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CLINICAL DECISION SUPPORT SYSTEMS IN TYPE 2 DIABETES MELLITUS

A thesis submitted in partial fulfillment for the
degree of Master of Physics and Technological Applications

by

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Declaration of Authorship

I, Saiti Kyriaki-Maria, declare that this thesis titled, 'CLINICAL DECISION SUPPORT SYSTEM IN TYPE 2 DIABETES MELLITUS' and the work presented in it are my own. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at the National Technical University of Athens in collaboration with CVUT v Praze.
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated.
- Where I have consulted the published work of others, this is always clearly attributed.
- Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work.
- I have acknowledged all main sources of help.
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself.

Signed: Kyriaki-Maria Saiti

Date: 07/07/2016

"There must be men clever than any given machine,but then again there might be other machines cleverer again, and so on."

Alan Turing (1912-1954)

Abstract

Why is so important to develop expert systems especially for diabetes mellitus and what are the characteristics of that disease? This disease afflict many people worldwide with rates steadily growing every year affecting the every lives of patients in many areas (e.g. socially , economically etc). This project describes the identity of diabetes mellitus,tested the data from patients and recognizes the effectiveness of the expert systems to confront with the requirements of that disease. Results from the processing of data (6 patients-two females and 4 males,between 27-47 years old) shows how important is to develop a system supporting patients in cooperation with experts to strengthen them take the optimum decisions.There are also some issues that arise from the data mining and the first one is about the quality of data.The need for information is so important as the quality of it in order to be able to make the right decision. ...

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Abbreviations

DM	**D**iabetes **M**ellitus
T1DM	**T**ype **1** **D**iabetes **M**ellitus
T2DM	**T**ype **2** **D**iabetes **M**ellitus
MODY	**M**aturity **O**nset **D**iabetes of the **Y**oung people
LADA	**L**atent **A**utoimnune **D**iabetes in **A**dults
BG	**B**lood **G**lucose
BL	**B**lood glucose **L**evels
GC	**G**lycemic **C**ontrol
HBA1c	**G**lycated **H**emoglobin
SI	**S**ysteme **I**nternational
DCCT	**D**iabetes **C**ontrol and **C**omplications **T**rial
IFCC	**I**nternational **F**ederation of **C**linical **C**hemistry
SMBG	**S**elf **M**onitoring of **B**lood **G**lucose
BMI	**B**ody **M**ass **I**ndex
BMR	**B**asal **M**etabolic **R**ate
TDEE	**T**otal **D**aily **E**nergy **E**xpenditure
EER	**E**nergy **E**stimated **R**equirement
GI	**G**lycemic **I**ntex
GL	**G**lycemic **L**oad
KB	**K**nowledge **B**ase
WEKA	**W**aikato **E**nvironment for **K**nowledge **A**nalysis

To my parents for supporting me every time...

Chapter 1

Introduction

Diabetes mellitus is a disease afflicting many people worldwide for many years. Polyuric diseases have been described for over 3500 years.The name "diabetes" comes from the Greek word for a syphon;the sweet taste of diabetic urine was recognized at the beginning of the first millennium , but the adjective "mellitus" (honeyed) was only added by Rollo in the late 18th century. [1]

The sugar in diabetes urine was identified as glucose by Chevreul in 1815.In the 1840s, Bernard showed that glucose was normally present in blood, and showed that it was in the liver (as glycogen) for secretion into the bloodstream during fasting. In 1889 , Minkowski and von Mering reported that pancreatectomy caused severe diabetes in the dog. In 1893, Laguesse suggested that the pancreatic "islets" described by Langerhans in 1869 produced an internal secretion that regulated glucose metabolism. Insulin was discovered in 1921 by Banting, Best, Macleod and Collip in acid-ethanol extracts of pancreas. It was first used for treatment in January 1922. [1]

Diabetes was subdivided on clinical grounds into diabete maigre (lean subjects) and diabete gras (obese) by Lancreraux in 1880, and during the 1930s by Falta and Himsworth into insulin-sensitive and insulin-insesitive types. These classifications were the forrunners of the etiological classification in type 1 and type 2 (non-insulin-dependent) diabetes. [1]

Physicians and biologists worldwide are trying to cope with the disease managing great progress.In recent years, the effort of these scientists have contributed and other scientists,such as mathematicians, physicists and programmers with a common goal of tackling the disease and support the patients.

Chapter 2

Diabetes Mellitus

Diabetes mellitus(DM) , commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar (glucose) levels over a prolonged period. People from all the academical communities use to give symbols to common diseases like DM in order to sensitizing more and more people all over the world. What is more, the purpose of the symbol is to give diabetes a common identity. It aims is to support all existing efforts ,raise awareness about diabetes ,inspire new activities and bring diabetes to the attention of the general public.

FIGURE 2.1: DM SYMBOL [2]

Diabetes has already affected more than 180 million people worldwide. This number is likely to reach 300 million by 2025. Diabetes is no longer restricted to developing or developed countries alone, but has become a global concern. The concern in the developing countries are much higher as the occurrence of diabetes at an early age can lead to untoward human suffering, disability and increased socioeconomic cost. Additionally while in developed countries most people with diabetes are above the age of retirement, in developing countries people aged between 35 and 64 years are those most frequently affected.Increased incidence in the younger age group during which the adults are most productive has obviously increased concerns in the developing countries like India which has incidentally been ranked as number one among the diabetes prevalent countries.Further, it has also been estimated that there will be a whopping 150% rise in diabetics in the developing countries.The concern is also growing among the developed countries as impaired glucose tolerance or the dysmetabolic syndrome, considered to represent pre-diabetic states, has been reported in about one-quarter of western populations. The cost of management of diabetic patients is reportedly more than twice as that of non-diabetic patients. This increased cost has been attributed to the high costs incurred while managing many of the diabetic complications. About 2-7% of the total national health care budgets of Western European countries are already being spent for diabetes and its related complications. Urbanization has been considered as one of the key factors globally that has lead to the increase in prevalence of diabetes. People living in cities (especially in developing countries) tend to be less physically active and are increasingly overweight or obese when compared to people in rural areas.[3]

2.1 Type 1 Diabetes Mellitus

The differentiation between the two main forms of diabetes mellitus - type 1 (previously known as insulin dependent or juvenile onset) and type 2 diabetes (non-insulin dependent or adult onset) - haw been possible for almost 50 years. Type 1 Diabetes Mellitus(T1DM) occurs when the immune system itself destroys the cells that produce insulin in the pancreas (beta-cells). Normally, the immune system fights the intruders such as viruses and bacteria. For unknown reasons the immune system attacks the body's cells. The result is an overall lack of the hormone insulin.[1]

Some people experience a form of diabetes which is called secondary diabetes, which resembles the type 1 diabetes, however, the beta cells are not destroyed by the immune system, but by some other factor, such as cystic fibrosis.

Typically, insulin is secreted by the pancreas in small quantities. When we eat a meal, sugar (glucose) from food mobilizes the pancreas to release insulin. The amount released is proportional to the amount required by the size of the meal.

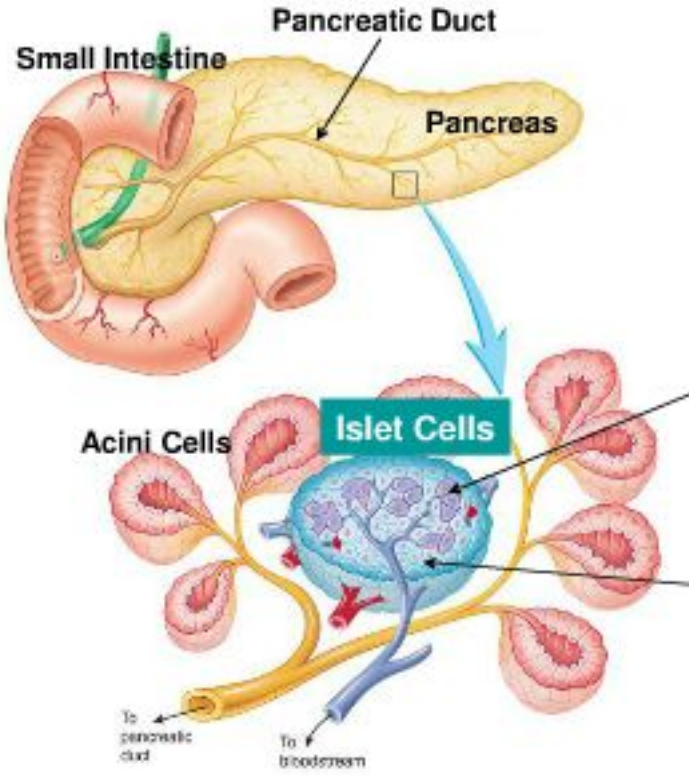


FIGURE 2.2: Insulin secretion

The main role of insulin is to transport nutrients -glucose primarily literary in the body's tissue cells. Cells use glucose and other nutrients from meals as an energy source to operate.

The amount of glucose in the blood decreases when entering the cells. Usually, it notifies the beta cells in the pancreas to reduce the amount of insulin secreted in order not to cause hypoglycemia. However, the destruction of beta-cells in the case of T1DM disrupts the whole process.

In patients with T1DM, glucose is not transferred to the cells, as there is no insulin available. When glucose builds up in the blood instead of being transferred to the cells of the body cells do not have the necessary nutrients so other body systems have to provide power in order to perform bodily functions. Accordingly, there is a large amount of glucose in the blood, which may cause:[1],[4]

1. **Dehydration**

In an effort to rid the body of unnecessary glucose, the result is frequent urination. When the kidneys lose glucose due to urination is lost while a large quantity of water, leading to dehydration.

2. **Weight loss**

   The loss of glucose in urine mean loss of calories provide energy. Thus, many people with diabetes lose weight. Dehydration also contribute to weight loss.

3. **Diabetic ketoacidosis**

   Without insulin, and its lack of cell energy, the body breaks down fat cells. Products of this degradation of fat are organic compounds called ketones, which are used for energy production. The levels of these substances are accumulated gradually in the blood, causing increased acidity. The liver continues to release the glucose during the process. As the body is unable to utilize the glucose without insulin, the level of glucose in the blood increases. The combination of high glucose content, dehydration and accumulated acids called ketoacidosis can be highly dangerous to health without immediate treatment.

4. **Damage to the human body**

   Over time, high levels of glucose in blood can cause damage to the nervous system and the tiny blood eye vessels, kidney and predispose an individual to atherosclerosis (hardening) of the arteries, which can lead to myocardial or stroke.

- Who is affected by T1DM?

  Although the disease usually occurs in people under 20 years, it is observed that type 1 diabetes can occur at any age. It is not very common disease, and the incidence of diabetes type 1 are only 5 % of patients with diabetes. It occurs more often in whites than blacks populations and equally affects men and women.

- What causes T1DM?

  Physicians do not know all the factors that cause type 1 diabetes are likely to develop the disease increase due to heredity. Physicians also say that one environmental factor plays a role in the disease. Type 1 diabetes probably occurs when something in the environment-a toxin or a virus- mistakenly activates the immune system to begin attacking the pancreas and destroys the beta cells to the point that they can no longer produce enough insulin. Signs of this disaster are autoantibodies, which are present in most patients with type 1 diabetes in fact, found in 85% to 90% of people with this type of diabetes, when blood glucose levels are high. As the disease is an autoimmune, can also be displayed along with other autoimmune diseases such as hyperthyroidism.

- What are the symptoms of T1DM?

  Symptoms of type 1 diabetes are often subtle but can be a significant problem. These include:

  1. Intense thirst
  2. Increased appetite
  3. Dryness in the mouth
  4. Nausea and occasionally vomiting
  5. Pain in the abdomen
  6. Frequent urination
  7. Unexplained weight loss
  8. Fatigue and weakness
  9. Blurred vision
  10. Heavy breathing
  11. Common skin infections, urinary or genital

  The worrying signs of an impending crisis are:

  - Shivering and confusion
  - Tachypnea
  - Unpleasant breath
  - Stomachache
  - Loss of consciousness (rare)

- Diagnosis of T1DM

  If there is suspicion of type 1 diabetes, first check for abnormalities in the blood (high blood glucose levels). At the same time, check if there are amounts of glucose or ketones in the urine. Currently, there is no way to prevent type 1 diabetes.

- How can patients deal with T1DM?

  Many diabetes' patients manage to live many years without major problems. The key to a good health is to maintain glucose at low levels, which can be achieved by proper diet, exercise and insulin treatment. All patients with type 1 diabetes must take insulin injections to control glucose levels in the blood.The levels of blood glucose should be checked regularly to make any necessary changes in insulin doses, diet and daily activities.

- What are the effects of T1DM?

  If the patient does not receive the necessary treatment can occur varied and dangerous problems such as:

  - Retinopathy

    This eye disease occurs in 80% of adults with type 1 diabetes for more than 15 years. The retinopathy in type 1 diabetes is extremely rare before puberty, regardless of the duration of the disease. The proper glucose control, the management of blood pressure and regulation of fat in the blood (eg cholesterol and triglycerides) are important factors to prevent retinopathy. Fortunately, vision loss can be prevented in most patients.

  - Damage to the kidneys

    About 20% to 30% of patients with type 1 diabetes show problems in the kidneys (nephropathy). The risk of retinopathy increases with the lapse of time and be increasing from 15 to 25 years after the initial presentation of the disease. The effect of renal disease can be kidney failure or heart disease.

  - Poor blood circulation and damage to the nervous system

    The damage to the nervous system and the hardening of the arteries leads to decreased sensation and poor circulation in the legs. This increases the chances of injury and reduces the body's ability to heal wounds, which in turn increases the risk of amputation. Also, damage to the nervous system can lead to problems in the digestive system, such as nausea, vomiting and diarrhea.

2.2 Type 2 Diabetes Mellitus

Type 2 Diabetes mellitus (T2DM) usually develops after the age of 40 years, but in recent years the age-ratios are coming down, mainly because its appearance is related to lifestyle. It involves 80-90% of diabetes cases. In this form of diabetes, the pancreas still produces insulin, but not enough and the body is unable to use it effectively. Specifically, people with type 2 diabetes have insulin resistance, a condition that forces the body to produce more and more insulin to overcome this resistance. This, however, results after several years (5-25, depending on the case) to running the pancreas does not produce another. So sometime and type 2 diabetics to enter and those in insulin. Of course, here we should note that the more correct one manage his condition, namely watches his diet, not thoughtlessly spends insulin, is exercised, maintains his weight at normal levels and regulate blood sugar with anti diabetic drugs, the more take long to get into

insulin. According to the World Health Organization 171 million people or else 2.8% of the world population has Diabetes and estimated that by 2030 this figure will have almost doubled.[1],[4]

- What causes T2DM?

  Although type 2 diabetes is more common than type 1, the causes are not fully specified. Probably caused by many factors, not a single event. We know so far that:

  - TheT2DM occurs in relatives in the family, but the exact way it is inherited and the identity of the gene is not known.
  - People with type 2 diabetes exhibit resistance to insulin action and relative deficiency of the secretion from the pancreas. These changes may have been present for several years before the onset of clinical diabetes. Progressively insulin secretion by the pancreas is reduced resulting in high blood sugar.

- What are the symptoms?

  Symptoms vary from patient to patient but the main ones are:

  1. Increased thirst
  2. Increased appetite
  3. Dry mouth
  4. Nausea and vomiting
  5. Polyuria
  6. Tiredness, exhaustion
  7. Vision problems
  8. Numbness or tingling in hands and feet
  9. Frequent inflammation of the skin, urinary tract and vagina
  10. Rare type 2 diabetes can be diagnosed after a transfer to the hospital in a coma

- T2DM diagnosis

  Physicians first measure the blood glucose levels and then the presence of the ketone bodies in urine. It also suspects that you may have diabetes from high cholesterol and especially triglycerides in the blood. Sometimes, DMT2 discovered accidentally by a routine in the bottom of the eye which may be the characteristic lesions of diabetes.

- T2DM treatment

  Many diabetes' patient live a long life and good health. The goal is to maintain blood sugar in good levels achieved by proper diet exercise and drug therapy with insulin pills. It also needs the frequent measurement of blood sugar.

- What are the complications?

  If diabetes is not properly adjusted can occur complications that are dangerous even for life. The main ones are:

  1. Retinopathy

     The damage to the retina of the eye are common in type 2 diabetes (hemorrhages, exudates) and become more common with the passage of time. Their appearance is prevented by delaying the good setting not only sugar and blood pressure and cholesterol. Fortunately blindness is uncommon complication

  2. Damage to the kidneys

     The risk of kidney damage increases with time. This complication is serious because it can lead to kidney failure and heart diseases.

  3. Reduced sensation and poor circulation

     Damage to nerves and hardening of the arteries leads to decreased sensation and poor circulation in the legs. This can lead to an increase in skin inflammations and ulcers that do not heal easily. Poor circulation can even lead to amputation. The nerve damage can also cause digestive disorders such as nausea, vomiting and diarrhea.

There are some similarities that are remarkable and under further consideration such as the maturity - onset diabetes of the young (MODY) , latent autoimmune diabetes in adult (LADA) and genetic variants affecting the insulin, amylin and mitochondrial pathways. Until recently, autoimmune T1DM was considered to be the predominant form of diabetes in children and young adults . Although recent studies have shown the possibility of an existing overlap between two types of DM. That factor necessitate, [1]

- detailed medical history-taking(e.g. family history of diabetes, mode of presentation and exposure to infection)
- complex physical examination (e.g. body leanness, microvascular complications , metabolic syndrome and associated cardiovascular complications)
- use of appropriate laboratory testing (e.g. autoantibodies against pancreatic antigens and genetic markers)

in order to allow physicians to refine the diagnosis and guide the treatment for the patients.

2.3 Glycemic control

"The overall goal of diabetes management is to achieve as near as normal physiological or ideal values as possible, without detriment to quality of life and, for glucose control in particular, without causing significant hypoglycemia." [5]

Diabetes is a disorder of glucose homeostasis . It currently affects 285 million of people worldwide and is expected to affect 435 million by 2039.For people without diabetes,glucose levels are maintained in the range of 4-6 mmol/L (80-110 mg/dL). When blood glucose levels increase as a result of glycogen conversion or eating carbohydrate - containing food, insulin is released restoring homeostasis through hepatic conversion of glucose to glycogen , and uptake of glucose to muscle and fat cells. Conversely, if blood glucose levels fall too low as a result of exercise or lack of food , glucagon is released causing hepatic conversion of glycogen to glucose.

People with T1DM lack the normal homeostatic mechanism to control levels of blood glucose, while people with type 2 diabetes mellitus (T2DM) have an impaired or absent response. In addition to insulin, which is the most important of the regulatory mechanisms, growth hormone, thyroxine and catecholamines are also important counter-regulatory hormones and lead to increases in BG levels. The aim of monitoring GC is to diagnose the nature of any impairment of homeostatic mechanisms, allow patients to understand the nature of their disorder , determine optimum times for initiating therapeutic intervention; and guide the day-to-day adjustment of management regimens.

Glycated hemoglobin (HBA1c) and BG are the two most frequently used measures of glycemia in current practice. Glycated hemoglobin provides information about overall control of glucose levels in the previous 6-8 weeks allowing assessment of the need for therapy and therapeutic response with minimal within-person variation in measurement. BG concentrations provide information about the day-to-day level of control, variation in control and response to therapeutic intervention. Measurement and interpretation of BG , however , may be difficult because of potentially wide within-person variations in measures other than when fasting. Prospective observational and intervention studies have shown that HBA1c levels are related to long-term disease outcomes .

Both BG levels and HBA1c therefore, along with a number of other tests , including measurement of urinary glucose for those who do not intend to aim for intensive GC,remain

an option for helping to identify poor glycemic control and to facilitate the adjustment of therapy to achieve optimal glucose controls. [5]

Nowadays, scientists continue to recommend that the diagnosis of diabetes is based on at least two laboratory measurements of BG $\geq$ 7mmol/L or random samples of $\geq$11.1 mmol/L. BG was traditionally given as whole blood values , but now we can measure only plasma GL in most laboratories. BG levels are expressed in SI unit as millimoles/liter (mmol/L) . The traditional unit for measuring BG is milligrams/decilitre (mg/dL) . To convert mmol/L to mg/dL , multiply by 18.

TABLE 2.1: Values for diagnosis of diabetes mellitus [1]

Time of measurement	**Glucose concetration (mmol/L)**$*$	
	Plasma	Whole blood
	Venous/Capillary	Venous/Capillary
fasting	$\geq$ 7.0 /$\geq$ 7.0	$\geq$ 6.1 /$\geq$ 6.1
2h after a glucose load	$\geq$ 11.1 /$\geq$ 12.2	$\geq$ 10.0 /$\geq$ 11.1

$*$ 1mmol/L=18mg/dL

TABLE 2.2: Correlation of HBA1c with average glucose [1]

HBA1c %	**Mean plasma glucose**	
	mg/dL	mmol/L
6	126	7.0
7	154	8.6
8	183	10.2
9	212	11.8
10	240	13.4
11	269	14.9
12	298	16.5

Glycated hemoglobin measurement is recommended to assess the maintenance of glycemic control and should be measured with high precision methods. Results should be presented in IFCC units (mmol/mmol) or eAG (mmol/L or mg/dL) alongside the DCCT aligned (%) units. As it is recommended , HBA1c measurements should be performed at least twice a year in patients meeting treatment targets and with stable glycemic control. An interval of 3 months between tests is usually preferred after changes in

therapy when levels are unstable, although a test after 2 months may add some more information. Self - monitoring of BG (SMBG) is a standard of care for patients with T1DM and absolutely necessary for them with T2DM. [1]

- Insulin

  Insulin is a potent anabolic hormone vital for life , it has a circulating of 15-20 mU/L in the fasting state and 60-80 mU/L post-prandially. Multiple-dose insulin therapy is the best way to reproducing the physiologic insulin profile in patients with lack of insulin secretion such as those with type 1 diabetes. The suggested way consist of a long-anting insulin preparation administered once or twice a day to meet the basal insulin requirements , with the injection of a short-acting insulin preparation with each meal. A number of different insulin injection regimens are available for patients with type 2 diabetes who may already be treated with non-insulin-based therapies. These include a once daily injection of a long - acting insulin, a once daily injection of a long-acting insulin with an injection of a shot-acting insulin with the main meal , twice a day injections of short mixtures , and multiple dose injections.

Table 2.3: Overview of insulin types [6]

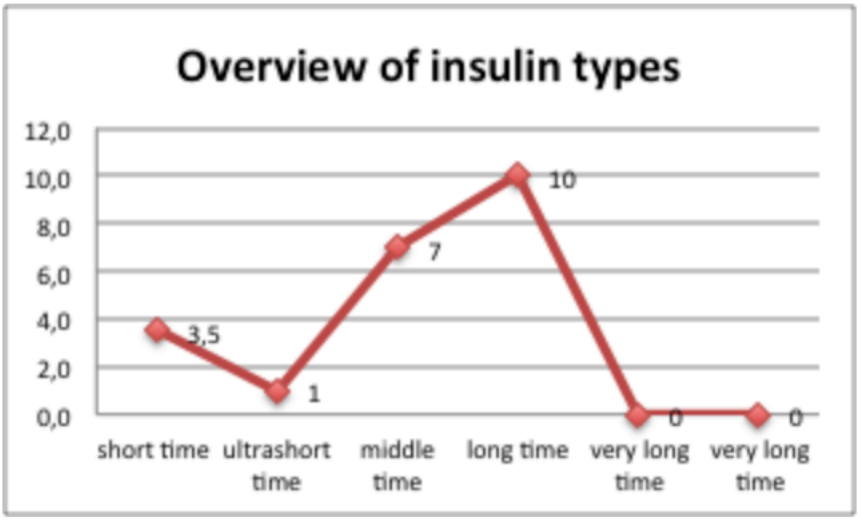
Onset the action	**Time of max. affection**	**Whole duration of action**
0,5-1h	2-5h	5-8h / short-time insulin types
5-15min	1h	3-5h / ultrashort-time insulin types
1-3h	6-8h	12-20h / middle-time insulin types
2-4h	8-12h	18-28h / long-time insulin types
1-2h	no pick point	24h / very long-time insulin types
1-1,5h	no pick point	24h / very long-time insulin types

- What is the most suitable insulin regimen ?

  Patients with T1DM and T2DM try a variety of treatment insulin regimens during their lives. There are many factors that affect on the decision for what is the best regimen and the most suitable in any case.

  – Selecting an insulin program for T1DM [1]

    For people with type 1 diabetes, is there really anything more personal and significant in your life than your insulin program; additionally, it is a fact that your insulin program defines your lifestyle. It can either dictate your meal, sleep, and activity schedules, or it can set you up for successful control of your diabetes. Unfortunately, most people are given little choice,education or knowledge on how to select the insulin program that best meets their needs. As a matter of fact, many people probably put more thought and effort into



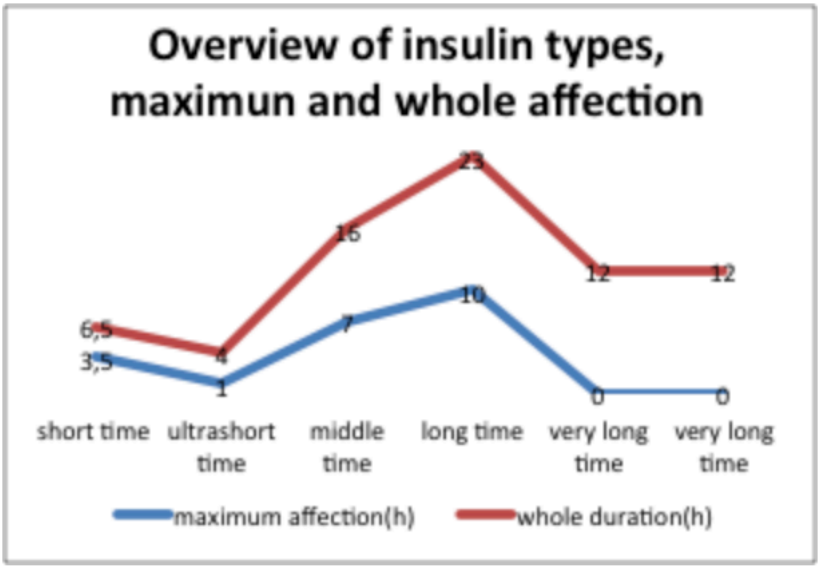


FIGURE 2.3: Insulin types and maximum affection(1),Insulin types,maximum and whole affection(2)

choosing −clothes or a car − perhaps because they have a better idea of what they are looking for.

All patients,except those that have been fortunate in such a way to become insulin independent following a pancreas or islet cell transplant, will require exogenous insulin to provide 24h background and meal time coverage. For many this is provided by the basal bolus regimen. Every insulin program for people with type 1 diabetes should include a basal, or background insulin. Basal insulin is necessary to cover the liver's secretion of glucose throughout the day and night, which provides the cells with a continuous supply of glucose to burn for energy. Insufficient basal insulin at any time will result in a sharp rise in blood glucose level and can also lead to the buildup of ketones, acidic

by-products of fat-burning that can accumulate in large amounts if no glucose is being burned simultaneously. If they do not care about high blood BG and ketones are not treated promptly, a life-threatening condition called diabetic ketoacidosis can develop.

Each patient′s basal insulin requirements are unique, but generally it is noticed that they are higher during the early morning and lower in the middle of the day. Basal insulin coverage can be supplied by a variety of insulins. Intermediate-acting insulin (NPH) is typically taken once or twice daily. NPH begins working within 1-3 hours (NPH belongs to middle time insulin types, as we can notice in table 2.3), provides peak coverage about 4-8 hours after injection, and tapers off about $12-24$ hours after the injection. The long-acting basal insulin analogs glargine (brand name Lantus) and detemir (brand name Levemir) offer relatively peakless background insulin for approximately 24 hours(belongs in the last group of long-time insulin types); They are usually injected once a day. Insulin pumps deliver rapid-acting insulin in small pulses every few minutes for basal coverage;this output can be adjusted and fine-tuned to match the body′s fluctuating basal insulin needs.

In addition to basal insulin, mealtime insulin boluses are needed to cover the rapid blood sugar rise that occurs after eating.After many researches they found that carbohydrates usually takes about $10-15$ minutes to begin raising your blood sugar level, with a high point occurring about $30-90$ minutes after eating (average time is 60 minutes after meals), depending on the portion size and composition of the meal. Ideally, mealtime insulin doses should be timed so that the insulin′s peak activity occurs simultaneously with the peak BG rise after the meal.

Each insulin has its share of pluses and minuses, and choosing the right combination of basal and bolus insulins is not a simple decision and needs time and probably many tests before doctors and patients and realize which the most suitable for them.

– Selecting an insulin program for T2DM

It is known that in many cases , patients with type 2 diabetes can follow the same insulin treatments with T1DM patients but in other cases , insulin initiation and intensification is a more gradual process. Most insulin$-$dependent patients with T2DM usually use a long-acting basal analogs as an add$-$on to existing oral therapy and show low rates of hypoglycemia compared to those you use NHP insulin (middle time insulin types). As a result, now physicians recommend patients to use long lasting insulin boluses and many health care professionals achieved satisfactory glycemic targets with this regimen.

- Starting insulin for the first time - Useful steps, [1]

  Session 1 -first steps of the treatment

  - **Patient and doctor or diabetes nurse have already discuss the need of insulin and patient went to a dietitian**
  - **A regimen will have been agreed upon and the first prescription has been obtained by the patient**
  - **A review of "what is diabetes" including what insulin does and the need for insulin injections usually takes place**
  - **Further discussion (e.g. sites and time of injection,where and how to obtain equipment,recognition and management hypoglycemia and hyperglycemia,self blood glucose monitoring etc)**
  - **Nurse explains the basics about insulin injection and patient tries it for the first time,24h contact details provide**

  Session 2
  (around 2 weeks after insulin initiation)

  - **Review of session 1**
  - **Nurse usually have had telephone contact over insulin injections and BG levels**
  - **Review of insulin injection technique**

  Session 3
  (around 4 weeks after insulin injection)

  - **Review of session 1 and 2**
  - **Further discussion about several issues (e.g. site and time of injections, where and how to obtain equipment etc.)**

  Session 4
  (around 10 weeks after insulin initiation)

  - **Review of previous sessions**
  - **Assessment of glycemic control and need for further doctor/nurse follow− up**
  - **Book follow− up clinic/surgery appointment**

Chapter 3

Pancreas

Pancreas is an exocrine and endocrine gland, a cone shaped organ with 12-15cm length and 85-100 grams weight. Anatomically is located deep in the upper abdomen in front of the spine. The pancreas is divided anatomically into head, body and tail. The head of the pancreas is located in the loop of the duodenum while the body and the tail pass in front of the spine and reach to the gate of the spleen. Along the pancreas is a tube that begins at the tail and reaches the head of the institution called main pancreatic duct or resource Wirsung. The main pancreatic duct empties into the duodenum.[7],[1]

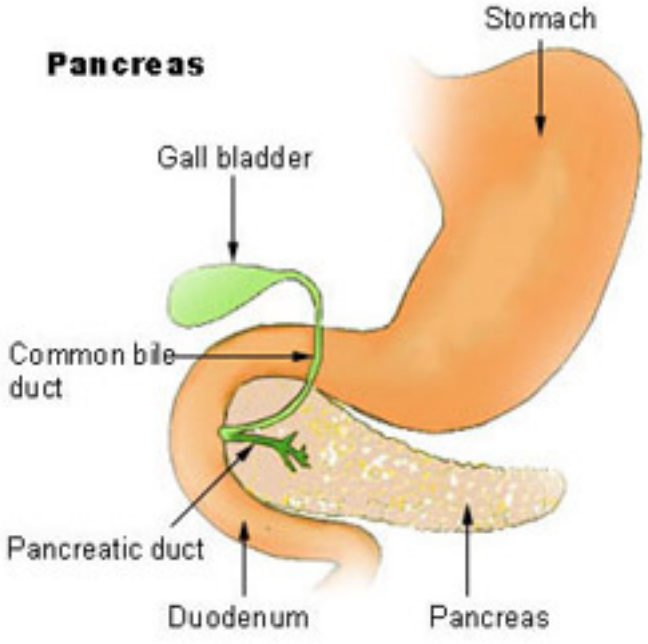


FIGURE 3.1: Pancreas [8]

The pancreas, as we referred is a gland with two basic functions. The exocrine function, relating to the production and secretion in the duodenum of pancreatic enzymes, which are absolutely essential for digestion and absorption of food particles and endocrine function, which mainly concerns the secretion of insulin which regulates the sugar level in blood. These two functions make the pancreas, essential for the smooth functioning of the body.

3.1 Exocrine function

The 85% of the cells of the pancreatic mass are cells that produce, store and secrete pancreatic enzymes. These enzymes are driven means of the main pancreatic duct at the cusp Vater, and after being mixed with bile reaches the middle of the bile duct from the liver, flowing in the background medium duodenal sphincter of Oddi. The combination of bile acids and the activated pancreatic enzymes necessary for the degradation and absorption of proteins, fats and carbohydrates in food. The major pancreatic enzymes are:[9]

1. Proteolytic (trypsin, chymotrypsin, elastase, carboxypeptidase)

   Secreted as inactive proenzymes, which are activated in the lumen of the duodenum from enzyme enterokinase. Purpose of proteolytic enzymes is the protein breakdown of food.

2. Lipase

   It is produced and secreted in the active form and is responsible for the breakdown of fats in foods. Amylase. It is produced and secreted in the active form and is responsible for the breakdown of glycogen, starch and carbohydrate foods.

3. The fosfolypasi A

   It is secreted as an inactive proenzyme and activated in the duodenum by trypsin. Active fosfolypasi A convert lecithin into lysolecithin bile which is detrimental to the cell membrane. Role of fosfolypasis mainly cleavage of cells foods such as disruption of the muscle cells in the digestion of food meat. If the operation of fosfolypasis done within the pancreatic ducts, lead to the disruption of pancreatic tissue and the onset of pancreatitis.

- CEPHALIC PHASE

TABLE 3.1: Enzymes of pancreatic juice [1]

Carbs	**Proteins**	**Fat**
amylase	Trypsin	Lipase
	Carboxypeptidase	Cholesterol esterase
	Aminopeptidase	Phospholipase
	Elastases	
	Nucleases	

Visual, olfactory, taste stimuli induce the generation of nerve signals from the cerebral cortex and the hypothalamus via the vagus nerve stimulates pancreatic secretion resulting moderate amount of enzymes which constitutes 20% of the total pancreatic secretion. However, minimum discharge flow to the intestine because they are produced a minimum of water and electrolytes.

- GASTRIC PHASE

  In gastric nerve stimulation phase for enzyme production continues resulting in the production of other 5-10% of the enzymes secreted after meal. Also in this phase of minimum amounts fed to the lumen of the duodenum remains because the lack of sufficient amount of liquid from the discharge.

- INTESTINAL PHASE

3.2 Endocrine function

The pancreatic cells,responsible for the endocrine function of the instrument, are only 2% of pancreatic mass. Islets are approximately spherical,with an average of 100-200 μm,and a health human pancreas may contain up to a million individual islets, each having its own complex anatomy , blood supply and innervation.

Hormones produced and secreted are:

- Glucagon, which is secreted from the A cells
- Insulin, which is secreted by B cells
- Somatostatin, which is secreted from the D cells
- The pancreatic polypeptide, which is secreted from the F cells

The principal action of pancreatic hormones are regulation of carbohydrate metabolism, blood sugar, the rate of production and degradation of glycogen, proteolysis and lipolysis.

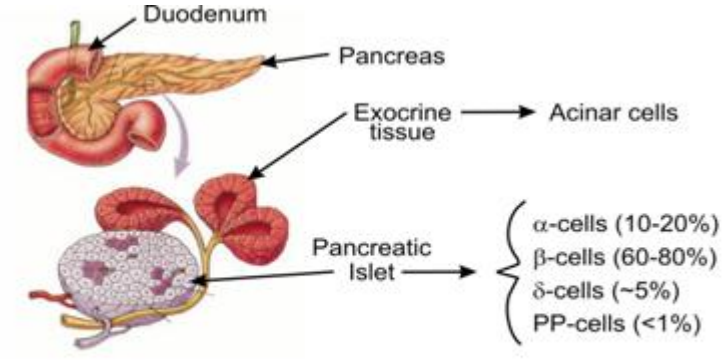


FIGURE 3.2: Pancreas anatomy [1]

Pancreatic $\beta-$ cells respond to small changes in glucose concentrations within a narrow physiological range. Glucose is transported to $\beta-$ cells via hight capacity glucose transporters (e.g. GLUT, GLUT2 in rodents, GLUT1,2,3 in humans) enabling rapid equilibration of extracellular and intracellular glucose concentrations. Once inside the $\beta-$ cell glucose is phosphorylated by glucokinase which is "sensitive" to glucose,coupling insulin secretion to the prevailing GL. Concentrations of glucose below 5 mmol/L do not affect rates of insulin release,and the rate of secretion increases progressively at extracellular GL between 5 and $\sim$ 10 mmol/L, with half−maximal stimulation at $\sim$ 8 mmol/L.[1]

3.3 Nutrition and Diabetes Mellitus

Modern insulins as well as knowledge equivalent carbohydrates can suport patients with type 1 and 2 diabetes mellitus in order to achieve the perfect setting and at the same time have a great variety in the daily diet. But as nutrition is the cornerstone for the correct setting of diabetes, what is vital to know about our diet and how we can make it better and more effective?

The setting of diabetes, in addition to medication, include weight loss, exercise and healthy eating (a combination of all three food categories ratio). The food ingredients are proteins (meat, fish, cheese, egg, milk), carbohydrates − which will be discussed in detail below; and fat (saturated and unsaturated).[10],[11] It is a myth that diabetics should not eat carbohydrates. This advised by doctors before insulin becoming available, because it was known that carbohydrates increase the BG levels. Today, however, diabetics can enjoy a healthy and balanced diet, which should include carbohydrates.

3.3.1 Carbohydrates

Carbohydrates are found in starchy foods, pasta, rice, potatoes, fruit, vegetables, milk, sugar. One gram of carbohydrate provides our body with 4 calories. With the equivalent carbohydrate, the patient can be accurately calculate the dose of ultrafast insulin to cover meals and reduces hypoglycaemia or hyperglycaemia levels which are a result of not counting the carbs correctly. Hyperglycemia occurs when more carbohydrates are consumed, not covered with insulin administered or pancreas did not produce enough or is not able to metabolize glucose consumed by the patient.As a result ,we need a balanced diet which can contain complex carbohydrates , so that the postprandial glucose (2 hours after a meal) can not be up to 140 mg / dl. If you have diabetes, the best diet for you is one that includes your favorites, but healthy foods in the right proportion and complex carbohydrates, not simple (refined) like sugar.[12]

Some useful recommendations for patients with T1DM/T2DM are:

- Prefer complex carbohydrates that are rich in fiber and untreated as brown bread or wholegrain, wholemeal pasta, rice husk.
- Eat all the fruits of his choice, but unripe.
- It is necessary to consume al dente pasta, not boiled for so long.
- Prefer raw vegetables , rich in fibers and delay the absorption of glucose.
- For diabetics are better when the main meals are separated in small meals with 3-4 hours gaps between them. They need variety, imagination and taste to achieve the desired result. Those who take pills and / or insulin should talk with their doctor about the best timing of meals and take insulin.

3.3.2 Glycemic Index and Glycemic Load

The glycemic index (GI) is a concept that shows how levels of sugar are increasing in the blood after $2-3$ hours of a meal which contains 50 grams of carbohydrates, compared to a reference food (glucose or white bread). GI provides a measure of the quality of carbohydrate, on a scale from 0 to 100 and does not refer to the quantity. GI remains the same whether we are talking about consumption of 10 or 100 grams of carbohydrate.

Another important concept to be resolved is the glycemic load (GL) referred to the quantity of carbohydrates consumed by an individual in conjunction with glycemic index. The glycemic load of food arises if we multiply the glycemic index of food for the content

of carbohydrate and divide it by a hundred.Practically, this means that a food with a low GI if consumed in large amounts can have a high glycemic load while foodstuff with moderate or high GI if consumed in a small amount will have a low glycemic load.[13],[14]

$$GI = \frac{BG\ tested}{BG\ bread} * 100$$

$$GL = GI * [GRAMS\ OF\ CARBS]/100$$

Foods with a high GI causing direct reaction of insulin resulting in sudden and large increase in blood sugar. Unlike the low GI foods because of slow digestion and absorption gradually increase insulin levels and blood sugar, and thus contribute to better glycemic control in diabetics. It has been shown to have proven benefits for health, contribute to a reduction of serum lipids in hyperlipidemia diseases, have been associated with higher levels of HDL−cholesterol concentrations and a reduced risk of diabetes and cardiovascular disease. Finally contribute positively to reduce weight, and help control appetite and delay hunger.

TABLE 3.2: Target values of diabetes compensation [15]

	Excellent price	**Good price**	**Unsatisfactory price**
BG before meal∗(mmol/L)	4,0-6,0	6,0-7,0	> 7,0
BG after meal∗∗(mmol/L)	5,0-7,5	7,5-9,0	>9,0
HBA1c (%)			
IFCC	<4,5	< 4,5-5,3	>5,3
IFCC	<6,5	< 6,5-7,0	>7,0
HBA1c(mmol/L)	<45	<53	>53
total cholesterol(mmol/L)	<4,5	1,1-0,9	>5,0
HDL cholesterol(mmol/L)	>1,1	<4,5-5,0	<0,9
LDL cholesterol(mmol/L)	<2,5	2,5-3,0	>3,0
Triglycerides (mmol/L)	<1,7	1,7-2,0	> 2,0
Blood pressure (mmHg)	<130/80		>130/80

Main factors that affect on GI :

1. **Maturation of the food** The more mature are fruits and vegetables, the more the GI are high. A typical example is the banana. The immature has GI: 43 and the ripe 74. That is why diabetics are advised to avoid eating ripe fruit.
2. **Presence of fiber** Food with high fiber content have lower GI values.
3. **Method and cooking time** Cooking and baking increase the GIs or softened vegetable food fibers or make them more digestible carbohydrates. Also the longer food is cooked more the GI increase.

4. **Edit suffered food** The shorter treatment has been the food, the lower GI has(e.g. wholegrain products have less GI compared with white)

5. **Recommendation lunch** The fat and the proteins affect glycemic response of the food. The fat slows down stomach emptying, whereas proteins stimulate insulin secretion. Therefore, the presence of fat in the meal lowers the GI.

Table 3.3: Categorize GI

Food	**GI**
Low GI	≤ 55
Medium GI	56-69
High GI	≥ 70

Table 3.4: Categorize GL

Food	**GL**
Low GL	≤ 10
Medium GL	11-19
High GL	≥ 20

High GI :

- White bread
- Processed breakfast cereals
- Potato
- Plain biscuits or crackers
- Cakes and muffins
- Fruits, such as bananas (especially ripe), watermelon, melon
- Honey
- Sugar
- soft candies
- Waffles

Low GI :

- Multigrain breads
- Cereals wholemeal
- Oats, muesli, porridge, All Bran
- Oat biscuits
- Vegetables

- Yoghurt
- Paddy rice (eg basmati)
- Fruits such as apples, pears, cherries, oranges, grapes
- Peanuts

To sum up,some nutritional points worthy of attention are presented:[15]

(a) Distribution of carbohydrates during the day

(b) Small frequent meals

(c) Variety of food consumption

(d) Eating a lot of fruits and vegetables each day

(e) Reducing saturated fat consumption

(f) Consumption of sugar and salt in moderation

(g) Increasing fiber intake (25-30 g. Per day). Good sources are fruits, vegetables, legumes and whole grains (breads cereals etc.).

(h) As for type 2 diabetes should be made meals at fixed times every day

(i) Keeping weight at normal levels

(j) Select healthy cooking (avoid the pan)

(k) Daily counting sugar

(l) The best treatment is prevention, diets of diabetics is what everyone must follow in order to be healthy.

3.4 Physical activity and diabetes

It is now clear that the exercise, apart from its benefits in maintaining good health in general, has much to offer in some specific conditions. One such case is diabetes. The benefits of exercise concern not only to better treat or delay the onset of disease but , also at the same time prevention of it.[1],[16] If somebody has diabetes and want to integrate exercise into his life, specialists recommend that the best way to start is to visit a doctor, who will get a detailed medical history and testes, focusing his attention to any symptoms related to heart and blood vessels, eyes, kidneys and nervous system. Some additional tests may be needed, if any of the following applies:

- You are over 35 years old.
- You have type 2 diabetes for more than 10 years.

- You have Type 1 diabetes for more than 15 years.
- Coexists another risk factor for coronary heart disease.
- Have a diagnosed microvascular disease.
- You have peripheral arterial disease.
- You suffer from anatomical neuropathy.

If you have a satisfactory metabolic rate can safely participate in most activities. But if you're middle-aged or belong to old age, will benefit from the exercise. The aging process leads to degeneration of muscles, ligaments, bones and joints, and the misuse of the body due to malfunctions and the existence of diabetes may exacerbate the problem. In all cases, the best suggestion is to begin gradually,set realistic goals and choose your activities carefully.

When you have diabetes, physical activity can shed the blood glucose levels. This does not apply to people who make use of insulin. Some pills can also have the same results.In order to avoid hypoglycemia,patients should always eat a small snack before starting practice,measure blood glucose levels to be sure it is not too low before exercise and have glucose tablets, a sugary drink or a snack with you during exercise, if you feel a hypoglycemia.If you do intense exercise, continue to check your glucose levels up to 36 hours after, to prevent any hypoglycemia later.

- Exercise and T2DM[17]
  - What kind of exercise?
    - Aerobics: First you should start with 10-15 minutes of exercise,which can be gradually increased to 30 minutes or three times of 10 minutes during the day. The primary goal is to lose weight, so the intensity must be low to moderate and duration gradually increased to 1 hour. Try to exercise 3-4 times a week of moderate-intensity exercise (e.g. walking) and other activities (e.g. cycling, swimming).If you take insulin, you can exercise daily in order to reduce the difficulty of balancing caloric needs and insulin dosage. If you're obese, you can exercise every day for more calorie burning and weight loss.
    - Muscle strengthening: Make a low intensity program with small weights, with 10-15 repeats set for the main muscle groups, at least two times a week.
    - Flexibility / Stretching: At least 2-3 times per week for 15-30minutes, repeating 2-4 times each dilatation. The aim of the program is to "burn" at least 1,000 calories a week with exercise to benefits your health or 2,000 calories to achieve weight loss.

  - What to concern about

    Especially for patients with T2DM,checking glucose levels before and after exercise is vital, to understand how body reacts to different activities. Physicians recommend them to wear even an ID wristband or exercise with friends.

- Exercise and T1DM[17]

  Most of the activities are recommended to type 1 diabetes patients,unless there are medical complications that do not allow them. You should exercise at least 4-5 times a week at a low or middle rhythm or about 30-40 minutes. Besides aerobic exercise, it is important to do strength training and flexibility.You should check glucose levels before and after exercise and also know your body's reactions to various exercise types. As for those who suffer from diabetes type 2, it is prudent to do gymnastics with friends and wear an ID of your diabetic condition. Furthermore, because you may get hypoglycemia, be sure to have with you in case of emergency, a food rich in carbohydrates.Patients also suggested not to neglect to consult your doctor regularly to help reduce the likelihood of diabetic complications. If there are complications in the eyes, kidneys or heart, it is important for your doctor to determine the intensities of your physical activity.It is now clear that especially T2DM, which is spreading rapidly worldwide, is associated with reduced levels of exercise and obesity. It is therefore imperative to add exercise in order to prevent the disease, and cope with this type of diabetes.For people with diabetes type 1, it is important to include exercise in the therapeutic part of the treatment and they can safely participate in all kinds of physical activities.

It is important to mention that it is useful to know the price some useful factors and what those represent .

TABLE 3.5: Useful factors

Factors	**Definition**
BMI	Body Mass Index
BMR	Basal Metabolic Rate
TDEE	Total Daily Energy Expenditure
EER	Energy Efficiency Ratio

- BMI[18]

  The BMI is an attempt to quantify the amount of tissue mass (muscle, fat, and bone) in an individual, and then categorize the person as underweight, normal weight, overweight, or obese based on that value. BMI equation :

$$BMI = \frac{mass\ (kg)}{height^2\ (m)} = \frac{mass\ (lb)}{height^2\ (in)} * 703$$

TABLE 3.6: BMI categories

Category	**BMI(kg/m2)**	
	from	**to**
very severely underweight		15
severely underweight	15	16
underweight	16	18.5
normal(healthy weight)	18.5	25
overweight	25	30
obese class 1 (moderately obese)	30	35
obese class 2 (severely obese)	35	40
obese class 3 (very severely obese)	40	

- BMR[19]

  Basal metabolic rate (BMR) is the minimal rate of energy expenditure per unit time by endothermic animals at rest. Basal metabolic rate (BMR) affects the rate that a person burns calories and ultimately whether you maintain, gain, or lose weight. Your basal metabolic rate accounts for about 60 to 75% of the calories you burn every day. It is influenced by several factors :

  - Muscle mass − that is, the amount of muscle tissue on your body. Muscle requires more energy to function than fat. So the more muscle tissue you carry, the more energy your body needs just to exist. (While most forms of exercise will help boost muscle, resistance or strength training is most effective: for example lifting weights and exercises that work against the resistance of your body weight such as pushups, squats and lunges.)
  - Age −As you get older, your metabolic rate generally slows. This is partly because of a loss of muscle tissue, and also because of hormonal and neurological changes. When babies and children go through periods of growth, their metabolism speeds up.
  - Body size−People with bigger bodies tend to have a larger BMR because they usually have larger internal organs and fluid volume to maintain. Taller people have a larger skin surface, which means their bodies may have to work harder to maintain a constant temperature.
  - Gender −As men are usually larger than women, they generally have faster metabolisms.
  - Genetics −This can also play a role in whether you have a slower or faster metabolism, and some genetic disorders can also affect your metabolism.

- Physical activity −Regular exercise increases muscle mass and encourages your body to burn kilojoules at a faster rate, even when at rest.
- Hormonal factors −Hormonal imbalances caused by certain conditions, including hypo- and hyperthyroidism, can affect your metabolism.
- Environmental factors − The weather can also have an effect on your metabolism; if it is very cold or very hot, your body has to work harder to maintain its normal temperature and that increases the metabolic rate.
- Drugs− Caffeine and nicotine can increase your metabolic rate, while medications including some antidepressants and anabolic steroids can contribute to weight gain regardless of what you eat.
- Diet −Certain aspects of your diet can also affect metabolism. For instance if you don't have enough iodine for optimal thyroid function, it can slow down your metabolism.

In order to calculate BMR , we use the Harris-Benedict formula:

$$for\ men:$$

$$BMR = 66.5+(13.75*weight\ (kg))+(5.003*height\ (cm))-(6.755*age\ (yrs))$$

$$for\ women:$$

$$BMR = 655.1+(9.563*weight\ (kg))+(1.850*height\ (cm))-(4.676*age\ (yrs))$$

TABLE 3.7: Determine recommended intake [19]

Category	**Daily kcals needed**
little no exercise	BMR∗1.2
light exercise(1−3 days/week)	BMR∗1.375
moderate exercise(3−5 days/week)	BMR∗1.55
heavy exercise(6−7 days/week)	BMR∗1.725
very heavy exercise(twice per day, extra heavy workouts)	BMR∗1.9

- TDEE[20],[21]

  Everyday your body burns a specific number of calories just by existing. This is known as your Basal Metabolic Rate.The BMR is based on your weight, height and age, as we have already shown. When you exercise or simply expend energy through physical activity, you burn additional calories. When you combine your BMR with the calories you burn through physical activity, you get your Total Daily Energy Expenditure(TDEE). As a result, we can calculate the TDEE knowing the BMR and the category of exercise that we

follow ,table 3.7 . It is simple to say that to gain weight you eat more than your TDEE and to lose weight you eat less.

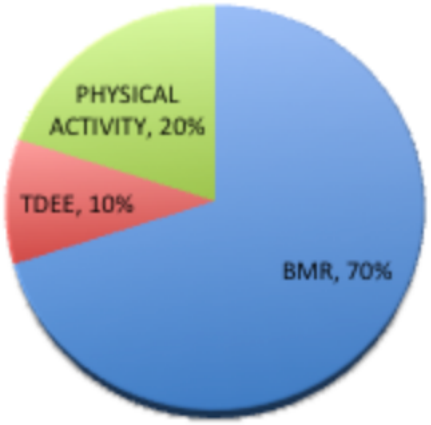


FIGURE 3.3: BMR,TDEE and Physical activity in every day life [22]

- EER

  Estimated Energy Requirement (EER) is the average dietary energy intake that is predicted to maintain energy balance in healthy, normal weight individuals of a defined age, gender, weight, height, and level of physical activity consistent with good health. In children and pregnant and lactating women, the EER includes the needs associated with growth or secretion of milk at rates consistent with good health.The EER predictive equations developed by the Institute of Medicine Equation were released in September 2002 and were used to formulate the new dietary guidelines for the U.S. in 2005 when the revised food pyramid (MyPyramid) was released. These equations were based on an extensive doubly labeled water database (considered the gold standard for Total Energy Expenditure measurement.) Total Energy Expenditure (TEE) is the sum of the basal metabolic rate, TEF (thermic effect of food), physical activity, thermoregulation, and the energy expended in depositing new tissues and in producing milk.

  When using the EER equations, it is important to distinguish between the 'Physical Activity Coefficients (PA) and the Physical Activity Levels (PAL). The physical activity coefficients are used in the EER equations to estimate energy requirements and are based on ranges of physical activity levels.The Physical Activity Level (PAL) is the ratio of total energy expenditure to basal energy expenditure (TEE/BEE). The Physical Activity Level categories were defined as sedentary (PAL 1.0-1.39), low active (PAL 1.4-1.59), active (PAL 1.6-1.89), and very active (PAL 1.9-2.5).[23]

Definitions about the classification of activities:[23]

- Sedentary: (Daily PAL range: 1.0 − 1.39): Typical activities of daily living such as gardening (no lifting), household tasks, light activity while sitting, loading/unloading car, mopping, mowing lawn (power mower), etc.
- Low Active: (Daily PAL range: 1.4−1.59): Typical activities of daily living such as gardening (no lifting), household tasks, light activity while sitting, loading/unloading car, mopping, mowing lawn (power mower), etc. and 30 to 60 minutes of moderate activity daily such as calisthenics (no weight), cycling (leisurely), golf (without cart), swimming (slow), walking 3−4mph, etc.
- Active: (Daily PAL range: 1.6− 1.89): Typical activities of daily living such as gardening (no lifting), household tasks, light activity while sitting, loading/unloading car, mopping, mowing lawn (power mower), etc. and 60 minutes of moderate activity daily such as calisthenics (no weight), cycling (leisurely), golf (without cart), swimming (slow), walking 3−4mph, etc.
- Very Active: (Daily PAL range: 1.9− 2.5): Typical activities of daily living such as gardening (no lifting), household tasks, light activity while sitting, loading/unloading car, mopping, mowing lawn (power mower), etc. and 60 minutes of moderate activity daily such as calisthenics (no weight), cycling (leisurely), golf (without cart), swimming (slow), walking 3−4mph, etc. PLUS additional 60 minutes of vigorous activity such as chopping wood, climbing hills (no load), cycling (moderately), jogging (10−min miles), rope skipping, skating, swimming, tennis (doubles), walking (5 mph) or 120 minutes of additional moderate activity.

Categorize people according to their age ,table 3.8 :

TABLE 3.8: EER - Estimated Energy Requirements [24]

Gender-Age(years)	**Sendetary/Moderately Active**	**Active**
child / 2-3	1,000 / 1,000-1,400	1,000-1,400
female/ 4-8	1,200 / 1,400-1,600	1,400-1,800
9-13	1,600 / 1,600-2,000	1,800-2,200
14-18	1,800 / 2,000	2,400
19-30	2,000 / 2,000-2,200	2,400
31-50	1,800 / 2,000	2,200
51+	1,600 / 1,800	2,200
male/ 4-8	1,400 / 1,400-1,600	1,600-2,000
9-13	1,800 / 1,800-2,200	1,600-2,000
14-18	2,200 / 2,400-2,800	2,800-3,200
19-30	2,400 / 2,600-2,800	3,000
31-50	2,200 / 2,400-2,600	2,800-3,000
51+	2,200 / 2,200-2,400	2,400-2,800

Kilojoules (food energy) are important for providing energy for your daily activities and body function. The aim is to balance the energy consumed through foods with the energy expended during the day. The more active you are the more kilojoules of food energy you need. If you are less active, your body needs fewer kilojoules of food energy to get you through the day.When you are choosing foods and drinks, take a look at the DIG .The Daily Intake Guide has been developed to show you how you can distribute your energy intake over a day. It's based on 3 main meals plus 2 smaller snacks.You can modify the guide to adapt it to your eating pattern on a given day.For example if you have a large breakfast (greater than 20% of your daily energy needs), you will need to modify (reduce) your intake amount for mid-morning and afternoon snacks, lunch or dinner.

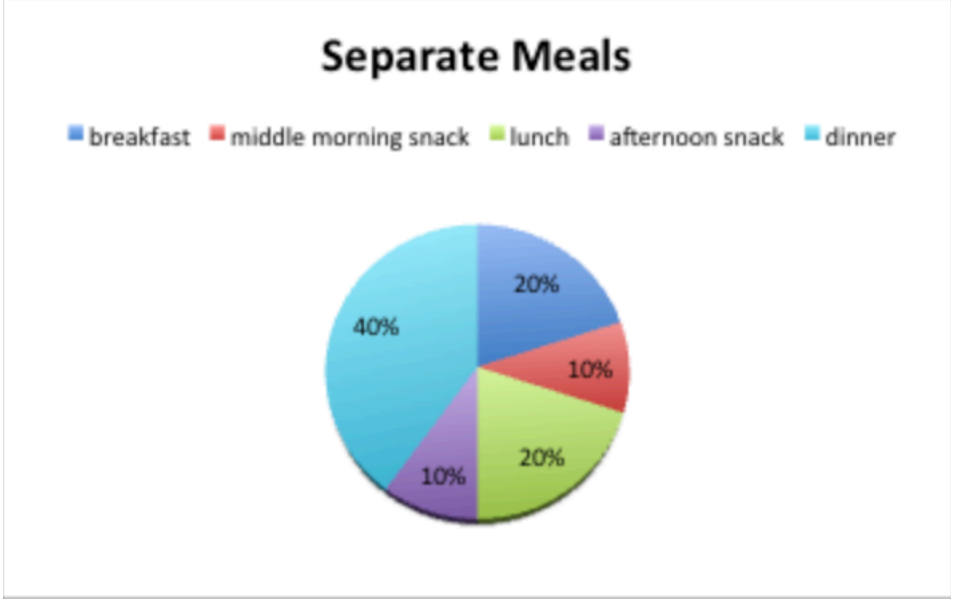


FIGURE 3.4: Ideal way to separate meals

Chapter 4

Clinical Decision Support Systems

Information technology (IT) is the use of any computers, storage, networking and other physical devices, infrastructure and processes to create, process, store, secure and exchange all forms of electronic data.Health Information Technology (HIT) is information technology applied to health and health care.A Clinical Decision Support System (CDSS) is a Health Information Technology system that is designed to provide physicians and other health professionals with clinical decision support (CDS), that is, assistance with clinical decision-making tasks. A working definition has been proposed by Robert Hayward of the Centre for Health Evidence: "Clinical Decision Support systems link health observations with health knowledge to influence health choices by clinicians for improved health care". CDSSs constitute a major topic in Artificial Intelligence in medicine. CDSS are set up to support the physicians and contribute to the correct diagnosis and support of patients.Studies show that the contribution of these systems has brought progress in various chronic diseases such as cardiovascular disease (CVD) , chronic obstructive pulmonary disease (COPD) , heart diseases and ambulatory/primary care setting. In this chapter , we will describe in detail the architecture of the systems and their application in patients with diabetes. Clinical DSSs are typically designed to integrate a medical knowledge base, patient data and an inference engine to generate case specific advice.

4.1 General Information about CDSS

Research into the use of artificial intelligence in medicine started in the early 1970's and produced a number of experimental systems. Some examples of CDSS

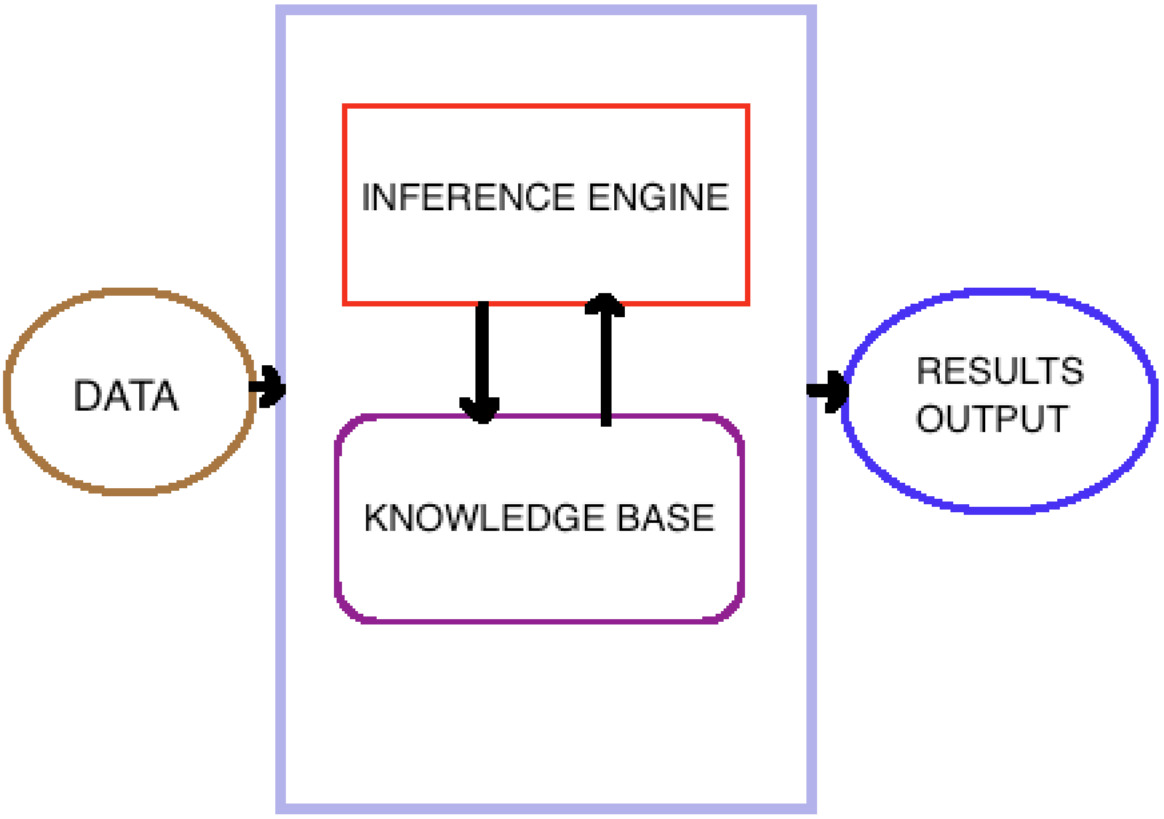


FIGURE 4.1: CDSS architecture

systems:

- AAPHelp: de Dombal′s system for acute abdominal pain (1972).[25]

  An early attempt to implement automated reasoning under uncertainty. De Dombal's system, developed at Leeds University, was designed to support the diagnosis of acute abdominal pain and, based on analysis, the need for surgery. The system's decision making was based on the naive Bayesian approach.

- INTERNIST I (1974)[25]

  Pople and Myers begin work on INTERNIST, one of the first clinical decision support systems, designed to support diagnosis, in 1970.

  INTERNIST-I was a rule-based expert system designed at the University of Pittsburgh in 1974 for the diagnosis of complex diagnosis of complex problems in general internal medicine. It uses patient observations to deduce a list of compatible disease states (based on a tree-structured database that links diseases with symptoms). By the early 1980s, it was recognized that the most valuable product of the system was its medical knowledge base. This was used as a basis for successor systems including CADUCEUS and Quick Medical Reference (QMR), a commercialised diagnostic DSS for internists.

- MYCIN (1976)[25]

  MYCIN was a rule-based expert system designed to diagnose and recommend treatment for certain blood infections (antimicrobial selection for patients with bacteremia or meningitis).It was later extended to handle other infectious diseases. Clinical knowledge in MYCIN is represented as a set of IF-THEN rules with certainty factors attached to diagnoses. It was a goal-directed system, using a basic backward chaining reasoning strategy (resulting in exhaustive depth-first search of the rules base for relevant rules though with additional heuristic support to control the search for a proposed solution). MYCIN was developed in the mid-1970s by Ted Shortliffe and colleagues at Stanford University.It is probably the most famous early expert system, described by Mark Musen as being "the first convincing demonstration of the power of the rule-based approach in the development of robust clinical decision-support systems" [Musen, 1999]. The EMYCIN (Essential MYCIN) expert system shell, employing MYCIN's control structures was developed at Stanford in 1980. This domain-independent framework was used to build diagnostic rule-based expert systems such as PUFF, a system designed to interpret pulmonary function tests for patients with lung disease.

- CASNET/Glaucoma [25]

  CASNET (Causal ASsociational NETworks), developed in the 1960s, was a general tool for building expert system for the diagnosis and treatment of diseases. The most significant Expert System application based on CASNET was CASNET/Glaucoma for the diagnosis and treatment of glaucoma. Expert clinical knowledge was represented in a causal-associational network (CASNET) model for describing disease processes. CASNET/Glaucoma was developed at Rutgers University and implemented in FORTRAN.

- PIP [25]

  PIP, the Present Illness Program, was a system built by MIT and Tufts-New England Medical Center in the 1970s that gathered data and generated hypotheses about disease processes in patients with renal disease.

- ABEL [25]

  Acid-Base and ELectrolyte program. An expert system, employing causal reasoning, for the management of electrolyte and acid base derangements. Developed at the Laboratory for Computer Science, MIT, in the early 1980s.

- ONCOCIN [25]

  A rule-based medical expert system for oncology protocol management developed at Stanford University. ONCOCIN was designed to assist physicians with the treatment of cancer patients receiving chemotherapy. ONCOCIN

was one of the first DSS which attempted to model decisions and sequencing actions over time, using a customised flowchart language. It extended the skeletal-planning technique to an application area where the history of past events and the duration of actions are important.

The potential benefits of using electronic decision support systems in clinical practice fall into three broad categories (Coiera quoting Sintchenko et al., 2002):

- Improved patient safety e.g. through reduced medication errors and adverse events and improved medication and test ordering.
- Improved quality of care e.g. by increasing clinicians;available time for direct patient care, increased application of clinical pathways and guidelines, facilitating the use of up-to-date clinical evidence, improved clinical documentation and patient satisfaction.
- Improved efficiency in health care delivery e.g. by reducing costs through faster order processing, reductions in test duplication, decreased adverse events, and changed patterns of drug prescribing favouring cheaper but equally effective generic brands.

Informal list of potential benefits :

- Automatic provision of relevant, personalized expert advice, expertise and recommendations sourced from up-to-date, best practice knowledge.
- Reduce variation in the quality of care.
- Can support medical education and training.
- Can help overcome problems of inefficient coding of data.
- Can be cost-effective after initial capital costs and update and maintenance costs.
- Can provide immediate feedback to patients.
- If integrated with an EMR, can help streamline workflow (history taking, diagnosis, treatment) and encourage more efficient data gathering.
- Can provide an audit trail and support research.
- Can maintain and improve consistency of care.
- Can supply clinical information anytime, anywhere it's needed.

Factors which may help determine the acceptance and use of CDSSs in clinical practice:

- Cost

- Attitude of targeted users: breadth and depth of commitment.
- Degree of user acceptance prior to and after installation.
- Ease of use−time needed to learn to use and to use.
- Type, timing, length of training to be provided.
- Availablility of support and maintenance.
- Interoperability: ease/extent of integration with legacy systems (hardware, other devices) and existing software programs (integration with patient record and/or any relevant clinical terminologies would avoid need to re-enter patient data).
- Ease of integration within organisational context and routine workflow - degee to which it entails aredesign of clinical processes.
- Legal and ethical issues.
- User interface: design, structure, number of forms.
- Style, manner of presentation of advice/ recommendations/ results to user.
- Patients' attitudes to use.
- Provision of evidence justifying advice and/or recommendations.
- Involvement of local users during development phase.
- The quality and reliability of a system and its knowledge base which should be populated with trusted, up-to-date and maintainable knowledge.
- In the last resort, widespread use of clinical decision support systems in clinical practice will not occur without electronic patient record systems using terminology and data standards that will allow them to be accessed effortlessly during routine patient care.

4.2 FEL EX Expert System

FEL EX Expert is a universal diagnostic expert system that is able to provide expert advice, decision or solution recommendation in a particular situation.

The importance of diagnostics is critical in a number of diverse areas, from medicine to engineering and automotive industries. In medicine, its concern is the detection of disease processes in the human body and an optimal treatment plan, while in the technical field its object is most often "fault detection" in non-living complex facilities, optionally including suggestion of effective repair actions. The expert system approaches both challenges in a similar way and replaces the presence of experts in analyzing relevant causes and/or consequences. FEL EX Expert has the capability to:

FIGURE 4.2: FEL EX Expert System [26]

(a) Accept requisite knowledge in the form of a knowledge base of rules and utilize them for specific cases to be evaluated.

(b) Infer the likelihood of events (hypotheses) from the knowledge base along with specific data for the diagnosed case (system).

(c) Communicate automatically with a database or directly with the user via a graphical user interface.

(d) Using additional modules, FEL EX Expert can be utilized in an automated monitoring mode for a connected device and provide notifications (alarm activation, sending an SMS, etc.) in case, a significant event occurs.

There is no official definition of the term "expert system". However, it can be said, that expert systems are computer programs simulating decision activity of an expert solving complex tasks and using properly coded, explicitly expressed special knowledge taken from the expert, with the goal of achieving in a selected problem area quality of decision at the level of an expert.

Expert systems can be divided into three types: diagnostic, planning and hybrid expert systems. Task of a diagnostic expert system is to provide diagnosis from the data retrieved from the real world. This type of an expert system is described in detail below. Task of a planning expert system is to find a plan (if possible optimal) consisting from operators (steps) which lead from known start to known stop state and satisfy known restrictions. Planning system has to use its knowledge base to limit number of generated steps leading from the current state and to evaluate found solution. Hybrid expert systems have a combined architecture− they use both concepts of diagnostic and planning systems. Examples of hybrid systems are intelligent tutoring systems (diagnosis of a student knowledge and planning of the next teaching process) or monitoring systems (when diagnostic part detects fault the planning part plans repair).

Diagnostic expert system provides interpretation of real world data with the goal of selecting the most corresponding goal hypothesis from the set of possible goal hypotheses. The inner current model is updated from retrieved data using the knowledge base by fixed inference engine.

In a dialog mode the control mechanism selects questions put to the user and manages updating of the current model. This is repeated until he system selects diagnosis for the consulted case. Process of consultation and updating is described below in detail. The knowledge base describing problem area solved by a diagnostic expert system is often expressed in a form of if-then rules and is separated from the control mechanism.

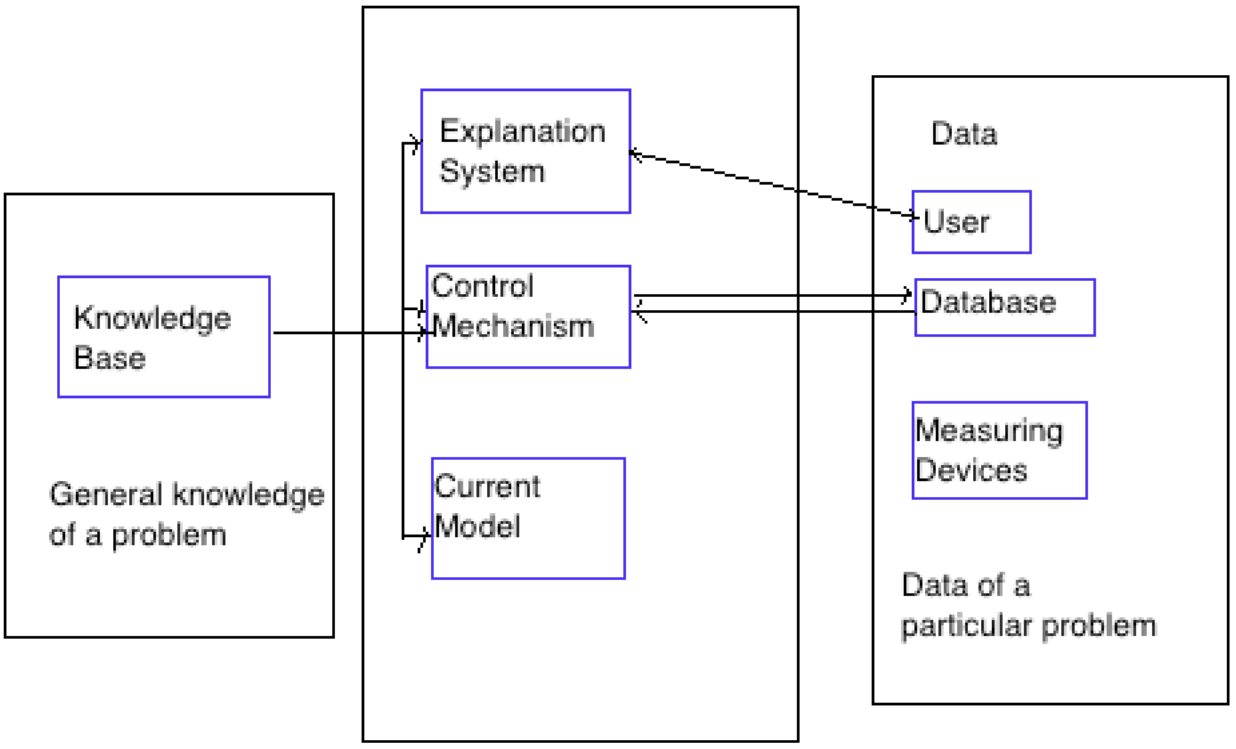


FIGURE 4.3: Fel Ex Expert system form

The first expert systems (for example DENDRAL, MYCIN, PROSPECTOR – were made whole dependent on one problem. From these systems can be extracted the core (the control and inference mechanism) and reused for other problems only by changing the knowledge base. Problem independent on an empty expert system is called shell. The expert system shell can be used for developing and testing the knowledge base and can thus form expert system for any area.It should be again mentioned that the quality of any expert system de- pends strongly on its knowledge base. The inference engine (control mechanism) is also important, but the knowledge base is critical.FEL Expert is a name for family of problem

independent expert system shells. The FEL Expert system in all versions uses probabilistic pseudobayesian approach to handling uncertainty both in the data and in the knowledge base. This approach is adapted from the PROSPECTOR system. This section describes the uncertainty handling in the FEL Expert system.

4.2.1 Inference Engine

The required KB for a rule-based diagnostic system, such as FEL EX Expert System, is expresses by rules. Rules are in the following form: [25]

$$if\ presumption\ E\ then\ conclusion\ H\ with\ probability\ P(H|E)$$

$$else\ conclusion\ H\ with\ probability\ P(H|\bar{E})$$

These rules are explained as : "If the presumption (evidence) E certainly holds then accept the conclusion H with measure (probability) P(H|E); if the negation of E certainly holds then accept the conclusion H with measure P(H|$\bar{E}$)",where E and H are hypotheses(statements). P(H|E),probability of H when E holds and P(H|$\bar{E}$) are subjective conditional probabilities. P(H|E) is called sufficiency measure of the rule while P(H|$\bar{E}$) is called necessity measure of the rule. These measures express uncertainty in the knowledge base,figure 4.4.

FIGURE 4.4: "If Then rules",E⟶H [25]

It should be noted that probability in this context and also in the rest of the thesis has a different meaning than in the classical statistical frequentist sense. The probability here is used to express uncertain knowledge and is subjective and thus has not necessarily to be objective in a statistical meaning, simply because in cases solved by expert systems we are not able to get such a characteristics. If we had such an objective probability we would not have to use expert system and its heuristics. However, to manipulate these probabilities classical statistical methods are often used here. Instead of probability the term pseudoprobability is used often in some publications. The set of the rules introduced above can be represented by a directed graph so that every hypothesis (statement) is represented by one node (vertex) and each rule is represented by one edge− see figure 4.5. This graph is called inference net.

FIGURE 4.5: Inference net [25]

Classify the types of nodes can be found in the inference net:[25]

- Top (goal) nodes are nodes from which there is no directed edge.These nodes represent so called goal hypotheses (usually possible results of diagnosis).
- Leaf nodes are nodes to which there leads no directed edge.These nodes represent so called leaf statements. The validity of these statements must be always obtained from an observation of the real world.
- Inner nodes are the other nodes which are neither goal nor leaf.They represent intermediate statements or hypotheses.

Every node can be askable or not askable. In the first case (askable node) the user can be asked about the validity of the corresponding statement1. In the second case (not askable node) it has no sense to ask the user about the corresponding statement. Each node N has assigned a parameter −aprior probability P(N) (pseudoprobability-subjective probability) of the corresponding hypothesis or statement. Aprior probability of a hypothesis expresses a measure of the validity of the hypothesis before any observation of the real world. Inference net is then weighted directed graph. Every node is weighted by the aprior probability while every edge is weighted by two measures P(H|E) and P(H|E). During the process of the consultation the probabilities of the hypotheses are updated (recomputed) by applying the Bayes rule(see below). All assigned numerical values are used in this process. The nodes described above are called bayesian nodes because of the name of the formula used for recomputing probabilities of them (see below). Besides this the system FEL Expert has also a possibility to express knowledge in the form of logical nodes. Using logical nodes it is possible to express logical functions and, or and not.For computing probabilities of logical nodes the formulas from the area of fuzzy logic are used (see below).

$$if\ presumption\ E1\ and\ E2\ then\ H\ with\ probability\ P(E1\ \&\ E2)$$

$$if\ presumption\ E1\ or\ E2\ then\ H\ with\ probability\ P(E1\ \vee\ E2)$$

$$if\ not\ E\ then\ H\ with\ P(\neg\ E)$$

There is a possibility to have unlimited number of presumptions (E1,E2,E3, . .) in the first two cases. The probabilities of conclusions (H) are computed only

from the probabilities of presumptions so the edges to logical nodes do not have assigned any additional numerical values as in the case of edges to bayesian nodes. Bayesian and logical nodes and rules between them form the basic inference net. In addition it is possible to use context or priority links to partially control the process of consultation. The system also offers a possibility of using taxonomy nets which can express a shallow knowledge above the inference net.

4.2.2 Uncertainty Factor

The FEL Expert system can handle uncertainty both in the knowledge base and in the data from the real world. Uncertainty in the knowledge base is expressed by necessity and sufficiency measures attached to the rules. Uncertainty in the data expresses user?s uncertainty in answers to questions put by an expert system.[25]

- Subjective Bayesian Updating

  In order to understand the way in which we can handle uncertainty it should be useful to follow Bayes rule.

  When the possibility H happens :$P(H|E) = \frac{P(E|\bar{H})*P(H)}{P(E)}$,and for the negation of H : $P(\bar{H}|E) = \frac{P(E|\bar{H})*P(\bar{H})}{P(E)}$.

  We define the prior odds on H to be

  $$O(H) = \frac{P(H)}{P(\bar{H})} = \frac{P(H)}{1 - P(H)}$$

  and the posterior odds to be

  $$O(H|E) = \frac{P(H|E)}{P(\bar{H}|E)} = \frac{P(H|E)}{1 - P(H|E)}$$

  The likelihood ratio is defined by

  $$\lambda = \frac{P(E|H)}{P(E|\bar{H})}$$

  so, the form of the Bayes rule is:

  $$O(H|E) = \lambda \ * \ O(H)$$

  This equation tells us how to update the odds on H given the observation of E. We assume that a human expert has given us the rule and has provided the likelihood ratio to indicate the strength of the rule. A high value of

$\lambda(\lambda \gg 1)$ represents, roughly speaking, the fact that E is sufficient for H, since the observation that E is true will transform indifferent prior odds on H into heavy posterior odds in favor of H. Notice that the underlying probabilities can be recovered from their odds by the simple formula

$$P = \frac{O}{O+1}$$

so that the odds and the probabilities give exactly the same information. Suppose now that we wish to update the odds on H given that E is observed to be false. So, according to we have already wrote ,

$$O(H|\bar{E}) = \bar{\lambda} \ * \ O(H)$$

where

$$\bar{\lambda} = \frac{1 - P(E|H)}{1 - P(E|\bar{H})}$$

Notice that $\bar{\lambda}$ must also be provided by the human expert; it cannot be derived from λ. A low value of $(0 \leq \lambda \ll 1)$ represents, roughly speaking,the fact that E is necessary for H, since the observation that E is false will be transform indifferent prior odds on H into odds heavily against H. Curiously, althoug λ and $\bar{\lambda}$ must be separately provided by the expert, they are not completely independent of each other as the equation below,

$$\bar{\lambda} = \frac{1 - \lambda \ * \ P(E|\bar{H})}{1 - P(E|\bar{H})}$$

.

As a result, if we exclude the extreme cases of P(E—H) being either 0 or 1, we see that $\lambda > 1$implies $\lambda < 1$,and $\lambda < 1$ implies $\lambda > 1$. Further,we have $\lambda = 1$if and only if $\lambda = 1$. This means that if the expert gives a rule such that the presence of E enhances the odds on H (i.e., $\lambda > 1$), he should also tell us that the absence of E enhances the odds on H (i.e. $\lambda < 1$). This mathematical requirement may violate the intuition. Expert can often say that ?The presence of E enhances the odds on H, but the absence of E has no significance.? In other words, the expert says that $\lambda > 1$, but $\lambda = 1$. An approach to solve this inconsistency will be discussed below.Also note that the knowledge of both λ and $\bar{\lambda}$ is equivalent to knowledge of both P(E|H) and P(E|$\bar{H}$) as we can see in equations below:

$$P(E|H) = \lambda \ * \ \frac{1-\bar{\lambda}}{1-\bar{\lambda}}$$

and,

$$P(E|\bar{H}) = \frac{1-\bar{\lambda}}{\lambda-\bar{\lambda}}$$

Thus, whether the expert should be asked to provide λ and $\bar{\lambda}$, P(E|H) and P(E|H), or some other equivalent information, is a psychological rather than a mathematical question. FEL Expert expects P(H|E) and P(H|$\bar{E}$) to provide this information.

– Achieving consistency

A useful way for achieving consistency would be to adjust the linear interpolation the linear interpolation function shown in figure 4.6. There are several possibilities, one of which is illustrated in figure 4.7. The linear function has been broken onto a piecewise linear function at the coordinates of the prior probabilities, forcing consistent updating of the probability of H given E'. This approach is used by the FEL Expert system. The analytical expression of figure 4.7 is

$$P(H|E') = \begin{cases} P(H|E-) + \frac{P(E|E')}{P(E)} * (P(H) - P(H|E')), & \text{for } 0 \leq P(E—E') \leq P(E) \\ \frac{P(H)-P(H|E)P(E)}{1-P(E)} + P(E|E')\frac{P(H|E)-P(H)}{1-P(E)}, & \text{for } P(E) \leq P(E—E') \leq 1 \end{cases}$$

4.2.3 Certainty factor

Certainty factor is used to provide possibility of qualitative responses. The idea is that a man can answer not only yes or no but also probably yes, I think yes, surely no, I don't know and so on. These answers can be for our purposes ordered on a numerical axis where the outer values correspond to the categorical answers surely yes and surely no (4.8). FEL Expert uses number -5 for surely no and +5 for surely yes, 0 then means I don't know. This number is called certainty factor R, where R ϵ <-5; 5>.[25]

The response in the form of the certainty factor has to be translated to a pseudoprobability that will be used for inference. This translation is made by a linear interpolation between three points (see 4.8). First point, certainty factor -5 means surely no and so corresponds to the probability 0. Similarly the certainty factor

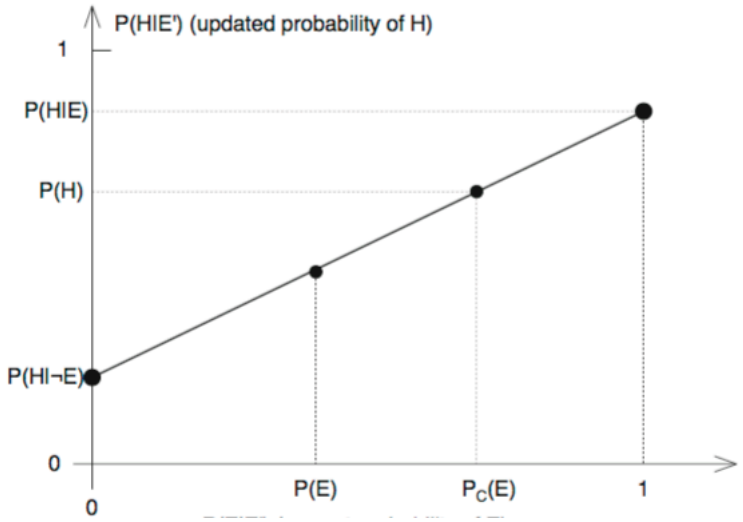


FIGURE 4.6: Inconsistent priors [25]

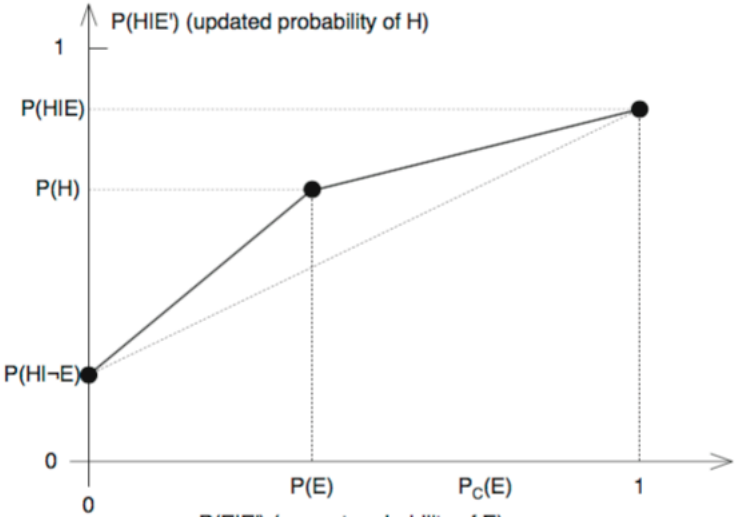


FIGURE 4.7: Consistent interpolation functions [25]

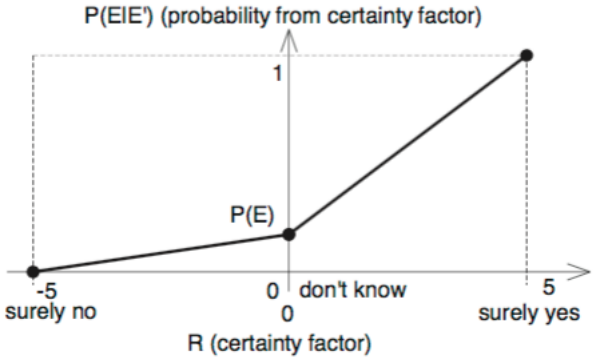


FIGURE 4.8: Certainty factor to a probability [25]

+5 corresponds to the probability 1. Certainty factor 0 means don't know, which is the case where the a prior probability has to be used. The pseudoprobability is calculated ,now, by equation

$$P(E|E') = \begin{cases} P(E) + \frac{1-P(E)}{P(E)} * \ (\frac{R}{5}), & \text{for R}\geq 0 \\ P(E) * (1 - \frac{R}{5}) & \text{for R}<0 \end{cases}$$

4.3 Numerical Value

Computing the probability from a single numerical value x is based on the following idea: The expert can provide the sufficiency measure (or subjective probability) for some important values. If the user enters any of these values the inference engine can use the corresponding values from the expert. Other values can be computed by a linear interpolation between values provided by the expert. The FEL Expert 3.2 used so called S-nodes to handle this type of input. Each S-node has assigned important values xi of an observed quantity. From each S-node must lead special rule with attached probabilities P(H|E,xi) which represent measures corresponding to the values specified in the S-node. In this way the value of P(H|E,x) is approximated and used to compute the probability of the successor node from the user's input.[25] In some cases the expert can declare the dependency explicitly. This case cannot be handled by the system FEL Expert 3.2 directly. However it can be transferred to the previous approximation by choosing important values and corresponding probabilities. In FEL Expert 4.0, the concept of translators was introduced, so S-nodes with special rules are no more used.

4.4 Links

The basic inference net described above specifies the relation between hypotheses, whether goal hypotheses or evidences or inner hypotheses. It is sufficient to describe relations but is not sufficient to describe the order of the node examination or the examination under specific conditions. To specify this FEL Expert uses priority and context links.[25]

- Priority Links Priority links specify unconditional order of the examination. It says that some node must be examined before the examination of some other node:

  $$Before\ investigating\ the\ node\ E1,\ investigate\ the\ node\ E2$$

  This is important for example when using external programs−to call them the system must know the values of certain nodes which are used as parameters before calling the external program. This can be ensured by using priority links.

- Context Links

  In some cases we do not want to examine certain hypotheses. For example it has no sense to ask whether a brother of a patient is genetically handicapped if we did not prove that the patient has a brother. To specify this conditional examination the context links can be used. The context link specifies that some node is examined only if a probability of some other node is in a given range (context):

  $$Investigate\ the\ node\ E1\ only$$

  $$if\ the\ probability\ of\ the\ node\ E2\ is\ in\ a\ given\ range$$

  If the second node is not yet examined the system examines it first (tries to satisfy the context) and than again looks whether the first node should be examined.

4.5 Taxonomies

Taxonomies are used to specify a shallow knowledge over the inference net. They are important especially for large knowledge bases. Taxonomies are used for attention focusing and for specifying hierarchies among hypotheses in the inference net. In the first case they can eliminate examining irrelevant hypotheses, in the

second case they can eliminate examining the statements for which we can estimate the answer from the other statements. The taxonomies form additional net (or nets) over the inference net and should be consistent with the inference net (the consistency check is made by finding cycles in the IIC graph (inference and inheritance compound graph).[25] Both taxonomy for attention focusing and for specifying hierarchical dependencies have a form of a tree graph where the nodes are the taxonomy classes. Edges represent dependencies between the taxonomy classes (hierarchy). Subclasses of any given class are classes on the paths from that class to leaves of the tree graph, superclasses of a class are classes on the path to the root of the tree graph. To each node in this graph a list of inference net nodes is assigned (this list can be empty)−in this way taxonomy specifies dependencies between group of hypotheses (inference net nodes). [27],[28],[29].

Chapter 5

Data Analysis - CDSS in DM(Results)

In order to be able to create a knowledge database for the CDS system we asked from patients with T1DM to record daily the foods they eat and what time,to take pictures of meals in order to have a way to calculate the size of the portions and recorded by a sensor the insulin levels and the values for blood glucose during one month. What is more, we recommended them to record the time that they use bolus insulin. Up to now, it has been captured the eating habits of 6 patients with diabetes mellitus type 1 , between 27-54 years old , two women and four men .

TABLE 5.1: Patients' basic information(1)

Sex	**Age**	**Weight(kg)**	**Height(m)**
F	27	74	1,55
M	54	88	1,84
F	45	70	1,73
M	47	92	1,89
M	45	86	1,85
M	35	102	1,92

TABLE 5.2: Patients' basic information(2)

Sex	**BMI**	**Total insulin dose (AVG)**	**HBA1c**
F	30,8	41,1	80
M	25,99	47,2	39
F	23,39	43,2	96
M	25,76	43,6	64
M	25	40	59
M	27,6	53	59

TABLE 5.3: Patients' basic information(3)

Sex	BMI	Complications
F	30,8	sumnik
M	25,9	no
F	23,3	Gastroparesis
M	25,6	Hypertension, hypercholesterolaemia, smoker
M	25,13	Hypothyreosis
M	27,67	no

5.1 Characterize patients according to their basic information

First of all, the patient is classified depending on the personal data and are characterized in order to figure out if they are obese or not (according to the BMI value). These are the basic calculations that we should do, plus BMR, TDEE and EER. These values are really important to be known in order to have one "first picture" of every patient.The calculation of BMR is according to the Harris-Benedict formula and the calculation of TDEE is according to the table 3.7. What is more, we can characterize patients' EER according to the table 3.8.

- patient No.1

TABLE 5.4: Patient no.1:(Information about BMI,BMR,TDDE(as sedentary motivate)

sex	F
BMI	30.8
BMR	1517 cals
TDEE(sedentary)	1821 cals

- patient No.2

TABLE 5.5: Patient no.2:(information about BMI,BMR,TDDE(as sedentary motivate))

sex	M
BMI	25,99
BMR	1824 cals
TDEE(sedentary)	2189 cals

- patient No.3

TABLE 5.6: Patient no.3:(Information about BMI,BMR,TDDE(as sedentary motivate))

sex	F
BMI	23,39
BMR	1426 cals
TDEE(sedentary)	1712 cals

- patient No.4

TABLE 5.7: Patient no.4:(Information about BMI,BMR,TDDE(as sedentary motivate))

sex	M
BMI	25,76
BMR	1951 cals
TDEE(sedentary)	2342 cals

- patient No.5

TABLE 5.8: Patient no.5:(Information about BMI,BMR,TDDE(as sedentary motivate))

sex	M
BMI	25,13
BMR	1863 cals
TDEE(sedentary)	2235 cals

- patient No.6

TABLE 5.9: Patient no.6:(Information about BMI,BMR,TDDE(as sedentary motivate))

sex	M
BMI	27,67
BMR	2185 cals
TDEE(sedentary)	2622 cals

According to the table 3.6 , we can summarize the results as below:

TABLE 5.10: Characterize patients

patient(sex)	**BMI**	**characterization**
F	30,8	moderately obese
M	25,99	overweight
F	23,39	normal(healthy weight)
M	25,76	overweight
M	25,13	overweight
M	27,67	overweight

As we can notice (diagram in figure 5.1) all men are overweight , the younger woman is (moderately) obese and only one woman has the normal (healthy) weight according to their personal data (e.g. age, sex, height and weight). This is not a satisfactory and positive fact if we consider that those people are T1DM patients and,as we explained before, one of the most vital factors in order to deal with this disease is to try to maintain in normal weight by control the food intake and by physical activity. So,why those people do not care about their good way of living?

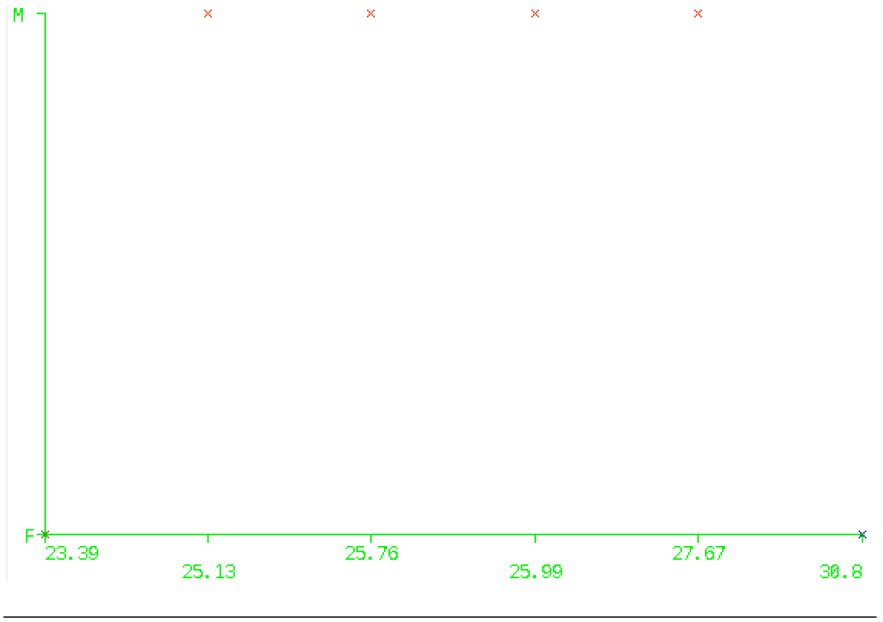


FIGURE 5.1: blue:moderately obese,red:overweight,green:normal(healthy weight). The graph shows how the patients are characterized depending on the sex and the BMI

One main problem is that they cannot calculate the cals of carbs that they eat in every meal , because it is a big deal generally to calculate them in the right way (we will discuss about it further) and it is known after many researches that carbs can "hide" in meals and food in a way that it is not so easy to recognize them (e.g. somebody would chose to drink milk (1,5% fat), but the difference between this and the whole milk is that in order to make the first one they add carbs instead of fat!). Examples like this, make the creation of a food KB very important in order to give patients the right instructions in order to avoid mistakes like this. What is more, it is well known that nowadays, people do not have enough time or they do not want to spend time to do exercises and activities mainly because of the bad modern west lifestyle but they cannot think how simple is to do some exercises without going to the gym. For example, they can choose to walk go their jobs instead of driving or taking trams,buses etc.,washing the dishes instead of using the dishwasher,wipe the floor instead of using vacuum cleaner,ride a bike or walk in the park ,go down the stairs instead of using the elevator and so on.We can see analytically, the cals that we can burn doing a variety of activities "outside" the gym (table 5.11).

As a result, it is very important to add all these information to the KB in order to suggest people and encourage them to do alternative activities in order to burn fat, maintain in normal weight and help them to manage the disease.Another useful statement is the avg BG levels (mmol/L) per month for every patient and how relatively is to BMI (which means how relatively is to the weight mainly)

TABLE 5.11: A variety of activities and calorie burn

description	calories per hour
walking at a moderate pace	287
vacuuming	193.7
dusting	173.6
painting	66
gardering,weeding	**287.8**
mopping floors	193.7
car washing	**234**
cleaning windows	180.3
ironing	113.1
shoveling snow	**400-600**

because,as we have already said, BG levels are affected by food and this is the main goal for every patient;how to manage the calories intake and BG levels.

As we can see in figure 5.2, avg BG levels are higher than the suggested and this situation is matched with the fact that most of the patients are overweighted. What is more, the first patient (female),who is characterized as obese, has the highest avg BG levels during one month.This is something expected according to the relationship between over weighted and BG levels. These assumptions reinforces the need to control the levels of glucose because,as mentioned,BG affects not only the quality of everyday life but also persistently high levels of glucose are responsible for the development of other diseases (high cholesterol, heart diseases etc.).

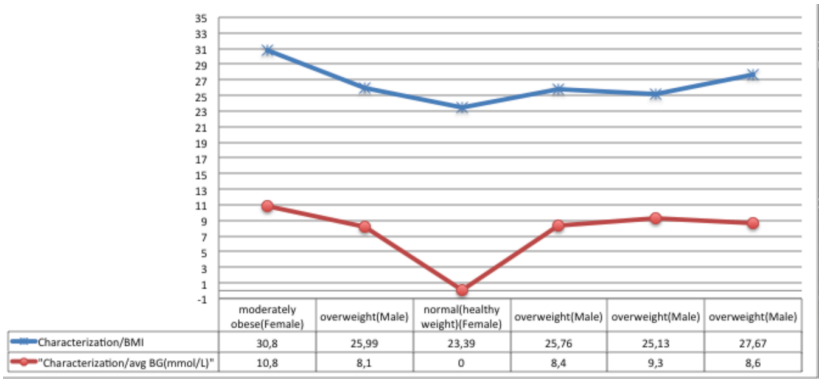


FIGURE 5.2: Comparison between avg Blood Glucose(BG) levels and Body Mass index(BMI),(∗ 0 point means that we do not have data about the patient's avg BG levels)

5.2 Food,calories intake and further analysis

In the following, we will try to examine food that was consumed by the patient and their effect on glucose levels in blood. We will study three different meals separately,breakfast,lunch and dinner and we will define the proper hours for these meals. Except for the portion size of food it is important to consume that at appropriate times because those habbits have great effect on metabolism.It is undeniable that calories play the most important role in the diet, but should be careful and times we eat every meal of the day. The time we eat affects our metabolism and accordingly regulates hunger. The control of the body weight is the result of three factors that regulate metabolism: brain, hormones and neurotransmitters, and metabolism. If any of these three factors trigger the feeling of hunger during the day, the metabolism slows down, the cravings are intensified and effort for weight loss falls on deaf ears. First, we must start our day with a good breakfast. Nutritionists recommend even to eat breakfast up to an hour after awakening, but not later. Thus, the metabolism goes into operation and our body realizes that it needs to save energy by storing calories. As we wait to eat breakfast, so slow to start, and the burning of calories.should not intervene more than three hours until the next meal or snack. This will maintain balance in the blood glucose levels and will not "run out" of energy.With decreasing daylight, both must be reduced and the calories we consume.The evening meal should not be consumed after 8 pm, to achieve the desired results. Our metabolism begins to slow down from 4 in the afternoon and the approaching bedtime.If you take several hours from the evening to sleep, you should choose fruits or a hearty and simultaneously light snack such as yogurt and nuts.In order to do this study we will use the WEKA program.Waikato Environment for Knowledge Analysis (Weka) is a popular suite of machine learning software written in Java, developed at the University of Waikato, New Zealand. It is free software licensed under the GNU General Public License.[30]

(a) Breakfast (around 6am - 9am)

We will present the food consumed by patients in these hours (6am-9am) as breakfast and their effect on glucose levels. ?he first to consider is how many times the consumption of meals leads to elevated glucose levels more than the regular (10 mmol/L). In figure 5.3 we can see that most of the times, after breakfast, the BG levels are less than 10 mmol/L and the predominate price is equal to 4.9 mmol/L but it is noteworthy to mention that in many cases the meals increased the BG levels (predominate price is 10.6 mmol/L).

In figure 5.4 we examine several breakfast meals (e.g. apple pie, coffee,tea, etc.) and their content of calories of carbs.Breakfast is the most important

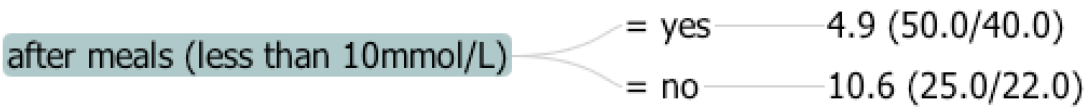


FIGURE 5.3: Estimate how many times the BG levels after breakfast are less than 10 mmol/L

meal of the day. After hours of nocturnal sleep, a correct and balanced breakfast provides our body with the necessary energy for a good start. As we have mentioned the breakfast should be the 20% of the daily EER and if we suppose that usually the EER for an adult is equal to 2,000 total calories , we can calculate the need in carbs as:

$$2,000 * 0.2 = 400 \; total \; calories$$

$$400 * 0.4 = 160 \; cals \; of \; carbs$$

After that, we can see that mostly patients consumed less than 320 cals of carbs which is something very encouraging in the control of carbohydrate intake and especially during breakfast where there is enough time in the rest of day to metabolize and burn those calories.

In figure 5.5 we examine the relationship between the calories of carbs and the BG levels in order to clarify the importance of controlling the carbs that we assume.We have already mentioned that after the meals, the BG levels must be less than 10 mmol/L (but not less than 4,9 mmol/L,this leads to hypoglycemia) and it is obvious that,in most cases,when the cals of carbs are <160 the BG levels are regular.Although, in some cases , the cals of carbs are less than 160 but the BG levels are more than 10 mmol/L and in this cases the patient should suggested to do exercise.

(b) Lunch (around 1pm)

We will present the food consumed by patients in these hours (around 1pm) as lunch and their effect on glucose levels.The first to consider is how many times the consumption of meals lead to elevated glucose levels more than the regular (10 mmol/L). In figure 5.6 we can see that most of the times, after breakfast, the BG levels are less than 10 mmol/L and the predominate price is equal to 7.8 mmol/L but it is noteworthy to mention that in many cases the meals increased the BG levels (predominate price is 11 mmol/L).

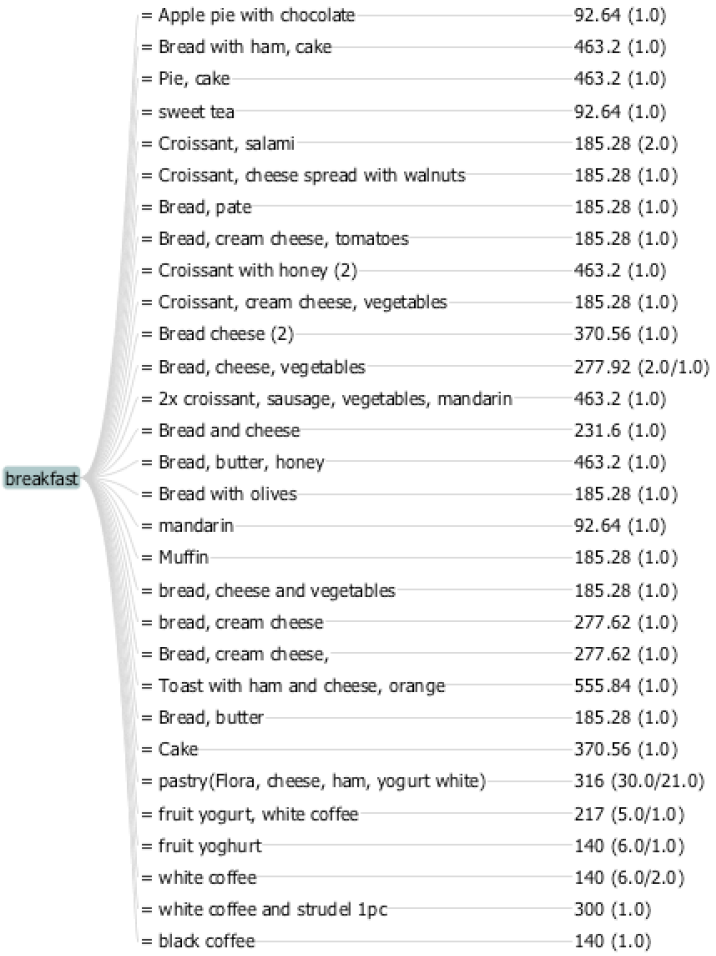


FIGURE 5.4: Several breakfast meals and cals of carbs

In figure 5.7 we examine several lunch meals (e.g. soup,breads,pasta etc.) and their content of calories of carbs.As we have mentioned the breakfast should be the 20% of the daily EER and if we suppose that usually the EER for an adult is equal to 2,000 total calories , we can calculate the need in carbs as:

$$2,000 * 0.2 = 400 \; total \; calories$$

$$400 * 0.4 = 160 \; cals \; of \; carbs$$

In figure 5.8 we examine the relationship between the calories of carbs and the BG levels in order to clarify the importance of controlling the carbs that we assume.We have already mentioned that after the meals, the BG levels must be less than 10 mmol/L (but not less than 4,9 mmol/L,this leads to hypoglycemia) and it is obvious that when the cals of carbs are < 160 the BG levels are regular.Although, in some cases , the cals of carbs are less than 160 but the BG levels are more than 10 mmol/L and in this cases the patient

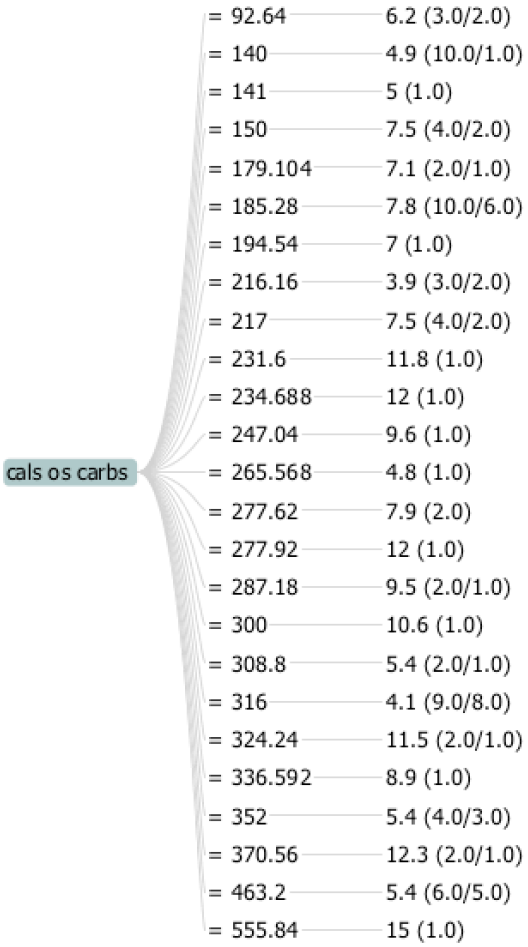


FIGURE 5.5: Cals of carbs and BG levels after breakfast meals

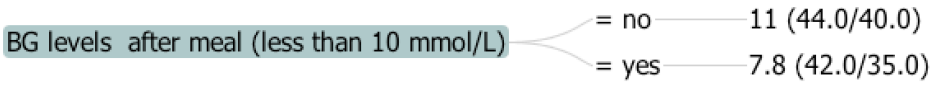


FIGURE 5.6: Estimate how many times the BG levels after lunch are less than 10 mmol/L

FIGURE 5.7: Several lunch meals and cals of carbs

should suggested to do exercise.The disappointing situation is that patients consumed mainly more than 160 cals of carbs (during lunch) and this leaded to high BG levels.Patients should recommended to exercise or do alternative activities and handle properly the insulin pumbs.

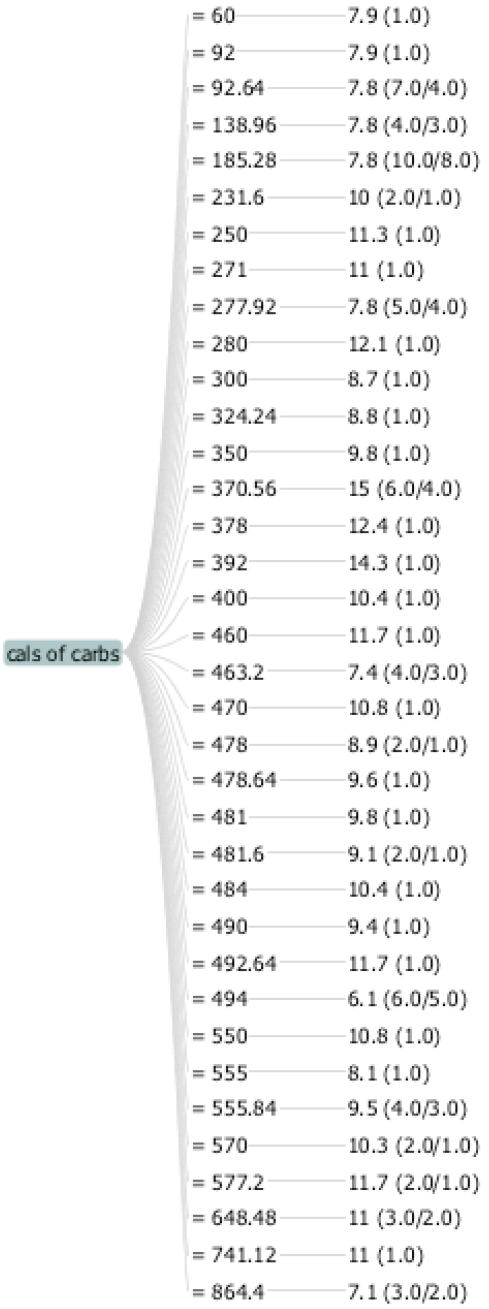


FIGURE 5.8: Cals of carbs and BG levels after lunch meals

The consumption of vegetables and fruits is remarkably reduced and is another useful suggestion to all patients because if they could replace the carbs (e.g potatoes,rice,pasta etc.) with vegetables the cals of carbs could reduced

(as the BG levels). Fruits and vegetables contain vitamins, fiber, minerals and thousands of other active substances when offered together in the body, acting in synergy and promote our health, significantly reducing the risk of various diseases.Vegetables are one of the six food groups. Classified into various categories depending on their color, their carbohydrate content, their usefulness, their content of vitamins A and C.The vegetables we can consume fresh, frozen, canned, dried or in juice form.The value of the vegetables with respect to the efficiency of energy is very small (10-15 kcal / 100 gr.). Almost all vegetables contain no fat and no cholesterol.What is more, vegetables are considered an important source of vitamins A, C and folic acid, minerals and fiber.

(c) Dinner (around 7pm - 9pm)

We will present the food consumed by patients in these hours (around 1pm) as dinner and their effect on glucose levels.?he first to consider is how many times the consumption of meals leads to elevated glucose levels more than the regular (10 mmol/L). In figure 5.9 we can see that most of the times, after dinner, the BG levels are less than 10 mmol/L and the predominate price is equal to 7.8 mmol/L but it is noteworthy to mention that in many cases the meals increased the BG levels (predominate price is 15 mmol/L).

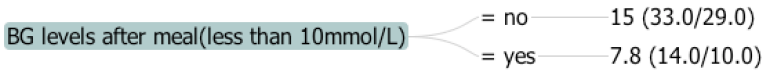


FIGURE 5.9: Estimate how many times the BG levels after dinner are less than 10 mmol/L

In figure 5.10 we examine several dinner meals (e.g. soup,breads,pasta etc.) and their content of calories of carbs.As we have mentioned the dinner should be the 40% of the daily EER and if we suppose that usually the EER for an adult is equal to 2,000 total calories , we can calculate the need in carbs as:

$$2,000 * 0.4 = 800 \; total \; calories$$

$$800 * 0.4 = 320 \; cals \; of \; carbs$$

In figure 5.11 we examine the relationship between the calories of carbs and the BG levels in order to clarify the importance of controlling the carbs that we assume.Dinner is the last meal of the day and very vital for our health.

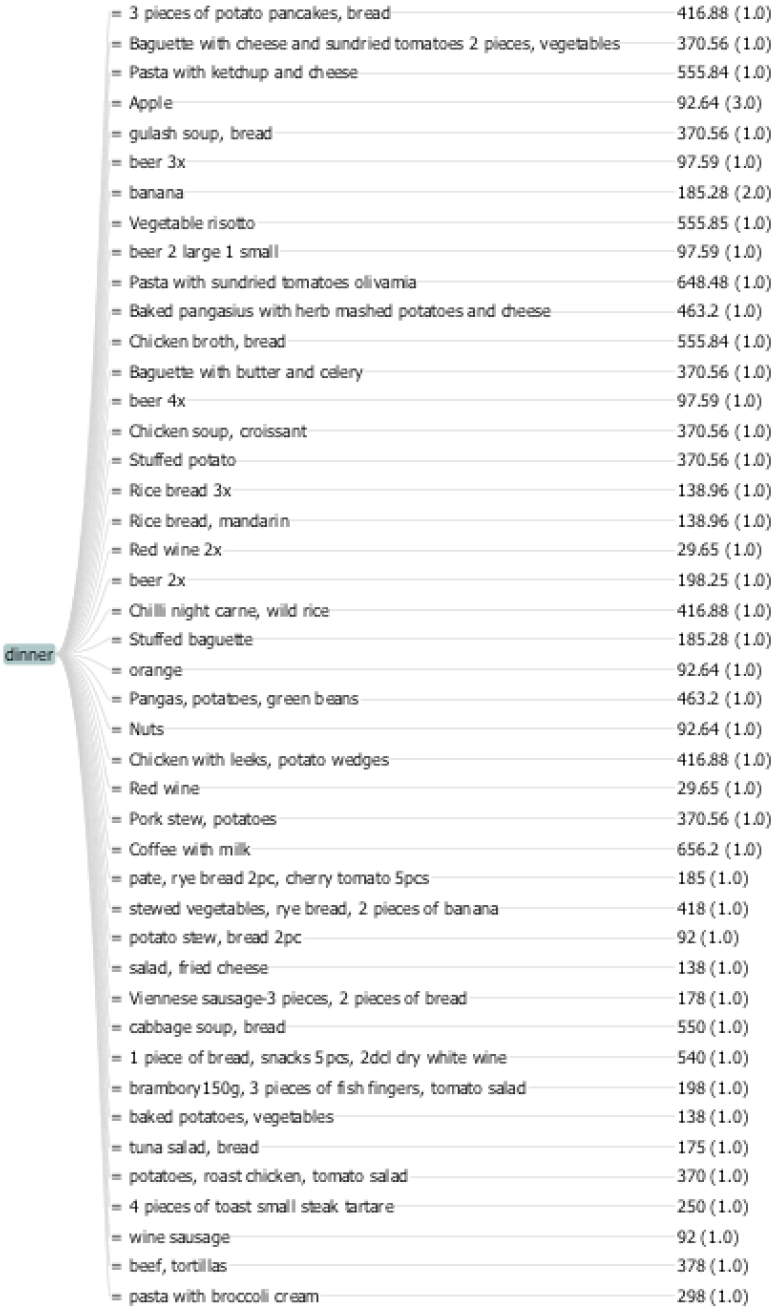


FIGURE 5.10: Several dinner meals and cals of carbs

After many studies, there is an increased incidence of obesity and diabetes in people who work during night hours and those who have deregulated biological clock because of abnormal sleep patterns.Human body metabolizes the food in a lower rate than during the rest of the day so we have to be careful of what we are having as dinner and eat the last meal 3-4 hours before going to sleep.

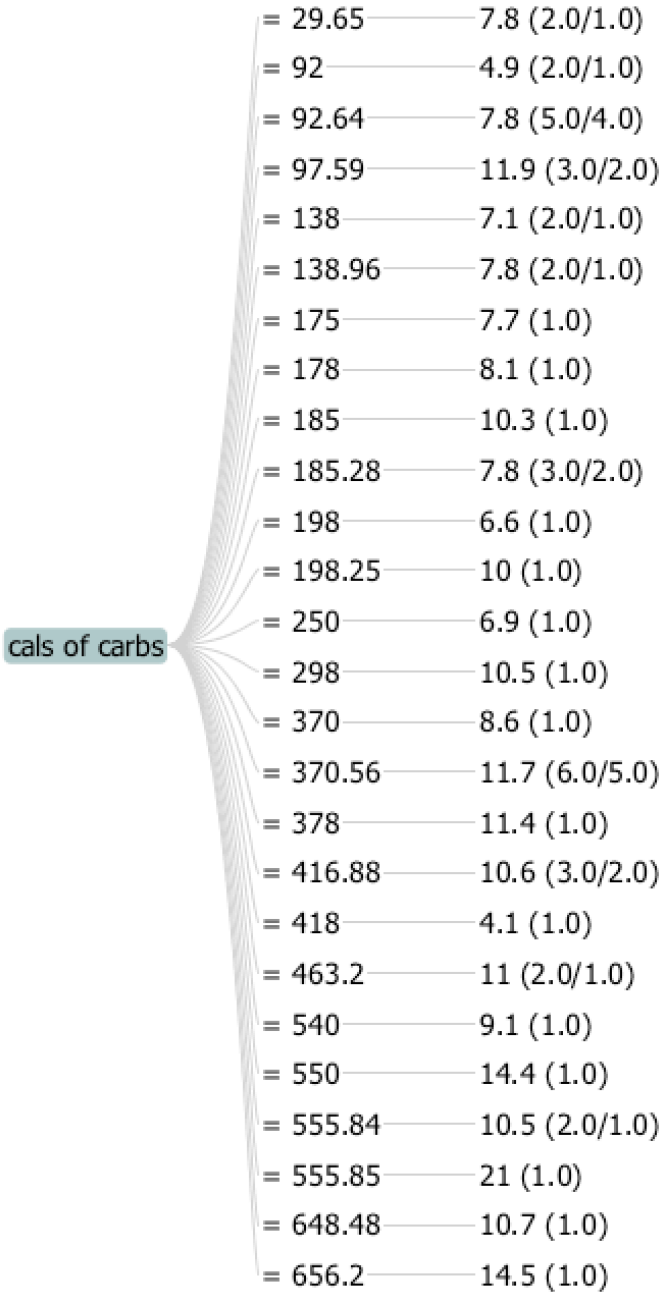


FIGURE 5.11: Cals of carbs and BG levels after dinner meals

To sum up, it is vital to make combinations of proteins and complex carbohydrates. Carbohydrates are broken down quickly into glucose, which the body uses to get energy through insulin. So if you eat a meal rich in carbohydrates and low in protein, your body will be stimulated for a while by the sharp rise in blood sugar levels, but then once levels start to fall, you will feel again tired and hungry. For this, add protein to this meal, so the glucose absorbed from the intestine and released into the bloodstream more slowly. That is why a seemingly "sinner" toast with ham will keep you fuller for longer than the innocent wholegrain cereals and juice. Dieticians recommend the consumption of 3 meals and 2 snacks per day and always take breakfast within one hour from the time you wake up, to keep glucose levels stable. It is also useful to combine foods from all food groups and eat every 2-3 hours.

5.3 Physical activities

For decades it has been accepted that exercise is an integral part of the treatment of diabetes. Recently, studies have confirmed the value of increased physical activity, after showing the benefits of exercise in diabetic person. Therefore, all diabetics should be informed and agree that regular physical activity and exercise is a key part of their treatment. Physical activity can help people with diabetes to achieve many goals, such as improving their physical fitness, increased energy, reduce price of their blood sugar by improving the action of their endogenous insulin, improving the lipid profile and achieving and maintaining weight loss. Today, it is generally accepted that regular aerobic or anaerobic exercise results in a significant improvement in glycemic control in adults with type 2 diabetes.Exercise lasting at least eight weeks, has been shown to reduce HBA1c by an average of 0.7% in people with type 2 diabetes, even if the change in body weight is not significant. Last, it proved that moderate to high physical activity levels are associated with a significant reduction in morbidity and mortality in both men and women with type 2 diabetes.

Generally, that patients do not spend much time on doing activities and gymnastics.This is something that we expected,as we explained in previous chapter, because western lifestyle supports sedentary lifestyle.The people waste many hours in the office because of their job and after that they do not have enough time for their personal life.It is important to understand how we can help our body to facing DM and in generally. In table 5.12 the most remarkable statement is that the second patient wh? recorded activities (e.g. cooking,cleaning the house,washing,ironing etc) every day during one month is the only one patient with healthy weight and

TABLE 5.12: Several activities(*the patient did not exercise),(**there are no data about activities)

Activities	**patient(sex)**	**activities/30 days**	**BMI characterize**
weekend trips	F	10	moderately obese
ride a bike	M	25	overweight
shopping	F	30	normal(healthy weight)
walking	M	0*	overweight
playing tennis	M	5	overweight
swimming	M	0**	overweight
washing windows			
cooking			
family celebrations			
cleaning house			
christmas decoration			
planting			
ironing			

also the lowest avg BG levels (during one month) as we can see in table 5.13.It is among the most accurate example to show practically that the disease can be controlled with the increase in activities.

TABLE 5.13: Patients and avg BG levels(mmol/L)

Patient(sex)	**avg BG levels(mmol/L))**
F	10,8
M	8,1
F	7,9
M	8,4
M	9,6
M	8,6

Chapter 6

Data Quality

After several surveys , some of the most indicative ways to record food data is to take photos before and after the meals, use proper rulers or text/voice records in order to clarify the portion size or the kind food or drink (such as the type of bread or the the kind of beer) . The sample of patients examined through those ways in order to estimate whether they have managed to record properly their eating habits or not and give a good justification to search for better ways to record data.Firstly,we can notice that women (table 6.1) are proofed to be more active on taking pictures than men, although conversely the age seems to play no role in that point.

TABLE 6.1: Characterize patients

patient(sex)	**use of rulers**	**%percent**
F	59/167	35,3
F	39/70	55,7
M	14/163	8,55
M	13/163	7,9
M	60/178	33,7
M	16/117	13,6

- The usefulness of the ruler.

  Obviously, the first factor than can plays a vital role to the best estimation of portion sizes is the ruler. What can patients use as a ruler and in which way?

  Apart from the rulers (figure 6.1) plus scales are often more handy and suggested to patients to use spoons, forks or knives and in some cases pens or pencils.We will initially examine the sample of patients on the use of rulers of all kind in order to discuss the results and notice the advantages and disadvantages of using them.What is more, after the examination we will present some better ways to improve pictures by using rulers.

FIGURE 6.1: Common ruler

TABLE 6.2: How often patients used rulers

patient	photos	use of rulers
1	167	59
2	163	14
3	70	39
4	163	13
5	178	60
6	117	16

The first thing that is easily noticeable is that the use of rulers according to the total registered meals is significantly reduced . What is more, there are many examples that shown the use of spoons, knives and forks as rulers as well as pen and pencils.Another fact is that patients prefer to use spoons,knives and forks plus pens than rulers. Addittionaly, it is very important for patients to realize the importance of recording the data properly in order to help themselves but at the same time , support other patients all over the world. As a result , we can present some disappointing examples and how to improve them. What is more , we can suggest the use of scale as another alternative way of reference ruler.In Figure 6.2,the patient decided to use a knife as a ruler,but fist of all it is not obvious what the patient wanted to measure so the first suggestion is to measure separately the ingredients and in different photos to help scientists to make conclusions. Additionally, it is not convenient to use knives (or spoons and forks) because there are many kinds and different scales .It is better to use a common rule,as in the Figure 6.1.It is remarkable that no patient used this ruler. In Figure 6.3,the patient decided to use a pen and a little spoon as rulers but it is clear the fact that this decision does not lead to the right estimations and cannot help the process of data analysis.Except that it would be much better to use a common ruler as previously, it is also important to take more photos in order to estimate them separately and

maybe,in the case of yogurt is better to use a common scale such as this in Figure 6.5.

FIGURE 6.2: The patient used a knife as a ruler

FIGURE 6.3: The patient used a pen as a ruler

FIGURE 6.4: Using a pencil as a ruler

- Photos before and after meals.

  The fact is that there is only two records from only one patient that can show picture of the meal before and after , as we can see in Figure 6.6 and 6.7.Diabetes mellitus (in both cases, type 1 and 2) is a disease that is affected mainly by the food and the nutrition plus the portion size. As a result,it would be really helpful to scientists to know exactly the amount of food is consumed from patients.

FIGURE 6.5: Scale as a ruler

FIGURE 6.6: Meal before consumed

FIGURE 6.7: Meal after consumed

Another important factor is to suggest the patients to take photos in such a way so as to provide as many information as possible.For example,images that show the size of a slice of bread or including the packages of food with useful details.

As we can notice in figure 6.8 the patient took pictures in such a way that we can clarify the size of the slice of bread and details about ham and cheese (written in the packages) ,so as in figure 6.9 we can see details about the yogurt(e.g grams,ingredients etc.).On the other hand, in figure 6.10 the picture is not so analytical and defective because we can not estimate the size of the slices and the patient included small pieces of cheese but with the whole package.

FIGURE 6.8: Meals included many details and pictures are taken in a useful point of view(1)

- Text and voice records.

  According to studies , another supportive factor would be to recommend patients not only to write down details about the meals but also tape record them which is easier especially nowadays due to smartphones and applications which are really friendly to users. In our sample , we did not found examples of tape record only text records, but we will present some not satisfactory examples and recommendations for better registers . In the case of food and drinks, unfortunately, images are not enough. It is vital to know some other information such as type of food , ingredients that we can not recognize or type of drinks. Another issue is that one of the patients did not record details and in this case it is really difficult to estimate portion sizes or to know

FIGURE 6.9: Meals included many details and pictures are taken in a useful point of view(2)

FIGURE 6.10: Meals with not so many details

the ingredients of a soup for example.We will further analyze , despite the quantity of data, the quality of them which is in some circumstances more important through some examples.

In Figure 6.11, we can see the picture of the meal, but there is lack of information.The patient had to refer the type of pasta, the way of cooking (bake, boil, fry,roast etc) and for how long . After investigation, it is a fact that the less you boil pasta the less starch and carbs are released.

FIGURE 6.11: Pasta with broccoli

In Figure 6.12, we can see the picture of a drink, but in order to build a useful database it is really vital to know the type of beer (blonde,brown,dark etc.) as we can see in figure 6.13.

FIGURE 6.12: Beer as a drink

Bread is one of the most common eating habits for everybody , but there are so many types that we have to be really careful if we want to manage the cals of carbs intake and deal with the diabetes mellitus. 6.14. In figure 6.15, we can see the different kinds of bread and the differences between them on how many cals of carbs they contain.

Top-Selling Beers	Calories Per 12-oz. Serving	Alcohol Content	Carbs (in grams)
Bud Light	110	4.2%	6.6
Coors Light	102	4.2%	5
Budweiser	145	5.0%	10.6
Miller Lite	96	4.2%	3.2
Natural Light	95	4.2%	3.2
Corona	148	4.6%	13
Busch Light	95	4.1%	3.2
Busch	122	4.6%	7.5
Miller High Life	143	4.7%	13.1

FIGURE 6.13: Different types of beer and cals of carbs

FIGURE 6.14: Different kind of breads

TYPE OF BREAD	CALORIES	TOTAL FAT (G)	SODIUM (MG)	CARBS (G)	FIBER (G)	SUGARS (G)	PROTEIN (G)
2 slices white bread	220	2	380	44	4	4	8
2 slices wheat bread	220	2	340	38	6	4	10
2 slices dark rye bread	320	0	640	68	4	0	12
2 slices marble rye bread	320	0	600	68	4	0	12
Whole wheat sandwich thin	100	1.5	170	19	5	3	6
Ciabatta roll	250	2.5	730	48	2	2	9
Kaiser roll	200	2.5	370	37	1	6	7
Wheat dinner roll	76	1.8	95	12.9	1.1	0.5	2.4

FIGURE 6.15: Different kind of breads and cals of carbs

To sum up , through a short analysis and with few data for processing and inference,the important role of qualitatively data is obviously one of the most vital factors and there are still many improvements in order to gain the best results .It is very claimantly to ask from patients to withstand with all these details that scientists need to analyze end export researches and they have to concern about the improvement of their lives. The first goal after this research is to give patients the right instructions in order to be able to keep useful notes and help the development of a strong Knowledge Base (KB).

Chapter 7

Conclusions

This study attempting to describe the disease and the relationship with the diet and exercise in order to make clear the benefits of a more balanced diet and exercise in addition to western life standards.The expert systems are developed in order to contribute to the support of patients with diabetes type 2,however, the present study is more a first pilot study in order to clarify the best way to collect data from patients highlighting all the problems resulting from the first analyzes and examinations.

The first estimates after the connection of the meal with the glucose levels shows the great need to consult patients about the correct way to combine food and to integrate gymnastics and activities in their everyday lives.These instructions would help patients to manage the disease and will inspire the prevention of it against the sedentary lifestyle that promote from the western society,mainly.

The first goal after this research is to improve the quality of the data (giving right and useful instructions to the patients) in order to build a strong knowledge base and make the system able to predict the blood glucose levels after a meal.Moreover, it is useful to use accelerometers in order to calculate the energy and the calories burning after doing an activity.

This study,though is in its beginning stage,promises to give many new features and to help effectively to face the DM and why no to give inspirations to another studies.

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