DATA AND KNOWLEDGE ACQUISITION IN CASE-BASED REASONING FOR
DIABETES MANAGEMENT

A thesis presented to
the faculty of
the Russ College of Engineering and Technology of Ohio University

In partial fulfillment
of the requirements for the degree
Master of Science

Anthony Maimone
August 2006
This thesis entitled
DATA AND KNOWLEDGE ACQUISITION IN CASE-BASED REASONING FOR
DIABETES MANAGEMENT

by

ANTHONY MAIMONE

has been approved for

the School of Electrical Engineering and Computer Science
and the Russ College of Engineering and Technology by

Cynthia R. Marling
Assistant Professor of Electrical Engineering and Computer Science

Dennis Irwin
Dean, College of Engineering and Technology
This thesis presents work in data and knowledge acquisition in case-based reasoning for diabetes management. Contributions include designing and implementing a database, designing and implementing a website, and acquiring knowledge to build cases for a Case-Based Reasoning (CBR) system. This work is the initial phase of a project that will provide automated insulin therapy adjustments to Type 1 Diabetics on insulin pumps. An Ohio University Institutional Review Board approved study is under way which collects and analyzes data from patients with Type 1 Diabetes for use in knowledge engineering. Data is interpreted and analyzed by physicians to find problems, create solutions, and adjust insulin therapy accordingly. Knowledge acquired from physicians is used to create cases for the CBR system. The cases embody problem solving knowledge that will be used to help future patients.

Approved:

Cynthia R. Marling
Assistant Professor of Electrical Engineering and Computer Science
Acknowledgments

I would like to thank all of my friends, family, and professors for all of their support while I was working on my thesis. Specifically, Professor Cynthia Marling, Wesley Miller, Dr. Frank Schwartz, and Dr. Jay Shubrook for all their hard work regarding our project. Also, I would like to thank Prof. Marling for proofreading my thesis, Steven Diehl for guiding me through \LaTeX{} problems, and Kathryn Brady for helping me in every way.
Table of Contents

Abstract .......................................................... 3
Acknowledgments .................................................. 4
List of Figures ..................................................... 8
List of Tables ...................................................... 9

1 INTRODUCTION ................................................. 10

2 BACKGROUND .................................................. 16
  2.1 Diabetes ...................................................... 17
    2.1.1 Type 1 Diabetes .......................................... 18
    2.1.2 Traditional Treatment/Therapy for Type 1 Diabetes .... 21
    2.1.3 Emerging Trends in the Management of Type 1 Diabetes .. 23
  2.2 How Can Case-Based Reasoning Help? ......................... 24
  2.3 Diabetes Research Systems .................................. 26
    2.3.1 Telematic Management of Insulin-Dependent Diabetes Mellitus 27
    2.3.2 VIE-DIAB ............................................... 28
    2.3.3 Controlled Assisted Meal Related Insulin Therapy ....... 28
  2.4 Commercially Available Software ........................... 29
    2.4.1 Medtronic MiniMed ....................................... 29
    2.4.2 Unmet Needs ............................................. 32
  2.5 Preliminary Study .......................................... 32

3 DATA AND KNOWLEDGE ACQUISITION .......................... 35
  3.1 Initial Knowledge Acquisition to Identify Case Features .... 37
  3.2 Database Design and Implementation ........................ 40
    3.2.1 Patient History .......................................... 41
    3.2.2 Normal Daily Schedule ................................... 43
    3.2.3 Daily Events ............................................. 44
    3.2.4 Insulin Usage and Blood Glucose Measurements .......... 44
    3.2.5 Hypoglycemic Events ...................................... 45
    3.2.6 Illness and Stressful Events ............................. 46
    3.2.7 Other Events ............................................. 46
    3.2.8 Too Much Data Now? ...................................... 47
  3.3 Website ................................................... 48
    3.3.1 Registration Pages ........................................ 49
A  Website Views ................................................................. 113
   A.1  Registration pages .................................................. 113
   A.2  Non-Registration pages ........................................... 123
   A.3  Administrator pages ............................................... 136

B  Artificial Intelligence Scenarios ....................................... 140

C  Patient Informed Consent Form ....................................... 143

D  Preliminary Study Protocol Timeline ................................ 147

E  Intelligent Decision Support Survey ................................. 149
## List of Figures

3.1 An Example Case for Patient 1. ........................................ 62
3.2 An Example Case for Patient 2. ........................................ 64
3.3 The Next Case for Patient 2. ........................................ 66

A.1 The Login Page. .................................................. 114
A.2 The Greetings Page. .................................................. 115
A.3 The Second Registration Page. ..................................... 116
A.4 The Complications Page. .......................................... 117
A.5 The Relatives with Diabetes Page. ................................. 118
A.6 The Chronic Illnesses Page. ....................................... 119
A.7 The Medications Page. ............................................. 120
A.8 The Basal Rates Page. ............................................. 121
A.9 The Daily Schedule Page. ......................................... 122
A.10 The Home Page. ................................................... 124
A.11 The Daily Exercise, Work, and Sleep Page. ...................... 125
A.12 The Meals Page. .................................................. 126
A.13 The Foods Page. .................................................. 127
A.14 The Measurements Page. ......................................... 128
A.15 The Fingerstick Measurements Page. ............................ 129
A.16 The Temporary Basal Rates Page. ................................. 130
A.17 The Bolus Measurements Page. ................................ 131
A.18 The Infusion Set Page. ............................................ 132
A.19 The Hypglycemic Episode Page. .................................. 133
A.20 The Other Events Page. .......................................... 134
A.21 The Daily Log Page. ............................................. 135
A.22 The Administrators Intervention Page. .......................... 137
A.23 The Administrators Change Password Page. .................... 138
A.24 The Administrators Add Patient Page. ............................ 139

D.1 The Study’s Protocol Timeline. ................................. 148
List of Tables

3.1 Table Names from our Database ........................................ 42
Chapter 1

INTRODUCTION
This thesis presents work in data and knowledge acquisition in case-based reasoning for management of type 1 diabetics on insulin pump therapy. This work is the initial phase of a project to create an automated insulin therapy advisory system. This system will help regulate patients’ blood glucose levels based on previous experiences using Case-Based Reasoning (CBR), which is a subfield of Artificial Intelligence (AI).

This work is interdisciplinary and of importance to both Medicine and AI. It is important to Medicine because controlling diabetes leads to fewer complications. Diabetes is a disease where the body does not produce or properly use insulin [Wray, 2006]. Type 1 Diabetes results from the body’s complete lack of producing insulin from destruction of the beta cells in the pancreas [Association, 2003]. A ten year study called the Diabetes Control and Complications Trial (DCCT) was created by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in 1983 to learn if keeping blood glucose levels under control could prevent complications [Association, 2003]. “Researchers found that after 10 years, practicing tight control reduced the risk of developing eye disease (retinopathy) by 76 percent, kidney disease by 50 percent, nerve disease by 60 percent, and cardiovascular disease by 35 percent” [Association, 2003]. Those who have Type 1 Diabetes need to regulate their blood glucose levels to prevent long term complications. This is done with insulin therapy that is designed by the physician and controlled by both the physician and patient. The patient controls blood glucose levels by monitoring their levels and tracking food.
consumption and daily activities. The physician adjusts therapy during the patient visits to his practice every three to four months. The physician will interpret data maintained by the patient, find problems, create solutions, and adjust the patient’s therapy accordingly to help control long term complications.

One definition of AI is “the study of how to make computers do things at which, at the moment, people are better” [Rich and Knight, 1991]. This work is important to AI because physicians are able to change therapy regimens for diabetics on insulin pump therapy, but computers are not. Medtronic MiniMed, the current “world leader in insulin pump therapy” [MiniMed, 2006c], “does not practice medicine or provide medical services or advice” [MiniMed, 2001]. This company has created the Bolus Wizard® Calculator which contains a numeric algorithm for setting bolus insulin dosages based on limited data [MiniMed, 2006a]. They do not attempt to manage basal insulin or lifestyle factors including blood glucose control. There are no formal algorithms for controlling type 1 diabetes, but previous research systems have attempted to use reasoning methods, including Rule-Based Reasoning (RBR) and Model-Based Reasoning (MBR). These systems include T-IDDM [Schmidt et al., 2001, Bellazzi et al., 2002, Montani and Bellazzi, 2002], VIE-DIAB [Popow et al., 2003], and CAMIT [Schrezenmeir et al., 2002]. However, research systems have not yet focused on insulin pump therapy, which allows for tighter control, because it is new and except for T-IDDM, they have not included CBR. Physicians
find problems and solutions to a patient’s insulin therapy based on their previous experiences, which is the basis of CBR.

Case-based reasoning adapts the solutions to old problems to solve new problems that are presented to the system. The previous problems are stored in a case base along with their solutions and outcomes. Cases have features relating to problems that distinguish them from each other. These features are used as indexes into the case base, so that the most applicable previous cases will be retrieved and used for the new problem. CBR is an appropriate approach because there are no formal algorithms for all type 1 diabetics, but we do have a large experience base from our physician. CBR has been successfully applied to other complex medical problems [Bichindaritz and Marling, 2006].

The primary contributions of the thesis are:

- Design, in collaboration with two other graduate students, of a database to store patient information
- Implementation of the database
- Knowledge Acquisition from physicians as they adjust patient therapy based on information stored in the database

Additional contributions include:

- Design and implementation of a website to collect patient information
• Teaching patients in an experimental study how to enter data into the database via the website

Data and knowledge are acquired from our physician in two aspects of our project. The first portion was finding which data points needed to be collected for the physician to be able to accurately diagnose a patient’s problem. To do this the author shadowed Dr. Frank Schwartz to learn about Type 1 Diabetes and how the disease is managed by the patient and physician. Information provided by the physician and patients allowed the author and two other graduate students to design a database that would facilitate case acquisition. Forty-four tables are included in the database, which was solely implemented by the author. The database is used to acquire knowledge needed to develop cases for the CBR system. The website was designed and implemented by the author using HyperText Markup Language (HTTP) and Hypertext Preprocessor (PHP) programming languages. The website allows the patient to enter information into forms and insert information into the database, where it can be analyzed by the physician.

Data is then collected and analyzed from an Ohio University Institutional Review Board (IRB) study involving twenty patients. Data is reviewed by Dr. Schwartz and Dr. Jay Shubrook to identify patient problems and determine appropriate therapy adjustments. This is the second portion where knowledge has been acquired from our physicians. Knowledge acquired from these review sessions is organized into cases containing problems, solutions, and outcomes. Cases will be used to retrieve
previous knowledge of a problem to solve new problems. Situation assessment will mimic how the physician finds problems in the patient’s data and will send the new problem to the CBR portion to be solved. Creation of a case-based reasoner with an efficient indexing strategy, memory structure, and two similarity metrics will be the last portion of the project to be completed. Each piece will contribute to our system giving automated insulin therapy advice to physicians, and possibly even to patients, once the entire project has been completed.

This thesis is organized as follows. Chapter 2 contains the background and gives an in depth explanation of Diabetes, Type 1 Diabetes, Case-Based Reasoning, and our preliminary study. Chapter 3 details the data and knowledge acquisition, including the design and implementation of a database and web site and the use of the database to acquire knowledge for case construction. Chapter 4 describes research in AI in Medicine, CBR in Medicine, and diabetes research systems related to this thesis. Chapter 5 presents an evaluation of work to date and details future work, including construction of a CBR prototype, future enhancements, and extensions. Finally, Chapter 6 contains the summary and conclusion of the thesis.
Chapter 2

BACKGROUND
This Chapter provides a background on:

- Diabetes and its management
- How case-based reasoning can help
- Recent related research systems
- Commercially available software for Type 1 diabetics on insulin pump therapy
- The preliminary study to provide intelligent decision support for Type 1 diabetics on insulin pump therapy

2.1 Diabetes

The medical term for diabetes, diabetes mellitus, comes from words with Greek and Latin roots. Diabetes has a Greek root, meaning “to siphon”, while mellitus has a Latin root meaning “sweet like honey” [Manis, 1995a]. Diabetes is a disease in which the body does not produce or properly use insulin [Wray, 2006]. It is speculated that 20.8 million people have diabetes, or 7% of the United States population has some form of diabetes [Wray, 2006]. There are 800,000 new cases diagnosed in the United States each year [for Disease Control and of Health, 2004]. There are two main types of diabetes, type 1 and type 2, along with pre-diabetes. Pre-diabetes is explained by blood glucose levels that are higher than normal, but not high enough to be classified as diabetes. Type 1 diabetes refers to the fact that the body cannot produce insulin,
while type 2 diabetes results from an insulin resistance in the body. Both pre-diabetes and diabetes can be tested by using either the Fasting Plasma Glucose Test (FPG) or the Oral Glucose Tolerance Test (OGTT) [Wray, 2006]. With the FPG, a fasting blood glucose level of 100-125 mg/dl signals pre-diabetes, while a level greater than 126 mg/dl indicates diabetes. During the OGTT test, the patient first fasts and then drinks a glucose-rich beverage. After two hours, their blood glucose level is taken. Results ranging from 140-199 mg/dl indicates pre-diabetes while results above 200 mg/dl indicates diabetes [Wray, 2006].

2.1.1 Type 1 Diabetes

Type 1 Diabetes results from the body’s lack of producing insulin. Insulin is a hormone that is created by beta cells in the pancreas. Type 1 diabetics have an autoimmune deficiency where the beta cells in the pancreas are destroyed causing no insulin to be produced. With this absolute lack of insulin, the body will respond in the following ways: excessive thirst, frequent urination, extreme hunger, extreme fatigue, and weight loss [Association, 2003]. There are many different types of insulin being produced today. These include beef, pork, beef and pork combined, or synthetic human [Manis, 1995b]. In our study, patients were using one of two brands of synthetic human insulin, Humalog or Novolog. When patients are first diagnosed with type 1 diabetes, they are given an insulin therapy regimen to use to cope with
diabetes. Without intensive insulin therapies, patients would not survive for very long.

When a patient is first diagnosed with type 1 diabetes, they need to learn about diabetes and how it will affect their lives. Among this patient education is nutritional support, self glucose monitoring, and long-term glycemic control. Patients learn about how different foods affect their lifestyles and their blood glucose levels, concentrating on carbohydrates and the glycemic index. The glycemic index is a ranking of carbohydrates in a foods base and how they affect blood glucose levels [Brand-Miller, 2006]. Simple carbohydrates will act differently than complex carbohydrates on a person’s blood glucose levels. Glucose monitoring is the process of monitoring one’s blood glucose with a glucose meter. A person will prick their finger with a diabetic tool called a lancet and that will make them bleed [Association, 2003]. They will then drip the blood onto a test strip and then place the strip in the blood glucose meter. The meter will give the value of their blood glucose measurement.

Long-term control refers to keeping blood glucose values within prescribed high and low ranges as much as possible. This will help the patient stay away from complications down the road and will help lower the HbA1c value of the patient. HbA1c is the “glycated hemoglobin, the concentration of hemoglobin molecules that have glucose attached to them” [Association, 2003]. Your HbA1c will give your average blood glucose reading from the last two to three months and will predict further complications. “In general, every percentage point drop in HbA1c blood tests results
(from 8.0% to 7.0%) reduces the risk of microvascular complications (eye, kidney, and nerve diseases) by 40%" [Davis, 2005]. When patients keep their blood glucose levels within their low and high target ranges, fewer problems tend to occur. The worse the control, the greater the risk of complications occurring. These complications include: retinopathy, impotence, gastroparesis, depression, foot ulcers, heart attack, stroke, blindness, amputation, dialysis, and kidney transplant.

Some common conditions stemming from type 1 diabetes are hypoglycemia, hypoglycemia unawareness, hyperglycemia, and ketoacidosis [Association, 2003]. Hypoglycemia occurs when the body’s blood glucose levels go too low to provide enough energy for the body’s activities. Hypoglycemia unawareness occurs when a person has no symptoms of hypoglycemia. Hyperglycemia occurs when the body’s blood glucose levels are much higher than normal. Ketoacidosis is the build up of acids in the blood, usually to dangerously high levels. Ketones in the blood mean that the body is burning fat to get energy [Association, 2003]. Known causes of ketoacidosis are not getting enough insulin (hyperglycemia), not eating enough food (usually when sick), when blood glucose levels are low, and psychological or social pressures stopping people from taking their insulin [Association, 2003]. By controlling blood glucose values on a daily basis and keeping these common conditions to a minimum, long-term complications are kept to a minimum.

A person without diabetes will only get as much insulin as their body needs after each meal, which their pancreas controls. Their blood glucose levels will then spike
and begin to trend downward directly after each meal or snack. This also includes a small amount of insulin throughout the day which will help keep this person in normal blood glucose ranges when not consuming foods. For a diabetic to do this, they would take an injection of long-lasting insulin when they awoke and take an injection of insulin prior to each meal. A patient diagnosed with type 1 diabetes will receive an insulin therapy regimen that they need to adhere to for their blood glucose levels to remain as normal as possible.

2.1.2 Traditional Treatment/Therapy for Type 1 Diabetes

To keep control of their diabetes, patients must manage how much insulin they take for each meal and many other factors. All of this information must be stored since it is hard for humans to remember accurately what has happened over the past week, let alone the past few months or years. Diabetes patients have been using paper data log sheets to keep track of information that should be useful to physicians. On most log sheets, patients will record their blood glucose values, their insulin values, the amount of carbohydrates consumed, and when each of these values occurred. Patients have been taught to track their blood glucose values and to adjust their insulin dosages based on past experiences. This should help the patient control their diabetes by maintaining good glycemic control and help with avoiding long-term complications.
While it may help some patients in managing their type 1 diabetes, for others it is still not enough. Most patients only take 4-6 blood glucose values per day. While this information can be very useful, it can also be quite misleading. What if the blood glucose readings are all within the patient’s target ranges but the patient is missing the highs and lows that are occurring? What if the patient is missing morning readings of AM hypoglycemia prior to breakfast because the patient is not taking a pre-breakfast blood glucose reading? What if the patient is experiencing overnight hypoglycemia and is not having any reactions that would make the patient wake up in the middle of the night? The 4-6 blood glucose readings are not enough to estimate daily insulin requirements.

When the patient visits the physician, they bring in these paper log sheets since their last visit. The physician will view these sheets, looking for trends that are not positive for long-term care and change the treatment to help the patient. The physician could be looking at four data point values for each day for multiple weeks worth of data. This can be considered data overload for the physician. Furthermore, no memory of past experiences of how a patient responds to a situation is recorded in the paper logs. Therefore, it is dependent on the physician or patient to recall how they reacted. A physician may be managing over 1000 patients at any given time, which would make it extremely difficult to remember how each patient reacts to a particular treatment.
2.1.3 Emerging Trends in the Management of Type 1 Diabetes

Insulin pumps

While the majority of Type 1 diabetics still use multiple insulin injections and paper logs to manage their diabetes, new technologies are now available. These are recommended and used by the physicians of Ohio University’s Diabetes and Endocrine Center. Insulin pumps change the way that patients take their insulin and allow patients to store some data pertaining to their day. Information that can be stored includes: when the patient eats, the amount of carbohydrates, when the patient boluses, the bolus value, the basal rate, when the patient exercises, and when the patient suspends the pump. All of this information is very useful and does help the patient with managing their daily lives while allowing easy access to their insulin. Unfortunately, the pump does not allow the patient to enter other information that is very important to the physician. This information includes: what foods the patient ate, how hard the patient exercised and duration of exercise, when the patient went to and returned from work, when the patient started or ended a nap, stressful events, and miscellaneous events.
CGMS Sensors

Continuous Glucose Monitoring Systems (CGMS) are a newly developed way of collecting blood glucose information from a patient. Most sensors take a blood glucose reading every five minutes for three days, giving the physician 288 readings per day. The patient is currently unable to see the data in real-time although newer CGMS systems are addressing this issue. While this system gives readings every five minutes, fingersticks are still used to calibrate the system. This is done to be sure that there are no miscalculations in the readings. These systems indicate the trend and direction of blood glucose values. They are used to gather more information on blood glucose levels than fingersticks and are also used to check overnight lows of a patient. While CGMS gathers more information on blood glucose levels, it offers no help with other factors that need to be collected.

2.2 How Can Case-Based Reasoning Help?

Case-based reasoning (CBR) is a subfield of Artificial Intelligence (AI), which may be viewed as the study of how to make computers perform tasks that are currently performed better by humans than by computers [Rich and Knight, 1991]. Currently in diabetes management, humans support type 1 diabetics better than computers can. “In case-based reasoning, a reasoner remembers previous situations similar to the current one and uses them to solve the new problem” [Kolodner, 1993]. Case-
based reasoning is made up of cases which must be retrieved, reused, revised, and retained. A case represents “knowledge at the operational level; that is, they make explicit how a task was carried out or how a piece of knowledge was applied to what particular strategies for accomplishing a goal were used” [Kolodner, 1993]. An index is included in each case which allows cases to be searched and the most relevant information to be retrieved from the case base. The matching case will not be an exact replica of the new problem, so it will be adapted to solve the new problem. Revision includes testing the adapted solution to see if it would work in the real world, if it does not, it should be adapted again. When a sufficient solution is found, it should be retained by the case base so if this problem were to come along again, it would be solved very easily [Kolodner, 1993].

There are no formal algorithms that can be universally applied to all type 1 diabetics, but we have a large experience base. One of the physicians that we are currently working with treats over 1,000 type 1 diabetics on insulin pump therapy. The idea is to use individual case experiences from patients with type 1 diabetes to develop treatment strategies that may be applied to individual patients with diabetes.

A CBR system may be able to automatically recognize problems requiring therapy adjustment, remember similar problems in the patient’s history and what therapy was effective or ineffective in the past, detect similar problems among other patients and use previously learned solutions to make suggestions in the next patient’s management. CBR has been applied successfully to other complex medical problems,
such as: diagnosing heart diseases, supporting the diagnosis and treatment of psychiatric eating disorders, diagnosing intoxication by drugs, and supporting the long-term follow-up care for stem cell transplant patients [Bichindaritz and Marling, 2006]. Applications of Case-Based Reasoning in Medicine are described in Chapter 4.

2.3 Diabetes Research Systems

This section introduces three research systems that have the goal of helping diabetics manage their disease. Only one of the three employs CBR and only two employ AI. While we can learn from their attempts, our research differs considerably. First, none of these projects included diabetics on insulin pump therapy. This means that available treatment options and parameters vary from those we are considering. Second, none of these research systems explored CBR as a primary reasoning method, so our AI approach is distinct. Third, we are actively pursuing partnerships with commercial pump and meter companies. The following research has not resulted in commercially available tools for Type 1 diabetics on insulin pump therapy. More detail about these research systems is given in Chapter 5, Related Research.
2.3.1 Telematic Management of Insulin-Dependent Diabetes Mellitus

The Telematic Management of Insulin-Dependent Diabetes Mellitus (TIDDM) project [Bellazzi et al., 2002] is the only known research system to employ Case Based Reasoning to assist with insulin therapy recommendations for a patient. Case-based reasoning was initially tried in the TIDDM’s Medical Unit module, when its primary rule-based reasoning module could not give a sufficient answer [Bellazzi et al., 2002]. It used past cases to “specialize the rule behavior in the problem identification and in the therapy revision step, by setting proper rule parameters to specific values, selected on the basis of the situation at hand” [Bellazzi et al., 2002].

In a second T-IDDM experiment, Rule Based Reasoning (RBR) is initially used for therapy adjustment, but if the results are not good enough it will attempt to use Model Based Reasoning (MBR). If MBR does not create a sufficient answer to the problem, then CBR is used. Retrieved cases that are similar are analyzed and the best solution is chosen to apply insulin adjustments to the patient’s current treatment [Montani et al., 2003]. An example problem that would allow this to happen in this system is the “Somogyi effect”, because “a clear causal effect of insulin doses on the Blood Glucose Levels cannot be identified” [Montani et al., 2003]. This same effect is also referenced by [Schmidt et al., 2001, Montani and Bellazzi, 2002].
2.3.2 VIE-DIAB

The VIE-DIAB system [Popow et al., 2003] creates a daily color-coded graph plot of patient data allowing the physician to easily track patient management of diabetes. To receive data, patients send messages from a Java application that is loaded onto their mobile phones to the physicians VIE-DIAB system. This data is then visualized by the physician using graph plots and feedback is returned to the patient. Their aim is to improve diabetes control and to reduce long term complications. They are currently not using any AI techniques, but are looking into them for further studies [Popow et al., 2003].

2.3.3 Controlled Assisted Meal Related Insulin Therapy

The Controlled Assisted Meal Related Insulin Therapy (CAMIT) [Schrezenmeir et al., 2002] study tests whether or not computer aided decision making improves patients insulin therapy. In the study 50 people are split into two distinct 25 person groups, one with Multiple Subcutaneous Injections (MSI) and the other with the CAMIT pocket computer. CAMIT adapts the insulin dose to the patients current situation. The study showed the CAMIT group received better results over the study, which can be explained by better “better metabolic control due to more consistent insulin dosage adaption” [Schrezenmeir et al., 2002]. No AI techniques were used in CAMIT, but this study does show that computer aided treatment can be effective.
2.4 Commercially Available Software

2.4.1 Medtronic MiniMed

“For more than 20 years, Medtronic Diabetes has been at the forefront of diabetes management” [MiniMed, 2006c] by offering hardware products and software products that allow patients to more easily manage their diabetes. The state of the art in commercially available software is the Bolus Wizard® Calculator, which was released in July 2003 [MiniMed, 2006b]. The Bolus Wizard® Calculator “recommends proper insulin dosages to patients and keeps track of insulin used by the body” [MiniMed, 2006b] based on an arithmetic formula. Another portion of Medtronic MiniMeds software will allow patients to choose different types of boluses depending on the type of food they are eating and how they believe the insulin should be dispensed.

Bolus Wizard® Calculator

This calculator uses six parameters to determine a bolus dosage for the patient, which include: food (grams), carbohydrate ratio (grams per unit), current blood glucose measurement (mg/dL), blood glucose target (mg/dL), insulin sensitivity (mg/dL/unit), and active insulin (mg/dL) [Minimed, 2005]. The food parameter accounts for the amount of carbohydrates to be consumed for this meal. The carbohydrate ratio is the amount of insulin that should be taken to offset the number of carbohydrates eaten in a particular meal. Current blood glucose measurement and
blood glucose target are self-explanatory. Insulin sensitivity determines how one unit of insulin will lower the patient’s blood glucose level. Active insulin is determined based on the “previous insulin bolus and the insulin type” [Minimed, 2005]. The majority of insulin is absorbed in the first few hours, but a small amount is still available for a few more hours. The Bolus Wizard ® Calculator determines this and uses it in the formula. The formula is Estimate = Food Estimate + Correction Estimate - Active Insulin OR

\[
Est = \left(\frac{Food}{CarbRatio}\right) + \left(\frac{CurrentBG - BGTarget}{InsulinSens.}\right) - ActiveIns.
\]  

[Minimed, 2005]

On applying this formula:

- “Active Insulin only reduces the correction portion of the estimate, not the food portion” [Minimed, 2005].
- “If the active insulin is more than the correction insulin, the correction portion of the estimate will be changed to zero (0)” [Minimed, 2005].
- “If the current BG is lower than the target, the correction portion of the estimate will reduce the total estimate” [Minimed, 2005].
- “If a Dual Wave bolus is less than the estimate due to the max bolus limit or user change, the square portion is reduced first” [Minimed, 2005].

By using the Bolus Wizard ® Calculator, the patient receives three advantages over manual bolus calculations:
1. Clinical advantage - “bolus estimators calculating a bolus results in less correction boluses” [Minimed, 2005] and it may be helpful in preventing hypoglycemia.

2. Accuracy advantage - it can be used in conjunction with other hardware to eliminate user data entry error.

3. Ease of use - no more manual calculations.

**Meal Bolus Options**

There are three different choices for meal boluses when using Medtronic MiniMed software: Normal, Square Wave, and Dual Wave. A Normal Bolus is “delivered at one time as soon as the bolus is activated” [Minimed, 2005] and is for low fat meals. A Square Wave Bolus is “given over a 30 minute to 8 hour period of time in 1/2 hour increments” [Minimed, 2005] and is for meals high in fat or eaten over a long period of time. A Dual Wave Bolus is “divided to give some of the insulin as a normal bolus and some as a square” [Minimed, 2005] and is for meals high in both carbohydrates and fat, like pizza. This gives the patient more freedom to eat foods they prefer while still maintaining a healthy blood glucose level by altering how the insulin is injected. The patient may also avoid later correction boluses if they choose the correct bolus method for each meal. The choice of bolus method is left to the patient, not calculated by the system.
2.4.2 Unmet Needs

The resources provided by Medtronic MiniMed falls short of our current research goal of being able to give advice on a patient’s overall insulin therapy regimen. The current software allows control focuses on how much insulin should be injected with each meal. It is only using a simple arithmetic formula and is not giving advice to the patient. Our aim is to be able to change the patient’s basal rates, insulin sensitivity, carbohydrate ratios, and other related factors, which can currently be done only by an experienced physician. Our research goal is to go above and beyond what current commercially available software can offer. Toward this end, we have begun the preliminary study described next.

2.5 Preliminary Study

A preliminary study was initiated to see if it is possible to have computer software analyze glucose patterns throughout the day from data downloads and Continuous Glucose Monitoring Systems (CGMS), learn from previous adjustments, and generate advice on what adjustments to make in insulin dosages. This study was approved by the Ohio University Institutional Review Board (IRB) on February 16, 2005. In this study, artificial intelligence is used to analyze blood glucose patterns and provide advice as a tool in aiding the patient’s daily control. We use personal blood glucose
records, CGMS data from Medtronic MiniMed glucose sensors, and daily event diaries containing other daily data which impacts blood glucose levels.

The preliminary study will collect and analyze data from twenty subjects for use in software development. To be a subject in our preliminary study, an individual must be a patient of the University Medical Associates (UMA) Diabetes/Endocrine Center with Type 1 Diabetes Mellitus on insulin pump therapy. Patients must be under the care of Dr. Frank Schwartz or Dr. Jay Shubrook and must agree to participate in the study. Suitable patients are identified by the physicians and asked if they would like to participate. Patient ages vary from 18-75. Patients that decide to participate in the study are not compensated, but will receive a new pump and software if needed. The study lasts for 6 weeks for each participant. During this time, patients are asked to measure their blood glucose levels 6-10 times per day via fingersticks and record the values obtained. On three separate occasions, a patient is asked to wear a CGMS sensor for three days to obtain additional information for the study. The sensor is worn at the beginning of the study, after two weeks, and at the end of the study. Patients are also asked to keep accurate food and activity diaries. Before a patient can begin participating in the study, he or she must read, understand, and sign an informed consent form. This form appears in Appendix C.

There are three contributions that the author made to the preliminary study: database design and implementation, website design and implementation, and knowledge acquisition. The database is used to store all of the information that is entered
by each patient. The website is a user friendly way for the patient to insert their daily activities into the database. Knowledge acquisition was initially used to determine the relevant features for inclusion in the database. Once data was entered into the database, knowledge acquisition was used to build cases for our Case-Based Reasoning prototype. Without knowledge about how physicians use data to adjust insulin therapy, our system would not be able to progress past being a database. Each of these contributions will be explained in the following chapters.
CHAPTER 3

DATA AND KNOWLEDGE ACQUISITION
In CBR, the basic knowledge representation is the case, which consists of a description of the problem, solution to the problem, and the outcome [Kolodner, 1993]. The description of the problem will include all information explicitly taken into account in solving the problem and information people normally include when describing problems of this type [Kolodner, 1993]. Therefore, acquiring cases interleaves acquiring data and acquiring knowledge. We must first collect patient data in order for the physician to identify a problem. Once the physician determines a solution to the problem, he tells the patient of the solution. We must then collect additional data to evaluate the outcome of the solution.

The first step was to design and implement a database to contain the information taken into account to solve the problem and information normally used to describe the problem. This data is not readily available to physicians in electronic format in its entirety. If historical data were available, it would have been of limited use, as we could not retroactively suggest solutions and observe their outcomes. To get both types of information, the author shadowed the physicians, spoke with patients, and researched diabetes.

The second step was to design and implement a web-based system so that patients could enter data into the database. Patients enrolled in an IRB-approved clinical trial where artificial intelligence is used to analyze blood glucose patterns and provide advice as a tool in aiding the patients daily control. This study will allow us to
collect and analyze data from twenty subjects for use in our system and is further explained in Section 2.5.

The third step was to observe physicians as they identified problems and solutions and to track the results of their solutions in the required data. This last step allowed us to acquire knowledge and construct cases for use in a Case Based Reasoning system. To date, 25 cases have been built for five patients.

3.1 Initial Knowledge Acquisition to Identify Case Features

To solve the problem of giving automated insulin therapy advice to a type 1 diabetic, we first needed to acquire the knowledge needed to identify case features. Our group, comprised of four graduate students and our advisor, met with Dr. Frank Schwartz in his office in Parks Hall at Ohio University. This initial meeting was to help us understand type 1 diabetes in general. He explained how a patient uses insulin, how exercise can affect blood glucose levels, and diabetic terms like hypoglycemia, hyperglycemia, and ketoacidosis. He also explained that our study would only involve those patients who are currently using insulin pumps and that he was currently advising over 1000 of these patients. We would be creating a system that would help recommend insulin therapies to any of these patients. He explained that patients are currently using paper data log sheets to store their information and he
would receive them during a patient’s visit. We need to gather this information and more to be able to make the same decisions that he would make automatically. He explained that we would need IRB approval for this project since we would be using human subjects in building and testing of our system. At the end of our initial meeting, he explained that we should shadow him in order to get first-hand knowledge of how he treats diabetes.

Over the next few weeks each student took turns shadowing the physician, each spending at least two visits in his practice. When shadowing the physician, we took notes and wrote questions that we would like to get answers to about the process that the physician goes through to create an alteration in therapy. The physician explained that there are too many factors to explain at the current time, but gave an example. He explained that the patient had three days in a row with morning hypoglycemia and that is a problem that needed to be fixed. He did not explain what was causing it or exactly how he went about fixing this current problem, just that we would learn that part later. We each also heard about diagnostic tests, for example the HbA1c test, and also testing for the patient’s current complications. The physician wanted us to see how different people cope with diabetes. This is one way we gathered information from experience about data that needed to be stored to solve our problem.

Every week after our initial meeting, our group met to discuss the information collected from shadowing and to continue the design of our preliminary study. All
of this information was written down and logged by us to keep track of information that we thought was important. Examples of information that was initially deemed important are exercise, age, carbohydrates, and insulin dosages. The preliminary study included creating our IRB approval form so we could get the information from patients using our system. During this meeting, we created a general plan to solve the automated decision problem. We would use a database to store the data we are currently gathering and case base reasoning to solve the problem of automated advice on insulin therapy in the future. This data is being collected because the physician uses his knowledge with this data to find problems in the patient’s therapy. We need to store this information so we can do the same in our system. The data that is used to find the problem will become the features of a case that will be stored in our case based reasoner. The knowledge needed for a case based reasoner is gathered one case at a time.

Following this meeting, usually the next day, our group would meet with the physician to explain the information we had gathered from shadowing him and from our group meetings. The physician would confirm our suspicions that some information was needed to give advice. During this meeting, our physician also gave us a handout that included 12 Artificial Intelligence scenarios. A copy of this handout is shown in Appendix B. This handout gave us even more information that we were currently missing and it explained why particular problems would occur.
The following weeks involved the same routine: shadow, group meeting, physician meeting. After three weeks of this schedule, we finished shadowing the physician and we had a meeting to combine all of the data collected to make a final submission to the physician. We had compiled approximately 50 data items that are considered to be important. This information was taken to the physician and most was confirmed, with new information also being added. This information was used to design the database described next.

### 3.2 Database Design and Implementation

Patients traditionally use paper data log sheets to help manage their daily diabetes information. When a physician sees a patient for a checkup, the patient will bring in their paper logs since their last visit. This presents a problem for the physician: he may be overloaded by the quantities of data while still not having the right data to make good decisions. In our preliminary study, we are asking patients to record all the information that they have been storing on paper logs and other events that occur in their day-to-day lives that they were not previously recording. While having patients record more information than before is time consuming, it will help lead to more accurate analysis because of the information that will be available to the physician. What needed to be created was a way to store information that would be standardized and easily available for use by the patient and physician.
Rather than storing information on paper, a database was created to electronically store patient information for our IRB approved preliminary study. This database represents a major contribution of this thesis. It was designed in collaboration with two other graduate students, Kathleen Evans-Romaine and Wesley Miller. It was implemented solely by the author. The website and front end for the database were designed and implemented by the author.

The database currently contains 44 tables, which are listed in Figure 3.1. The tables in Figure 3.1 have been grouped by their relationship to each other.

### 3.2.1 Patient History

Tables numbered 1 - 15 in Figure 3.1 contain the patient’s medical history and registration information for our study. Each of these tables contains information that seldom changes over the course of the preliminary study. BG_Target is a table that holds the patient’s high and low blood glucose targets. The Carb_Ratio table holds information relating to the patient’s insulin to carbohydrate ratio. This ratio is established by the physician and explains the amount of insulin that should be taken to offset the number of carbohydrates eaten in a particular meal. If a patient has a ratio of one unit of insulin for every 15 grams of carbohydrates and the patient eats 60 grams of carbohydrates for dinner, they should have an injection of four units of insulin. The Chronic_Disorders and Complications tables store the patient’s chronic disorders and complications. Chronic disorders are conditions that will affect the
Table 3.1: Table Names from our Database

<table>
<thead>
<tr>
<th>Number</th>
<th>Table</th>
<th>Number</th>
<th>Table</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BG_TARGET</td>
<td>2</td>
<td>CARB_RATIO</td>
</tr>
<tr>
<td>3</td>
<td>CHRONIC_DISORDER</td>
<td>4</td>
<td>COMPLICATIONS</td>
</tr>
<tr>
<td>5</td>
<td>DOCTOR</td>
<td>6</td>
<td>HBA1C</td>
</tr>
<tr>
<td>7</td>
<td>INSULIN_SENSITIVITY</td>
<td>8</td>
<td>INSULIN_TYPE</td>
</tr>
<tr>
<td>9</td>
<td>LOGIN</td>
<td>10</td>
<td>MEDS</td>
</tr>
<tr>
<td>11</td>
<td>OCCUPATION</td>
<td>12</td>
<td>PATIENT</td>
</tr>
<tr>
<td>13</td>
<td>PUMP</td>
<td>14</td>
<td>RELATIVE</td>
</tr>
<tr>
<td>15</td>
<td>WEIGHT</td>
<td>16</td>
<td>DAILY_EXERCISE</td>
</tr>
<tr>
<td>17</td>
<td>DAILY_SCHEDULE</td>
<td>18</td>
<td>DAILY_NAP</td>
</tr>
<tr>
<td>19</td>
<td>DAILY_SNACK</td>
<td>20</td>
<td>DAILY_WORK</td>
</tr>
<tr>
<td>21</td>
<td>EXERCISE</td>
<td>22</td>
<td>FOOD</td>
</tr>
<tr>
<td>23</td>
<td>MEAL</td>
<td>24</td>
<td>NAP</td>
</tr>
<tr>
<td>25</td>
<td>SLEEP</td>
<td>26</td>
<td>WORKS</td>
</tr>
<tr>
<td>27</td>
<td>BASAL</td>
<td>28</td>
<td>BOLUS</td>
</tr>
<tr>
<td>29</td>
<td>TEMP_BASAL</td>
<td>30</td>
<td>INFUSION_SET</td>
</tr>
<tr>
<td>31</td>
<td>PUMP_FAILURE</td>
<td>32</td>
<td>CGMS</td>
</tr>
<tr>
<td>33</td>
<td>FINGER_STICK</td>
<td>34</td>
<td>HE_ACTION</td>
</tr>
<tr>
<td>35</td>
<td>HE_SYMPTOMS</td>
<td>36</td>
<td>HYPO_EVENT</td>
</tr>
<tr>
<td>37</td>
<td>MEASUREMENT</td>
<td>38</td>
<td>ILLNESS</td>
</tr>
<tr>
<td>39</td>
<td>ISYMPTOM</td>
<td>40</td>
<td>STRESSOR</td>
</tr>
<tr>
<td>41</td>
<td>INTERVENTION</td>
<td>42</td>
<td>MENSES</td>
</tr>
<tr>
<td>43</td>
<td>MISC_EVENT</td>
<td>44</td>
<td>NUTRITION</td>
</tr>
</tbody>
</table>

individual for long periods of time, for example: asthma, lupus, and cystic fibrosis.

Complications are health related problems that stem from diabetes and include nerve complications, heart complications, stroke, and amputation, to name a few.

The Doctor table tells us which physician the patient is seeing. The HbA1c table specifies the patient’s HbA1c level at the beginning and end of the study. HbA1c is the “glycated hemoglobin, the concentration of hemoglobin molecules that have glucose attached to them” [Association, 2003]. Insulin_Sensitivity holds information on the
patient’s insulin sensitivity, the amount that 1 unit of fast-acting insulin would lower
the patient’s blood glucose level. For example, an insulin sensitivity of 1:100 shows
that one unit of insulin will lower the blood glucose level 100 points. Insulin_Type
tells us the brand of insulin that is being used. The Login table holds the patient’s
login name and password, which is an md5 checksum for security purposes.

The Meds table stores the patient’s medications. The Occupation table stores
information about the patient’s occupation. The Pump table stores information about
the type of insulin pump the patient is currently using. The Patient table is the main
table in the database and most other tables relate to the patient ID that is held within
this table. The Relative table contains information about the patient’s relatives with
diabetes. The Weight table stores information about the patient’s weight over the
study.

3.2.2 Normal Daily Schedule

Tables 16 - 20 in Figure 3.1 are the Daily_Exercise, Daily_Schedule, Daily_Nap,
Daily_Snack, Daily_Work tables. Each of these tables contains information about the
patient’s usual daily routine. These tables keep track of when they would normally
go to work, sleep, eat meals, eat snacks, and when they exercise. Storing all of this
information is important because it gives us a better understanding of the patient’s
average daily activities, so we know when patients deviate from their normal routines.
3.2.3 Daily Events

Tables numbered 21 to 26 in Figure 3.1 store information about a patient’s daily activities. These tables are the Exercise, Food, Meal, Nap, Sleep, and Works tables. They tell us exactly when they eat, go to or from work, go to sleep or wake up, exercise, and take a nap. This allows us to see the type and duration of exercise and what foods they are eating at each meal. For example, a patient may walk for 45 minutes one day and jog 25 minutes the next. These activities will have different effects on the blood glucose levels of the patient. Seeing exactly what the patient eats, rather than just the number of carbohydrates, is also important. These are two of the things that we capture that other systems may not.

3.2.4 Insulin Usage and Blood Glucose Measurements

Numbers 27 - 31 of Figure 3.1 refer to insulin. The Basal table stores the patient’s current basal rates. The basal rate is the “background release of fast-acting insulin by an insulin pump to control blood sugars when the patient is not eating” [Association, 2003]. This rate can change throughout the day, depending on the therapy for the patient. The Bolus table stores information about each bolus injection of insulin that is taken. A bolus is an injection of insulin into the patient’s system that is done prior to a meal or snack and can be used to bring the patient down from hyperglycemia. The Temp_Basal tables holds data for the patient’s temporary basal values. A temporary basal rate is a change from the normal basal rate, usually a
lower rate when exercising and possibly a higher rate when the patient is feeling ill.
The Infusion Set table holds information for when the infusion set was changed and
where it was placed. The Pump_Failure table stores information about the patient’s
pump not working correctly and when it began working again.

Number 32 and 33 of Figure 3.1 refer to blood glucose readings from the patient.
The CGMS table holds data from a CGMS sensor that the patient wears for three
days at a time, three times during the study: the first week, third week, and sixth
week. The CGMS sensor takes a reading every five minutes providing 288 data points
per day worn. The Finger Stick table holds information pertaining to the patient’s
self blood glucose monitoring.

3.2.5 Hypoglycemic Events

Numbers 34 to 37 of Figure 3.1 relate to hypoglycemic reaction. While paper logs
tend to just keep track of a hypoglycemic blood glucose level and when it occurred,
our system also keeps track of how the patient was feeling during the event and the
action taken to correct the event. These are important for multiple reasons: finding
how the patient feels when a hypoglycemic reaction occurs and checking for over or
under correction of a hypoglycemic event. The Hypo_Event table stores when and to
which patient the event occurred, while the HE_Symptoms table holds the symptoms
that occurred during the event. The Measurement table contains the blood glucose
information that occurs during the hypoglycemic episode and the HE_Action table contains the action that was taken to correct the episode.

3.2.6 Illness and Stressful Events

Numbers 38, 39, and 40 of Figure 3.1 deal with illnesses and stress. The ISymp-tom tables stores information on the patient’s symptoms and the Illness table stores information on what illness the patient has been diagnosed with. These are important to keep track of because illnesses effect blood glucose readings. The Stressor table stores stressful events that have occurred in the patient’s daily activities.

3.2.7 Other Events

Numbers 41 to 44 of Figure 3.1 are grouped together because they really do not fit into any other grouping. The Intervention table stores information on a patient’s therapy, how and why it was changed, and if the change created a successful result. The Menses table stores information on when a female patient has begun menstruating. This information is important because changes in hormones will affect blood glucose levels. The Nutrition table stores detailed information for particular foods that are eaten by patients. This table is not currently being used, but would be useful for future work. The Misc_Event table stores information for anything that we did not include in our preliminary study. This was our catch-all for other information a patient may want to supply.
3.2.8 Too Much Data Now?

All of the data that is being stored in the database is not being stored by other companies and research ventures. This information is being gathered to see how the patient’s daily life affects their blood glucose levels. Without this information, we would not be able to build the rest of our system to help in the management of type 1 diabetes. Since we are looking to take the endocrinologist’s knowledge and create a system that will be able to make recommendations for patient therapies, all information that the physician uses to make judgements is extremely useful.

Now there is even more information for the physician to sort through compared to the paper data log sheets. The physician was manually looking through pages of paper log sheets while attempting to find patterns that are occurring and trying to interpret them. The amount of data can be phenomenal while still missing key information from the patient. On average, patients will take 4-6 fingersticks and record them on their paper log sheets. This information alone is inadequate to estimate the adjustments needed in a patients’ daily insulin requirements. The use of a CGMS sensor allows the physician to see 72 hours worth of continuous blood glucose data.

Yes, the study is gathering more information than on paper logs, but we are also simplifying the way the physician views the data. We are actually making the patients do more work than they have previously because of the additional time it will take to record the needed information. The patients are not using paper based sheets to
record their information; they are now using a website to keep track of their daily
information, as will be explained shortly.

While there is more information for the physician to view, the physician will
not see the data in a paper based format. Wesley Miller, another Ohio University
graduate student in the Computer Science Department, has created a graphical user
interface (GUI) that will allow the data to be easily viewed by the physician.

3.3 Website

A website was designed and implemented as an easy way for the patient to insert
their daily information into the database. The website is currently made up of 24
different pages and was created using HyperText Markup Language (HTML) and
Hypertext Preprocessor (PHP) programming languages. These pages are broken
down into three different sections: registration, non-registration, and administrator
pages. The nine registration pages all refer to data that will seldom be changed.
The 12 non-registration pages relate to information that will be entered daily. The
three administrator pages are only seen by the administrator and are used rather
infrequently. Screenshots of each page are available in Appendix A.
3.3.1 Registration Pages

Initially, the administrator must log into the website and add the patient via the Add Patient web page, which will be explained later. After the administrator logs out, the patient can then log in with their newly chosen password. The Login page contains a text box for the patient’s username and password. Their password is typed in text and then translated to a 32-bit character string using the md5checksum algorithm. This new string is then tested against the md5 version of their original password and if they match, they are logged into the website.

Once logged into the website, the patient will insert information into the registration pages. The registration pages can only be accessed in order and the patient cannot go back to the previous page. The first page is called the Greetings page. Here the patient inserts some personal information like their date of birth, gender, height, age when diagnosed with diabetes, pump start date, and who is their physician. When the user chooses the submit button and no data entry errors occur, the information will be correctly inserted into the Patient, Occupation, and Weight tables in the database. The next page is then loaded, which is the Registration page.

The Registration page includes: pump manufacturer, pump model, insulin type, blood glucose targets, insulin sensitivity, carbohydrate ratio, and most recent HbA1c value. This information will be stored into the following tables: Pump, Insulin_Type, BG_Target, Insulin_Sensitivity, Carb_Ratio, and HbA1c. After inserting this information, the next page is the Complications page.
The Complications page allows the user to insert information about their current complications and when they began. The previous pages only allowed the inserting of information once, but this page can be used multiple times. By choosing the “Add Complication” button, the information is inserted into the Complications table and the same page is viewed again. The user can then enter more complications, or choose Submit to move to the following page.

The Relatives page allows the user to enter information regarding their relatives with diabetes. Information that is collected is: the person’s relation, type of diabetes, age of onset, which side of family, and their complications. The information will be inserted into the Relative table in the database. This page also allows the user to enter information for multiple relatives by using the “Add Relative” button. When the user has finished entering data, the “Submit” button will be used to move to the next page.

The Chronic Illnesses page is next and here the user will enter the names of the chronic illnesses that they have been diagnosed with, if any. If there are none, the user should not enter any information and choose the “Submit” button. If the user has one illness, they should enter the information and choose the “Submit” button, which will enter the information into the Chronic_Illness table and then send them to the next page. If the user has multiple chronic illnesses, they should enter them one at a time, and use the “Add Illness” button until they are on their final illness, then use the “Submit” button.
The Medications page is next and information collected on this page includes the name of the medication, the dosage, and the dosage units. This page is similar to the previous few pages in that it allows for adding multiple entries into the database via the “Add Medications” button. The information is inserted into the Meds table when the user selects either the “Submit” or “Add Medications” buttons. After choosing the “Submit” button, the user is then moved to the following page, the Basal Rates page.

The Basal Rates page collects information regarding a patient’s basal rates. The information includes the time started on the basal rate and the rate for that time. The information is stored in the Basal table in the database. Again, the user can use the “Add Basal” button to insert information and come back to the same page to enter different information. When finished, the user should choose the “Submit” button to insert information and then move to the next page.

The final table in the registration pages is the Daily Schedule page. This page contains the typical daily schedule for each patient and involves quite a bit of information. Information needed for this page includes: when the user wakes up and goes to bed, eats meals, goes to and returns from work, when they exercise and what type of exercise, when they eat snacks (if any), and finally which days of the week the schedule is for. This information is stored in the Daily_Schedule, Daily_Work, Daily_Exercise, Daily_Nap, and Daily_Snack tables. Until the patient inserts infor-
mation for each day, the page will continually loop back to itself. When the user is finished, they will be transported to the beginning of the Non-Registration pages.

3.3.2 Non-Registration Pages

The non-registration pages are available to the patient whenever they log in to the website, after their initial login. The patient will enter at the Home page, which contains a short explanation about each of the menu links that are available. The menu links will take the user to the appropriate pages and allow them to insert particular information. In the non-registration pages, there is no set format that the user must adhere to when moving through pages. They are able to decide which pages to view and when to view them. When the patient is done entering data on a particular page, they may choose any of the eight links from the menu to switch pages. Also, each page allows the user to insert information from today to three days prior to today as a convenience to the patient. The pages will be explained in the order they are listed in the menu and also their sub-pages below them.

The second link available on the menu sends the user to the Daily Exercise, Work, and Sleep page. Information collected on this page pertains to the patient’s actual schedule and will allow us to see how they deviate from their normal schedule which they entered in the registration pages. Exercise data collected here includes when the patient began working out, the duration of the workout, the intensity of the workout, and the type of workout. Information collected about their work day includes when
they went to work, when they returned from work, and the physical intensity of work. Information obtained about the sleep schedule includes when did the patient wake up, go to bed, begin a nap, and end a nap. All of this information is saved into the Exercise, Work, Sleep, and Nap tables respectively.

The third link on the menu takes us to the Meals page. Information collected on this page deals with the time of a meal, which meal, and the carbohydrates consumed for that meal. Which meal is either breakfast, lunch, dinner, or snack, and the carbohydrate consumed can be between 0 and 999. This information will be saved to the Meal table in the database. When the patient enters this information, we would also like to know the foods that they have eaten. Clicking on the submit button will take the patient to the next page. It is the Foods page, which consists of the name and amount of the food and the units of measurement (cups, half, ounce(s), slice(s), tablespoon(s), teaspoon, whole) for the food. This information is saved into the Food table in the database. If the patient has eaten more than one type of food, they should select the “Add Food” button and they will be brought back to the Food page so they can enter the other food. Otherwise, they should choose the “Done” button and they will return to the Meals page and either continue to enter other meals or choose the next link.

The fourth link in the menu is the Measurements page. This webpage is not linked to the database but it does contain three links to other pages that are. They are the Fingerstick, Temporary Basal, and Bolus measurement pages. The first link is the
Fingerstick Measurement page and it is used to collect information on the patient’s fingersticks that are taken throughout the day. The page consists of entering a day, the time, and the value of the fingerstick. This information will be saved into the Finger Stick table in the database. If the patient has more than one fingerstick to enter into the database, they should use the “Add Fingerstick” button. This will allow them to insert the information into the database and then return to Fingerstick Measurements page. Otherwise, when they choose the “Done” button, they will be sent to the Measurements page.

The second link on the Measurements page is the Temporary Basal Measurement page. It is used to track the patient’s temporary basal rates that may occur throughout the day. Information entered into this page will be the day, when the temporary basal started and ended, and the rate that was used. This data will be stored in the Temp_Basal table in the database. If the patient has more than one temporary basal value to enter, they should choose the “Add Basal” button, which will store the data and let them return to the same page. Otherwise, the “Done” button should be used and the patient will be returned to the Measurements page.

The third link is on the Measurements page is the Bolus Measurement page. It is used to track the patient’s boluses for the current day. Data that will be entered includes the day, the time of the bolus, the bolus type, and the bolus dose. This information will be stored into the Bolus table in the database. If the patient has multiple boluses to enter, they should choose the “Add Bolus” button. This button
will allow them to store information and return them to the Bolus Measurements page. Otherwise, they will store the information and be sent to the Measurements page and may choose where to go from there.

The next link on the menu will take the patient to the Infusion Set page. This page allows the patient to insert information about their infusion set, such as: the day it was changed, the time it was changed, and where it was placed on the body. This information is stored in the Infusion Set table in the database.

The sixth link on the menu leads the patient to the Hypoglycemic Events page. This page allows the user to enter detailed information about a particular hypoglycemic event. This information includes the day and time it occurred, day and time it was corrected, how was it corrected, and the symptoms that occurred. It also includes information for fingersticks during and after the hypoglycemic event. All of this information is dispersed into five separate tables in the database: the Hypo_Event, HE_Action, HE_Symptoms, Measurement, and Finger_ Stick tables. The fingerstick data that is taken during the hypoglycemic event is stored in the measurement table, while the fingerstick after the event is stored in the finger_stick table. This is done because the value after the episode should not constitute another hypoglycemic event and they should therefore be separated from each other.

The seventh link on the menu sends the patient to the Other Events page. This page contains other information that should be saved in the database, but that really did not fit into any other category. This page covers information regarding illnesses,
stressful events, menses (for women only), pump failures, and miscellaneous events. For illnesses, the page asks for the date the patient fell ill, date recovered, type of illness, and symptoms. This information will be stored in the Illness and ISymptom tables in the database. Information on stressful events includes the time and date of the event, the type of event (family, financial, physical, work, other), and a description of the event. This information is stored in the Stressor table. The menses information includes the date that the patient began menstruating and is stored in the Menses table. This data field is only shown to female patients. Pump failures requests information explaining the time and date, how the pump failed, and when it began to work again. This information is stored in the Pump_Failure table. Miscellaneous events include anything that may have been overlooked in the previous pages but is still important for us to know. The time, date, and full description can be entered by the patient, and the data is stored in the Misc_Event table in the database. There is also a check box above the description area that will allow the message to be sent to the patient’s physician if they feel the physician should know immediately about this problem. The patient does not need to enter all the information on this page in order to have it saved to the database. Any data that is filled into the form will be entered into the database. For example, if a patient enters just a stressful event into the page, the only table that will be updated is the Stressor table.
The eighth and final link is the Daily Log page. This page contains a link to a Portable Document Format (PDF) file that contains a paper data sheet, in case the patient is unable to insert information into the website on a daily basis.

### 3.3.3 Administrator Pages

When the administrator logs in, this user will see the same non-registration pages that the normal users also see. There will be three additional links at the bottom of the menu that only the administrator is able to use. These three links are the Intervention, Change Password, and Add Patient pages.

The Intervention page is the first page that is administrator only and is located directly under the Daily Log link. The page allows the administrator to add an intervention made for a patient by the physician. Information that needs to be entered includes the patient ID, date of intervention, trend type, intervention type, reason, outcome, and description. This information is all entered into the Intervention table in the database. This information is important because it allows the programmers to keep track of cases and store them electronically.

The second administrator link that is available is the link to the Change Password page. With the correct information, the administrator is able to change a patient’s password. The information needed is the patient’s login, original password, and new password twice. This information will update the Login table. This is particularly
useful if the patient happens to lose their password. The administrator can login and change it to something different.

The last administrator link on the menu a link to the Add Patient page. This page allows the administrator to add a patient ad their password to the Login table. The information needed on this page is the new patient login, the new password, and a confirmation of that password. This information will be stored in the Login table.

3.4 Knowledge Acquisition to Build Cases

Once the database and website were completed and fully tested, the system was ready to go live. Before we could meet with any patients, we had to complete human subjects training. This training illuminated ethical aspects of working with human subjects and explained what is and what is not allowable during testing. After this was completed by each of us, we began our study with our first patient, aptly named Patient 1. He came to the clinic, a registered nurse explained the entire study to him, and when he was sure he wanted to participate, he signed the IRB informed consent form, located in Appendix C. He was then hooked up to a CGMS sensor and we were allowed into the room to meet the patient and register him and familiarize him with our website. After he registered, the system was explained in detail and he could begin entering his daily data when he returned home.

Every week after the patient began, our group of Professor Marling, Wes Miller, and I would meet with Dr. Frank Schwartz to go over the patient’s current data.
The physician would interpret the data to identify problems that were occurring. Adjustments to therapy would be made by the physician and documented by both the physician and our group. Later that day, the physician would contact the patient and recommend the changes that were brought up during the meeting. Within the following weeks, outcomes would be noticed in the patient’s data from the previous solution and these would also be noted.

As weeks passed, we gained other patients, added Dr. Jay Shubrook as another physician, and had multiple meetings to translate patient data into therapy adjustments. While the physicians would interpret the data to create adjustments, our group would pick up on why these changes were being made. By seeing why changes were being made, we were able to find some problems in our own meetings prior to our weekly meeting with the physicians. We learned to find problems on our own based on the therapy adjustment meetings, before the physicians saw the new data.

The therapy adjustments that occurred in our meetings are important to our system being able to give automated advice. They are the beginnings of cases that will be inserted into our case base. When the physician finds a problem in the patient’s data, he explains how he came to this conclusion by showing which pieces of data relate to the new problem. These key pieces of data will be used as features in cases to distinguish one case from another. The solution that is created for the problem is the second portion of our case and will explain how treatment should be changed to alleviate this problem. When an outcome is created, it is the final piece of information
in the case. When a case is finished being created, it will be entered into the case base where it can be used to solve different problems. When a new problem arises, the case base will be searched for the nearest case match. The resulting match provides knowledge about a previous problem and a solution that can be adapted to solve the new problem. Examples of cases built to date by Dr. Marling, based on knowledge we acquired, are provided in Figures 3.1, 3.2, and 3.3.

The first example happened in a meeting of ours with Dr. Schwartz. The problem that occurred is that Patient 1 was over-correcting for hypoglycemia. Notes were taken as to why this is a problem, when it occurs, how therapy was adjusted, and the outcome of the adjustment. Hypoglycemia occurs when blood glucose levels go below normal and an over-correction of this event will put the patient’s blood glucose levels above their high glucose target. Dr. Schwartz explained that a good correction was to consume approximately 30 grams of carbohydrates when this occurs. This problem was detected by the patient reporting a hypoglycemic event. His symptoms were sleepiness, weakness, dizziness, confusion, and irritability. He had a blood glucose level of 55 and he corrected by consuming orange juice, yogurt, and wheat sesame sticks, which together contain far more than 30 grams of carbohydrates. The patient then goes over his normal high target, as seen in his CGMS data, within two to three hours of the hypoglycemic episode. The solution to this problem of over-correcting for hypoglycemia is: (a) the patient should suspend the pump for 15 minutes, recheck blood glucose levels, and reconnect the insulin pump if within the normal blood glu-
cose range; (b) the patient should consume half of the orange juice, but none of the other food. The outcome of this case is that the patient was not comfortable suspending the insulin pump, but he did adjust his carbohydrate intake for the hypoglycemic event. This is one of the first problems that we saw in our study, and a case has been made of it. This case is shown in Figure 3.1.
Problem: Patient Overcorrected for Hypo Event
Patient: Patient 1
Physician: Schwartz
Dates: 2-16-06
   2-17-06
How Detected: Patient reports hypo event. One event occurred at 19:50 on 2-16-06 and another at 22:00 on 2-17-06. Symptoms were sleepiness, weakness, dizziness, confusion, irritability. Fingerstick was 55 on 2-16 and 49 on 2-17. Patient reports intake of OJ, yogurt and sesame wheat sticks on 2-16 and of OJ and banana on 2-17. Patient appears high on CGMS data 2 to 3 hours after reported event.
Generalization: Patient reports intake of more than 30 carbs.
Generalization: Use fingerstick data instead of CGMS data.
Differentiation: When patient does not report detecting and correcting a hypo event, but pattern of low followed by high occurs, you may have Somogyi phenomenon instead.

Solution:
Adjustment: For hypoglycemia, patient should suspend pump for 15 minutes, recheck blood glucose, reconnect pump if OK. Patient should have half the OJ, not all the other food.
Generalization: Suspend pump as above, cut back food intake to 30 carbs.
   Example: 2 glucose tablets
Repair: Remind patient to set an alarm for 15 minutes to signal the time to reconnect the pump.
Reason for Repair: Patient 1 forgot to reconnect pump for over an hour, until glucose level was too high, during a hypo event. Event occurred on 2-22-06 at 17:27. Patient reconnected at 18:51, when blood glucose was 176.

Outcome: Patient did about 80% of this. He wasn't comfortable suspending his pump, but he did adjust his carbs. This helped. The advice is sound for future patients.
Another example is that Patient 2’s blood glucose creeps up in the early morning, starting before breakfast and spikes up after breakfast. The physician interpreting the data was Dr. Shubrook. The problem was detected by reading the CGMS data. The upward trend appears all three mornings between 7 and 10 AM. The solution is to increase the early morning basal rate slightly. For this patient, the basal rate of .35 beginning at 7 AM was moved to start two hours earlier. The outcome of applying this solution was an improvement, but the problem was still occurring. Another adjustment was made, which then eliminated the problem. This case is shown in Figure 3.2.
Problem: Patient's Blood Glucose Creeps up in the Early Morning, Starting before Breakfast, and Spikes up after Breakfast.

Patient: Patient 2
Physician: Shubrook
Date: 3-14-06
Date: 3-15-06
Date: 3-16-06
How Detected: Looking at the CGMS data, you can see the upward trend on all three mornings. The problem appears between 7 and 10 AM.

Solution:

Adjustment: Increase early morning basal rate. The patient's current basal rate is .35 between 7:00 and 11:30 AM and .3 at other times. He adjusted the .35 basal rate to begin at 5:00 AM, two hours earlier.

Note: This is intended as a first step. Further increases in basal rate are anticipated as other problems come under control.

Outcome: Improvement was noted, but the patient was still spiking after breakfast and dropping low before lunch. This is the next problem for this patient. The basal rate was ultimately adjusted once more. The combination of the two adjustments eliminated the problem for the patient.
This final example is a continuation of the preceding case. The next problem for Patient 2 is that her blood glucose levels are spiking high after breakfast and then dropping low before lunch. This was again seen over three continuous days and was detected in CGMS data. The solution is to increase the patient’s morning basal rate by .05, increasing it from .35 to .40. The problem is due to the patient’s insulin sensitivity being decreased early in the morning, but increasing later in the day. Also, it is a long-term goal of the physician to increase the patient’s basal intake of insulin and decrease the bolus intake of insulin. The outcome is that this solution eliminated the problem. This case is shown in Figure 3.3.
Problem: Patient is Spiking Every Day after Breakfast and Then Dropping Low Before Lunch

Patient: Patient 2
Physician: Shubrook
Dates: 3-28-06, 3-29-06 and 3-30-06
How Detected: Examination of CGMS data

Solution:

Adjustment: Patient should raise her 7:00 to 11:30 AM basal rate to 0.4. (It is currently at 0.35.)

Note: Seeing the spike, you might think of giving a larger bolus before breakfast, but this would make the low even worse. What is happening is that the patient has decreased insulin sensitivity early in the morning, but becomes more sensitive to insulin later in the morning.

Note: We have a long-term goal of raising this patient's intake of insulin as basal and lowering her intake of insulin from boluses to even her out.

Outcome: This adjustment eliminated the problem.
In Case-Based Reasoning, knowledge is acquired and represented in cases. We have acquired knowledge from our physicians by tracking how they interpret patient data, and we are creating cases from these interpretations. Cases include a description of the problem, a solution, and an outcome. The cases will allow the system to solve similar problems in the future. We have already seen 25 problems, solutions, and outcomes for the first five patients in our IRB approved preliminary study. We will acquire knowledge and build cases for fifteen more patients in order to complete our system prototype.
Chapter 4

RELATED RESEARCH
The related research section covers three main topics: AI in Medicine (AIM), CBR in Medicine, and Diabetes research systems. When AI in Medicine began, diagnostic and educational systems were developed for diagnosis, but these usually did not go further than the research labs. CBR in Medicine takes AIM one step further, by using Case Based Reasoning to help solve problems in the medical field. Diabetes research systems introduces three systems that have the goal of helping diabetics manage their disease.

4.1 AI in Medicine

Artificial Intelligence in Medicine began back in the 1950s and has been growing since. There have been a few different eras that have come about to meet the goals of the physicians and to meet the goals of our world. The era of diagnosis was based on the idea that doctors needed help in diagnosing patient’s diseases. The era of managed care of chronic disease shows the evolution of physician care and how it changes the needs of AI in the doctor’s perspectives.

The Era of Diagnosis began in 1959 with a paper published by Ledley and Lusted entitled “The Reasoning Foundations of Medical Diagnosis” [Altman, 1999]. They pointed out that medical reasoning contained “well-recognized inference strategies: Boolean logic, symbolic inference, and Bayesian probability” [Altman, 1999] and that diagnostic reasoning could be created by using these three techniques. In 1965, Lawrence Weed was the first to demonstrate the use of electronic medical records and
he believed that structured data would be a major goal in the informatics community. The 1970s brought out the push for diagnostic performance. Kulikowski created the CASNET system, which “explored methods for using causal models for somewhat deeper diagnostic tasks” [Altman, 1999]. The MYCIN system used production rules to make expert-level diagnoses of infectious diseases. In 1982, the INTERNIST program’s goal was to “diagnose any problem within general internal medicine - any systemic disease between the neck and pelvis” [Altman, 1999]. The INTERNIST knowledge base associated diseases with two numbers: frequency of association and an evoking strength. An algorithm was written for finding and computing the most likely diagnoses.

All of these systems were evaluated and they performed near the level of human experts, but problems arose. Physicians never embraced the technology because of awkward interfaces, time consuming data insertion, not wanting help with their diagnoses, and diagnosing patients was a small part of their job. With new economic models for medicine, the physician’s financial incentives changed. Previously, the doctor would see as many patients as possible in order to make more money, also known as fee for service. Now the physicians needed to deliver a more “cost-effective, high quality care” [Altman, 1999] by charging a standard rate per patient, seeing patients less often, and having shorter hospital stays. The systems that were used in the physician’s offices needed to evolve from being able to diagnose to being able
to keep track of a patient’s diseases and how to combat those diseases. This would bring on the Era of Managed Care of Chronic Disease.

With the changes that were being made in doctor’s offices across the country, an AI in Medicine conference stated these subjects as concerns: “(1) the representation and manipulation of protocols and guidelines, (2) natural language and terminology, and (3) temporal reasoning and planning” [Altman, 1999]. Protocols and guidelines are an important way to standardize care and reduce variance. GLIF is a “syntax for specifying clinical protocols that contains representing actions, branch steps, and synchronization steps needed to specify a clinical guideline” [Altman, 1999]. Natural language and standardization terminologies are goals for the medical community to move away from using hand-written natural language. The Unified Medical Language System (UMLS) was designed in 1980 to include existing medical vocabularies and common semantic structure. The UMLS contains approximately 500,000 terms that are classified into about 150 semantic types with specified relationships. Temporal reasoning and planning are critical when the patients have chronic illnesses and episodic interactions with their physician. With temporal reasoning and planning, “nonmonotonic reasoning becomes essential: as new data are collected, we retract old inferences and assert different ones” [Altman, 1999]. Other applications of the era are telemedicine, intensive care medicine, and clinical trials.

The Era of Diagnosis got the ball rolling and showed physicians how AI could initially help them in the workplace. The Era of Managed Care of Chronic Dis-
ease changed the focus from diagnosing to keeping track of patient records electronically. Both eras prove that Artificial Intelligence belongs in medicine and will stay in medicine for many years to come.

4.2 CBR in Medicine

4.2.1 CASEY

CASEY combines CBR and Model-Based Reasoning (MBR) to diagnose heart diseases. It begins with a causal model and develops knowledge through its experiences. The system uses CBR first and if a solution is not sufficient, CASEY uses its model-based reasoning to create a sufficient solution. CASEY uses a discrimination network as its dynamic memory structure. If the CBR portion finds a solution that is not a copy of a previous case, it is stored into the case base. If the solution is a copy of a current case, then the case's importance is updated. If CBR fails to find a solution, the model-based solution is made, inserted into the case base and indexed.

CASEY is the first system that “(1) used associated reasoning for efficiency, (2) used model-based learning for robustness, and (3) learned from experience by combining the advantages of each technique while complementing their individual limitations” [Koton, 1989]. Prior to CASEY, CBR was only applied to domains that did not have a strong causal model. “The causal model is used to justify re-using previous solutions and to solve unfamiliar problems” [Koton, 1989]. CASEY resulted
in solutions that were identical to those made by a model-based system and was more efficient. The methods used are domain-independent and should be applicable in other domains with models of a similar form [Koton, 1989].

4.2.2 PROTOS

PROTOS is an approach to case-based concept learning and heuristic classification problem solving for diagnosing hearing disorders. For successful heuristic classification, the program must be able to “explain classifications, accommodate for incomplete case descriptions, and learn domain-specific knowledge for inferring case features need for classification” [Porter et al., 1990]. This is important because these dimensions are valuable for real-world problems. PROTOS supports these dimensions by using domain knowledge to fill its case base, one of the first systems to do so. Each case has a set of features and a category. PROTOS also has a set of relations and an explanation, which is a “chain of relationships between two features or a feature and a category” [Aamodt, 1990]. Explanations will be accepted when its strength is above a particular threshold.

During knowledge acquisition, a problem will be entered into PROTOS and PROTOS will produce an answer. If that answer is not correct, the expert can ask for another solution or can create their own solution and explain the reasoning behind the new solution. It continually learns by strengthening or weakening the relevant
features and when incorrect, adding new cases. PROTOS relies heavily on the user for its information.

4.2.3 ALEXIA

ALEXIA is a case-based problem solver and its application domain is the “determination of a patient’s hypertension etiology” [Bichindaritz, 2006]. It uses a combination of a qualitative model and CBR. Its cases are represented using three dimensions: intake, clinical, and biological. Exact values are used when they can be determined. Otherwise, theoretical values are used. Its ontology is a “set of classes and rules associated with the classes in frames represented in an Object-oriented kernel, called K language” [Bichindaritz, 2006]. ALEXIA was tested on both easy and difficult cases, some of which failed on a Bayesian network or expert system [Bichindaritz, 2006]. ALEXIA solved all 18 of the cases that were given to it.

4.2.4 MNAOMIA

MNAOMIA is another case-based reasoning system that helps clinical staff with psychiatric eating disorders for diagnosis, treatment, and research hypothesis recommendations [Bichindaritz, 2006]. Its cases are represented among multiple dimensions, including: general, behavioral, somatic, psychic, and biological. A case contains 2287 attributes and these come from questionnaires administered during a hospital stay. MNAOMIA’s ontology contains “diagnostic category prototypes” and its mem-


ory is structured to handle multiple points of view. Prognosis is given at the patient’s admission to the hospital and the accuracy of the prognosis comes from weeks of hospital care. MNAOMIA was tested on 115 cases with and without its prototypes. After the first 30 cases, both tested at about 94% accuracy but the previous 30 cases were very different. The version with the prototypes was approximately 80% accurate for the first 30 cases, while the version without the prototypes was much lower [Bichindaritz, 2006].

4.2.5 CARE-PARTNER

CARE-PARTNER is a multimodal system using CBR and RBR to give decision support to patients that have undergone a stem cell transplant [Bichindaritz, 2006]. Home care providers place contacts with long term follow-up of transplants on the Internet and are able to receive advice on the continuing follow-up. The cases are represented as a patient record and include problems, medications, laboratories, protocols, and risks [Bichindaritz, 2006]. The system is comprised of patient cases plus experimental and theoretical memory, including 91 clinical pathways [Bichindaritz, 2006]. Prototypical cases are stored and can be reused within CBR for actual cases that are similar. The system was evaluated by medical experts and received an overall rating of 94.5% that the results were acceptable by the medical experts.
4.2.6 INRECA

The INRECA (Induction and Reasoning from Cases) Approach is “aimed at developing information technology for building systems for solving diagnosis and identification problems by using past history” [Althoff et al., 1998]. They address the problem of diagnosing intoxication by drugs. They used Russian toxicologists for their knowledge acquisition, since they have valuable experience in the field. Its main goals were to make quick decisions, help inexperienced medical staff, and make its experience useful to multiple sites.

There were 8 different medicines covered and 86 parameters identified for diagnosis. The program’s requirements were: short response time, justifiability of results, dealing with incomplete information, dealing with vague relationships, measured values and conceptual terms. The solution was to use CBR to deal with the lack of information, vague relationships, and to allow different attributes. The indexing strategy used is the Inreca-Tree, a multi-dimensional binary search tree that helps by creating shorter response times. The branches of the tree represent constraints on attributes, while the leaves contain all cases which fulfill all constraints [Althoff et al., 1998]. A recursive search is used for retrieval.

The system was tested against a highly specialized system, called the AS algorithm, and an induction system [Althoff et al., 1998]. Overall, this system met all of its domain and task requirements and showed a “very high classification accuracy”, which was slightly worse than the AS algorithm, but better than the induction sys-
tem. The INRECA system also required a lower developmental effort compared to the AS algorithm that it was tested against.

Another successful toxicology approach is the SETH approach. SETH’s goals are to give users advice on treating and monitoring drug poisoning. It has been in use since April 1992 [Darmoni et al., 1995] and takes into account toxicological task delay, sign, and dose. It works for both known and unknown intoxication. If known, it gives inexperienced physicians advice on treating the poisoning, and if unknown, it is used to identify the toxins. “The SETH approach underlines that computer based decision support in the toxicology field is very helpful” [Darmoni et al., 1995].

4.2.7 SMARTHOUSE

Another system that offers CBR with specialized retrieval is SMARTHOUSE. Its cases consisted of a person’s needs along with the assisted living devices that are available to help them. The two biggest issues for the retrieval only system are case representation and an iterative retrieval strategy that used similarity matching, but could also handle multiple case reuse [Wiratunga et al., 2004]. Case representation was done by manually translating text cases into feature pairs for knowledge representation. There are binary valued and multi-valued pairs for holding knowledge. A total of 108 features with 64 “to describe the problem in terms of the person, their home, abilities, and needs; and a further 44 features to describe the solution” [Wiratunga et al., 2004]. Each set of features is then grouped based on
similarities to allow retrieval to look into each sub-task separately. A decision tree index formed by using “C4.5’s information gain ratio heuristic [Quilan, 1993] additionally provides useful means to explain the underlying reasoning behind the retrieval” [Wiratunga et al., 2004]. The Nearest Neighbor Algorithm is also used to find the most similar cases. SINGLE is a retrieval method that applies the Nearest Neighbor algorithm to the entire case base and does not use indices, while MULTIPLE also applies the Nearest Neighbor algorithm but uses multiple indices to “enable reuse of multiple cases to solve different sub-tasks” [Wiratunga et al., 2004]. Eleven real cases are in the case base with another twelve cases that were created by their domain expert.

The system was evaluated by using two separate methods, leave-one-out testing and user testing, and their two different retrieval methods, SINGLE and MULTIPLE. Leave-one-out testing involves removing a case from the case base and running the tests on the remaining cases while user testing is the “comparison of the system’s and expert’s solutions” [Wiratunga et al., 2004] for new problems. The leave-one-out testing showed MULTIPLE with a significant improvement over SINGLE but later states that “system generated solutions should not be taken on board as the all encompassing solution” [Wiratunga et al., 2004]. This was stated because MULTIPLE made a very expensive suggestion that could gradually reduce a patient’s movements. User testing showed that MULTIPLE again performed better than SINGLE, but they found another flaw in device groups containing more than five devices. The
authors conclude that “multiple indicies enabled re-use of different cases to solve different parts of a given test case, thereby encouraging best use of the relatively small database” [Wiratunga et al., 2004] and that a better realistic evaluation will be needed before the approach is completely justified.

4.2.8 WHAT

“Wellworks/Heartworks Advisor/Trainor (WHAT) is a prototypical training system for beginning sports medicine students in the Wellworks and Heartworks programs at Ohio University” [Evans-Romaine and Marling, 2003]. Students are taught how to create exercise prescriptions for patients based on their past experiences. There are a set of rules that are used to teach students exactly how to create these prescriptions. In Wellworks/Heartworks, the patient starts in a exercise regimen that is ranked from 0 to 12 in intensity, with 11 and 12 being the maintenance levels for each program. The program is limited to showing students where a patient should begin and gives two different outputs, one which is rule-based and the other of which is the best matching case from the case-base. The case base of the WHAT program is made up of eighteen previous examples of patients and what exercise regimen they were given.

WHAT was tested by the leave-one-out method, while using the left out case as the new test case. WHAT’s case based output produces more expert prescriptions than the rule-based reasoner. While the CBR portion recommended more strenuous
regimens, it was less likely to place a participant in too high a regimen. The rule-based reasoner was a level too high 33% of the time, while the CBR portion was a level too high 18% of the time [Evans-Romaine and Marling, 2003]. From this testing, it is shown that the CBR portion of WHAT out performs the RBR portion and gives more precise exercise regimens.

4.2.9 AUGUSTE

The Auguste Project [Marling and Whitehouse, 2001] is an effort to “provide decision support for planning the ongoing care of Alzheimer’s Disease (AD) patients, using CBR and other thought processes natural to members of geriatric interdisciplinary teams” [Marling and Whitehouse, 2001]. Its cases have approximately 100 features to represent the problem and the solution for the case. The problem description is the patient’s medical history and current physical, emotional, behavioral, and cognitive status, while the solution explains which neuroleptic was chosen, if one was chosen at all. The system initially screens out patients without behavioral problems and those already on neuroleptics. Then Mini Mental Status Examination (MMSE), a test of cognitive status, is used to find similar cases in the case base. Nearest neighbor matching is used to find the most similar case out of the MMSE initial findings by examining features like: “agitation; anxiety; hallucinations; paranoia; wandering; caregiver stress; external support services; current Parkinson’s disease; and problems with dressing, bathing, or transfer” [Marling and Whitehouse, 2001]. The case with
the highest similarity, that was above a cutoff, is the nearest neighbor and then decisions are made. If the case involves giving a neuroleptic, then the RBR comes into play and decides which neuroleptic will be given to the patient.

The system was evaluated by introducing new cases, examining the output, and demonstrating the system to 12 clinicians, of whom 8 completed evaluation questionnaires. All of the cases that were tested by the CBR portion were correctly classified even though one value fell below the cutoff threshold. Out of these cases, three were prescribed neuroleptics. Of these three cases, the system only managed to successfully predict one neuroleptic correctly. This could have been caused by errors or omissions in charts or different drugs being favored based on slightly differing results. The system’s positives were ease of use, understandable and thorough suggestions, helpful comparisons, and usefulness to general practitioners and geriatric interdisciplinary teams. It is not easy for one system to deal with “multiple perspectives of professionals from different healthcare disciplines, cases that change over time, and ethical points of view” [Marling and Whitehouse, 2001]. Clinicians agreed that the system’s suggestions are comparable to that of a knowledgeable clinician and that the system would be useful for those who are in training, general practitioners, and geriatric interdisciplinary teams.
4.2.10 Breast Cancer Systems

Rossille describes a new hybrid system for breast cancer, which will eventually
be used for all cancers [Rossille et al., 2005]. They create a hybrid RBR-first, CBR-
last system to support physicians in atypical cases, the first like it in their area.
Their initial phase is to design and model the architecture, with the next phase
including searching and a similarity metric. They created a model using Unified
Modeling Language (UML). Their Decision Support System (DSS) contains a case
base, knowledge base, processing engine, and an interface [Rossille et al., 2005]. As
new cases are entered, the system compares the case to a particular guideline and
enters information into the classification table relating to the case and guideline. This
will allow the system to identify related cases and do a more specific comparison of
those matching cases. To make their future system completely automated, they would
need all of the patient data to be completely acquired from their hospital’s database.
This system needs to be fully implemented and tested before we will know how useful
the system is.

Shin-Yuan Hung created a decision support system that uses CBR and applies
computer-aided detection (CAD) to mammographic images because CAD picks up
“barely visible [Hung and Chen, 2006]” lesions so radiologists do not miss them. Once
a lesion is found, the radiologist needs to classify the lesion correctly using the Breast
Imaging Report and Data System (BI-RADS ®). By creating this system, Hung
was looking to support the radiologists in their decisions by giving them the most
relevant cases and hopefully “avoiding some unnecessary biopsies for benign breast lesions [Hung and Chen, 2006]”. The testers were 34 experienced radiologists and they seemed to be “more confident in their own judgment when interpreting mammography [Hung and Chen, 2006].” This could be why the testers did not rate it as high as the authors would have hoped. The system’s main limitation is that it is only for decision support, it cannot currently replace a human interpretation, it can only help them. This is because “the system cannot read mammographic images and medical diagnosis is still an art” [Hung and Chen, 2006]. The author concludes that the system could help less experienced doctors learn how to treat breast cancer.

Bilska-Wolak and Floyd also created a CBR program to help in “reducing the number of biopsies performed on benign lesions” [Bilska-Wolak and Floyd, 2002]. They are predicting biopsy results from BI-RADS® technology. They have ten major features that represent their cases and are testing using leave-one-out, Receiver Operating Characteristic (ROC) analysis, and bootstrap. Their inference engine uses two algorithms, Hamming distance and Euclidean distance, to find the most influential features in their case base. The authors conclude that the best features from the Hamming and Euclidean distances contradicted each other, except for mass margin, calcification morphology, and age [Bilska-Wolak and Floyd, 2002]. They do not include other useful information, such as medical history or clinical data [Hung and Chen, 2006], but the authors believe that their tool is useful for the classification of mammographic lesions.
4.3 Diabetes Research Systems

These systems were introduced in Chapter 2 and are described here in more detail.

4.3.1 Telematic Management of Insulin-Dependent Diabetes Mellitus

Schmidt, Montani et al. [Schmidt et al., 2001] are working on a multi Modal Reasoning (MMR) paradigm, which is the beginning of the Telematic Management of Insulin-Dependent Diabetes Mellitus. Inside of this paradigm, they need to handle the following things: “identify metabolic problems, generate a set of suggestions, and apply suggestions to the current insulin protocol” [Schmidt et al., 2001]. To accomplish this, they use a RBR and CBR system to come up with their conclusions. The RBR tool was created to “fire specialized procedures for data analysis and metabolic indicators extraction” [Schmidt et al., 2001]. The CBR tool has data generalized into classes allowing for easier classification. Initially, the raw data is analyzed by Temporal Abstractions (TA) and states are abstracted [Schmidt et al., 2001]. A Blood Glucose Level (BGL) modal day is created with probabilities of each abstraction in different time periods. Case based retrieval is then used to classify similar classes and a “Naive Bayes technique” [Schmidt et al., 2001] is used to find similar classes. The RBR tool will typically suggest solutions, but when the problems are more complex
CBR retrieval is used. The retrieval is done using the Nearest Neighbor technique and then the newly found corrections can be applied to the patient’s protocol.

The authors conclude that the RBR tool can handle simple problems but for more challenging ones, the CBR tool is “very helpful for the definition of a proper therapy” [Schmidt et al., 2001]. If the case library is poor though, the retrieved results may not be the best protocol. When this is the case, the RBR will be used, even if it is too conservative of a solution. In time, new cases will be created and the competence gaps in the case library will hopefully be filled. If new cases are found and they are not in the current case library, they can also help fill the library.

The following year, the Telematic Management of Insulin-Dependent Diabetes Mellitus (T-IDDM) project was funded by the European Union and carried out in 2001 [Bellazzi et al., 2002]. The system’s main goals were to “(a) supply effective treatment by balancing insulin therapy, diet, and physical exercise, (b) supply patients with continuous care outside of a hospital setting, (c) allow continuous education to patients, (d) create a cost-effective system to handle many patients” [Bellazzi et al., 2002]. This system was created using two modules, the Patient Unit (PU) and the Medical Unit (MU), that are connected via the Internet. “The MU integrates a visit-by-visit assistance for the physician with the possibility of providing telecare to patients, via the telecommunication link between the hospital and patient’s house. The PU gives day-to-day support to the patients, allowing for telecommunication” [Bellazzi et al., 2002]. This system again used RBR and CBR for its Multi-Modal Reasoning methodology.
This system’s initial clinical results were: “(a) 9% reduction in patient’s mean BGL (from 146.3 to 133.9 mg/dl); (b) 11% reduction in median BGL (from 158 to 141.3 mg/dl); (c) 9% reduction in HbA1c (from 7.77 to 7.1%)” [Bellazzi et al., 2002]. These results are very good, but the number of patients involved was only three. The system’s pilot clinical validation was with 12 patients and was heavily testing the MU. “The MU advice influences the insulin daily requirement with a maximal increase of 16%, a maximal decrease of 13%, and a mean absolute variation of 5.5%” [Bellazzi et al., 2002]. The clinicians involved agreed that the system worked well. The outcomes show that telemedicine is feasible and the system does help the patients with their management of diabetes. “In particular, it could permit to perform a tighter control of the patients’ metabolic situation, in a cost-effective way, without requiring additional visits and personal contacts between patients and physicians” [Bellazzi et al., 2002].

In 2002, Stefania Montani uses RBR and CBR to create an MMR Knowledge Management (KM) system for diabetes patients. This model uses RBR first and then tailors the results using CBR. This was tested by two diabetologists that were asked to preform a “fully-crossed, blind review of therapies proposed by RBR, MMR, and two colleagues” [Montani and Bellazzi, 2002]. Both the RBR and MMR worked well, but no benefit was found by exploiting MMR.

In 2003, Montani and Bellazzi propose a MMR system that uses a tight integration of RBR, CBR, and MBR, which is based on the previous T-IDDM system.
“Case-based retrieval and the mathematical model are used as a means for specializing the behavior set of production rules, and for computing the optimal therapeutic suggestion” [Montani et al., 2003]. The physician will be able to use the CBR tool, use the case library, and rebuild patient histories over time. The CBR can be seen as “independent operative KM methodology” [Montani et al., 2003]. If the case library contains insufficient information, CBR-RBR results will lead to “sub-optimal therapeutic advice” [Montani et al., 2003]. This can be changed by adding a MBR strategy to go alongside the RBR to provide a well tailored solution. By adding the MBR to the system, the authors are able to “detect a complex situation and to handle them in a more robust way” [Montani et al., 2003].

The T-IDDM system focuses on helping patients with their blood glucose control by regulating the amount of insulin intake per meal. The data being collected includes blood glucose measurements, diet readings, insulin measurements, and some personal data. Since the papers do a poor job of explaining the data they are collecting, it is difficult to create comparisons between the their data and ours. Their study is collecting just enough information to be able to decide how much insulin should be taken at each meal. Our study collects extra data because we are dealing with a different goal, to create suggestions in insulin therapy to tighten blood glucose control for patients. This system also changes the types of reasonings that it uses from using CBR alongside RBR to CBR, RBR, and MBR together, while our system exclusively uses CBR. While T-IDDM is using telemedicine to receive patient data, our study
is using the Internet and a form-based website to collect patient information. Our patients also have the benefit of using an insulin pump which helps control the amount of insulin per meal, which will be explained further in the chapter.

4.3.2 VIE-DIAB

VIE-DIAB [Popow et al., 2003] creates a 4x7 graph plot that shows patient days broken down into six separate daily times, ranging from early morning (3am to 8am) till night (10pm till 3am). The blood glucose readings from each time is categorized into five different categories, ranging from hypoglycemia (<60 mg/dL) to extremely high (>350 mg/dL). Each category is then color-coded for the physician’s ease-of-use. Their aim, like ours, is to improve diabetes control and reduce long term complications [Popow et al., 2003].

They speculate that “patient compliance could be improved and the clinical workload reduced at the patients side by using mobile phone or hand-held computer technology for automated data transmission and at the caretaker’s side by preprocessing the data applying automated data visualization and artificial intelligence techniques” [Popow et al., 2003]. The system’s architecture relies on three main ideas: (a) continuous data from the patient, (b) visualization of data by the physician, and (c) feedback to the patient. The data collected is date and time, serum glucose value, insulin dosage, treatment type, carbohydrate intake, and notes. The data is visualized by day into six time periods: early morning, 3am - 8am; morning, 8am - 11
am; noon, 11am - 2pm; afternoon, 2pm - 5pm; evening, 5pm - 8pm; night, 8pm - 3am. The blood glucose value is displayed in this time period by either the highest value or both the high and low, if the patient had a dangerously low value. Those values are then color coded for an easier representation in a chart. Each of these small graphs represents a single day and the small plots are combined in a large graph plot involving the last 28 days (four rows by seven columns). Other detailed views of the patient’s data is also available in a scatter plot showing all blood glucose levels, a histogram showing blood glucose, carbohydrates, and insulin doses, and a spreadsheet containing all the raw data [Popow et al., 2003]. The system also has a recommendation processor that gives an initial recommendation of four types: not enough data, control is good, control needs help - make these improvements, or control is poor - contact your physician.

The advantages of the system are that it’s user-friendly for the physicians - they are able to see the data in an easy to read format very quickly - and that the system creates simple advice based on the last seven days of user input. The disadvantages are that the user must send multiple messages per day to the physician’s server and the increased workload on the physicians having to create weekly responses. Another disadvantage is that only 14 patients were involved, but the next study was to include 36 patients. The system’s approach seems useful and further testing would reveal how helpful the visualization is and if changes are needed to improve portions of the system.
The VIE-DIAB system explains that it is able to “produce (simple) suggestions for patients advice” [Popow et al., 2003], but never explains them in detail. The level of detail is given above, but the system is not looking to be able to give advice to drastically change a patient’s insulin regimen. This system uses telemedicine in the form of mobile phones running a Java application while our system is a form-based website. The visualization tool that is also provided for physicians from this system graphically displays information, as does ours. Our system collects more information and will also display more information on each graph. By not collecting more information, this system is missing data to make more detailed diagnoses in changes for their patients. CBR is also not used in this application.

4.3.3 Controlled Assisted Meal Related Insulin Therapy

Another study was conducted to test whether or not computer assistance helps a patient with insulin therapy. Of the 50 diabetics in the study, they were randomly split into two distinct 25 person groups. The first group used Multiple Subcutaneous Injection (MSI) treatment with their usual intensive regimen. The other group was treated with the Computer Assisted Meal Related Insulin Therapy (CAMIT) which is aided by a pocket computer. The CAMIT program was written in C and adapts the insulin dose to the current situation of the patient based on the patient’s “blood glucose value, carbohydrate content of next meal, intended physical activity, and events (such as hypoglycemia symptoms, illness, stress)” [Schrezenmeir et al., 2002]. The
MSI group was also documenting the following data: “blood glucose values, carbohydrate intake, sports, events, and injected insulin doses” [Schrezenmeir et al., 2002].

The MSI group was a control group to test against the CAMIT group and the results were good. In each of the tests, the CAMIT group received better results than the MSI group. This can be explained by “better metabolic control due to more consistent insulin dosage adaption” [Schrezenmeir et al., 2002] in the CAMIT group. “The improvement in the metabolic situation in the CAMIT group was associated with an increase in the insulin sensitivity, a reduction of hypoglycemic episodes, and HbA1-values” [Schrezenmeir et al., 2002].

This system is similar to newer commercially available software that is used in insulin pumps. It is able to predict the amount of insulin needed per meal based on the patients carbohydrate ratio, current blood glucose measurement, blood glucose target, insulin sensitivity, and carbohydrates to consume. With our patients all having this insulin pump software and an insulin pump, they are already having this benefit that the CAMIT system was providing. Our system is collecting more information via a form-based website and using this information to generate advice for patients insulin regimen. While no CBR or AI was used, this is another study that successfully shows that computer aided treatment is effective for type 1 diabetics.
Chapter 5

Evaluation and Future Work
5.1 Evaluation of Work to Date

To evaluate the ease with which data can be acquired and the usefulness of the acquired knowledge, feedback was solicited from physicians and patients.

5.1.1 Physician Feedback

Both physicians have been extremely positive with the current progress of our software. They agree that “prototypical tools developed for expanded daily event data collection and graphic presentation allow participating physicians to identify trends more readily and adjust therapy more effectively, resulting in improved glucose control” [Marling et al., 2006]. They also know that “physician review of self glucose monitoring and CGMS data along with extensive daily patient logs can improve glucose control. However, the time required for analysis and data overload precludes most physicians from doing so. Intelligent decision support tools may assist” [Marling et al., 2006]. Dr. Frank Schwartz had this to say about a one of his patient’s data that was received during our study, I have been following this patient for 10 to 12 years and I have never seen this data. We have been flying by the seat of our pants.

5.1.2 Patient Feedback

An exit survey was administered to solicit feedback from patients in the preliminary study. All four patients who finished the preliminary study have also taken our
exit survey, which is available for reference in Appendix E. The results are summarized below.

All patient characterized their blood glucose levels as being “fairly well controlled” at the beginning of our study. During the course of the study, three patients felt that their blood glucose control improved while one felt it stayed the same. All four patients agreed that the increased contact with health care providers during the study was beneficial to managing their blood glucose levels. All four patients indicated that immediate feedback with advice concerning their blood glucose levels from an automated system would be beneficial to managing their diabetes. One felt it would be very beneficial, while the other three felt it would be fairly beneficial. This feedback indicates that knowledge about blood glucose control is important to patients and that patients are open to using a CBR system.

Patients answered that it would take them anywhere between 15 and 60 minutes to use the system, with an average time of 41 minutes. A study has shown that diabetics must spend between two and three hours each day managing their diabetes to fully comply with the recommendations of the American Diabetes Association [Shubrook and Schwartz, 2006]. It is anticipated that the time spent on the system could be reduced through eventual integration with commercial pump and meter software.

Three patients felt that the internet computer data entry system was easy to use, while one thought it was fairly difficult to use. Of the first three, one thought it
was very easy to use, while the other two felt it was fairly easy to use. Three of the patients would prefer to have a computerized therapy adjustment wizard on their pumps, while one would like it on their Palm or Blackberry. Dr. Schwartz is working with pump and meter manufacturers in hopes of eventually making this transition.

All patients said they would be very likely to adopt a therapy adjustment recommended by their doctor. All four patients would also be very likely to adopt a recommended therapy adjustment if it were made by a computerized therapy adjustment wizard. One patient answered very likely and wrote in “until it proves to be inaccurate or improper.” This feedback supports the idea that a CBR system would be used by and useful to patients.

Patients were split on whether they would be willing to wear a continuous glucose sensor at all times if the technology is released soon. One patient would be willing only if “it were less obtrusive and more comfortable.” Two other patients who would not wear a continuous glucose sensor wrote in: “not unless it was integrated with the pump’s infusion set” and “unless it was a closed loop system or did not require additional inserts into skin.” Medtronic Minimed is currently working on integrating glucose sensors with insulin pumps.

Our final question on the exit interview was open ended and asked the patient what other factors contribute to your blood glucose going high or low that we have not considered. Patients answers included:

- Unexpected blockage of infusion set
• Unexpected development of air bubbles in insulin delivery line

• Guessing amount of carbohydrate intake versus knowing exact amount

• Would like to focus on minimizing or decreasing the standard deviation of my glucose results

These open ended suggestions will be incorporated into future work.

5.2 Finishing the Construction of the CBR Prototype

There are two major areas that need to be finished before our prototype is in full working order. The major areas are trends analysis and the creation of a case base for our prototype. We are currently conducting an Ohio University Institutional Review Board (IRB) approved clinical trial, in order to obtain the data we need for these future tasks. Data from 20 type 1 diabetics will be collected over the next several months via this study.

5.2.1 Trends Analysis

Since we already have the website to allow the user easy access to inserting their data to the database, the next logical area would be working on finding a patient’s problems. Trends analysis is needed for our project to spot problems in
data that could be more tightly controlled. Our doctor initially gave us twelve scenarios to implement for trends analysis. These scenarios are dawn phenomena, Somogyi phenomena, AM hypo/hyperglycemia, pre-meal hypo/hyperglycemia, post-meal hypo/hyperglycemia, other erratic glucose levels, the effect of the menstrual cycle on glucose levels, effects of stress on glucose levels, and effects of exercise on glucose levels. Each of these scenarios can have multiple causes or effects on a patient’s glucose levels and can often occur in diabetes management. When a trend is spotted, for example, hyperglycemia prior to lunch for three consecutive days, it will be matched against the case base. If a similar case can be found, its solution will be adapted to suit the current patient and a result will be sent back to the user or physician.

5.2.2 Creation of a Case Base

Once the trends analysis is completed, the next step is the creation of a case base to store the cases that we are currently creating. Dr. Frank Schwartz and Dr. Jay Shubrook have been doing the trends analysis to find the problems within the patient’s data and then creating solutions to problems by adjusting the patient’s therapy. After a week or two with the new solution, an outcome is determined based on how responsive the patient has been to the created solution and how successful the therapy adjustment has been. Each problem, its solution, and outcome will be structured into a case for the case base to enable automatic reasoning about similar problems. Each case will need to be converted from human readable format into a
computer recognized format that will be used by the CBR prototype. Other aspects of the case base that need to be created are an efficient memory structure, an effective indexing strategy, and a practical similarity metric. The case base is taking shape and this future work will be culminating in a thesis within the next year.

5.3 Future Enhancements and Extensions

Future enhancements and extensions of our project will occur after the initial study has been completed and we see that our work provides support to type 1 diabetics. We would like to add a nutritionist’s expertise into our project, upgrade our website, expand the number of patients using our system, and add more cases to our case base.

5.3.1 Nutritionist

Including a nutritionist into our project would be very beneficial. A nutritionist would help us create an extension to our project that would test the food eaten by the patient based on carbohydrates, calories, and glycemic index. This could be done by creating or using an existing database that contains nutritional information about many different types of foods. By testing the patient’s foods for this information, the extension would be able to give advice on the carbohydrates and the glycemic index. Patients currently base their insulin intake per meal mainly estimated on
carbohydrates. If a patient is not estimating carbohydrates correctly, their blood glucose levels could be going high or low each time they eat a particular food. This system would help find these problems and educate the patient and physician based on how a patient estimates their carbohydrates.

The system would also suggest other foods that the patient could be eating to help lower their glycemic index for that meal. Reducing the glycemic index of their meals can lead to “improved diabetes control, increase the body’s sensitivity to insulin, reduce the risk for heart disease, reduce blood cholesterol levels, reduce hunger, and prolong physical endurance” [Brand-Miller, 2006]. The addition of this extension into our project will help our diabetic patients improve their carbohydrate counting ability and help them manage their diabetes more efficiently.

5.3.2 Upgrading the Website

The website that we currently use only allows the patient to insert their data, not to view any data or to receive any advice. We would like to be able to show the patient their current history, diabetes related information, current therapy, and recently created advice from the system on our website.

Their current history would show the current data that they have inserted into the database. This could be shown in either a textual or graphical format depending on the data that they would wish to view. We already have a program that displays their data in a graphical format and this would be the precursor to showing patients their
blood glucose data on a graph. This would be useful for the patient and physician to see how the patient was doing on a day-to-day basis. This would be useful for the patient to see how their days are going, what medication they are taking (and when). It would be useful for the physician to be able to check against previous medications and other ailments that the patient has had.

The patient’s current therapy would also be available online. In our current prototype, we are going to initially give the advice to the physician for the purpose of testing. We would like the patient to see the system’s recommendations in real-time. The advice would be exactly the same that we would give to the physician unless we could not find a valuable solution or we did not have enough data to create a solution. When the system has no recognized solution, we would have the patient contact their physician. This would show the problems in the past that they have had, how we have attempted to correct these problems, and whether or not the solutions worked. This would give the patient a lot of information to see how their current therapy is working and how well they are following it, because of the instant feedback available on the website. The physician would also benefit from this by being able to login to the website and choose which patient’s information to view. It would allow for the doctor to always have the information at his/her fingertips and would allow for quicker consultations.

In general, these updates to the website would allow the patient to see their own data, view their current therapy, and hopefully give the patients a tighter control of
their blood glucose values over time by letting them see how they have been affected by their therapies and life. The updates will allow the physician to easily find the patient’s current history, to access the data when questions are asked, and to change a current therapy and quickly see if the patient has followed through with the changes. This is not a small problem, but rather a large project that would need to be worked on for some time before it could be added into our project.

5.3.3 Expanding the Number of Patients

Once our initial study is finished, we would like to expand our study to a larger population, beginning with Southeast Ohio and then moving into other Appalachian areas. We would eventually like this to be used across the United States for any doctor that would be willing to try it with their patients. Many major upgrades in software and hardware would need to be made for such a large group of patients. The website would again need to be updated for a more user friendly approach, a dedicated server would need to be bought and set up, a more efficient strategy for backing up our data would be needed, and a much larger hard drive or preferably a jukebox with multiple RAID hard drives would be required. I am sure there are other upgrades that we would also need, but these are the major ones that would allow us to expand past our initial study and into a much larger area.
5.3.4 Including Other Types of Cases

There are many different types of studies that can be done following our initial study. These include detailed studies of diabetics at different stages of life, such as early childhood or adolescence. They could also include the effects of prolonged exercise, pregnancy, or menopause on diabetics. Each of these life stages and events has a direct effect on a patient’s blood glucose levels. In each case, we would like to have as much information as possible on the effects on the patient’s diabetes management. What happens for one person could be similar to what happens for another, and every case that we can learn from allows us to solve more problems.

Pregnancies would have to be followed for the full nine months, or from the time the conception is confirmed. Following women with pregnancies could be useful because of the ways a woman’s hormones change throughout her pregnancy and how they could possibly affect her insulin sensitivity and her baby.

Teenagers have special needs which we have not yet addressed. Data collected before and after puberty would be very useful. Young men and women change greatly in the course of two or three years, and their therapy changes along with them. Children could be studied as well, so that their special needs could be incorporated into our system. Menopause is another example of a person’s body changing quickly over time and it would be useful to see how blood glucose levels are affected by it.
Chapter 6

SUMMARY AND CONCLUSION
This thesis has presented work in data and knowledge acquisition in case-based reasoning for diabetes management. This work has been conducted in the context of a project to create an automated insulin therapy advisor. This system will help regulate patients blood glucose levels based on previous experiences using Case-Based Reasoning. This work is interdisciplinary and of importance to both Medicine and Artificial Intelligence. It is important to Medicine because controlling diabetes leads to fewer complications. It is important to Artificial Intelligence because physicians are able to change therapy regimens for diabetics on insulin pump therapy, but computers are not.

Contributions of the thesis include:

- Design and implementation of a database to store information
- Design and implementation of a website to collect information
- Knowledge acquisition from physicians as they adjust patient therapy based on information stored in the database

To design the database, the author learned about Type 1 Diabetes by shadowing Dr. Frank Schwartz and observing the strategies he used to create therapy revisions based on patient data. Shadowing the physician allowed the author to determine the information used to make therapy revisions. This information was then used to design a database with two other graduate students. The author then implemented the database to hold patient data during a preliminary study. With the database
complete, the website and front end for the database was designed and implemented by the author using HyperText Markup Language (HTML) and Hypertext Preprocessor (PHP) programming languages. Both the database and the website have been available for use by subjects in an Ohio University Institutional Review Board (IRB) approved preliminary study, which started on February 16, 2006.

This preliminary study will allow us to determine if computer software can analyze glucose patterns from data downloads and Continuous Glucose Monitoring Systems (CGMS), learn from previous adjustments, and generate advice on what adjustments to make in insulin dosages. Data is being collected and analyzed from twenty subjects for six weeks each for use in software development.

Once data is received from patients in the study, knowledge is acquired from physicians to build cases for a Case-Based Reasoning (CBR) system. During weekly meetings, Dr. Frank Schwartz and Dr. Jay Shubrook interpret their patients data, find problems in current therapy, decide on solutions, and recommend adjustments. Outcomes of each adjustment are noted in subsequent meetings. Cases are made up of problems, solutions, and outcomes from the physicians’ therapy adjustments. Problems contain features used to distinguish cases in the CBR system. Each created case allows for another problem to be recognized and solved. There are currently 25 cases created from five patients who have participated in the study. Fifteen more patients will be enrolled in the study and their data will also be interpreted and
analyzed by the physicians to create cases which will further enhance the knowledge that our CBR system has accumulated.

Future work includes finishing the construction of the case-based reasoning prototype. Trends analysis is currently being implemented as are initial cases for the case base. Future enhancements and extensions include upgrading the website, expanding the number of patients after the preliminary study, creating more cases from new patients, and involving a nutritionist in the project.

Evaluation of work to date was conducted by soliciting feedback from the physicians and patients involved in the study. The physicians, Dr. Frank Schwartz and Dr. Jay Shubrook, are excited to see the system take shape and to see the author learn how they make changes in therapies. Regarding Patient 4 of our study, Dr. Schwartz commented “I have been following this patient for ten to twelve years now and I have never had this data. We have been flying by the seat of our pants.” Patients are also enthusiastic about this study because they believe it will help them in their daily lives and they wish to be a part of it. Patients are so excited that we currently have a waiting list for patients to begin the study. The four patients who have finished participation in the study provided highly positive feedback on a structured exit survey. In conclusion, the work that is described here is the beginning of a system that will provide automated insulin therapy adjustment advice to patients. It lays solid groundwork for the future portions of this system.
Bibliography


Appendix A

Website Views

This appendix contains views of the website that was created for patients to enter data to the database. They are listed in three different sections: Registration, Non-registration, and Administrator pages.

A.1 Registration pages

The registration pages allow the patient to enter information to the database that seldom changes. This sequence of pages can only be viewed once by the patient. This occurs when they begin the study and are introduced to the website. The pages are viewed in the order that they are listed here.
Experimental System for Diabetes Patient Support

Please log in:  username: password: log in  Clear

Figure A.1: The Login Page.
Greetings!

Please enter the following basic information:
- Date of Birth (mm/dd/yyyy):
- Gender (m/f):
- Height (in inches):
- Age when diagnosed (in years):
- Date pump start (mm/dd/yyyy):
- Date you last checked your weight (mm/dd/yyyy):
- Weight:

Please enter the following occupational information:
- Job Start Date (mm/dd/yyyy):
- Physical intensity of the job (1-10):
- Job Title:

Who is your doctor?:

Submit
Clear

Log Out

Figure A.2: The Greetings Page.
Figure A.3: The Second Registration Page.
Figure A.4: The Complications Page.
Experimental System for Diabetes Patient Support

Relatives

Please enter the information regarding diabetic relatives:
This persons relation to you is:
Their diabetes type (1 or 2):
The age they were at onset of diabetes:
Which side of the family:

Their complications:

- Add Relative
- Submit
- Clear

Log Out

Figure A.5: The Relatives with Diabetes Page.
Experimental System for Diabetes Patient Support

Chronic Illnesses

Please enter the information regarding Chronic Disorders:
Type of disorder: __________________________

Add Illness  To add another Chronic Illness
Submit  To move onto the next Page
Clear

Log Out

Figure A.6: The Chronic Illnesses Page.
Experimental System for Diabetes Patient Support

Medications
Please enter the information regarding Medications:
Name of the Medication:
Dose (number only):
Units (for above dosage number):

Add Medication
Submit
Clear

Figure A.7: The Medications Page.
Figure A.8: The Basal Rates Page.
Experimental System for Diabetes Patient Support

Daily Schedule

Please enter the information regarding your daily schedule:

- The date this became your typical day (mm/dd/yyyy)
- Time you normally wake up (hh:mm AM/PM)
- Time you normally go to bed (hh:mm AM/PM)
- Time you normally eat breakfast (hh:mm AM)
- Time you normally eat lunch (hh:mm AM)
- Time you normally eat dinner (hh:mm AM)
- Time you normally go to work (hh:mm AM)
- Time you normally return from work (hh:mm PM)
- Time you normally exercise (hh:mm PM)
- Time you normally take a nap (hh:mm PM)
- Time you normally wake up (hh:mm PM)
- What time do you have your snack #1 (hh:mm PM)
- What time do you have your snack #2 (hh:mm PM)
- What time do you have your snack #3 (hh:mm PM)
- What time do you have your snack #4 (hh:mm PM)
- Please choose which days that this reflects your schedule.
  - Monday
  - Tuesday
  - Wednesday
  - Thursday
  - Friday
  - Saturday
  - Sunday

Submit
Clear
Log Out

Figure A.9: The Daily Schedule Page.
A.2 Non-Registration pages

This set of pages contains information that may be entered daily. These pages are arranged by the order that they occur in the menu on the left hand side of each page. Some pages may be listed on the menu, while others are only available after entering information on a previous page.
Welcome to the Experimental System for Diabetes Patient Support Home Page. Using this website, you will be able to input information into a database. The "links" on the left hand side of the webpage will allow you to move through the website, entering only the data that needs to be inserted.

**Home** - Will bring you directly back to the page that you are currently visiting.

**Daily** - This page consists of information regarding your daily exercise, work, and sleep habits. This page should be visited daily.

**Meals** - This page allows you to enter information about each of the meals or snacks that you have eaten throughout the day. This page should be visited daily.

**Measurements** - This page allows you to enter information about your daily fingersticks, basal, and bolus information. This page should be visited daily.

**Infusion Set** - This page allows you to enter information about the last time you changed your infusion set.

**Hypo Events** - This page allows you to enter data about any hypoglycemic events that have happened.

**Other Events** - This page allows you to enter information about stressful events, illnesses, pump failures, and other events that may happen.

**Daily Log** - This page allows you to get a new Daily Log book.

Figure A.10: The Home Page.
Experimental System for Diabetes Patient Support

Daily Schedule

Please enter the information regarding your Exercise:
- The time you started working out (h:mmPM):
- Duration of your workout (number of minutes):
- Intensity of the workout (1-10):
- Type of workout:

Please enter the following information about your work day:
- The time you went to work (h:mmAM):
- The time you came home from work (h:mmPM):
- Intensity of your work day (1-10):

What time did you wake up (h:mmAM):
What time did you (or will you) go to bed (h:mmPM):

If you took a nap, please enter the following information:
- The time you began your nap (h:mmAM):
- The time you ended your nap (h:mmAM):

Submit
Clear
Log Out

Figure A.11: The Daily Exercise, Work, and Sleep Page.
Experiment System for Diabetes Patient Support

**Meals**

Please choose which day to enter information for:

Please enter the information regarding Meals:

The time of the meal (hh:mm PM):

Which meal:

Estimated Carbs (number only):  

Submit  
Clear 

Log Out  

Figure A.12: The Meals Page.
Foods for meal

Please enter the following information regarding the food you ate for the meal:

Name of food:

Amount of food:

Amount in units:

Add Food  To add another food
Done  To enter your food and return to the Meals Page
Clear

Log Out

Figure A.13: The Foods Page.
Choose a type of measurement below. You will be directed to the data entry page for that type of measurement.

Fingerstick Measurements
Temporary Basal Measurements
Bolus Measurements

Figure A.14: The Measurements Page.
### Experimental System for Diabetes Patient Support

#### Fingerstick Measurements

Please choose which day to enter information for:

Please enter the information regarding your finger sticks:

- **The time of the fingerstick (hh:mm:PM):**

- **Fingerstick measurement:**

  - [Add Fingerstick](#) To add another Fingerstick measurement
  - [Done](#) To enter your Fingerstick measurement and return to the Measurements Page
  - [Clear](#)

---

**Figure A.15:** The Fingerstick Measurements Page.
Figure A.16: The Temporary Basal Rates Page.
Figure A.17: The Bolus Measurements Page.
Figure A.18: The Infusion Set Page.
Hypoglycemic Episode

Please enter the information regarding a hypoglycemic event:

- The time of this event (hh:mmPM):
- The time you corrected the hypoglycemia (hh:mmPM):
- The action you took to correct the hypoglycemia:
- Symptoms you had:

If you took a fingerstick measurement during the event, please enter the following:

- The time you took the measurement (hh:mmPM):
- Fingerstick measurement:

If you took a fingerstick measurement after your hypoglycemic episode, please enter the following:

- The time of the fingerstick (hh:mmPM):
- Fingerstick measurement:

Submit
Clear
Log Out

Figure A.19: The Hypoglycemic Episode Page.
Other Events

Please enter data regarding any illnesses:
- Date you fell ill (mm/dd/yyyy): [Field]
- If you have recovered, enter your recovery date (mm/dd/yyyy): [Field]
- Type of illness: [Field] (e.g., Cold, Flu)
- Illness Symptoms: [Field] (separate by commas)

Please enter the information regarding Stressful Events:
- The time and date of the stressful event (hh:mm PM): [Field]
- The type of stressful event: [Field] (Please Choose One)
- Description of the event: [Field]

Please enter data regarding any pump failures:
- Time and date the pump failed (hh:mm PM): [Field]
- Description of how the pump failed: [Field]
- Time and date the pump started working again (hh:mm PM): [Field]

If there were any other miscellaneous events that you think we should be aware of but that have not been covered above, please record the time and description:
- Time and date of the event (hh:mm PM): [Field]
- Please check here to email this description directly to your doctor.

Description of the event:

Submit
Clear
Log Out

Figure A.20: The Other Events Page.
Experimental System for Diabetes Patient Support

**Daily Log**

If you need to print a new Daily log book, select the following link

Daily Log Book

Log Out

Figure A.21: The Daily Log Page.
A.3 Administrator pages

These pages are only available to the administrator of the website. They are listed based on their order on the website’s menu, which is only viewable to the administrator.
Intervention

Please enter the information regarding Interventions (changes requested by Dr. Schwartz):

Date of Intervention (mm/dd/yyyy):
Trend Type:
Intervention Type:
Reason:
Outcome:
Description:

Submit
Clear

Figure A.22: The Administrators Intervention Page.
Change User Password

Please enter the information to change a patient's password:

Patient id:
Old Password
New Password
Confirm Password

Submit
Clear

Log Out

Figure A.23: The Administrators Change Password Page.
Figure A.24: The Administrators Add Patient Page.
Appendix B

Artificial Intelligence Scenarios

This is a handout from Dr. Frank Schwartz to our group at the beginning of our project. It highlights particular scenarios and what their causes are most likely to be. Our Artificial Intelligence in the project should be able to spot these problems and give advice on how to treat them when the project is completed.

1. **Dawn Phenomena**: Early morning rise in insulin requirements due to the release of counter-regulatory hormones such as; growth hormone, cortisol, epinephrine, and glucagon. Requires increase in basal insulin from early AM on.

2. **Somogyi Phenomena**: Rebound AM hyperglycemia due to nocturnal hypoglycemia and release of same counter-regulatory hormones. Requires a bedtime snack and a decrease in PM basal insulin from bedtime until at least 3:00 AM.

3. **Causes of AM Hypoglycemia**: Too much basal insulin, inadequate snack at bedtime, prolonged effects of exercise the night before, loss of the counter-regulatory hormones over time (glucagon) or autonomic neuropathy (epinephrine).

4. **Causes of AM Hyperglycemia**: Inadequate basal insulin, Dawn and Somogyi Phenomena, Sleep Apnea, Stress, and Depression

5. **Causes of Pre-Meal Hyperglycemia**: Inadequate basal insulin, asymptomatic hypoglycemia with rebound, high fat meal with delayed gastric emptying or
absorption, effects of exercise in face of inadequate insulin (muscle cannot utilize glucose due to lack of insulin and signals liver to produce more glucose).

6. Causes of Post-Meal Hyperglycemia: Failure to bolus prior to meal, inadequate bolus/inaccurate carbohydrate counting, effect of different food components (fat, protein, and carbohydrates) on glucose absorption, use of single wave bolus when square or dual wave would work better.

7. Causes of Post-Meal Hypoglycemia: Too much bolus, over estimation of food intake, delayed gastric emptying (Gastroparesis), and increased physical activity after meal.

8. Causes of Pre-Meal Hypoglycemia: Increased physical activity with no change in basal rates.

9. Other Causes of Erratic Glucose Levels: Stress, erratic absorption of insulin from infusion site, loss of biological activity of insulin, empty syringe, catheter kinking or pulling out, depression.

10. Effect of Menstrual Cycle on Glucose Levels: During follicular phase, female hormones are low and little effects on glucose levels, as luteal phase occurs increasing doses of progesterone induce insulin resistance and insulin requirements, during menses female hormones are at their lowest and insulin requirements are at their lowest unless there are painful menses (dysmenorrheal), which can elevate glucose levels.
11. **Effects of Stress on Glucose Levels**: Usually increases glucose levels due to increases in stress hormones. Some individuals will paradoxically go low with stress.

12. **Effects of Exercise on Glucose Levels**: Increase glucose utilization increases glucose demand and usually lowers glucose immediately and depending on intensity/duration, the effect can last up to 18 hours. If patient has inadequate insulin on board, glucose cannot be taken up in muscle and utilized, the liver produces more glucose and fat produces ketones.
Appendix C

Patient Informed Consent Form

Ohio University Adult Informed Consent Form

Title of Research: Intelligent Decision Support for Type I Diabetics on Insulin Pump Therapy

Principal Investigators:
Frank L. Schwartz, MD, FACE, Specialty Medicine, Ohio University College of Osteopathic Medicine
Cynthia Marling, PhD, School of Electrical Engineering and Computer Science, Russ College of Engineering and Technology

Federal and university regulations require signed consent for participation in research involving human subjects. After reading the statements below, please indicate your consent by signing this form.

Introduction to Informed Consent

You are being asked to participate in a project to develop artificial intelligence software to assist in the daily management of your diabetes mellitus. Similar to the Bolus Wizard on the Medtronic MiniMed insulin pump, we are trying to develop a Therapy Adjustment Wizard which will automatically analyze the glucose monitoring data downloaded from your meter, learn how you respond to insulin dosage adjustments made by Dr. Schwartz in response to different situations, and then learn to suggest changes in your insulin doses.

For you to be able to decide whether you want to participate in this program, you should understand what the program is about, as well as the possible risks and benefits in order to make an informed decision. This process is known as informed consent. This consent form describes the purpose, procedures, possible benefits and risks of the program. This form will also explain how your personal information will be used and protected. Once you have read this form, and your questions about the program answered, you will be asked to sign this form. This will allow your medical information to be collected and used as described below for medical research.

You do not have to participate in this research project. If you do not want to sign this form, your decision will have no effect on your medical care at this institution regardless of your decision to participate or not. Read this information carefully and if you have any questions please ask the doctor.

Explanation of Study

This is a feasibility study to see if it is possible to develop computer software which will be capable of analyzing glucose patterns throughout the day from the data downloads from your monitor or Continuous Glucose Measuring Sensor (CGMS), learn from past experiences with your adjustments, and then generate advice on what adjustments to make in your insulin dosage each time you access the software. This approach will use "artificial intelligence" technologies to analyze glucose patterns throughout the day and hopefully result in a new tool which could potentially aid you in your day to day glucose control. We are seeking approval to use your personal glucose monitoring records, data
from three Continuous Glucose Monitoring System (CGMS) with the Medtronic MiniMed Glucose Sensor, and your event diaries which contain other critical information about the impact of stress, physical activity, and food eaten on your glucose levels to develop the software. Your participation in this project will help us develop a program that eventually helps persons with diabetes mellitus automatically adjust their basal or bolus insulin doses based on the pattern analysis of your glucose monitoring data points.

**Procedures to be followed**

Persons who agree to participate will be asked to monitor their glucose levels 6-10 times per day and record them in a glucose monitor with data management software. You will also be asked to wear the CGMS for three days on three separate occasions to obtain additional information for the programmers so that they can develop the computer program. The CGMS will provide glucose points every 5 minutes for the three days that you wear the Sensor in addition to your normal testing. The CGMS will be worn at the beginning of the study, after two weeks and at six weeks which is the end of the study. We will ask you to send us your meter downloads either via the internet or bring your meter in and download it directly in the clinic every 7-10 days for the 8 weeks of the study. *(You may always contact the OUCOM Clinical Research Unit (740-593-2410) or the Answering Service (740-594-2416) if your blood sugars are out of control and you feel you need to contact the doctor sooner than the protocol asks for).*

We will also ask that you really keep accurate food and activity diaries to help the programmer learn how various life events affect your glucose levels. Computer engineers from the Ohio University Russ College of Engineering and Technology will attempt to develop programs which analyze your glucose records and suggest insulin adjustments. If the preliminary study is successful, we may ask you to participate in an extension of this study testing its accuracy and reliability. Fingerstick HGB-A1C levels will be obtained at the start of the project and then at three and six months afterward to see if this intervention has any long term benefits on your glucose control.

**Duration of your participation in the program**

The feasibility portion of this study will be 8-10 weeks in length. You may be asked to participate in a future, longer interval study if the software is successful in learning to help you to adjust your pump insulin infusion rates.

**Risks and Discomforts**

There are no significant risks associated with participation in this program other than the potential release of personal medical information to non-medical personnel (the programmers). Your personal medical information will be maintained in a manner which assures patient confidentiality and meets all HIPAA and other regulatory requirements. Each patient will be asked individually for permission to participate in the program and all personal identifiers will be eliminated prior to release of the glucose data points and other clinical information to the computer engineers.
Benefits

As you know, Diabetes is associated with many acute and chronic complications which are directly related to overall glucose control. Intensive glucose control, and insulin pump therapy in particular has been shown to significantly reduce the risk of these complications. This project is trying to determine if software based on artificial intelligence can potentially improve control of a person's diabetes by providing automatic advice for insulin adjustments directly to the individual patient by continuously assessing patterns of self-glucose monitoring and suggesting insulin adjustments.

Alternative Treatments

Again, you do not have to take part in this research. Your decision not to participate will have no effect on your medical care at this institution. If you do agree, you can be reassured that any research done must be approved by an Institutional Review Board (IRB) before it can be performed.

Confidentiality and Authorization to Collect and Use Your Medical Records For Biomedical Research

All medical records are kept in strict confidentiality according to HIPAA regulations (See clinic brochure on HIPAA Regulations). The clinical information compiled by in the UMA Diabetes/Endocrine Center is encrypted (personal identification blocked) and no personally identifiable information will be released to the engineers or any outside agency from this program, other than the Department of Health and Human Services and other governmental agencies which oversee this center. If you sign this form, you allow the Ohio University College of Osteopathic to collect and use your data for the purposes stated above.

Compensation

There is no direct compensation for the participation in this research project. You will be provided a new glucose meter with data management software if you do not already have one.

Contact Information

If you have any questions regarding this study, please contact
Frank L Schwartz, MD FACE or Cammie Starner RN, CCRC
Ohio University College of Osteopathic Medicine
102 Parks Hall, Athens, OH 45701
740-593-2410

If you have any questions regarding your rights as a research participant, please contact
Jo Ellen Sherow, Director of Research Compliance
Ohio University, 117 RTEC, Athens, OH 45701
740-593-0664
I certify that I have read and understand this consent form and agree to participate as a subject in the research described. I agree that the known risks to me have been explained to my satisfaction and I understand that no compensation is available from Ohio University and its employees for any injury resulting from my participation in this research. I certify that I am 18 years of age or older. My participation in this research is given voluntarily. I understand that I may discontinue participation at any time without penalty or loss of any benefits to which I may otherwise be entitled.

I certify that I have been given a copy of this consent form to take with me.

1) I agree to participate in this study. I will allow my glucose records to be released to the computer engineers involved in the development of this software and to wear the CGMS three times and send in my glucose records and personal diet and activity diary to the Center every 8-10 days throughout the project.

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Signature	 Date

Printed Name

Witness Signature	 Date

Printed Name
Appendix D

Preliminary Study Protocol

Timeline
<table>
<thead>
<tr>
<th>Time Line for Artificial Intelligence Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB # <strong>05X002</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Activity</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5</th>
<th>Week 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consent</td>
<td>First Day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Research Nurse Inserts Sensor</td>
<td>First Day</td>
<td>x</td>
<td></td>
<td></td>
<td>3 Days Before Final Visit</td>
<td></td>
</tr>
<tr>
<td>Initial HbA1c (for patients not tested within past 6 weeks)</td>
<td>First Day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Computer Engineer Collects Initial Data from Patient</td>
<td>First Day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Computer Engineer Shows Patient How to Enter Data</td>
<td>First Day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Returns CGMS Sensor and May Ask Nurse to Remove It</td>
<td>3 Days After Insertion</td>
<td>3 Days After Insertion</td>
<td>3 Days After Insertion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Downloads Pump Data (every four to five days, as usual)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Patient Returns Paper Daily Log Sheets</td>
<td>At Time of Sensor Insertion</td>
<td></td>
<td>At Beginning of Week</td>
<td>At End of Week</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Enters Daily Log Data into System (at least every three days, more often if possible)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Computer Engineers &amp; Dr. Schwartz Meet Wednesdays at 8:00 AM</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Final HbA1c</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>At End of Week</td>
</tr>
</tbody>
</table>

Figure D.1: The Study’s Protocol Timeline.
APPENDIX E

Intelligent Decision Support

Survey
Intelligent Decision Support Study Exit Survey

Thank you very much for participating in our study, “Intelligent Decision Support for Type I Diabetics on Insulin Pump Therapy.” We appreciate your valuable assistance. To complete your participation in the study, please answer the following questions as honestly as possible. Your candid feedback will help us to design the best possible intelligent decision support tools. To answer the first ten questions, simply circle the best choice for each question or statement. The last question asks you to write a short answer. Again, thank you for your help!

1. At the beginning of this study, I would characterize my overall blood glucose levels as:
   a) very well controlled
   b) fairly well controlled
   c) not well controlled

2. During the course of this study, my blood glucose control:
   a) improved a lot
   b) improved somewhat
   c) stayed the same
   d) got worse

3. Do you feel that the increased contact with health care providers during this study was beneficial in managing your blood glucose levels?
   a) yes
   b) no

4. Do you feel that immediate feedback with advice concerning your blood glucose levels by an automated system would be beneficial in managing your diabetes?
   a) very beneficial
   b) fairly beneficial
   c) not very beneficial
   d) confusing and intrusive

5. Approximately how many minutes each day did it take you to use the internet based computer data entry system?
   a) 60 minutes
   b) 30 minutes
   c) 15 minutes
   d) less than 15 minutes
6. The internet computer data entry system was:
   a) very easy to use
   b) fairly easy to use
   c) fairly difficult to use
   d) very difficult to use

7. In what format would you prefer to use a computerized therapy adjustment wizard?
   a) a web browser on a desktop or laptop computer
   b) a small handheld computer (Palm) or BlackBerry
   c) included on my meter
   d) included on my pump

8. How likely are you to adopt a therapy adjustment recommended by your doctor?
   a) very likely
   b) somewhat likely
   c) not very likely

9. If a computerized therapy adjustment wizard were to recommend a therapy adjustment, how likely would you be to adopt it?
   a) very likely
   b) somewhat likely
   c) not very likely

10. Would you be willing to wear a continuous glucose sensor at all times if the technology is released soon?
    a) yes
    b) no

11. What other factors contribute to your blood glucose going high or low that we haven't considered in our experimental computer system?