# M.S. Thesis

2019

# CLINICAL DECISION MAKING SYSTEM FOR EARLY DIAGNOSIS OF TYPES OF SMA DISEASE

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IŞIK UNIVERSITY 2019

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Submitted to the Graduate School of Science and Engineering in partial fulfillment of the requirements for the degree of Master of Science in Information Technologies

> IŞIK UNIVERSITY 2019

# IŞIK UNIVERSITY GRADUATE SCHOOL OF SCIENCE AND ENGINEERING PROGRAM OF INFORMATION TECHNOLOGIES

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# CLINICAL DECISION MAKING SYSTEM FOR EARLY DIAGNOSIS OF TYPES OF SMA DISEASE

## Abstract

Spinal muscular atrophy (SMA) is a strict neuromuscular disease that is the most common in infancy, and the third one among young people under 18 years. Diagnose of this diseases can be delayed because symptoms of them can be confused with another diseases. Thus life quality of patient has reduced. Meanwhile, with progression of disease treatment has gotten hard. After diagnose, disease can be treated with different methods such as treatment with medicine, care closely. Applications that conducive early diagnose such as decision making system has recruitted to wipe diseases out.

My project is a decision making system that shows us to probability of diseases when patients symptoms are entered to the system. It consist of a software system and Excel tables that keeping data and doing mathematical operations. Thanks to this, diagnose process has gotten shorter and it enables to early diagnose.

Main focus on my project is to gather maximum number of data that I can obtain and giving of program to the most correctly results. Doctor who uses it has logged in ID number of patient to interface, this file saved with named this ID number. Then age and gender informations are entered and main screen which consist of symptoms has come. Doctor can choose the symptoms of patient easily. After that, according to this symptoms probability of diseases are showed on the screen.

#### Keywords: Spinal muscular atrophy (SMA), diagnosis, application

# KLİNİK KARAR SİSTEMİ İLE SMA HASTALIĞININ TİPLERİNİN ERKEN TEŞHİSİ

# Özet

Spinal Müsküler Atrofi (SMA) hastalığı, spinal kordda bir yıkım nedeniyle oluşur ve motor nöronlar motor nöronları etkilemektedir. SMA dört tip olarak görülür ve en tehlikeli tip Tip 1'dir. SMA hastalıklarının belirtileri çocuklarda görülür. Yutma, nefes almada zorluk, zayıflık, desteksiz oturamama ve yürüyememe belirtileri ile tanısı konulduktan sonra ilaçlı tedavi alan hastaya nitelikli yaşam sunulmaktadır.

Tezimde, geliştirilen karar verme sistemi ile hastanın belirtileri sisteme girildiğinde hastalık tiplerinin oranları verilerek hastanın hangi tip hastalığa yakın olduğu ön görülür. Böylece tanı süresi kısa kısaltılarak erken tedavinin önü açılmış olur.

Bu projedeki odak noktam, maksimum hasta verisi toplayarak geliştirilen sistem ile hastalığa yakalanma olasılığını yüksek doğrulukta göstermektir. Sistemi kullanan doktor hastanın bilgilerini girer ve hasta verileri kayıt edilmiş olur. Sonra yaş verileri ve belittileri kolayca girilir. Belirtilere göre, hastanın SMA olma olasılığı, gösterilen sistem tarafından hesaplanır. SMA sonucu için optimum bir sayısal değer belirlenir. SMA'nın sistemde hesaplanması olasılığı, kontrol edilen nümerik değerin üzerinde veya altında olarak kontrol edilir. Sonuçlara göre hastalar üzerinde muayeneler yapılabilir.

Anahtar kelimeler: SMA hastalığı, SMA tipleri, belirtiler, karar sistemi

# Acknowledgements

First of all, I thank Çiğdem Gülsüm Çavdaroğlu who my project supervisor to work with us. Through all interest and teaching I gained new point of view to in my research.

Many thanks to hospital, association for supporting by giving information about SMA disease.

I would like to thank a doctor for my interview about SMA disease by answering my questions allowing time for me. Besides, I thank managers who are Mehmet Nuri Nasliç in Borda Technology, Mustafa Durna to provide me to make interview with my valuable mentioned doctors. And thanks to people who can go out although fight against SMA to respond my short questions.

The last, I thank a lot to Çağla Somuncu, Buğra Öner, Can Erhan, Muhittin Demirboğa for valuable ideas and to manage my needs on my subject, methods and software part. And my parents, thanks a lot for your patient deeply.

To All SMA Patients And Companions...

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# List of Abbreviations

$\mathbf{SMA}$	$\mathbf{S}$ pinal Muscular Atrophy	
$\mathbf{CNS}$	Central Nervous System	
PNS	$\mathbf{P} eripheral \ \mathbf{N} ervous \ \mathbf{S} ystem$	
$\mathbf{MS}$	$\mathbf{M} ultiple \ \mathbf{S} clerosis$	
ALS	$\mathbf{A} myotrophic \ \mathbf{L} ateral \ \mathbf{S} clerosis$	
FDA	${\bf F}{\rm ood}$ and ${\bf D}{\rm rug}$ ${\bf A}{\rm dministration}$	

# Chapter 1

# Introduction

SMA (Spinal Muscular Atrophy, Loose Infant Syndrome) is a genetic disease of the nerves of the spinal cord. It is occurred because of destruction of the nerves system. The pathological sign of SMA is degeneration of the lower muscle neurons at the head, leading to progressive denervation of the skeletal muscle, atrophy of the proximal muscles, and paralysis there.

The treatment of SMA disease has not been found but the progression of the disease can be slowed down by the use of the FDA approved a drug which name is "Nusinersen". The definitive solution is to control the carriage of the SMA gene for the couples to be married.

SMA disease is seen as 4 types. Type 4 is a mild form of SMA disease that occurs in adults. But it cannot be necessary to examine it, the problems are similar.

The other 3 types are separated by function [1].

- 1. Unable to sit Never sit (0-6 months old) Age of death <2
- 2. Able to sit Never stand (7-18 months) Age of death > 2
- 3. Able to Walk Stands and walks (> 18 months) Age of death is a dult

Physicians confronted with children experiencing hypotonia and weakness should develop a high rate of suspicion for the diagnosis of SMA. The frequency is 8-11 per 100.000 live births but one person over 35/50 carries its autosomal recessive gene [2]. To put this suspicion into a numerical data by using the algorithm that I will create based on complaints or findings. In this way, it is necessary to provide rapid diagnosis of SMA disease caused by wrong marriages. With the early diagnosis I will be carried out by taking the respiratory, digestive and excretory functions, physiological functions and care methods of people with SMA patients. Thus, the life of SMA patients can be prolonged and the quality of life may be increased.

My project is a decision making system that includes software system and interface. Probability distribution is calculated with combining of mathematical operations and demographic data of patient that are entered into the system and symptoms of patient. In this way diagnosing process gets easy and speed up.

In the process, I recognized the lack of knowledge of doctors about the diseases. Then, I decided to generate a project to get easy the process of their treatment and to save their life.

After my studies about this decision making system, I realised that this project can make easier doctors and patient decision process. When this decision making system is combined and expanded with other diseases, important developments will be happened in health sector.

# Chapter 2

## Literature Survey

#### 2.1 Nervous System

The nervous system is a special group of cells known as the nervous system and neurons that transmit signals between different regions of the body. Basicly electrical connection of electricity. It controls both voluntary movement (conscious movement) and external movements (breathing) and sends signals to different regions of the sector. The central nervous system includes the brain and spinal cord. The peripheral nervous system is central to other parts of the body. As a structure, the nervous system is seperated as two parts whic are the central nervous system and the peripheral nervous system. According to the National Institutes of Health, the central nervous system is composed of spinal cord and nerves. The peripheral nervous system was composed of sensory neurons, ganglions (neuron clusters), and nerves bound together at the central nerve center. Functionally, the nervous system features two main subpart which are somatic or voluntary selection; and autonomic or involuntary part [1]. (2.1) shows the nervous system of human body.

#### Nervous System:

- 1. Central Nervous System
- 2. Peripheral Nervous System
  - (a) Somatic

- (b) Autonomous
  - i. Sympathetic
  - ii. Parasympathetic

#### 2.1.1 Central nervous systems (CNS)

The system that manages the body, the cells, organs and systems that work together and provide regular work, responding to stimulation from the environment, internal organs or muscles, mind, intelligence, thinking, learning, speech, writing, memory, walking, such as the system that enables the realization of voluntary movements are called the centralized system. The central nervous system consists of billions of neurons. The nerves from the brain and spinal cord are distributed throughout the body, including eyes, lips, teeth, and fingertips. The central nervous system includes mainly of two parts which are the brain and the spinal cord. The cerebellum and spinal cord are the parts of the brain [1]. There are four organs in the central nervous system for this reason as brain, cerebellum, spinal cord and spinal bulb.

In neurology, the term motor neuron classifies nerve cells (neurons) in the central nervous system and controls the muscles directly or indirectly. Axons in the CNS transmit the information to other nerve cells. Motor neurons transmit signals from the spinal cord to the muscles to perform the movement [1].

#### 2.1.2 Peripheral nervous system

It is the peripheral nervous system that receives the warnings from the environment, internal organs or muscles, transmits these warnings to the central nervous system, transmits the response of the central nervous system to the incoming stimuli to the muscles or organs, and provides the transmission between the organs and muscles in the body and the central nervous system. The peripheral nervous system is composed of nerves that are formed by the connection of neurons and that surround the body as a network. The nerves that make up the peripheral nervous system exit from the brain and spinal cord and go to the muscles and organs in the body [1].

#### Nervous systems that may affects systems are [1]:

- 1. Immune System
- 2. Muscle System: The body's muscles, movement, blood flow and other bodily functions, which consists of approximately 650 metaphors. There are three types of muscles which are the skeletal muscle that is attached to the bone and provide the free movement, the smooth muscle that is inside the organs and provide to move the substances between the organs and the heart muscle that is inside the heart and helps to pump the blood.
- 3. Respiratory System
- 4. Skeletal System
- 5. Urinary System

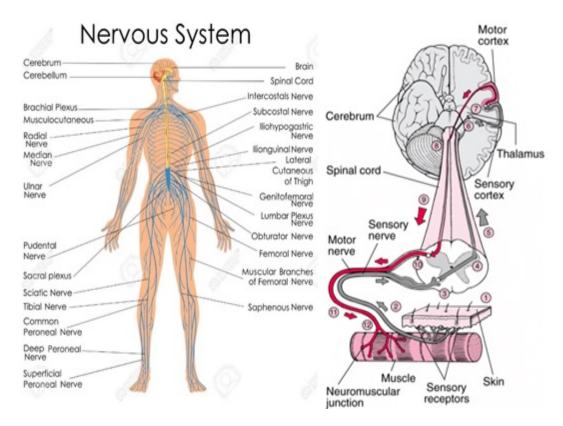


Figure 2.1: Nervous System of Human Body [3].

# Brain [4][5]:

It is called an organ between two skull bones, consisting of two hemispheres, the outer surface of which is protruding and a protective membrane on the outer surface and consisting of billions of neurons. The cerebellum and spinal cord bulb are the sections of the brain

# Function of the Brain [4][5]:

Performs voluntary movements. Learning, memory, imagination, thinking, memory, evaluation, perception, writing, reading, speaking.

- It evaluates the stimuli from the five sensory organs (eyes, ears, nose, tongue, skin), reacts and the centers of the five sensory organs (centers of vision, hearing, smell, taste, feeling) are here.
- Manages and controls the body with the help of other organs of the central nervous system.

- It allows the body to move. (It orders the muscles to move the body).
- Adjusts blood pressure and body temperature.

# Cerebellum [4][5]:

In the posterior and lower part of the brain, between the brain and the spinal cord, is composed of two hemispheres, the outer surface is folded and covered with a protective membrane, the so-called small brain called cerebellum or tree of life.

## Function of the Cerebellum [4][5]:

- It provides the balance of the body with the semicircle channels in the ear. (Evaluates the information coming from the semicircle channels.).
- Ensures balanced and regular working of the muscles in the body and ensures the movements are balanced.

## Spinal Bulb [4][5]:

At the back and bottom of the brain, the organa is called the spinal bulb, located between the brain and the spinal cord, covered with a flat and protective membrane.

## Function of spinal bulb [4][5]:

- It provides the passage of excitations between brain and spinal cord (ie organs).
- It provides working of internal organs (heart, kidney, stomach, intestines, liver).
- It controls and controls activities such as breathing, swallowing, chewing, heartbeat, contraction, relaxation, sneezing, coughing and vomiting.
- Controls the operation of non-request systems (respiration, circulation, excretion, digestion).

# Spinal cord [4][5]:

In the spinal cord located in the spine of the spine, the spinal cord is called a spinal cord. The nerves that move from the organs in the body to the brain, from the brain to the organs pass through the spinal cord and these nerves are crossed in the spinal cord. The nerves from the right side of the body go to the left hemisphere of the brain, the nerves from the left of the body to the right hemisphere of the brain.

### Function of the spinal cord [4][5]:

- It enables the sudden movements, reflexes.
- It allows the passage of the nerves between the brain and the organs.
- It enables the realization and control of habit movements, ie, acquired reflexes with the brain.

#### 2.2 Nervous System Diseases

Epilepsy, caused by abnormal electrical discharge from the brain cells caused by seizures [6].

<u>Parkinson's disease</u> with progressive neuropathy affecting movement [6].

Multiple sclerosis (MS), in which the protective lining of the nerves is attacked by the body's immune system [6].

<u>Amyotrophic lateral sclerosis (ALS)</u>, also known as Lou Gehrig's disease, is a motor neuron disease that weakens the muscles and decreases physical function [6]. <u>Huntington's disease</u>, a hereditary condition that causes degeneration of nerve cells in the brain [6].

Alzheimer's disease, encompasses a wide range of diseases that affect mental functions, especially memory [6].

SMA (Spinal Muscular Atrophy)

#### 2.3 Effect To Economy

Most of research conducted shows that health status related with economical development. In societies which bring up to the mark to economical development, sources that reserved for health have increased and also health conscious is on the rise. Thus, development of health level accelerates economical development by the way of increased productivity. Developing of health level of most of societies affects development of country positively. In experimental studies about this subject, health affects economical growing positively. So experiments supports to connection between health and economy as well [7].

#### 2.3.1 Health Expenses

Inside of gross domestic product (GDP) rate of total health expense in Turkey is 7.7% in 2004 (2.2). This rate is very low than 8.9% which is average of OECD countries. Also Turkey just high than Republic of Korea, Slovak Republic, Poland, Mexico, Ireland, Czech Republic and Finland from inside of 30 OECD countries.

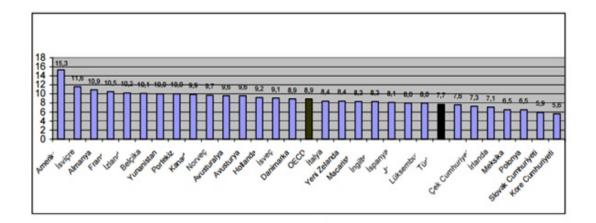


Figure 2.2: Proportion of health expense inside of gross domestic product (GDP).

Turkey is at the end of the list in terms of health expenses in all OECD countries (Per capita 580 USD) (2.3). Average of OECD countries is per capita 2550 USD. The countries that have the most health expense per capita are USA (6102 USD), Luxemburg (5089 USD) and Switzerland (4077 USD).

Annual growth rate of health expense per capita is higher in Turkey (8.6%) than OECD average (3.7%). This result is encouraging for our health sector.

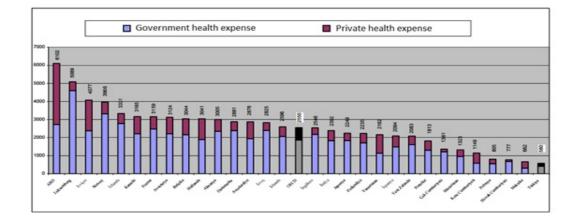


Figure 2.3: Health expense per capita[7].

Proportion of medicine expenses inside of total health expense of Turkey is 24.8% and this rate is higher than average of OECD (17.58%) according to 2004 data. The lowest medicine expenses are in Luxemburg (8.5%) and Denmark (9.4%). The highest medicine expenses are in Slovak Republic (38.5%) and Poland (29.6%)(2.4).

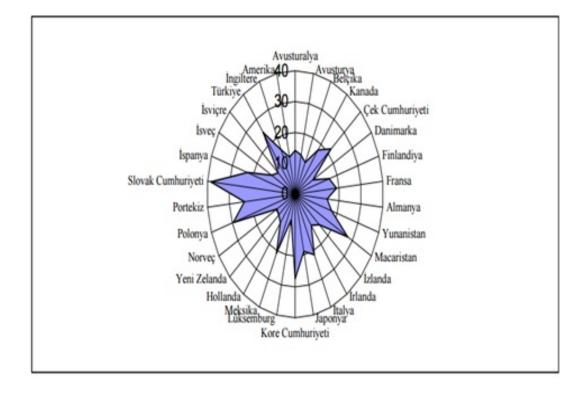


Figure 2.4: Rate of medicine expense of OECD countries inside of total health expense [7].

Medicine of Nusinersen Sodium for SMA disease is generally used. The price of the medicine (SPINRAZA 12 MG / 5 ML 1 VIAL) is 90.000 Euro and four doses are seen as sufficient for one year. It is calculated as more than 1 million TL annually.

#### 2.3.2 The Number of Patients Per Neurologist

In Turkey the least three cities in terms of number of doctor are Bayburt(74), Tunceli(86) and Ardahan(97) respectively; in Turkey the most three cities in terms of number of doctor are Istanbul(7.500), Ankara(5000) and Izmir(4000) respectively [8].

Turkey's records have known 2000 neurologists. Normally, a doctor should separate 20 minutes per a patient. However, this time is limited with few minutes due to insufficient number of doctors. A neurologist examines about 40 people a day, and look 40 people results. According doctor's interview, neurology, pediatrics and dermatology are the most common densities of the patients. In Ankara Training and Research Hospital, the number of patients in the neurology and dermatology clinics are 150, in the pediatric clinics number of patients are 200 and in the surgical clinics number of patients are 80 [8].

#### 2.4 Why Did We Prefer To Do Decision Support System?

As a result of my searches, I determined that diagnose of many diseases takes a long time because of health system in our country and early diagnosis even though it is very important - can't be done in many diseases. This led us to doing a thesis about support decision system. Furthermore another reason of prefering this subject is that I wanted to work on hospital system after graduated. There is 3 reasons of that I chose SMA diseases which are type 1, type 2 and type 3 out of all diseases :

- They are not common diseases
- Because of their symptoms, they can be confused with another diseases or unknown and can occur problems in diagnose.
- Doctors who are not neurologist have not enough knowledge about this diseases.

My support decision system will be easier to SMA types recognition and diagnose, and also it will be accelerate process.

#### 2.5 Decision Support System

#### 2.5.1 What Is Decision?

Decision that have focused on selection of the best option from a selection between two or more overlooked or possible options. Decision is proportional to produce information accurately and timely [9].

#### 2.5.2 How Are Decision Taken?

Recently, Making a decision has became complicated and process of making a decision was extended for each sector. I can substantiate as formless of hierarchy steps, uninformed or inexperience of staff.

#### 2.5.3 What is DSS?

Decision Support System (DSS) is the system to simplify of solving of complex problem and making a decision.

The main idea to reach with respect to data, information, knowledge [10].Decision support system provides to increase efficiency and quality of health sector. Moreover, confidence of patient to doctor is increased thus, success rate of treatment is raised up [11].

Generated some clinical decision support systems that is from 1960s to nowadays are below.

# DeDOMBAL'IN LEEDS ABDOMINAL PAIN SYSTEM

• End of the 1960s, De Dombal and his assistants was generated a decision system tahat related symptom process of abdominal diseases benefiting Bayesian theorem at Leeds niversity [10].

## DR.CAD

Dr.CAD (Computer Aided Diagnosis) is a useful and internet based diagnosis support system. It provides us to reach diagnosis most correctly by saving madical data as symptoms of diseases, examination and lab result, ECG, EEG, EMG [12].

# MYCIN

• In 1970s, MYCIN was generated Stanford niversity to make a significant estimation of doctors. The purpose that generates determination diagnosis and treatment methods of blood infection [13].

# POEMS (Post Operative Expert Medical System)

• POEMS is urgent care medical system after operation in 1992. The deci-sion support system was planned to evaluate the symptoms and to make recommendation for less experienced medical staff [14].

# OIRS

OIRS (On-Line Incident Reporting System) was generated at Osaka University to manage medical risks. Principles of the system are " do it - control it - continue setting it " [15].

# PERSIVIA

• The company was generated diagnosis platform called smartPath, that consists components for clinical decision support, order sets, analytics, and public health recording and real time monitoring. Clinical Decision Support part scans all available patient data to specify gaps in care, and develope effective treatment strategies [16].

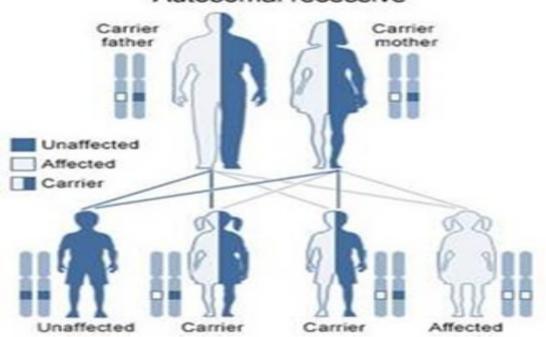
#### SAPHIRE

• SAPHIRE was started as project of EU in 2006. It has continued with participation of Turkey, France, Greece, Romania and Germany. Applications as stool blood tests, rektal tests, cervical cancer screening, practice of pelvic and thorax, smoking cessation are occured [17]. Application of health information system is to raise quality of life of people who are old and have chronic disease. [18]Advanced decision support tools are emerging from research labs, can be integrated with patient care systems that is using in hospital and clinics, and beginning to keep a prevalent effect on the way medicine is practiced as well [19]. Medical decision support system (MDSS) also provide a decision care that is rapid, accurate and valid with knowledge based for family physicians, internists to guide the patients, medical emergency services [20][21][22][23]. Medical decision support system (MDSS) is also useful for neurology clinics for diagnosis and treatment of diseases of nervous system as SMA types. The system will be developed and also design more useful formation if doc-tors and patients support the system. Thus, saving time and reducing the cost will be realized after while. a During the research my target is to generate an integrated medical decision support (MDSS) tool to diagnose of SMA types due to determine of diseases that causes the nervous system of a human body by answering the questions as "yes" or "no" simply.

#### 2.6 SMA Diseases (Type 1, Type 2, Type 3)

The disease is issued by homozygous removing or mutations in the survival motor neuron SMN1. In reality, the SMN gene is found in two ways in the human genome that are SMN1, ancestral telomeric copy, and SMN2 are centromic paralogy that arise through replication in recent evolution [24]. SMA patients lack SMN1, but their portrait in SMN2 is not compatible with the lifestyle at least one time - a complete SMN. Together, the SMN2 protein is only the remote region: SMN2 exon7 is a critical, translationally silent single nucleotide C to T transition 6bp, where the linkage is deeply here, 90% of the protein here is unstable and distorted. For SMN1 deficiency. The severity of the disease is inversely proportional to the SMN2 copy number[2]. Enhanced SMN2 addition therapies

The method of insertion switching oligonucleotide (SSO) treatment may provide modification of expression from the SMN2 gene and the production of SMD protein is now a clinical design with the approval of nuccinates. Therein, it is difficult to prepare invasive intrathecal injections in the central nervous system (CNS). The SMA Foundation funded a study examining alternative ways of managing SSOs [25]. Hammond et al. In a pay model of Oxford University's SMA, set that SSOs provide an effective systemic setting of binding of a peptide, including the CNS, and that the doses provide a lower order of magnitude than is only required for SSOs. 2.5 and 2.1 are explanation of assuming the birth prevalence.



Autosomal recessive

Figure 2.5: Assuming A Birth Prevalence [26].

# Assuming A Birth Prevalence of 8.5 per 100,000

SMA Type Estimated Prevalence (a) Estimated Prevalence (b)

• -		
Type 1	1455	1067
Type 2	3567	3330
Type 3	3504	3504
Total	8526	7901

(a) User Published Survival Estimates from US Literature Only

. . . .

(b) User Combined Published Survival Estimates from US, Europe and Australia

Assuming A Birth Prevalence of 9.4 per 100,000			
SMA Type	Estimated Prevalence (a)	Estimated Prevalence (b)	
Type 1	1610	1180	
Type 2	3944	3682	
Type 3	3875	3875	
Total	9429	8737	
(a) User Published Survival Estimates from US Literature Only			

(a) User Published Survival Estimates from US Literature Only

(b) User Combined Published Survival Estimates from US, Europe and Australia

Assuming A Birth Prevalence of 10.5 per 100,000			
SMA Type	Estimated Prevalence (a)	Estimated Prevalence (b)	
Type 1	1764	1293	
Type 2	4322	4035	
Type 3	4247	4247	
Total	10333	9575	
(a) User Published Survival Estimates from US Literature Only			

(b) User Combined Published Survival Estimates from US, Europe and Australia

Table 2.1: Assuming A Birth Prevalence [24].

#### 2.6.1SMA Type 1

Type 1 is called Werdnig Hoffmann Disease and sometimes referred to as infantile onset SMA or Werdnig-Hoffmann's disease. (2.6) and (2.7) shows the examples of Type 1. Type 1 begins to affect infants up to 6 months from birth, babies need to show signs of disease at 3 months. This is the most severe form of SMA. This disease is seen from the newborn period and is the most restrict form of the disease. In prenatal ultrasound follow-up, she may suspect that the movements in the mother's womb are inadequate<sup>[2]</sup>. There are findings such as insufficiency in the movements of the newborn baby after birth, the state of slack, which we call prominent hypotonia, difficulty in sucking and swallowing, and dimness in voice. These infants with severe respiratory failure need mechanical ventilator support and often can lose their lives without growing

too much.

Unable to sit- Never sit (0-6 months old) - Age of death  ${<}2$ 

# 2.6.1.1 Symptoms of Type 1

- Weakness
- Unable to Sit
- Respiratory Difficulty
- Looseness in Joint



Figure 2.6: SMA Type 1[27].



Figure 2.7: SMA Type 1[28].

## 2.6.1.2 Patients Live With SMA in Turkey

#### Do they communicate with specialists of the neuro-pneumonia? [29]

Yes, there is: 30

No: 31

5 people did not reply to this question.

Patients who can go to hospital can communicate with neurology department, not neuromuscular department.

#### Where Are Their Diagnosis And Which Test Results? [29]

Istanbul University: 20

Hacettepe University: 23

Ege University: 6

EMG and biopsy. There are some people who say that DNA testing has been done, but these centers do these tests outside. Because SMN analysis cannot be done. There are centers where we can make these analyzes.

#### Medicines<sup>[29]</sup>

23 patients have used Carnitine or are still using. Or8 patients have used VPA.- Six patients are using Coenzyme Q10. - Six patients using salbutamol. Two patients are using Neurontin.

#### Welcome To The Dietary With Nutrition On Nutrition? [29]

Yes: 17

No: 49

No answer to this question. 15

And we're talking about fresh-organic nutrition. There is no diet program for the metabolism of this disease. However, the standard information on this issue is now. At the beginning of the TREAT-NMD page, the file file is also described in the sma environment. While information about this subject can be given to 2-3 central patients in our country, it is the subject of treatment programs in a neuromuscular room in this country in our country.

#### Are They Using Wheelchair? [29]

Yes: 36

No: 30

It hasn't answered this question: 9

Those who use a manual chair cannot go on their own. They are not providing social security. When it came to getting help, the patient receives a certificate of poverty from the responsible staff.

#### Does The Vehicle - Use? [29]

Yes: It's using 30 patients. (Which vehicle-tools are used)

Tools supplies; ventilator and necessary equipment for this device, aspirator, steam engine, crutch, night mold, korean, patient lift, leg fixing instrument, walker.

#### Is Rehabilitation Applied? [29]

Yes: 17
No: 50
Partially: 3
Myself. : 4
It hasn't answered this question: 13
In general, rehabilitation was evaluated as physical therapy and 17 of our patients who gave this response were given physical therapy. Users can make 3 sessions per month.

#### Do You Need Home Maintenance? [29]

Yes there is: 44 Sometimes: 6 It did not answer this question: 6

#### Does It Work? (In the menu of the age of 18) [29]

Yes: 10 patients.

Electricity. Webmaster, accounting, architect, mathematician, worker, technician, teacher, artisan.

#### 2.6.2 SMA Type 2

Type 2 begins to affect children aged 7-18 months. Children can sit independently, but cannot walk. This form may be more moderate to severe. The symptoms start before the age of 1.5. It can not walk. It can hold his head and sit. However, it cannot go from sitting position to sitting position. It is a medium weight table. (2.8) is an example of Type 2. Able to sit- Never stand (7-18 months) - Age of death>2

#### 2.6.2.1 Symptoms of Type 2

- Inability to Walk
- Never Standing
- Muscle Strength Loss
- Weakness of Arms and Legs



Figure 2.8: SMA Type 2 [30].

#### 2.6.3 SMA Type 3

Type 3, also known as Kugelberg-Welander syndrome or child SMA, seen or begins to affect children at the age of 18 months or as a teenager, the symptoms start before the age of 1.5. Children can be able to walk independently but they have weakness in their arms and legs, and they often fall down. This is the lightest form of SMA in children. It can hold his head and sit. However, it cannot go from sitting position to sitting position. It is a medium weight table. (2.9) is an example of Type 3 disease.

Able to Walk- Stands and walks (> 18 months) - Age of death is adult

# 2.6.3.1 Symptoms of Type 3

- Unable to Walk (After a while)
- Unable to Swallowing
- Unable to Chew
- Shake
- Weakness of Arms and Legs



Figure 2.9: SMA Type 3 [31].

#### 2.6.4 Why Can Not The Diseases Diagnose Early?

According to health system in Turkey, patients go to the family physicans, firstly. If the family physicans has enough knowledge about this nervous system diseases, doctor sends to the patient to respective department directly. If doctor has not enough knowledge, firstly doctor tries to simple medicine treatment. For instance, a SMA patient goes to the family physicans. The doctor favors medicines like analgesics. After that, it is realized that this method is useless. In this way other treatment methods are tried and the problem is searched. This process causes to delay of diagnose and progression of disease. Also, patients has different symptoms and it causes to patients go to different units of hospitals. For instance, a SMA patient goes to internal medicine due to visual impairment. If the doctor has not enough knowledge, determined exact reason of this problem and diagnosis of SMA can delay. Chapter 3

# Approach

#### 3.1 Flow Of The Project And Theory

First of all I started to research diseases which belong nercous system. According to research, I wanted to choose three types of SMA diseases on nervous system which are SMA Type 1, SMA Type 2 and SMA Type 3. I researched in general how the diseases occurs, which department of hospital is related, what the symptoms of the diseases are. I had an interview about disease with some hospitals that I interned. These are Istanbul University Hospital in Istanbul, Liv Hospital Ulus, and society which is SMA Benimle Yuru. My target to get patient's data as soon as possible from hospitals. By the way, I continued to research about disease and to find symptoms of the disease as well. I executed my subject in hospitals and data centers accepted that I can get patient's limited data and to work with us. Some of hospitals that I requested couldn't accept to work because of lack of patient data or limited patient data.

I was quided to interview in short time with a doctor who is interested in Neurology thus I got information from her by discussing about diseases that I researched and its gripes and symptoms. Even if lack of data, department of medical archive of some hospital shared and data centers prepared limited patient's data (42 units) that including SMA Type 1 (25 units), SMA Type 2 (13 units), SMA Type 3 (4 units) and anamnesis with me. Actually, these data are not enough. I analyzed the all anamnesis and data in detail, I compared gripes and symptoms with myself that I found before and I interfiled of these data as an excel. Then, I setted flow diagram by using Visio, classify according to age range of patients on total patient numbers as diseases. (3.1) and (3.2) show the diagram. The target of shematization is to analyze the data deeply and to calculate probability of decision-making system.



- F1: 0-6 Month
- F2: 6-18 Month
- F3: 18-84 Month
- F4: 7-20 Years

Table 3.1: Age ranges of diseases in Visio.

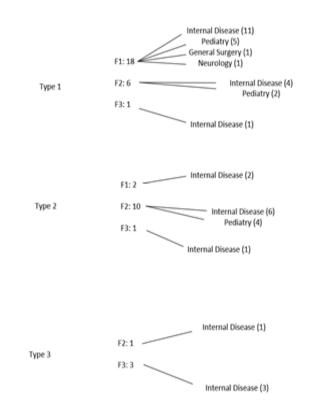


Table 3.2: According to SMA Type, Number, Age, Clinics Distribution of Diseases.

The project has simple and beneficial program, application and theorem such a Excel, Visio, Xcode and Bayes' Theorem. Excel is necessary to enter all patient data and to use Bayes' Theorem that is formula to calculate the probability of disesase. Visio is used for seperating the patient data. Xcode is also used to design interface by codding for user.

### 3.1.1 Excel

I got gripes and symptoms from anamnesis and created excel table. Then, I compared types and symptoms and calculated frequency and normalization. While I were calculating frequency, I divided by symptoms to total patient number of types. Then, I find possibility of symptom within total patient of a disease. While I also were calculating normalization, I divided by symptoms to total patient number of all diseases. Thus, I find possibility of each symptom for each types of disease within total patient of a type.

				Normalization						
	SMA Type 1	SMA Type 2	SMA Type 3	<ul> <li>Total</li> </ul>	٠	SMA Type 1 *	SMA Type 2 *	SMA Type 3 *	Total *	
Patient Number		25	13	4	42	1	1	1	1	
Weakness		6	2	1	9	0.24	0.153846154	0.25	0.21428571	
inability to walk		2	9	2	13	0.08	0.692307692	0.5	0.30952381	
Inability to sit		19	1	0	20	0.76	0.076923077	0	0.47619048	
Never Stand		4	11	0	15	0.16	0.846153846	0	0.35714286	
Inability to sleep		0	0	0	0	0	0	0	0	
Respiratory Difficulty		21	0	0	21	0.84	0	0	0.5	
Muscle Strength Loss		6	5	1	12	0.24	0.384615385	0.25	0.28571429	
Looseness in Joint	1	14	1	2	10	0.56	0 230769231	05	0.45238005	

Table 3.3: Calculation of Normalization.

I calculated possibility of symptom of each type disease with bayes' theorem. (3.3) shows the normalization calculation. Then, I reached results by multiplying disease's all of probability for each dis-ease. Maximum result shows that having disease's possibility.

I setted my system by comparing the types of symptoms of the diseases of pa-tients who come different symptom. The system shows patient is closed SMA and types of it. Thus, doctor can determine the prone to disease by entering the patient's symp-tom into the system immediately. 1-0 expressions that vary by symptom change my scale and the system is to help for diagnosis of the diseases, it is to prevent wrong treatment as well.

#### 3.1.2 Bayes' Theorem

Clinical data are progressive of treatment are inaccurate, so health professionals have hard choices. Probability means of expressing uncertainty. In this framework, probability (p) defines a clinician's opinion about the possibility of an event as a number between 0 and 1. An event that is certain to occur has a probability of 1; an event that is certain not to occur has a probability of 0. The probability of event A is given p[A]. The sum of the probabilities of all possible, collectively detailed outcomes of a chance event must be equal to 1. The probability of event A and event B occurring together is denoted by p[A&B] or by p[A, B]. Suppose that events A and B are considered independent and both of them occuring, thus probability formula is given,

$$p[A, B] = p[A] \ge p[B]$$
(3.1)

**Bayes' theorem** is a quantitative method for calculating probability. Recall that a conditional probability is the probability that event A will occur given that event B is known to occur. In general, I would like to know the probability that disease is present (event A), given that the test is known to be positive (event B). I indicate the presence of disease as D, its absence as D, a test result as R, and the pretest probability of disease as p[D]. The probability of disease, given a test result, is written p(D|R). Bayes' theorem is [32]:

$$p[D|R] = \frac{p[D]xP[R|D]}{P[D]xp[R|D] + p[-D]xp[R|-D]]}$$
(3.2)

					Normalization				Bayes Tablosu		
	SMA Type 1	SMA Type 2 🔹 💌	SMA Type 3 🔹 💌	Total 🔹	SMA Type 1 🔻	SMA Type 2 🔻	SMA Type 3 🔻	Total 🔻	SMA Type 1 💌	SMA Type 2 💌 S	SMA Type 3 💌
Patient Number	25	13	4	42	1	1	1	1	0.333333333	0.3333333333	0.3333333333
Weakness	6	2	! 1	9	0.24	0.153846154	0.25	0.21428571	0.08	0.051282051	0.083333333
Inability to walk	2	9	2	13	0.08	0.692307692	0.5	0.30952381	0.026666667	0.230769231	0.166666667
Inability to sit	19	1	. 0	20	0.76	0.076923077	0	0.47619048	0.253333333	0.025641026	0
Never Stand	4	. 11	. 0	15	0.16	0.846153846	0	0.35714286	0.053333333	0.282051282	0
Inability to sleep	C	(	) 0	(	0	0	0	0	0	0	0
Respiratory Difficulty	21	. (	) 0	21	0.84	0	0	0.5	0.28	0	0
Muscle Strength Loss	6	5	i 1	12	0.24	0.384615385	0.25	0.28571429	0.08	0.128205128	0.083333333
Looseness in Joint	14	. 3	2	19	0.56	0.230769231	0.5	0.45238095	0.186666667	0.076923077	0.166666667

Table 3.4: Calculation of Bayesian.

You can find the calculation of Bayesian as in (3.4).

#### 3.1.3 Programming Language (Swift 5.0)

The Swift is a Programming Language easy to reach and to use. It provides us a lot of open sources as library for iOS Platforms. Database can be created through the Swift. The application is available for iPad and iPhone products. Xcode also provides to write code, to find mistakes and to create class by using Swift. It gives more effective result. Some design working can be made on Xcode by using Swift for User Interface. To understand the user, some interfaces can be created with Xcode UI by designing.

For my Decision Making System as it is represented students study with together IT and Biomedical Engineering, I designed own file by using Swift. As a result, the system speeds up the decision making processing and experts can be made use of the system.

### 3.1.3.1 Code File

#### **Entering Screen**

```
import UIKit
class AcilisViewController: UIViewController {
     override func viewDidAppear(_ animated: Bool) {
        super.viewDidAppear(animated)
        DispatchQueue.main.asyncAfter(deadline: .now() + 1) {
            let storyboard = UIStoryboard(name: "Main", bundle: nil)
            let mainNavigationController =
    storyboard.instantiateViewController(withIdentifier: "MainNavigationController") as!
    UINavigationController
        self.present(mainNavigationController, animated: false, completion:
        null)
        }
    }
}
```

}

#### Symptoms Screen

import UIKit
<pre>class BelirtilerViewController: UIViewController {</pre>
<pre>@IBOutlet weak var tableView: UITableView!</pre>
private var belirtiler = [
BelirtiModel(name: "Kuvvetsizlik", type1HastaSayisi:
6, type2HastaSayisi: 2, type3HastaSayisi: 1),
BelirtiModel(name: "Yuruyememe", type1HastaSayisi:
2, type2HastaSayisi: 9, type3HastaSayisi: 2),
BelirtiModel(name: "Oturamama", type1HastaSayisi:
19, type2HastaSayisi: 1, type3HastaSayisi: 0),
BelirtiModel(name: "Ayakta duramama", type1HastaSayisi:
4, type2HastaSayisi: 11, type3HastaSayisi: 0),
BelirtiModel(name: "Yatamama", type1HastaSayisi:

```
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Solunum Zorlugu", type1HastaSayisi:
21, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Kas Kuvveti Kaybi", type1HastaSayisi:
6, type2HastaSayisi: 5, type3HastaSayisi: 1),
                BelirtiModel(name: "Eklemde Gevseklik", type1HastaSayisi:
14, type2HastaSayisi: 3, type3HastaSayisi: 2),
                BelirtiModel(name: "Dilin Segirmesi", type1HastaSayisi:
1, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Zayif Aglama", type1HastaSayisi:
4, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Kilo kaybi", type1HastaSayisi:
2, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Yorgunluk", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 1),
                BelirtiModel(name: "Sirt Agrisi", type1HastaSayisi:
2, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Emme Zorlugu", type1HastaSayisi:
2, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Deride Kizarma", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Omurga Egriligi", type1HastaSayisi:
3, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Karin Siskinligi", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Oksurme", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Gebelik beklentisi uzun", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Bogaz agrisi", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Adet d zensizligi", type1HastaSayisi:
 0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Yanaklarda sivilcelenme", type1HastaSayisi:
 0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Kilo alimi", type1HastaSayisi: 0, type2HastaSayisi:
0, type3HastaSayisi: 0),
                BelirtiModel(name: "Titreme", type1HastaSayisi: 7, type2HastaSayisi:
0, type3HastaSayisi: 3),
                BelirtiModel(name: "Bas agrisi", type1HastaSayisi: 1, type2HastaSayisi:
0, type3HastaSayisi: 0),
                BelirtiModel(name: "Can seklinde govde", type1HastaSayisi:
3, type2HastaSayisi: 1, type3HastaSayisi: 0),
                BelirtiModel(name: "Kanama fazlaligi", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Cinsel isteksizlik", type1HastaSayisi:
```

```
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: " igneyememe", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 2),
                BelirtiModel(name: "Asiri Terleme", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Ruh halinde degisim", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Bas donmesi", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
                BelirtiModel(name: "Bayilmalar", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
               BelirtiModel(name: "Istahsizlik", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 0),
               BelirtiModel(name: "Yutkunamama", type1HastaSayisi:
0, type2HastaSayisi: 0, type3HastaSayisi: 3),
                BelirtiModel(name: "Kol ve bacaklarda zayiflik", type1HastaSayisi:
 0, type2HastaSayisi: 8, type3HastaSayisi: 3)
       ]
        override func viewDidLoad() {
        super.viewDidLoad()
                               title = "Belirtiler"
        print(HastaModel.protokolNo, HastaModel.ayOlarakYas,
HastaModel.yas, HastaModel.cinsiyet)
       }
        @IBAction func ileriButonuTiklandi(_ sender: UIButton) {
                                var seciliBelirtiler = [BelirtiModel]()
                for belirti in belirtiler {
                        if belirti.isExist {
                                                        seciliBelirtiler.append(belirti)
                        }
                }
                let storyboard = UIStoryboard(name: "Main", bundle: nil)
                let sonucViewController = storyboard.instantiateViewControlle
r(withIdentifier: "SonucViewController") as! SonucViewController
                sonucViewController.belirtiler = seciliBelirtiler
                navigationController?.pushViewController(sonucViewController, animated: true)
        }
```

```
// MARK: - UITableViewDelegate, UITableViewDataSource
extension BelirtilerViewController: UITableViewDelegate, UITableViewDataSource {
    func tableView(_ tableView: UITableView, numberOfRowsInSection section: Int) -> Int {
        return belirtiler.count
    }
    func tableView(_ tableView: UITableView, cellForRowAt indexPath: IndexPath) ->
UITableViewCell {
        let cell = tableView.dequeueReusableCell(withIdentifier: "BelirtiCell") as!
BelirtiCell
        cell.configure(with: belirtiler[indexPath.row])
        return cell
    }
}
```

#### Symptom Cell

}

```
import UIKit
class BelirtiCell: UITableViewCell {
   var belirtiModel: BelirtiModel?
   @IBOutlet weak var belirtiLabel: UILabel!
   @IBOutlet weak var belirtiSwitch: UISwitch!
   override func awakeFromNib() {
        super.awakeFromNib()
        // Initialization code
       belirtiSwitch.isOn = false
   }
    override func setSelected(_ selected: Bool, animated: Bool) {
        super.setSelected(selected, animated: animated)
        // Configure the view for the selected state
   }
   func configure(with belirtiModel: BelirtiModel) {
        self.belirtiModel = belirtiModel
        self.belirtiLabel.text = belirtiModel.name
        self.belirtiSwitch.isOn = belirtiModel.isExist
   }
   @IBAction func switchChanged(_ sender: UISwitch) {
```

```
self.belirtiModel?.isExist = sender.isOn
}
```

#### Symptom Model

```
import Foundation
import UIKit
class BelirtiModel {
       let smaType1toplamHastaSayisi = 25
       let smaType2toplamHastaSayisi = 13
        let smaType3toplamHastaSayisi = 4
   var name: String
   var isExist: Bool = false
        var smaType1Normalizasyon: Float = 1
       var smaType2Normalizasyon: Float = 1
       var smaType3Normalizasyon: Float = 1
       var smaType1Bayes: Float = 1
       var smaType2Bayes: Float = 1
       var smaType3Bayes: Float = 1
       init(name: String, type1HastaSayisi: Int, type2HastaSayisi: Int, type3HastaSayisi
: Int) {
        self.name = name
                smaType1Normalizasyon = Float(type1HastaSayisi)
/ Float(smaType1toplamHastaSayisi)
                smaType2Normalizasyon = Float(type2HastaSayisi)
/ Float(smaType2toplamHastaSayisi)
                smaType3Normalizasyon = Float(type3HastaSayisi)
/ Float(smaType3toplamHastaSayisi)
                smaType1Bayes = smaType1Normalizasyon == 0 ? 1 : smaType1Normalizasyon / 3
                smaType2Bayes = smaType2Normalizasyon == 0 ? 1 : smaType2Normalizasyon / 3
                smaType3Bayes = smaType3Normalizasyon == 0 ? 1 : smaType3Normalizasyon / 3
   }
}
```

### **Patient Information Screen**

```
import UIKit
import PersistenceKit
class GirisViewController: UIViewController {
```

```
@IBOutlet weak var cinsiyetSegmentedControl: UISegmentedControl!
@IBOutlet weak var protokolNoTextField: UITextField!
@IBOutlet weak var yasTextField: UITextField!
@IBOutlet weak var ileriButon: UIButton!
@IBOutlet weak var yasSegmentControl: UISegmentedControl!
        override func viewDidLoad() {
        super.viewDidLoad()
                ilerButonAktiflikDegisti(aktiflik: false)
                protokolNoTextField.addTarget(self, action:
#selector(textFieldDidChange(_:)), for: .editingChanged)
                yasTextField.addTarget(self, action:
#selector(textFieldDidChange(_:)), for: .editingChanged)
    }
        @IBAction func ileriButonTiklandi(_ sender: UIButton) {
                guard let protokolNo = Int(protokolNoTextField.text!),
let yas = Int(yasTextField.text!) else {
                        return
                }
                HastaModel.protokolNo = protokolNo
        var yil: Int?
        var ay: Int?
        switch yasSegmentControl.selectedSegmentIndex {
        case 0:
            yil = yas
        case 1:
            ay = yas
        default:
            break
       }
        HastaModel.yasHesapla(ay: ay, yil: yil)
                let storyboard = UIStoryboard(name: "Main", bundle: nil)
                guard let belirtilerViewController =
 storyboard.instantiateViewController(withIdentifier: "BelirtilerViewController")
as? BelirtilerViewController else {
                        return
```

```
}
                navigationController?.pushViewController(belirtilerViewController,
 animated: true)
       }
        @IBAction func cikisButonTiklandi(_ sender: UIButton) {
                exit(0)
       }
        @IBAction func cinsiyetDegisti(_ sender: UISegmentedControl) {
                HastaModel.cinsiyet = sender.selectedSegmentIndex == 0 ? .erkek : .kadin
       }
        @objc func textFieldDidChange(_ textField: UITextField) {
                if protokolNoTextField.text?.count == 7 && yasTextField.text?.count != 0 {
                        ilerButonAktiflikDegisti(aktiflik: true)
                } else {
                        ilerButonAktiflikDegisti(aktiflik: false)
                }
       }
       func ilerButonAktiflikDegisti(aktiflik: Bool) {
                ileriButon.isEnabled = aktiflik
                ileriButon.alpha = aktiflik ? 1 : 0.5
       }
   @IBAction func sonuclariGosterButonuTiklandi(_ sender: UIButton) {
        let storyboard = UIStoryboard(name: "Main", bundle: nil)
        guard let sonuclarListesiViewController =
storyboard.instantiateViewController(withIdentifier: "SonuclarListesiViewController") as?
 SonuclarListesiViewController else {
            return
       7
        navigationController?.pushViewController(sonuclarListesiViewController,
animated: true)
   }
   }
```

#### **Patient Model**

```
import Foundation
class HastaModel {
```

```
static var protokolNo: Int = 0
```

```
static var yas: Int?
    static var ayOlarakYas: Int?
        static var cinsiyet: Cinsiyet = .erkek
    static func yasHesapla(ay: Int?, yil: Int?) {
        if let ay = ay {
            HastaModel.ayOlarakYas = ay
            return
        }
        if let yil = yil {
            HastaModel.yas = yil
        }
   }
}
enum Cinsiyet {
        case erkek
        case kadin
}
```

#### **Result Screen**

```
import UIKit
class SonucDetayViewController: UIViewController {
    var sonucModel: SonucModel!
    @IBOutlet weak var tableView: UITableView!
    override func viewDidLoad() {
        super.viewDidLoad()
       title = "Detaylar"
   }
}
extension SonucDetayViewController: UITableViewDataSource, UITableViewDelegate {
    func tableView(_ tableView: UITableView, numberOfRowsInSection section: Int) -> Int {
       return sonucModel.belirtiler.count + 4
    }
    func tableView(_ tableView: UITableView, cellForRowAt indexPath: IndexPath)
-> UITableViewCell {
        let cell = tableView.dequeueReusableCell(withIdentifier: "detayCell")!
        switch indexPath.row {
        case 0:
```

```
cell.textLabel?.text = "Protokol No"
        cell.detailTextLabel?.text = "\(sonucModel.protokolNo)"
    case 1:
        cell.textLabel?.text = "Hastalik"
        cell.detailTextLabel?.text = sonucModel.hastalik
    case 2:
        cell.textLabel?.text = "Yas"
        cell.detailTextLabel?.text = sonucModel.getYasTexti()
    case 3:
        cell.textLabel?.text = "Belirtiler :"
        cell.detailTextLabel?.text = ""
    default:
        cell.detailTextLabel?.text = sonucModel.belirtiler[indexPath.row - 4]
        cell.textLabel?.text = ""
    }
   return cell
}
```

}

#### **Result List Screen**

```
import UIKit
class SonucDetayViewController: UIViewController {
    var sonucModel: SonucModel!
      @IBOutlet weak var tableView: UITableView!
    override func viewDidLoad() {
      super.viewDidLoad()
      title = "Detaylar"
    }
}
extension SonucDetayViewController: UITableViewDataSource, UITableViewDelegate {
    func tableView(_ tableView: UITableView, numberOfRowsInSection section: Int) -> Int {
      return sonucModel.belirtiler.count + 4
    }
    func tableView(_ tableView: UITableView, cellForRowAt inderPath: InderPath)
```

```
-> UITableViewCell {
        let cell = tableView.dequeueReusableCell(withIdentifier: "detayCell")!
        switch indexPath.row {
        case 0:
            cell.textLabel?.text = "Protokol No"
            cell.detailTextLabel?.text = "\(sonucModel.protokolNo)"
        case 1:
            cell.textLabel?.text = "Hastalik"
            cell.detailTextLabel?.text = sonucModel.hastalik
            case 2:
            cell.textLabel?.text = "Yas"
            cell.detailTextLabel?.text = sonucModel.getYasTexti()
        case 3:
            cell.textLabel?.text = "Belirtiler :"
            cell.detailTextLabel?.text = ""
        default:
            cell.detailTextLabel?.text = sonucModel.belirtiler[indexPath.row - 4]
            cell.textLabel?.text = ""
        }
       return cell
    }
```

```
}
```

#### **Result Model**

```
import Foundation
import PersistenceKit
struct SonucModel: Codable, Identifiable {
    static var idKey = \protokolNo
    var protokolNo: Int
    var hastalik: String
    var yasYilOlarak: Int?
    var yasAyOlarak: Int?
    var belirtiler: [String]
      func getYasTexti() -> String {
        if let yasYilOlarak = yasYilOlarak {
            return "\(yasYilOlarak)"
        }
```

```
if let yasAyOlarak = yasAyOlarak {
    return "\(yasAyOlarak) Ay"
}
return ""
}
```

#### **Result List Detail Screen**

```
import UIKit
import PersistenceKit
class SonuclarListesiViewController: UIViewController {
   var sonuclar = [SonucModel]()
   let sonucStore = UserDefaultsStore<SonucModel>(uniqueIdentifier: "sonuclar")!
   @IBOutlet weak var tableView: UITableView!
    override func viewDidLoad() {
        super.viewDidLoad()
       title = "Sonuclar"
        sonuclar = sonucStore.allObjects().sorted(by: { $0.protokolNo < $1.protokolNo })</pre>
        self.navigationItem.setRightBarButton(UIBarButtonItem(title: "Temizle", style:
.done, target: self, action: #selector(temizleButonuTiklandi)), animated: false)
   7
   @objc func temizleButonuTiklandi() {
       let alertController = UIAlertController(title: "Tum sonuclar temizlenecek",
 message:
 "Tum sonuclari temizlemek istediginize emin misiniz?", preferredStyle: .alert)
        let okAction = UIAlertAction(title: "Temizle", style: .default) { (okAct) in
            self.sonucStore.deleteAll()
            self.sonuclar.removeAll()
            self.tableView.reloadData()
       }
       let cancelAction = UIAlertAction(title: "Vazgec", style: .cancel, handler: nil)
        alertController.addAction(okAction)
        alertController.addAction(cancelAction)
```

```
present(alertController, animated: true, completion: nil)
    }
}
extension SonuclarListesiViewController: UITableViewDelegate, UITableViewDataSource {
        func tableView(_ tableView: UITableView, numberOfRowsInSection section: Int) -> Int {
        return sonuclar.count
    }
    func tableView(_ tableView: UITableView, cellForRowAt indexPath: IndexPath)
 -> UITableViewCell {
        let cell = tableView.dequeueReusableCell(withIdentifier: "cell")!
        let sonuc = sonuclar[indexPath.row]
        cell.textLabel?.text = "\(sonuc.protokolNo), \(sonuc.hastalik),
 \(sonuc.getYasTexti())"
        return cell
    }
    func tableView(_ tableView: UITableView, didSelectRowAt indexPath: IndexPath) {
        let storyboard = UIStoryboard(name: "Main", bundle: nil)
        guard let sonucDetayViewController = storyboard.instantiateViewController
(withIdentifier: "SonucDetayViewController")
 as? SonucDetayViewController else {
           return
        }
        sonucDetayViewController.sonucModel = sonuclar[indexPath.row]
        navigationController?.pushViewController(sonucDetayViewController, animated: true)
        tableView.deselectRow(at: indexPath, animated: true)
    }
}
```

```
Result View Screen
```

```
import UIKit
import PersistenceKit
class SonucViewController: UIViewController {
    var belirtiler = [BelirtiModel]()
    var smaType1 : Float = 1
```

```
var smaType2 : Float = 1
        var smaType3 : Float = 1
   @IBOutlet weak var kaydetButonu: UIButton!
    @IBOutlet weak var smaType1SonucLabel: UILabel!
        @IBOutlet weak var smaType2SonucLabel: UILabel!
        @IBOutlet weak var smaType3SonucLabel: UILabel!
        @IBOutlet weak var maxSonucLabel: UILabel!
        @IBOutlet weak var maxTypeLabel: UILabel!
        override func viewDidLoad() {
        super.viewDidLoad()
        title = "Sonuc"
        self.navigationItem.setRightBarButton(UIBarButtonItem
(title: "Ana Sayfa", style: .done, target: self, action:
#selector(anasayfaButonuTiklandi)), animated: false)
        for belirti in belirtiler {
                smaType1 *= belirti.smaType1Bayes
                smaType2 *= belirti.smaType2Bayes
                smaType3 *= belirti.smaType3Bayes
                7
        smaType1 = smaType1 == 1 ? 0 : smaType1
        smaType2 = smaType2 == 1 ? 0 : smaType2
        smaType3 = smaType3 == 1 ? 0 : smaType3
                        let maxValue = max(smaType1, smaType2, smaType3)
                switch maxValue {
                case smaType1:
                        maxTypeLabel.text = "SMA Type 1"
                case smaType2:
                        maxTypeLabel.text = "SMA Type 2"
                case smaType3:
                        maxTypeLabel.text = "SMA Type 3"
                default:
                        break
                }
                smaType1SonucLabel.text = "\(NSNumber(value: smaType1).decimalValue)"
                smaType2SonucLabel.text = "\(NSNumber(value: smaType2).decimalValue)"
                smaType3SonucLabel.text = "\(NSNumber(value: smaType3).decimalValue)"
                maxSonucLabel.text = "\(NSNumber(value: maxValue).decimalValue)"
```

}

```
@objc func anasayfaButonuTiklandi() {
        dismiss(animated: true, completion: nil)
    }
        @IBAction func kaydetButonuTiklandi(_ sender: UIButton) {
        UIView.animate(withDuration: 0.5) {
            self.kaydetButonu.isEnabled = false
            self.kaydetButonu.alpha = 0.5
       }
        var belirtiTextleri = [String]()
        for belirti in belirtiler {
           belirtiTextleri.append(belirti.name)
        }
        let sonucModel = SonucModel(protokolNo: HastaModel.protokolNo, hastalik:
 maxTypeLabel.text!, yasYilOlarak: HastaModel.yas, yasAyOlarak:
 HastaModel.ayOlarakYas, belirtiler: belirtiTextleri)
        let sonucStore = UserDefaultsStore<SonucModel>(uniqueIdentifier: "sonuclar")!
        try! sonucStore.save(sonucModel)
        }
    @IBAction func tumSonuclariGorButonuTiklandi(_ sender: UIButton) {
        let storyboard = UIStoryboard(name: "Main", bundle: nil)
        guard let sonuclarListesiViewController = storyboard.instantiateViewControlle
r(withIdentifier: "SonuclarListesiViewController") as? SonuclarListesiViewController else {
            return
       }
       navigationController?.pushViewController(sonuclarListesiViewController, animated: true)
   }
}
```

# Chapter 4

# **Results and Discussion**

I choice 3 patients in my data for testing. First patient has SMA type 1 disease. He is 5 months old and his symptoms are inability to sit, respiratory difficulty, abdominal bulge, anorexia. After these symptoms are signed, results are as in (4.1) and (4.2).

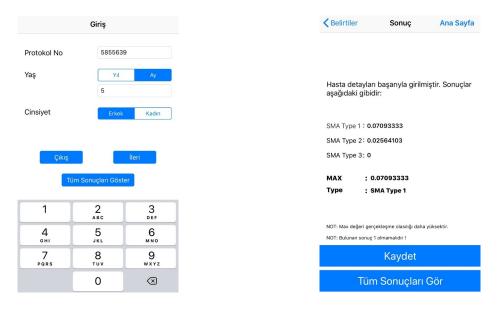


Figure 4.1: Information page in system about patient 1.

Figure 4.2: Results of patient 1.

Second patient has SMA type 2. She is 7 year s old. And his symptoms are throat ache, inability to walk, muscle strength loss. After these symptoms are signed, results are as in figure (4.3) and figure (4.4).

	Giriş			Belirtiler	Sonuç	Ana Say				
otokol No	345268	1								
′aş	Yd Ay 7			Hasta detayları başarıyla girilmiştir. Sonuçlar aşağıdaki gibidir:						
insiyet	Erkek	Kadın		SMA Type 1 : SMA Type 2 :	0.002133333 0.0295858					
Çıkış		İleri		SMA Type 3:	0.01388889					
Т	üm Sonuçları Göst	er			: 0.0295858 : SMA Type 2					
1	2 ^BC	3 DEF								
4 вні	5 JKL	6 MNO		_	gerçekleşme olasılığı daha nuç 1 olmamalıdır !	yüksektir.				
7 pqrs	8 TUV	9 wxyz			Kaydet					
	0	$\overline{\mathbf{X}}$		Т	üm Sonuçları	Gör				

Figure 4.3: Information page in system about patient.

Figure 4.4:	Results	of patient	2.
-------------	---------	------------	----

Third patient has SMA type 3. She is 15 years old and her symptoms are weakness inability to sit, fatigue, headache. After these symptoms are signed, results are as in (4.5) and figure (4.6).

Giriş			Belirtiler	So	nuç	Ana Sayfa	
Protokol No	951476	I					
Yaş	Yıl 15	Ау		Hasta deta aşağıdaki ç		/la girilmiş	tir. Sonuçlar
Cinsiyet	Erkek	Kadın		0141 T			
					: 0.0002702		
				SMA Type 2	2: 0.00131492	24	
Çıkış		İleri		SMA Type 3	3: 0.0069444	45	
Т	üm Sonuçları Göst	er		МАХ Туре	: 0.006944 : SMA Type		
1	2 ABC	3 DEF					
4 вні	5 JKL	6		-	ri gerçekleşme ol sonuç 1 olmamalıc		ksektir.
7 PORS	8 TUV	9 wxyz			Кау	/det	
	0	$\langle X \rangle$		٦	lüm Son	uçları G	ör

Figure 4.5: Information page in system about patient.

Figure 4.6: Results of patient 3.

## Chapter 5

## Conclusion

In this Project, I worked on decision making system and SMA diseases type 1, type 2, type 3. These diseases are not endemic disease and they differ from each other and other diseases in terms of symptoms. However process of treatment, if disease is not diagnosed, can be risky. Actually even if it is diagnosed, the risk can continue.

My target of Project is that accelerates process of the diagnosis not to delay for treatment and to have an idea generating decision making system. Family physicans and experts who work in hospital can see possibility of being disease with interface. as symptoms simple For testing, I visited family physicans in Sile and some experts. As I know function of the family physicans are that to follow the their own recorded patients and to diagnose or to treat the disease if patient has a disease. However as I predict, I saw the doctors who are less knowledgeable for this disease. When I conversated with them, they said me that they do not encounter and if patient who has one of the these diseases came, doctors send the patient to expert. Thus, process of diagnosis has been prolonged and patient will be under the risk. I determined to go to these departments of the Hospital that I work with because the patients who have one of the diseases went to there. Although they are avaliable, they are not interested in what I told and they did not want to test. The surgeon general is as well. He said me, my system should be done writing on paper and should be gave to doctors like that because of more useful.

I disagree with him. As a result, lots of doctors and hospitals are closed to innovation. Lots of family physicans and experts have less knowledgement. Hospitals and doctors should be integrated to these electronic systems but the process seems to take a long time. End of the project, I developed decision making system and the system works. However I worked with limited number of patient data so, I cannot obtain my desired result especially SMA. If patient data was much more for all disease, as I shematised I could develop decision making system according to age. In future prediction, SMA types can be change according to ages groups. The reason of it is changing of environmental factors day by day. After that effects of environmental factors SMA interval be on and age can examine. I reached my goals to generate decision making system for disease. According to patient's symptoms I produced the probability of disease as knowledge. In my project that is first step to biomedical engineer, I learnt steps of hierarchy, process of the diagnosis and treatment, problems in health sector, I saw how develop the solution for these problem and how is the reporting of them as well, the last conflict and communication between doctors and biomedical engineers. To sum up, recommendation is that developed system is available and in-service at present. So more effective results can be obtained with more patient data. Actually, using to developed systems are parallel level of development of the institution. However the main difficulty is integration of these systems. So, some seminars or educations should be given to staff of hospital and doctors to integrate of the electronic systems. To continue development in health sector, patient data and steps of diseases should be kept records. If and only if the existing systems can be developed and can be made decisions accurately in that way.

## References

- F. T. Farooq, M. Holcik, and A. MacKenzie, "Spinal muscular atrophy: Classification, diagnosis, background, molecular mechanism and development of therapeutics," pp. 15–16, 2013.
- [2] V. Valsecchi, M. Boido, E. De Amicis, A. Piras, and A. Vercelli, "Expression of muscle-specific mirna 206 in the progression of disease in a murine sma model," *PLOS ONE*, vol. 10, pp. 1–17, 06 2015.
- [3] shorturl.at/ejkX4, 2019.
- [4] K. T. P. Gary A.Thinboden, Anatomy and physiology. Mosby, fourth ed., 1999.
- [5] S. Silbernagl and F. Lang, *Color Atlas of Pathophysiology*. Thieme electronic book library, Thieme, 2000.
- [6] K. A. Zimmermann, Nervous System: Facts, Function Diseases. Live Science Contributor, 2018.
- [7] F. Ersoy, "Turkiye ile oecd ulkelerinin saglik duzeyleri ve saglik harcamalarinin analizi," *statistikciler Dergisi*, pp. 95–104, 2008.
- [8] "Turk saglik-sen." https://www.turksagliksen.org.tr, 2010.
- [9] L. R. Beach, "Broadening the definition of decision making: The role of prechoice screening of options," *Psychological Science*, vol. 4, no. 4, pp. 215– 220, 1993.

- [10] M. A. Musen, M. Blackford, and G. Robert, *Clinical decision-support sys*tems, pp. 643–674. United Kingdom: Springer London, 1 2014.
- [11] O. Yay, "Karar destek sistemleri (kds) decision support systems (dss)." https://bidunyasi.wordpress.com/, 2009.
- [12] B. A., "Uzman sistemlerin tipta teshis amacl kullanimi," Master's thesis, Gazi Universitesi, 2000.
- [13] S. R. Haug PJ, Rocha BH, "Decision support in medicine: Lessons from the help system," *International Journal of Medical Informatics*, vol. 69, pp. 273– 284, 2003.
- [14] C. A. Sawar MJ, Brennan TG, "Representing knowledge in medical decision support systems," in *Proceedings of IJCA191 One Day Workshop*, 1991.
- [15] N. K. Takeda H, Matsumura Y, "Health care quality management by means of an incident report system and an electronic patient record system," *International Journal of Medical Informatics*, vol. 69, pp. 285–293, 2003.
- [16] Persivia, "Global clinic al decision support system (cdss)."=http://persivia.com/.
- [17] D. S. B and T. RG., Basic 2nd clinical biostatistics. Connecticut: Appleton-Lange, 1994.
- [18] A. P and B. G., Statistical methods in medical research. Massachusetts:Science, third ed., 1994.
- [19] E. Shortliffe and J. J. Cimino, Biomedical Informatics: Computer Applications in Health Care and Biomedicine. 01 2014.
- [20] F. Burstein, F., C. Holsapple, and C., Handbook on Decision Support Systems 1: Basic Themes. 01 2008.

- [21] M. Gaynor, M. Seltzer, S. Moulton, and J. Freedman, "A dynamic, datadriven, decision support system for emergency medical services," in *Computational Science – ICCS 2005* (V. S. Sunderam, G. D. van Albada, P. M. A. Sloot, and J. J. Dongarra, eds.), (Berlin, Heidelberg), pp. 703–711, Springer Berlin Heidelberg, 2005.
- [22] A. Zerger and D. Ingle Smith, "Impediments to using gis for real-time disaster decision support," *Computers, Environment and Urban Systems*, vol. 27, pp. 123–141, 03 2003.
- [23] S. Zhu, J. Abraham, S. Paul, M. Reddy, J. Yen, M. Pfaff, and C. Deflitch, "R-cast-med: Applying intelligent agents to support emergency medical decision-making teams," pp. 24–33, 07 2007.
- [24] S. Ogino and R. B Wilson, "Spinal muscular atrophy: Molecular genetics and diagnostics," *Expert review of molecular diagnostics*, vol. 4, pp. 15–29, 02 2004.
- [25] V. Christie-Brown, J. Mitchell, and K. Talbot, "The sma trust: The role of a disease-focused research charity in developing treatments for sma," *Gene therapy*, vol. 24, 05 2017.
- [26] "University of rochester medical center rochester, ny, neurology clinical study of spinal muscular atrophy (sma)." https://www.urmc.rochester. edu/neurology/sma/about/genetics.aspx., 2019.
- [27] R. S. Finkel, "Natural history of sma and impact of standards of care on survival and motor function," pp. 1–4, 2016.
- [28] https://thegsf.org/blog/detail/project\_mariposa\_october\_recap\_ grants\_71-74/.
- [29] F. gretir, Spinal Muskuler Atrofi Hastalarinin Yasamlari. SMA Grubu, 2019.
- [30] http://ellas-corner.blogspot.com/2012/05/ mama-bracelets-re-opens.html, 2019.

- $[31] \ \texttt{https://smauk.org.uk/jasmine-fundraises-for-a-wheelchair}, \ 2019.$
- [32] D. Owens and H. Sox, Applications in Health Care and Biomedicine, Bayes' Theorem. Biomedical Informatics, 2014.