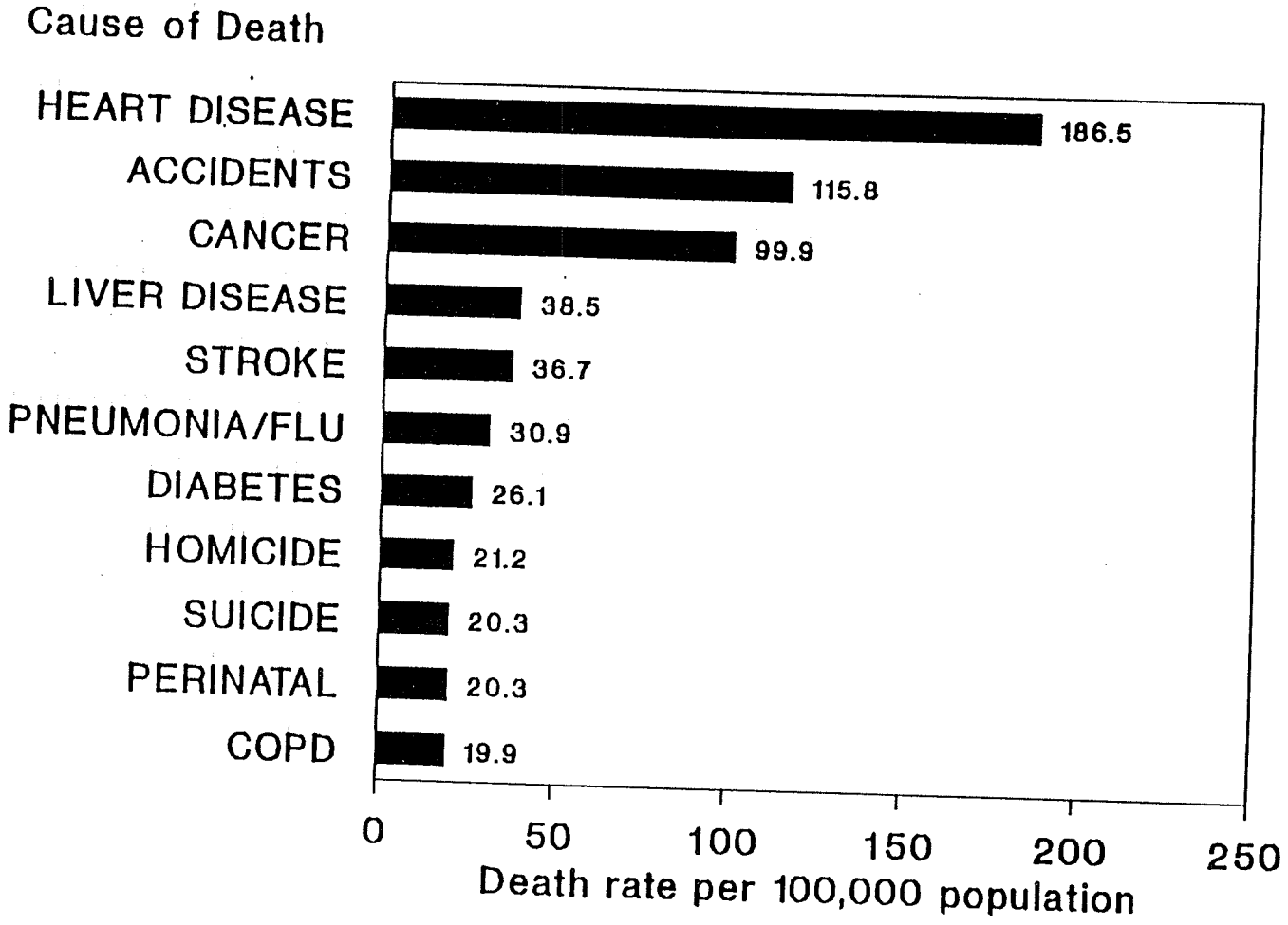
Recommendations have been made that include continued investigation in the following areas: epidemiologic studies, clinical prevention strategies, compliance with diabetic medical regimens, and disability issues related to LEA in reserve settings.

APPENDICES

APPENDIX A

AAIHS Leading Causes of Death Age-Adjusted Mortality Rates

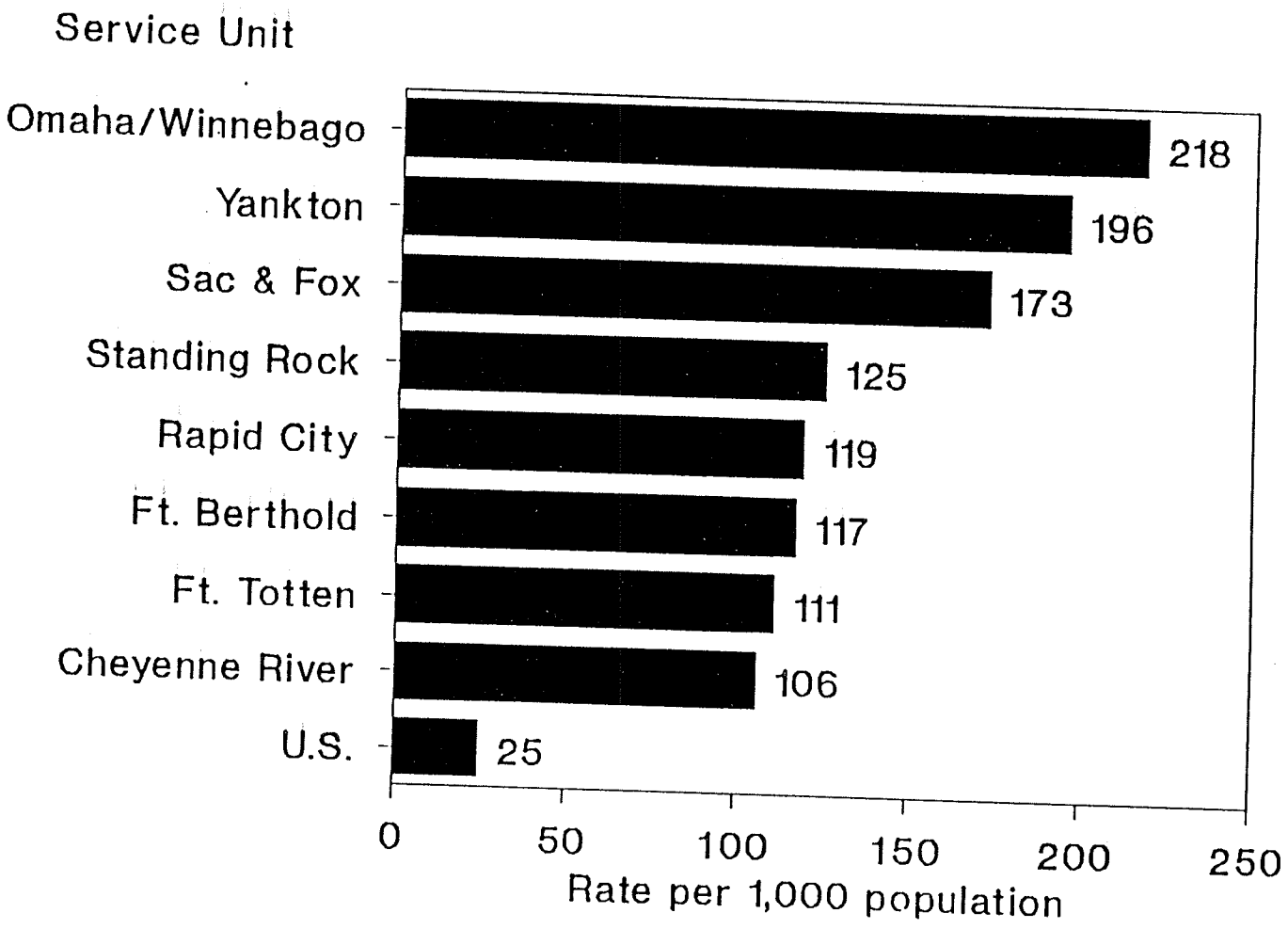
ABERDEEN AREA LEADING CAUSES OF DEATH
AGE-ADJUSTED MORTALITY RATES: FY 1985-87



APPENDIX B

AAIHS Prevalence of Diabetes

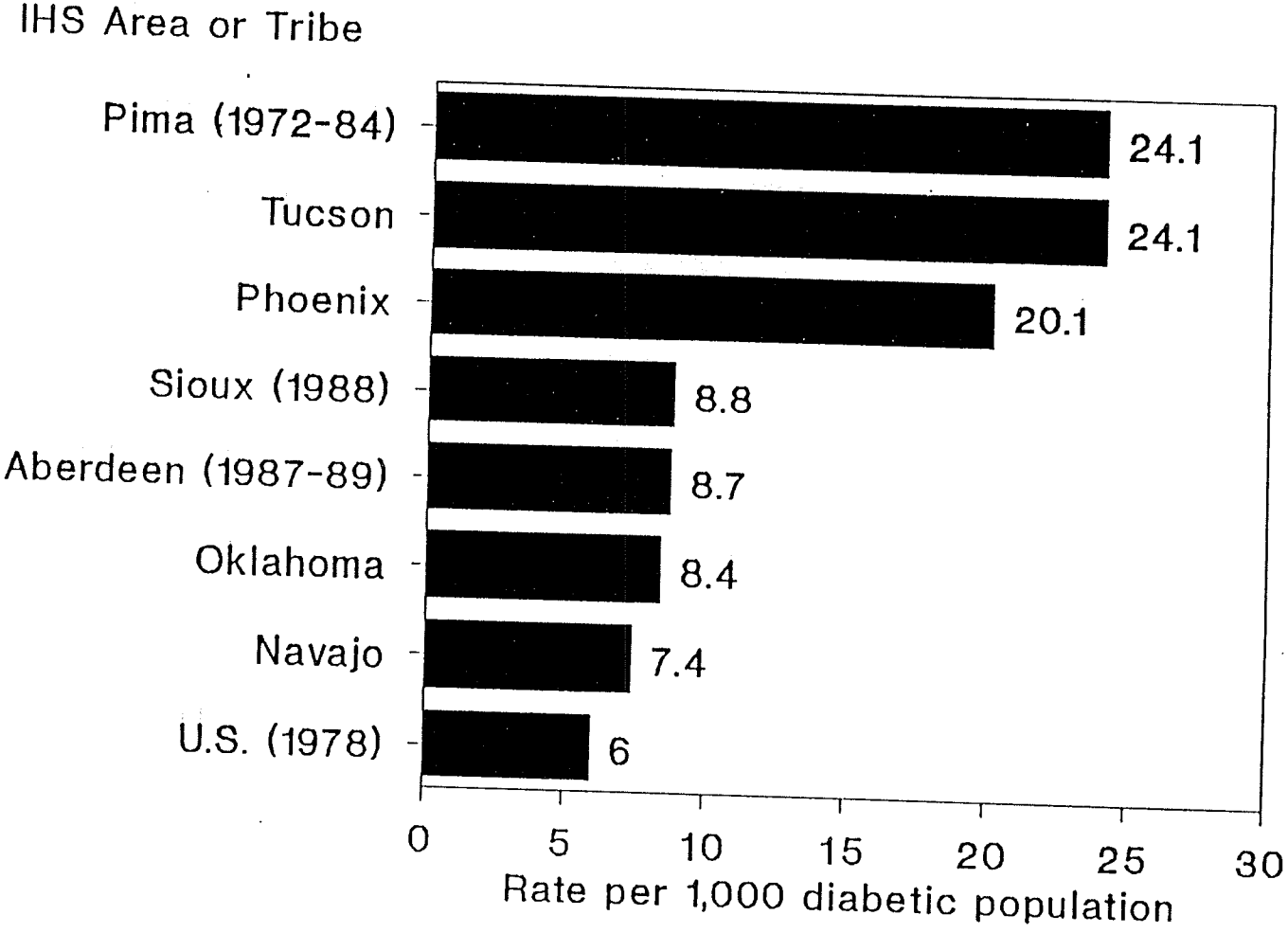
PREVALENCE OF DIABETES - FY 1987
ABERDEEN AREA SERVICE UNITS



APPENDIX C

Incidence of LEA among American Indian / Alaska Natives

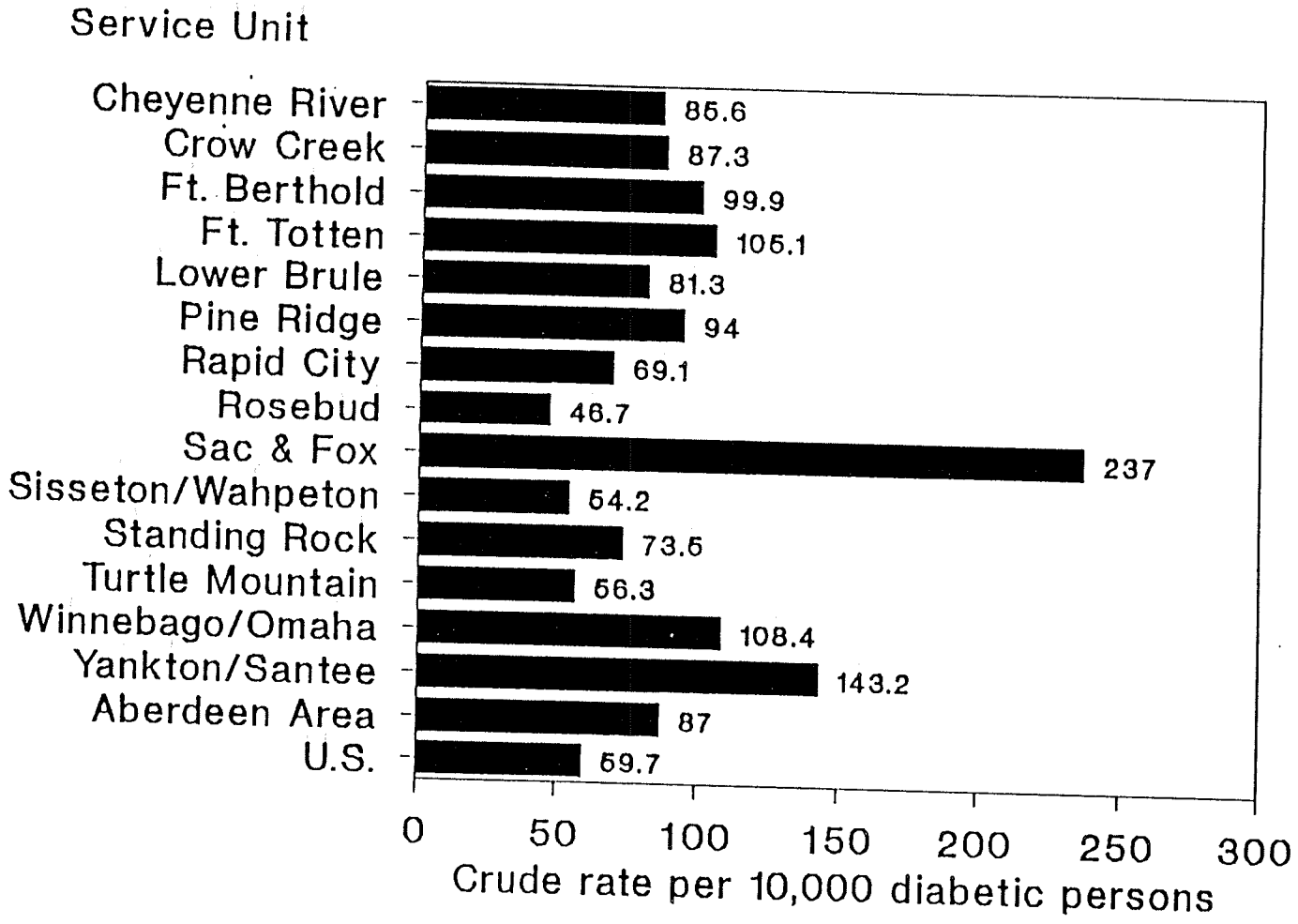
INCIDENCE OF LEA: 1982-87
AMONG AMERICAN INDIANS/ALASKA NATIVES



APPENDIX D

AAIHS Incidence of LEA

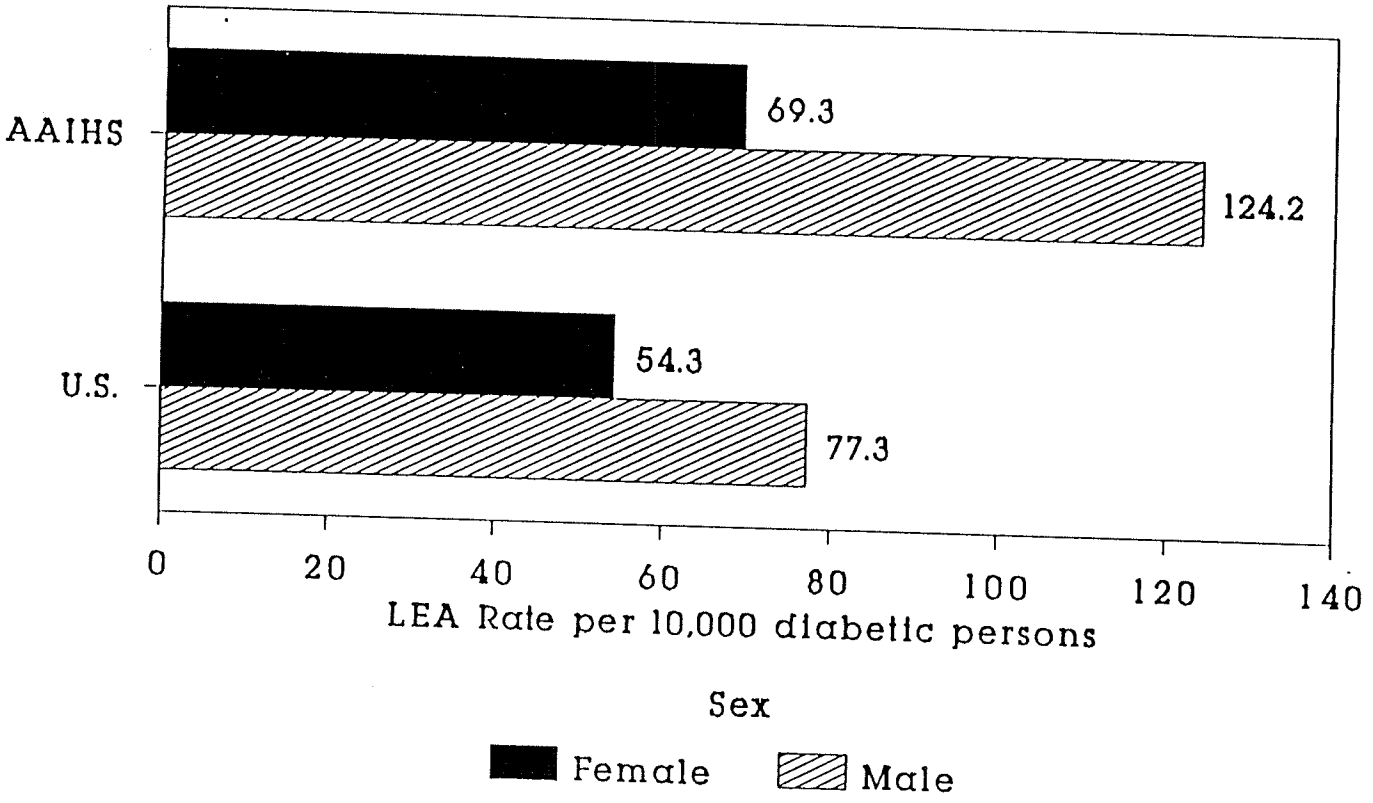
ABERDEEN AREA IHS
INCIDENCE OF LEA - FY 1987-89



APPENDIX E

Comparison of AAIHS Incidence of LEA to U.S. Incidence of LEA

ABERDEEN AREA IHS DIABETES PROGRAM
LOWER EXTREMITY AMPUTATIONS
FY 1987 - 1989



APPENDIX F

Fort Totten Diabetes Audit Form

FORT TOTTEN DIABETES AUDIT-1990

AUDIT DATE_____ REVIEWER_____

NAME_____ SEX_____ CHART NUMBER_____

DOB_____ CHECK ONE: NIDDM_____ IDDM_____ IGT_____ GEST_____

DOX:_____ IN OBVIOUS PLACE ON CHART Y N

CURRENT PATIENT: Y N NUMBER OF VISITS IN LAST YEAR:_____

IF DIED IN PAST YEAR: DATE:_____ CAUSE:_____

FLOW SHEET PRESENT Y N
FLOW SHEET CURRENT Y N

HEIGHT_____ IN OBVIOUS LOCATION ON CHART Y N

WEIGHT:_____ DATE_____ IDEAL BODY WEIGHT _____
WEIGHT ONE YEAR AGO_____ DATE_____
WEIGHT RECORDED EACH VISIT Y N

LABORATORY

BLOOD SUGAR RECORDED EACH VISIT Y N R(refused)
LAST THREE BLOOD SUGARS 1._____ F R DATE_____
F-FASTING R-RANDOM 2._____ F R DATE_____
3._____ F R DATE_____
HGBA1C_____ DATE_____

CALCULATE THE INDEX OF GLUCOSE CONTROL BY THE FOLLOWING FORMULA:
ACCEPTABLE 3 VALUES FBS $\leq$ 140 OR RBS $\leq$ 200
FAIR 1 - 2 VALUES FBS < 140 OR RBS $\leq$ 200 (circle one)
POOR 0 VALUES FBS $\leq$ 140 OR RBS $\leq$ 200
UNKNOWN CANNOT ASSESS FROM AVAILABLE INFORMATION

PROTEINURIA(greater than 300mg) LAST THREE VISITS Y N
UA IN PAST YEAR Y N R(refused)
BUN/CREAT IN LAST YEAR Y N R
CREATININE $\geq$ 2.0 MG LAST YEAR (VALUE_____) Y N
CHOLESTEROL IN LAST YEAR Y N R
VALUE_____ DATE_____
TRIGLYCERIDES IN PAST YEAR Y N R
TRIG LEVEL_____ DATE_____
HDL_____ DATE_____
LDL_____ DATE_____
EKG BASELINE DONE Y N R

PNEUMOVAX GIVEN ONCE Y N R
dT IN PAST 10 YEARS Y N R
PPD RESULTS: POSITIVE_____ NEGATIVE_____ UNKNOWN_____
IF POSITIVE, INH TREATMENT COMPLETE Y N R U
IF NEGATIVE,PPD SINCE DOX OF DIABETES Y N R U
(U-unknown)

EXAMINATIONS

EYE EXAM IN PAST YEAR(dilated or fundus photo) Y N R WN
(WN-NEWMAN)
FOOT EXAM IN LAST YEAR Y N R
(with sensation and pulses) Y N R
DENTAL EXAM IN PAST YEAR Y N R

EDUCATION

DIET INSTRUCTION IN PAST YEAR(by dietician) Y N R
DIET INSTRUCTION BY ANYONE Y N R
EXERCISE INSTRUCTION BY ANYONE Y N R
EDUCATION PLAN ON CHART Y N R
DOCUMENTATION OF PATIENT EDUCATION AT LEAST ONCE Y N R

THERAPY-check one

DIET ALONE_____ INSULIN_____ ORAL AGENT_____
ORAL AGENT PLUS INSULIN_____ UNKNOWN_____

PRIMARY CARE

BLOOD PRESSURE CHECKED EACH VISIT Y N R
HYPERTENSION PRESENT(diagnosed or undiagnosed) Y N
LAST BLOOD PRESSURES _____/_____ _____/_____ _____/_____
MEAN OF LAST 3 SYSTOLICS $\geq$ 140 Y N
MEAN OF LAST 3 DIASTOLICS $\geq$ 90 Y N
IF FEMALE, PAP SMEAR WITHIN PAST YEAR Y N R
IF FEMALE, BREAST EXAM WITHIN PAST YEAR Y N R
IF FEMALE, MAMMOGRAPHY PER NCI GUIDELINES Y N R
(every yr. if 50-70 yrs. old; every 2 yrs if 40-49 yrs. old)
ALL PATIENTS, RECTAL EXAM W/STOOL GUIAC IN PAST YEAR Y N R

COMPLICATIONS

AMPUTATION Y N
IN PAST YEAR Y N

ON DIALYSIS Y N
IN PAST YEAR Y N

RETINOPATHY Y N

LASER RX EVER Y N
IN PAST YEAR Y N

COMPLICATIONS(con't)

CATARACTS Y N
IN PAST YEAR Y N

HOSP FOR STROKE Y N
IN PAST YEAR Y N

HOSP FOR MI Y N
IN PAST YEAR Y N

HOSP FOR DIABETES IN PAST YEAR Y N

ALCOHOL PROBLEM DOCUMENTED ON PROBLEM LIST Y N

PATIENT SMOKES CIGARETTES Y N U TEACHING DONE_____

PATIENT HAS HIGH RISK FEET_____

PATIENT HAS PICKED UP MEDICATION AT
LEAST SIX TIMES IN THE LAST YEAR Y N

COMPLIANCE RATING_____ [2- (NONCOMPLIANT)-6(MOST COMPLIANT)]

COMMENTS:

APPENDIX G

AAIHS DCP Patient Amputation Registry

ABERDEEN AREA

DIABETES CONTROL PROGRAM

PATIENT AMPUTATION REGISTRY

Service Unit:_____

Patient's Name:_____

Patient's Birthdate:_____

Chart Number:_____

Sex: Female_____ Male_____

Date of Amputation: (check one)

Above Knee _____

Below Knee _____

At the ankle (whole foot) _____

Partial foot _____

Great toe _____

Other toe _____

Other _____

Reason for Amputation: (primary reason)

Trauma _____

Non-healing _____

Infection _____

Other _____

Does this patient have diabetes? Yes _____ No _____

Reported by: PHN _____ CHR _____ CHS _____

DCC _____ Other _____
(specify)

Please return completed from to:

Ruggles M. Stahn, M.D., M.P.H.
Diabetes Control Officer, AAIHS
PHS Indian Health Hospital
3200 Canyon Lake Drive
Rapid City, SD 57702

APPENDIX H

Confidentiality Pledge for Volunteers on Research Projects in AAIHS

ABERDEEN AREA INDIAN HEALTH SERVICE
OFFICE OF EPIDEMIOLOGY

Confidentiality Pledge

I, _____ understand that data obtained for subjects of research projects are confidential.

I will not reveal to unauthorized persons any patient's name or any identifying information or any other information obtained from subjects or their charts involved in any epidemiologic investigation.

I will not allow any persons who are not authorized members of the Indian Health Service facility staff or research team to have access to any information collected from or about the subjects.

I will properly store the data forms, computer printouts and other documents in locked file cabinets or drawers to protect confidentiality.

I understand that breach of this confidentiality pledge is ground for termination of this research study.

I will share all data with the Program Officer/Preceptor when my research terminates.

_____
Program Officer/Preceptor

_____
Epidemiology Program Management Officer

_____
Date

APPENDIX I

AAIHS Service Units

Aberdeen Area Indian Health Service
U.S. Public Health Service

REFERENCES

Aberdeen Area Indian Health Service, Diabetes Control Program (1991).

Acton, K., Rith-Najarian, S. & Gohdes, D. (1993). Implications of the Diabetes Control and Complication Trial. The IHS Primary Care Provider,18, 185-187.

Agency for Health Care Policy and Research (1991). Prevalence of chronic diseases: A summary of data from the survey of American Indians and Alaska Natives. National medical expenditure survey: Data summary 3. AHCPR Publication No. 91-0031. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service.

American Diabetes Association (1992). Clinical Practice Recommendations 1991-1992: Foot care in patients with diabetes mellitus. Diabetes Care,15, Suppl. 2, 19-20.

American Indian Health Care Association (1993, January). "The forgotten minority": Delivering health care to American Indians, 23-27.

Apelqvist, J., Ragnarson-Tennvall, G., Persson, U., & Larsson, J. (1994). Diabetic foot ulcers in a multidisciplinary setting: An economic analysis of primary healing and healing with amputation. Journal of Internal Medicine, 235, 463-471.

Assal, J.P., et. al. (1985). Patient education as the basis for diabetes care in clinical practice. Diabetologia, 28, 602-613.

Attvall, S., Fowelin, J., Lager, I., Von Schenck, H., & Smith, U. (1993). Smoking induces insulin resistance: A potential link with the insulin resistance syndrome. Journal of Internal Medicine, 233, 327-332.

Bailey, T.S., Yu, H.M. & Rayfield, E.J. (1985). Patterns of foot examinations in a diabetes clinic. American Journal of Medicine, 78, 371-374.

Barnett, A.H., et.al. (1981). Diabetes in identical twins: A study of 200 pairs. Diabetologia, 20, 87-93.

Beauregard, K., Cunningham, P., & Cornelius, L. (1991). Access to health care: Findings from the Survey of American Indians and Alaska Natives (AHCPR Pub. No. 91-0028). National Medical Expenditure Survey Research Findings 9, Agency for Health Care Policy and Research. Rockville, MD: Public Health Service.

Barett-Connor, E. (1989). Epidemiology, obesity, and non-insulin dependent diabetes mellitus. Epidemiologic Reviews, 11, 172-181.

Bennett, P.H., Burch, T.A., & Miller, M. (1971). Diabetes mellitus in American (Pima) Indians. Lancet, 2, 125-128.

Bild, D.E. Unpublished manuscript.

Bild, D.E., Selby, J.V., Sinnock, P., Browner, W.S., Braveman, P. & Showstack, J.A. (1989). Lower-extremity amputation in people with diabetes. Epidemiology and prevention. Diabetes Care, 12, 24-31.

Bjorntorp, P. (1988). Abdominal obesity and the development of non-insulin-dependent diabetes mellitus. Diabetes Metabolism Review, 4, 615-622.

Boulton, A.J.M. et. al. (1986). Impaired vibratory perception and diabetic foot ulceration. Diabetic Medicine, 3, 335-337.

Brod, T.M. (1975). Alcoholism as a mental health problem of Native Americans: A review of the literature. Archives of General Psychiatry, 32, 1385-1391.

Bronfenbrenner, U. (1979). The Ecology of Human Development, Harvard Press: Cambridge.

Brosseau, J., Eelkema, R., Crawford, A. & Abe, T. (1979). Diabetes among the Three Affiliated Tribes: Correlation with degree of Indian inheritance American Journal of Public Health, 69, 1277-1278.

Brosseau, J.D. (1993). Increasing prevalence of diabetes among the Three Affiliated Tribes. Diabetes Care, 16, 248-249.

Brunner, L.S. & Suddarth, D.S. (Eds.) (1988). Textbook of medical-surgical nursing, 6th edition. Philadelphia: J.B. Lippincott.

Chantelau, E., Kushner, T. & Spraul, M. (1989). How effective is cushioned therapeutic foot wear in protecting diabetic feet? A clinical study. Diabetic Medicine, 7, 355-359.

Chiu, K.C., Province, M.A., & Permutt, M.A. (1992). Glucokinase gene is genetic marker for NIDDM in American Blacks. Diabetes, 41, 843-849.

Christlieb, R., Krolewski, A., Warram, J. & Soeldner, S. (1985). Is insulin the link between hypertension and obesity? Hypertension, 7, Suppl II, II-54 - II-57.

Connell, F.A., Shaw, C., & Will, J. (1989). Lower extremity amputations among persons with diabetes mellitus - Washington, 1988. MMWR, 40, 737-739.

Cowie, et.al., (1993). Effect of multiple risk factors on differences between Blacks and Whites in the prevalence of non-insulin-dependent diabetes mellitus in the United States. American Journal of Epidemiology, 137, 719-732.

Dean, A.G., Dean, J.A., Burton, A.H., 7 Dicker, R.C. (1990). Epi Info Version 5. Centers for Disease Control: Atlanta.

DeFronzo, R.A. & Ferrannini, E. (1991). Insulin resistance: A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care, 14, 173-194.

Del Aguila, M.A., Reiber, G.E., & Koepsell, T.D. (1994). How does provider and patient awareness of high-risk status for lower-extremity amputation influence foot-care practice? Diabetes Care, 17, 1050-1054.

Delbridge, L, Appleberg, M., & Reeve, T.S. (1983). Factors associated with development of foot lesions in the diabetic. Surgery, 93, 78-82.

Dinneen, S., Gerich, J., & Rizza, R. (1992). Carbohydrate metabolism in non-insulin-dependent diabetes mellitus. The New England Journal of Medicine, 327, 707-713.

Donahue, R.P. & Orchard, T.J. (1992). Diabetes Mellitus and macrovascular complications: A epidemiological perspective. Diabetes Care, 15, 1141-1155.

Dyck, P.J. (1992). New understanding and treatment of diabetic neuropathy. The New England Journal of Medicine, 326, 1287-1288.

Farrell, M.A. & Miner, K. (1988). The prevention of amputations in diabetic patients: An IHS hospital's perspective. The IHS Primary Care Provider, December.

Elkeles, R.S. & Wolfe, J.H. (1991). The diabetic foot. British Medical Journal, 303, 1053-1055.

Engel, G.L. (1977). The need for a new medical model: a challenge for biomedicine. Science, 192, 129-136.

Freeman, W., Hosey, G., Diehr, P. & Gohdes, D. (1989). Diabetes in American Indians of Washington, Oregon, and Idaho. Diabetes Care, 4, 282-288.

Fuller, J.H. (1985). Epidemiology of hypertension associated with diabetes mellitus. Hypertension, 7, 113-117.

Garro, L.C. (1995). Individual or societal responsibility? Explanations of diabetes in an Anishinaabe (Objibway) community. Social Science and Medicine, 40, 37-46.

Gavin, J.R. & Davidson, J.A. (1992). Type II diabetes in minorities, Current Concepts, Upjohn: Kalamazoo.

Gavin, L.A., Stess, R.M., & Goldstone, J. (1993). Prevention and treatment of foot problems in diabetes mellitus: A comprehensive program. Western Journal of Medicine, 158, 47-55.

Genuth, S. (1990). Insulin use in NIDDM. Diabetes Care, 13, 1240-1264.

Gilmore, J.E., Allen, J.A., & Hayes, J.R. (1993). Autonomic function in neuropathic diabetic patients with foot ulceration. Diabetes Care, 16, 61-67.

Ginsberg, H.N. (1991). Lipoprotein physiology in nondiabetic and diabetic states: Relationship to atherogenesis. Diabetes Care, 14, 839-855.

Gohdes, D. (1986). Diabetes in American Indians. Diabetes Care, 9, 609-613.

Greene, D. (1988). The pathogenesis and prevention of diabetic neuropathy and nephropathy. Metabolism, 37(2), Suppl.1, 25-29.

Greene, D.A., Lattimer, S.A. & Sima, A.A.F. (1988). Pathogenesis and prevention of diabetic neuropathy. Diabetes Metabolism Review, 4, 201-221.

Gregory, R., Tattersall, R.B., & Allison, S.P. (1994). Peripheral neuropathy as a presenting feature of Type 2 diabetes: A case-controlled study. Diabetic Medicine, 11, 407-409.

Haffner, et.al. (1990). Incidence of type II diabetes in Mexican Americans predicted by fasting insulin and glucose levels, obesity, and body-fat distribution. Diabetes, 39, 283-288.

Harati, Y. (1987). Diabetic peripheral neuropathies. Annals of Internal Medicine, 107, 546-559.

Hassard, T. Unpublished manuscript, p. 74.

Heath, S.W., Ornelas, R., & Marquart, C. (1993). An action plan for American Indian and Alaska Native elders. The IHS Primary Care Provider, 18, 81-86.

Henly, S.J., Klebe, K.J. & Dudeck, R. (1989). Adaptive and conventional versions of the DAT: The first complete test battery comparison. Applied Psychological Measurement, 13, 363-371.

Hintze, J.L. (1991). Number Cruncher Statistical System, Version 5.03. Hintze: Kaysville, UT.

Hosmer, D.W. & Lemeshow, S. (1989). Applied Logistic Regression. New York: Wiley.

Hosmer, D.W., Taber, S. & Lemeshow, S. (1991). The importance of assessing the fit of logistic regression models: A case study. American Journal of Public Health, 81, 1630-1635.

Houston, M. (1989). Treatment of hypertension in diabetes mellitus. American Heart Journal, 118, 819-829.

Hrabovsky, S., Welty, T., & Coulehan, J. (1989). Acute myocardial infarction and sudden death in Sioux Indians. Western Journal of Medicine, 150, 420-422.

Indian Health Service (1988). Summary of Leading Causes for All Outpatient Visits: IHS Direct and Contract Facilities. Public Health Services, U.S. Department of Health and Human Services.

Indian Health Service (1990). Trends in Indian Health. Public Health Services, U.S. Department of Health and Human Services.

Indian Health Service (1992). Trends in Indian Health. Public Health Services, U.S. Department of Health and Human Services.

Ingelfinger, J.A., Bennett, P.H., Liebow, I.M., & Miller, M. (1976). Coronary heart disease in the Pima Indians: Electrographic findings and post-mortem evidence of myocardial infarction in a population with a high prevalence of diabetes mellitus. Diabetes, 25, 561-565.

Janka, H.U. & Dirschedl, P. (1985). Systolic blood pressure as a predictor for cardiovascular disease in diabetes: a 5 year longitudinal study. Hypertension, 7, Suppl II, II-90 - II-94.

Janka, H.U., Standl, L. & Mehnert, H. (1980). Peripheral vascular disease in diabetes mellitus and its relation to cardiovascular risk factors: Screening with the Doppler ultrasonic technique. Diabetes Care, 3, 207-213.

Joe, J. (1988). Interview in Non-insulin dependent diabetes mellitus in Native Americans: A roundtable discussion. Kalamazoo: Upjohn.

Johnson, A. & Taylor, A. (1991). Prevalence of chronic diseases: A summary of data from the Survey of American Indians and Alaska Natives (AHCPR Pub. No. 91-0031). National Medical Expenditure Survey Data Summary 3. Agency for Health Care Policy and Research. Rockville, MD: Public Health Service.

Kannel, W.B. & McGee, D.L. (1985). Update on some epidemiologic features of intermittent claudication: The Framingham study. Journal of the American Geriatrics Association, 33, 13-18.

Klein, B.E., Moss, S.E., & Klein, R. (1987). Longitudinal measure of glycemic control and diabetic retinopathy. Diabetes Care, 10, 273-277.

Kleinman, A. (1978). Concepts and a model for the comparison of medical systems as cultural systems. Social Science and Medicine, 12, 85-93.

Kleinman, A. (1988). The illness narratives. New York: Basic Books.

Knowler, W.C., Pettit, D.J., Saad, M., & Bennett, P.H. (1990). Diabetes mellitus in the Pima Indians: Incidence, risk factors and pathogenesis. Diabetes Metabolism Reviews, 6(1), 1-27.

Kriska, A.M., LaPorte, R.E., Pettitt, D.J. et. al. (1993). The association of physical activity wit obesity, fat distribution and glucose intolerance in Pima Indians. Diabetologia, 36, 863-869.

Kunzelman, C.L., Knowler, W.C., Pettitt, D.J., & Bennett, P.H. (1989). Incidence of proteinuria in type 2 diabetes mellitus in the Pima Indians. Kidney International, 35, 681-687.

LaDuke, W. & Churchill, W. (1985). Native America: The political economy of radioactive colonialism. Journal of Ethnic Studies, 13, 107-131.

Lang, G.C. (1985). Diabetics and health care in a Sioux community. Human Organization, 44, 251-260.

Lang, G.C. (1989). "Making sense about diabetes: Dakota narratives of illness. Medical Anthropology, 11, 305-327.

Lasker, R.D. (1993). The diabetes control and complications trial: Implications for policy and practice. The New England Journal of Medicine, 329, 1035-1036.

Lee, E.T., et. al. (1990). American Journal of Epidemiology, 132, 1141-1143.

Lee, J.S., Lu, M., Lee, V.S., Russell, D., Bahr, C., & Lee, E.T. (1993). Lower-extremity amputation: Incidence, risk factors, and mortality in the Oklahoma Indian Diabetes Study. Diabetes, 42, 876-882.

Leichter, S.B., Schaeffer, J.C. & O'Brian, J.T. (1991). New concepts in managing diabetic foot infections. Geriatrics, 46, 24-30.

Lewis, O. (1970). Anthroplological Essays. Random House: New York.

Lienhard, G.E., Slot, J.W., James, D.E., & Mueckler, M.M. (January, 1992). How cells absorb glucose. Scientific American, 86-91.

Lillioja, S., Young, A.A., Cutler, C.L., et.al. (1987). Skeletal muscle capillary density and fiber type are possible determinants in vivo insulin resistance in man. Journal of Clinical Investigation, 80, 415-424.

Lillioja, S., Mott, D.M., Howard, B.V., et.al.(1988). Impaired glucose tolerance as a disorder of insulin action: Longitudinal cross-sectional studies in Pima Indians. The New England Journal of Medicine, 318,, 1217-1225.

Lillioja, S., Mott, D.M., Spraul, M., et.al. (1993). Insulin resistance and insulin secretory dysfunction as precursors of non-insulin-dependent diabetes mellitus: Prospective studies of Pima Indians. The New England Journal of Medicine, 329, 1988-1992.

Lithner, H. & Tornblum, N. (1984). Gangrene localized to the feet in diabetic patients. Acta Medica Scandinavia, 215, 75-79.

Litzelman, D.K., Slemenda, C.W., Langfeld, C.D., et.al. (1993). Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitus. Annals of Internal Medicine, 119, 36-41.

Ludtke, R. & Pan, S. (August, 1994). Do most Native Americans have a usual source for health care services? National Resource Center on Native American Aging at the University of North Dakota, Report 94-1.

Most, R.S. & Sinnock, P. (1983). The epidemiology of lower extremity amputations in diabetic individuals. Diabetes Care, 6, 87-91.

Muhlhauser, I. (1994). Cigarette smoking and diabetes: An update. Diabetic Medicine, 11, 336-343.

Muneta, B., Newman, J., Wetterall, S., & Stevenson, J. (1993). Diabetes and associated risk factors among Native Americans. Diabetes Care, 12, 1619-1620.

Murdock, S.H. & Schwartz, D.F. (1978). Family structure and the use of agency services: An examination of patterns among elderly Native Americans. The Gerontologist, 18, 475-481.

Nathan, D.M. (1990). Hemoglobin A_{Ic} -- infatuation or the real thing? New England Journal of Medicine, 323, 1062-1064.

National Diabetes Data Group (1984). Diabetes in America. NIH publication No. 85-1468. National Institutes of Health, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, U.S. Department of Health and Human Services.

Nelson, R.G., Gohdes, D.M., Everhart, J.E., Hartner, J.A., Zwemer, F.L., Pettitt, D.J., & Knowler, W.C. (1988). Lower extremity amputations in NIDDM: 12 year follow-up study in Pima Indians. Diabetes Care, 11, 8-16.

Nelson, R.G., Kunzelman, C.L., Pettitt, D.J., Saad, M.F., Bennett, P.H., & Knowler, W.C. (1989). Albuminuria in type 2 (non-insulin dependent) diabetes mellitus and impaired glucose tolerance in Pima Indians. Diabetologia, 32, 870-876.

Nutting, P.A., Helgerson, S.D., Welty, T.K., Kileen, M.J. & Jackson, M.Y. (1990). A research agenda for Indian Health, part 5: Researchable questions in chronic disease. The IHS Primary Care Provider, 15(3), 29-38.

Office of Technology Assessment. (1986). Indian Health Care. Washington, DC: Office of Technology Assessment.

Ohlson, L.O., et.al. (1985). The influence of body fat distribution on the incidence of diabetes mellitus: 13.5 years of follow-up of the participants in the study of men born in 1913. Diabetes, 34, 1055-1058.

O'Neil, J.D. (1986). The politics of health in the fourth world: A northern Canadian example. Human Organization, 45, 119-127.

Pagano, G., Bargero, G., Vuolo, A., & Bruno, G. (1993). Prevalence and clinical features of known Type 2 diabetes in the elderly: A population-based study. Diabetic Medicine, 10, 475-478.

Palumbo, P.J. & Melton, (1985). Peripheral vascular disease and diabetes. In Diabetes in America. NIH publication No. 85-1468, National Institutes of Health, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, U.S. Department of Health and Human Services.

Pecoraro, R.E., Reiber, g.E., Burgess, E.M. (1990). Pathways to diabetic limb amputation: Basis for prevention. Diabetes Care, 13, 513-521.

Pirart, J. (1978). Diabetes mellitus and its degenerative complications: Prospective study of 4,400 patients observed between 1947 and 1973. Diabetes Care, 1, 168-188, 253-263.

Prochazka, M., Lillioja, S., Tait, J.F., Knowler, W.C., Mott, D.M., Spraul, M., Bennett, P., & Bogardus, C. (1993). Linkage of chromosomal markers on 4q with a putative gene determining maximal insulin action in Pima Indians. Diabetes, 42, 514-519.

Raboudi, S.H., et.al. (1989). Type II diabetes mellitus and polymophism of insulin-receptor gene in Mexican-Americans. Diabetes, 38,, 975-980.

Rate, R.G., et. al. (1983). Diabetes mellitus in Hopi and Navajo Indians: Prevalence of microvascular complications. Diabetes, 32, 894-899.

Ravussin, E., Valencia, M.E., Esparza, J., Bennett, P.H., & Schulz, L.O. (1994). Effects of a traditional lifestyle on obesity in Pima Indians. Diabetes Care, 17, 1067-1074.

Reaven, G.M. (1991). Insulin resistance, hyperinsulinemia, hypertriglyceridemia, and hypertension: Parallels between human disease and rodent models. Diabetes Care, 14, 195-202.

Reiber, G.E., Pecoraro, R.E., & Koepsell, T.D. (1992). Risk factors for amputation in patients with diabetes mellitus: A case-control study. 117, 97-105.

Rhoades, E.R., Hammond, J., Welty, T.K., Handler, A.O. & Amler, R.W. (1987). The Indian burden of illness and future health interventions. Public Health Reports, 102(4), 361-368.

Rith-Najarian, S., Stolusky, T., Mayfield, J.A., & Gohdes, D. (February, 1993). Reducing amputations caused by diabetes in American Indians: A simple strategy. The IHS Primary Care Provider.

Rith-Najarian, S., Stolusky, T., & Gohdes, D. (1992). Identifying diabetic patients at high risk for lower-extremity amputation in a primary health care setting: A prospective evaluation of simple screening criteria. Diabetes Care, 15, 1386-1389.

Ritenbaugh, C. & Goodby, C. (1989). Beyond the thrify gene: Metabolic implications of prehistoric migration into the new world. Medical Anthropology, 11, 227-236.

Scheper-Hughes, N. (1990). Three propositions for a critically applied medical anthropology. Social Science and Medicine, 30, 189-197.

Schlesselman, J.J. (1982). Case-Control Studies: design, Conduct, and Analysis. New York Press.

Schraer, C.D., Lanier, A.P., Boydo, E.J., Gohdes, D. & Murphy, N.J. (1988). Prevalence of diabetes mellitus in Alaskan Eskimos, Indians, and Aleuts. Diabetes Care, 11, 693-700.

Secretary's Task Force on Black and Minority Health (1986). Report, Volume II: Crosscutting Issues in Minority Health. U.S. Department of Health and Human Services.

Shaten, B.J., Smith, G.D., Kuller, L.H., & Neaton, J.D. (1993). Risk factors for the development of Type II diabetes among men enrolled in the usual care group of the Multiple Risk Factor Intervention Trial. Diabetes Care, 16, 1331-1339.

Shkilnyk, A.M. (1985). A Poison Stronger Than Love: The Destruction of an Ojibwa Community. Yale University Press: New Haven.

Sievers, M.L. & Fisher, J.R. (1984). Diabetes in North American Indians. In Diabetes in America, NIH publication no. 85-1468, XI. 1-20. National Institutes of Health, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, U.S. Department of Health and Human Services.

Singer, M. (1990). Reinventing medical anthropology: Towards a critical realignment. Social Science and Medicine, 30, 179-187.

Siperstein, M.D. (1988). Diabetic microangiopathy, genetics, environment, and treatment. The American Journal of Medicine, 85, 119-129.

Skolnik, A.A. (1992). Foot care program for patients with leprosy also may prevent amputations in persons with diabetes. Journal of the American Medical Association, 267, 2288.

Slotnik, Henry, University of North Dakota School of Medicine, Personal communication.

Stahn, R.M., Gohdes, D., & Valway, S.E. (1993). Diabetes and its complications among selected tribes in North Dakota, South Dakota, and Nebraska. Diabetes Care, 16, 244-247.

Steffes, M.W. & Maurer, S.M. (1991). Towards a basic understanding of diabetic complications. New England Journal of Medicine, 325, 883-884.

Stern, M.P. (1991). Primary prevention of Type II diabetes mellitus. Diabetes Care, 14, 399-410.

Stolar, M.W. (1988). Atherosclerosis in diabetes: the role of hyperinsulinemia. Metabolism, 37(2), Suppl 1, 1-9.

Szathmary, E.J.E., Ritenbaugh, C., & Goodby, C.S. (1987). Dietary change and plasma glucose levels in an Amerindian population undergoing cultural transition. Social Science and Medicine, 24, 791-804.

Szathmary, E. (1989). The impact of low carbohydrate consumption on glucose tolerance, insulin concentration, and insulin response to glucose challenge in Dogrib Indians. Medical Anthropology, 11, 329-350.

Taylor, A. & Johnson, A. (1991). Prevalence of chronic diseases: A summary of data from the Survey of American Indians and Alaska Natives (Agency for Health Care Policy and Research Publication No. 91-0031). National Medical Expenditure Survey Data Summary 3. Agency for Health Care Policy and Research. Rockville, MD: U.S. Public Health Service.

Teisberg, P. (1993). Genetics of non-insulin dependent diabetes mellitus. Journal of Internal Medicine, 234, 439-440.

Tesh, S. (1981). Disease causality and politics. Journal of Health Politics, Policy, and Law, 6, 369-390.

Thomas, P.K. (1992). Diabetic neuropathy: Models, mechanisms, and mayhem. Canadian Journal of Neurological Science, 19, 1-7.

Toubbeh, J.I. (1985). Handicapping and disabling conditions in Native American populations. American Rehabilitation, 11 (11), 3-8, 30-32.

Trost, B.N., Weidmann, P. & Beretta-Piccoli, C. (1985). Antihypertensive therapy in diabetic patients. Hypertension, 7, Suppl II, II-102 - II-108.

United States Department of Health and Human Services, (1990). Healthy People 2000: National Health Promotion and Disease Prevention Objectives. DHHS Publication No. (PHS) 91-50212.

Vionnet, N., Stoffel, M., Takeda, J., et.al. (1992). Nonsense mutation in the glucokinase gene causes early-onset non-insulin-dependent diabetes mellitus, Nature, 356, 721-722.

Waitzkin, H. (1978). A Marxist view of medical care. Annals of Internal Medicine, 89, 264-278.

Walters, D.P., Gatling, W., Mullee, M.A., & Hill, R.D. (1992). The distribution and severity of diabetic foot disease: A community study with comparison to a non-diabetic group. Diabetic Medicine, 9, 354-358.

Weiss, K.M., Ulbrecht, J.S., Cavanaugh, P.R. & Buchanan, A.V. (1989). Diabetes mellitus in American Indians: Characteristics, origins, and preventive health care implications. Medical Anthropology, 11, 283-304.

Welty, T.K. & Coulehan, T. (1994). Cardiovascular disease among American Indians and Alaska Natives. The IHS Primary Care Provider, 19, 70-75.

Wendorf, M. (1989). Diabetes, the ice free corridor, and the Paleoindian settlement of North America. American Journal of Physical Anthropology, 79, 503-520.

Wendorf, M. & Goldfine, I.D. (1991). Archaeology of NIDDM: Excavation of the "thrifty genotype". Diabetes, 40, 161-165.

West, K.M. (1974). Diabetes in American Indians and other native populations of the new world. Diabetes, 23, 841-855.

West, K.M. (1978). Diabetes in American Indians. Advances in Metabolic Disease, 9, 29-48.

West, K.M., et. al. (1983). The role of circulating glucose triglyceride concentrations and their interactions with other "risk factors" as determinants of arterial disease in nine diabetic population samples from the WHO multinational study. Diabetes Care, 6, 361-369.

Wiedman, D.W. (1989). Adiposity or longevity: Which factor accounts for the increase in type II diabetes mellitus when populations acculturate to an industrial technology? Medical Anthropology, 11, 237-254.

Windom, R.E. (1988). Journal of the American Medical Association, 260, 1346.

Woolbridge, J. & Moreno, L. (1994). Evaluation of the costs to Medicare of covering therapeutic shoes for diabetic patients. Diabetes Care, 17, 541-543.

Young, T.K. (1990). Cardiovascular Diseases and Risk Factors among North American Indians. Northern Health Research Unit: University of Manitoba, Canada.

Young, T.K. (1993). Diabetes mellitus among Native Americans in Canada and the United States: An epidemiological review. American Journal of Human Biology, 5, 399-413.

Young, T.K., McIntyre, L.L., Dooley, J., & Rodriguez, J. (1985). Epidemiologic features of diabetes mellitus among Indians in northwestern Ontario and northeastern Manitoba. Canadian Medical Association Journal, 132, 793-797.

Young, M.J., Veves, A., & Boulton, A.J.M. (1993). The diabetic foot: Aetiopathogenesis and management. Diabetes/Metabolism Reviews, 9, 109-127.

Zimmet, P.Z. (1992). Challenges in diabetes epidemiology: From West to the rest. Diabetes Care, 15, 232-252.

Zwemer, F.L. (1990). Amputations in diabetic Native Americans. Indian Health Service Primary Care Provider, 15(8), 117-120.