A Process Design for Rare Diseases Patients in Turkey

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Abstract. This paper is conducted to establish a better pathway for rare disease patients and doctors especially in Turkey. Through the project, contacts made with numerous rare disease patients, geneticists who expertise in this field, academicians, students of medicine department, and many more. After collection and evaluation of the raw data, the analysis is made to implement it for real life improvement scenarios. The analysis technique of this project was value stream mapping, which is broadly used to find the bottlenecks and slacks in the healthcare sector. Afterwards, final suggestions are explained on the last section. To conclude, the patient flow analysis for rare disease patients and especially the detailed flow for cystic fibrosis patients presented that a comprehensive strategy should be designed and plans should be made for rare diseases case in Turkey. This project was the first step for this mission, and also, the first project focusing on the rare diseases field from an engineering perspective.

Keywords: Rare diseases · Cystic fibrosis · Patient flow · Value stream mapping · Engineering analysis method

1 Introduction

Today health is the most essential field for any society as it has a significant effect on the development of humanity. The increased medical treatment and technological solutions are used more and more to cure patients. Especially the actions in the rare diseases field is gaining more importance in Europe and many other societies. Unfortunately, the awareness, actions and resources are very inadequate in Turkey. There is only one source of publication about rare diseases in Turkey, which is also gathering most of the information from foreign resources. Developments should be carried out on this field by starting an engineering analysis of the rare disease patient flow in Turkey.

Almost 9 years ago, it is stated by the Council of the European Union that, necessary plans and strategies should be developed to increase the synergy between local, national and transnational centres [2]. Turkey is way behind in that sense and an action to guide and unite all the rare disease patients should be taken. To begin with, the pathway of the rare disease patients in Turkey is researched and analysed carefully. In this project, a flow analysis is made for current and future states through findings from

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the interviews and surveys together with the focus group with doctors. Finally, a pathway of diagnosis and treatment of rare disease patients in Turkey is created with Value Stream Mapping technique. As a conclusion, recommendations are added accordingly.

2 Literature Review

A rare disease is any disease which is observed very uncommonly worldwide. Although it has many definitions, the main idea is to state that these diseases do not appear commonly and therefore, the physicians might not be able to diagnose and treat the patients. According to EURORDIS, it is called as rare disease, if a disease is observed less than 1 in each 2,000 people [5]. In another words, around 37,000 people is affected by a rare disease in Europe by taking the total population of Europe is 742,855,349 based on the assumptions of United Nations.

Many associations and organizations or non-governmental organizations have been established in order to provide economic, psychological and social support to patients and their families. In addition to this, these associations not only provide assistance but also create awareness about rare diseases. When associations in Turkey examined, it is observed that many associations just represent people with the same disease and unfortunately, there is no common work. Combining associations under a single roof will provide an effective communication as well as the sound of a strong community that cannot be underestimated in our country, in which 23.2% of the consanguineous marriages.

3 Fıeld Research

A field research study is conducted on rare diseases patients and doctors as online surveys, face-to-face interviews and focus group study. Prof. Dr. Melih Bulut and Prof. Dr. Ugur Ozbek helped us through all the stages of our study, who are the field expert doctors in Turkey and in contact with many patient organisations. The total duration of the study was approximately 10 weeks. An average of 80 answers on each survey is collected. Main outcomes of this study can be stated as follows: the diseases, which are observed in Turkey are analysed, the duration of the testing and diagnosis phases are examined, the knowledge of patients about their diseases and similarity of different diseases are analysed, the range of the patients ages and genders are gathered, the examination time of doctors on patients for one visit is gathered, active patient organizations are observed and contacted, the obstacles of the doctors about the diagnosis are analysed, and finally, suggestions and wishes of both patients and doctors are collected and analysed.

After analysing the data pool, the details of cystic fibrosis disease are explained more in detail. The following outcomes are achieved and used for value stream mapping: The average age of diagnosis is gathered, patient waiting times are collected and analysed, the misdiagnosis rate is calculated, the average number of the doctors that a patient visits is analysed, the average approximate time of the testing phase and

examinations is gathered, and previous and current situation of free of charge tests provided by public hospitals for CF patients are analysed.

There are some problems with rare diseases issue in Turkey. Firstly, the health data inappropriately to the E-Nabiz platform (Online Health Portal), currently used International Coding of Diseases ICD-10 does not cover many rare diseases and it should be updated with the ICD-11 instead. Secondly, beginning from the Ministry of Health, there is a lack of awareness and care about the rare diseases patients in Turkey. Our aim is to put a preceding step for this trainings as well. Other problems are low budget allocation and no budget plan, non-membership of EU and etc. Survey results can be stated as follows:

- The system is inadequate and the ministry of health needs to establish a policy. In total, there are 8000 diseases without a registry. For instance, asthma entered under the child diseases; albinism entered as a blindness. In our first survey, 70% of the patients stated that there is an inadequate knowledge of healthcare personnel about the causes of misdiagnosis. In this case, it should be handled by the ministry of health to create a programmed education and awareness.
- 10-min examination time is insufficient. It is impossible to diagnose a rare disease in 10 min. Most of the tests required for rare diseases are expensive and not paid by the government.
- The newborn heel-screening test is implemented for 4 kinds of diseases as follows Hypothyroidism, Phenylketonuria (PKU), Biotinidase Deficiency and Cystic Fibrosis respectively. Thanks to newborn screening program when started in 2015, real frequency of the disease in Turkey could be learn [11].
- The frequency of the Cystic Fibrosis in North America and Europe is around 1/2,500. The exact frequency in our country is unknown. However, it is thought to be from 1/3,000 to 1/4,000. According to TUIK 2018 data, Turkey's population of 2018 was 80,810,525 [3, 4]. In this case, from 20,203 to 26,937 people suffer from the Cystic Fibrosis. Such a large number represents a considerable community.
- When symptoms are first realised, patients are on average 1.5 years old. The age range is from 0 to 19.
- After realising the symptoms, patient waits an average of 66 days until the examination. Waiting times range from 0 to 1800 days.
- After make an appointment for the examination, expected time is 16 days and ranges from 0 to 450 days.
- After examination, full diagnosis takes an average of 98 days. This period ranges from 0 to 1800 days.
- The patients were 3 years old at the time of diagnosis. The ages range from 0 to 40 years.
- Patients go to 4.2 doctors, until the diagnosed. Misdiagnosis lead to prolong the duration of the diagnosis approximately 15 months and ranges from 0 to 180 months. 68% of the patients were misdiagnosed.
- When it is asked the patients who had been misdiagnosed, how many times were diagnosed wrongly, the answer is received as 2.2 times. The gender distribution of cystic fibrosis patients participating in the survey were equal.

- When adequacy of resources in Turkey is asked with 1–5 Likert scale, average answer as 2,1 is received.
- When similar diseases with the most common misdiagnosis is asked, 20 kinds of diseases are obtained. For instance, asthma and bronchitis are the ones that have almost inseparable symptoms.

4 Value Stream Mapping

4.1 Introduction

Value stream mapping (VSM) is a flowchart method to illustrate, analyse and improve the steps required to deliver product or service and uses a system of symbols to depict various work activities and information flows. In our study, the VSM technique is used because main problem was the astronomic numbers of cycle and waiting times, backward flowing pathways and loops on patient doctor interactions. For sure, there are other reasons, which are unmeasurable such as inadequate knowledge of patients and healthcare personnel. However, the focus group study with doctors has provide us valuable information about this issue as well. Before designing the VSM, a flow analysis designed for current and future scenarios. In this project, there are 2 current flows for patients born before 1st of January on 2015 and after 1st of January on 2015 due to the heel-screening test mentioned in the previous section. However, the future flow is only one and united flow with the rare diseases hub in Turkey.

4.2 Current Flow Analysis

(1) Current Flow Diagram: The flow is designed for a patient going to a state hospital as many rare disease patients first choice is a state hospital. There are 3 main stages in the patient flow; appointment and examination, testing, results and diagnosis.

Although it seems like the same flow of a regular illness, a flow for the rare disease patients have a huge difference compared to that, due to its start with patients experience of an intense disease symptom, unpredictable length of testing and diagnosis phase and loops created within this patient-doctor cycle until disease is truly diagnosed. This is the critical path for our research as it delays the diagnosis with an unpredictable time and results with fatal consequences for a patient. However, obstacle of diagnosing a disease cannot be assigned only to doctors, because it is quite challenging to make right diagnosis in 10 min appointment and even with available state hospital test results. Even for a normal disease, there is always a misdiagnosis probability. It is harder if disease has similar symptoms or test results with hundreds of many other diseases. This scenario is much more challenging for the rare disease patients because of the following reasons.

1. Inadequate options and resources for specific testings
   a. Lack of testing options in most of the hospitals
   b. High costs and long durations for specific tests
2. The healthcare personnel and doctors are lack of adequate knowledge about rare diseases due to
   a. Inadequate academic lecturing
   b. Underestimation due to lower prevalence rates compared to rare
   c. No trainings designed by the ministry of health

A general flow of the rare diseases patients in below indicated in Fig. 1.

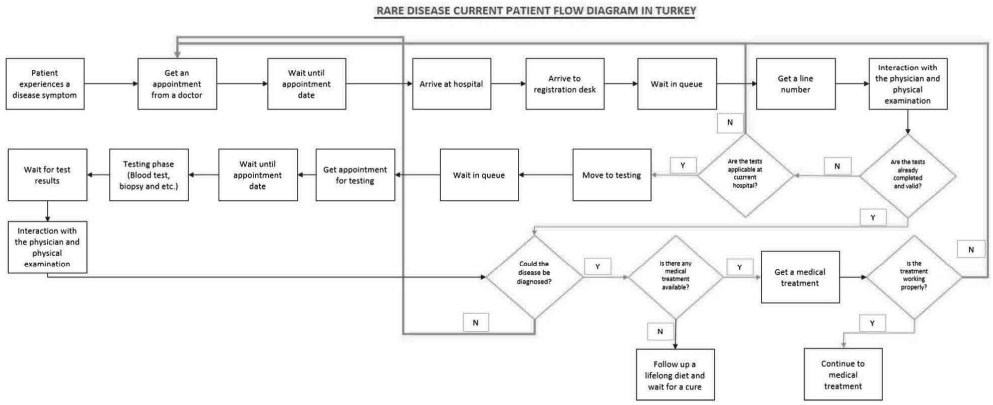

Fig. 1. Rare disease current patient flow diagram

On the figure, it can be clearly observed that the loops of taking an appointment might occur from three points: unavailability of test at the current hospital, undiagnosed disease by the current doctor, or ineffective treatment on the disease.

For the current cystic fibrosis flow of patients born earlier than year 2015, there are 4 backward paths observed. Two of them is the same for the general case of rare disease patients, which are tests unavailability at the current hospital, and the ineffectiveness of the treatment. Other 2 activities are different than the general case. Either patient actually is not a cystic fibrosis patient, or unavailability of medical treatment for cystic fibrosis patients at current hospital.

It can be clearly observed on flow that fully understanding that the patient is a Cystic Fibrosis patient is happening almost at the end of the flow. Therefore, there is a tremendous amount of time loss for these patients who are mainly children under serious health risks. On the other side, there is no backwards loop at the current flow of patients born after year 2015, which is a very good development as seen in Figs. 2 and 3 respectively.

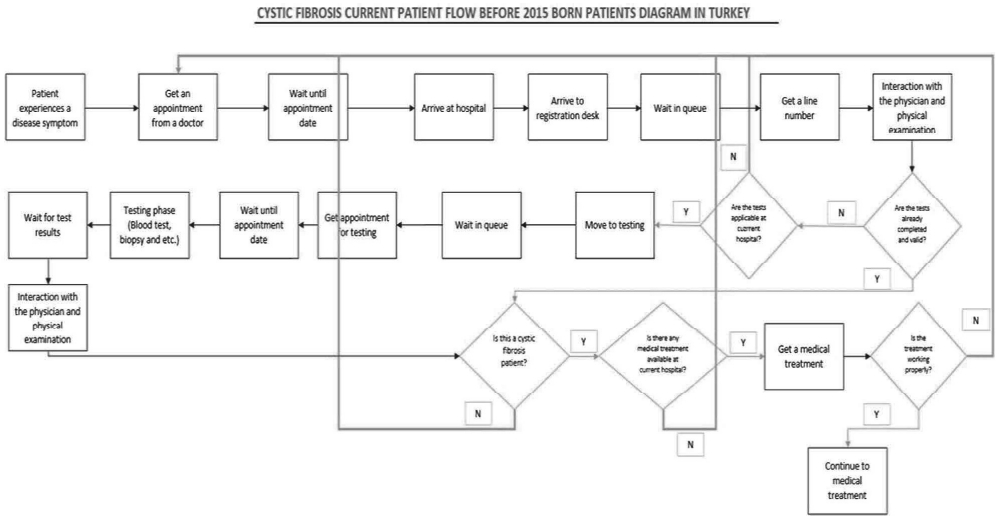

Fig. 2. Cystic fibrosis current patient flow: before 2015 born patients diagram

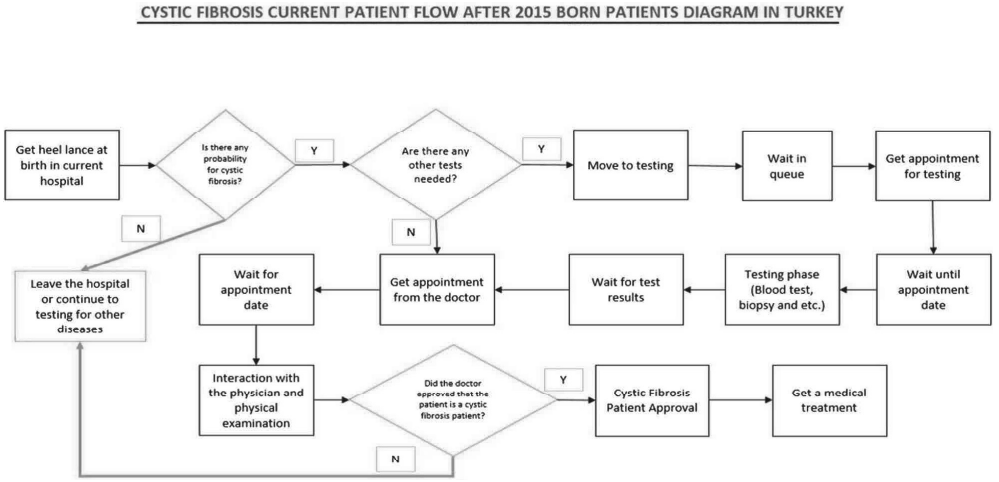

Fig. 3. Cystic fibrosis current patient flow: after 2015 born patients diagram

(2) Current State Map: After the evaluation of the 2 alternatives of CF patient flows a general current state map is created with average time values stated for each step. The value added times are

- Registration desk: The time spent during the patients process on the registration desk of the hospital to give her ID number to the person in charge, the control of personnel on the computer, whether the patient has already booked appointment, and approving appointment and giving a line number to the patient.
- Examination: The time interval of doctor examining a patient (Sector standard is 15 min in Turkey)

- Registration desk: The time of patient taking an appointment for testings stated by the doctor. The patient comes to desk, the personnel searches for the testings entered by the doctor on the system, personnel prints out and gives the line numbers for each testing to the patient.
- Test appointment: The total time of the actual the testing processes.
- Test examination: The real time required for the analysis of a test.
- Examination after testing: The patient's second visit to the doctor for the test results evaluation and examination. Again, the sector standards is the limit here.

The non-value added times are the waiting times in between the value-added activities, which is wanted to minimize as possible if the conditions held on real life. These are for example waiting on the lines, waiting because of unforeseen events such as process delays from previous patient, or time passed during changing clothes, wearing some tools before testing and etc. However, reducing these times are usually not possible due to many procedures, regulations and standards implemented on health sector. Therefore, minimizing them is beyond the topic of this study. Figure 4 shows the Cystic Fibrosis Patients Current Value Stream Map.

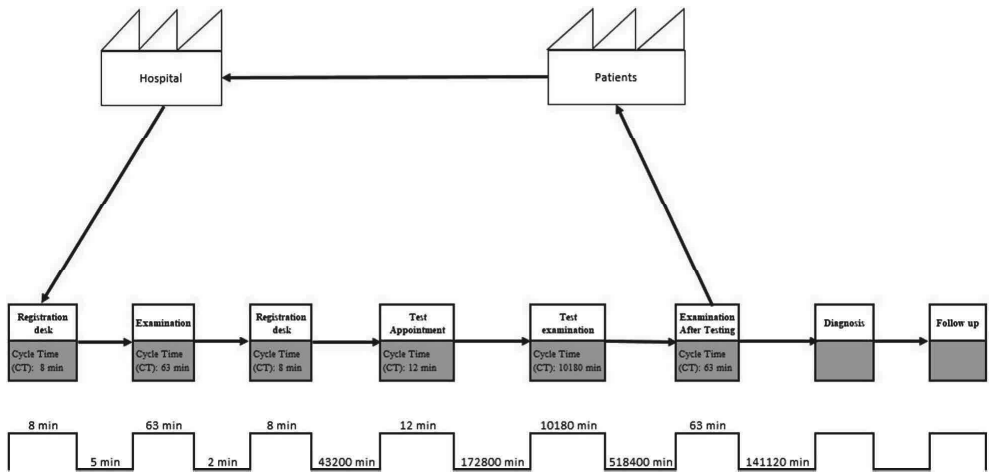

Fig. 4. Cystic fibrosis patients current value stream map

4.3 Future Flow Analysis

(1) Future Flow Diagram: The future flow analysis is designed based on the findings of the selected concept with AHP technique in the next section of this report. The selected concept to improve the rare disease patient flow is establishing a rare diseases hub in Turkey as a rare diseases hospital to serve only for these specific diseases. For the future flow there are some assumptions taken as stated below.

Assumption 1: The cloud based healthcare data storage system in Turkey (E-nabiz) will be improved including family genetics, and ICD-11 codes. ICD-10, current code system used in Turkey does not include rare diseases. ICD-11 codes are the new

disease codes announced by WHO including many rare diseases. (*ICD: International Classification of Diseases)

Assumption 2: Doctors and healthcare personnel are started to take trainings about rare diseases.

Assumption 3: The rare diseases hub will serve as a hospital under ministry of health.

Assumption 4: An area of profession for rare diseases will start to work in this hub as an intern or as a doctor.

Assumption 5: The European Reference Networks (ERN) for rare diseases will be followed.

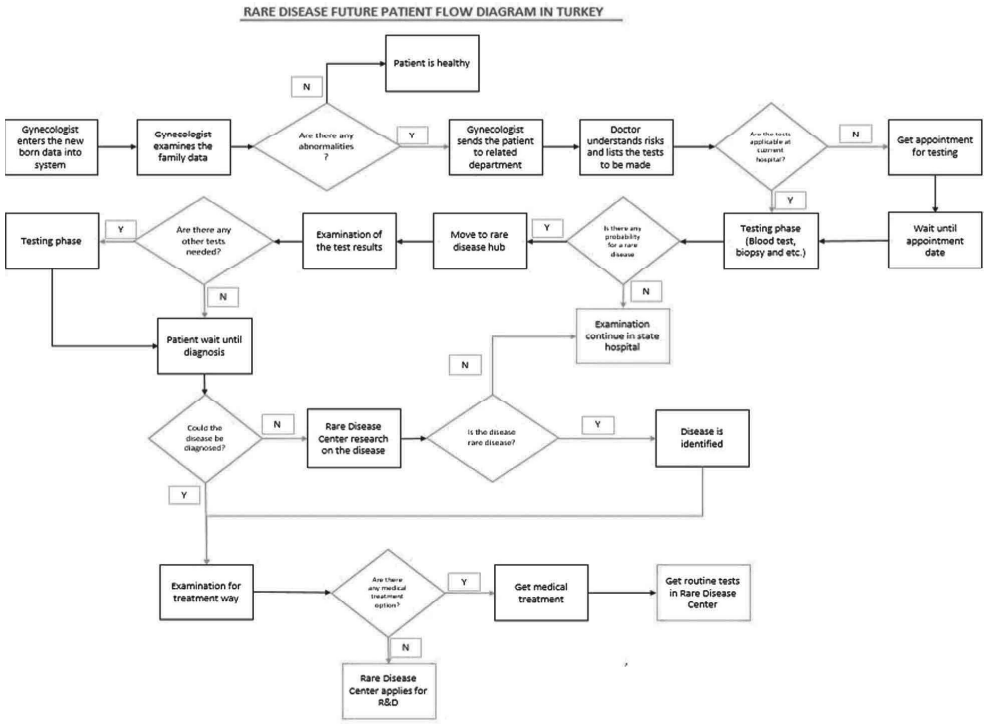

Fig. 5. Rare disease future patient flow diagram in Turkey

In the future flow given in Fig. 5, the steps are different than the current flow as the genetic data of a patient is analysed at the birth and necessary actions started earlier. If there is a rare disease possibility for this patient, the hospital sends the patient to the rare diseases hub and examinations continue at there. The centre makes necessary tests, search for the rare disease, search for treatment options and apply to ministry of health if there isn't any treatment yet. Basically, rare diseases hub will serve to the patients as a special centre such as the cancer treatment centres. After that, if the rare disease diagnosis is made patient gets the treatment and follows up the regular controls at this centre. If not diagnosed, patient goes back to a state hospital for following examinations.

The future flow for a cystic fibrosis patient is also created as special circumstances occur for every different disease. Figure 6 shows the cystic fibrosis patient flow design with the suggested rare disease hub. As it can be observed very clearly, there are no backward flows or loops created. The patient flow is on one and fluent direction with an establishment of rare disease hub, and other assumptions stated.

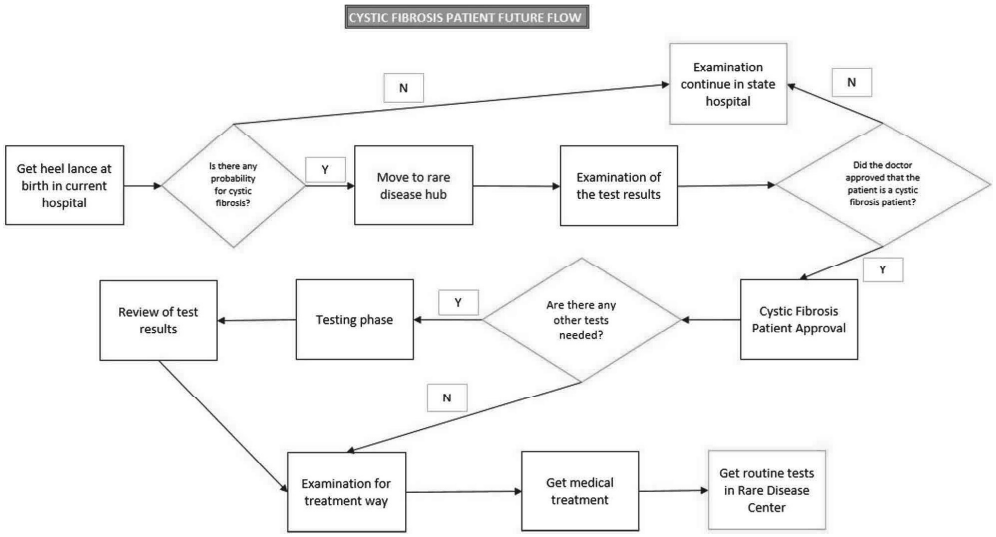

Fig. 6. Cystic fibrosis patients future flow in Turkey

(2) Future State Map: Then, a future state map is generated for cystic fibrosis patients in Turkey. The total value-added average cycle time is reduced from 10,334 min to 10,217 min with this suggested future flow. The cycle time of activities reduced significantly, due to lowering the visiting amount of a doctor to only once. Also, there are other effects such as healthcare personnel's and patient's increased knowledge about rare diseases, more resources availability and increased use of technology. Including all these quantitative and non-quantifiable affects the cycle time is reduced as given in Fig. 7.

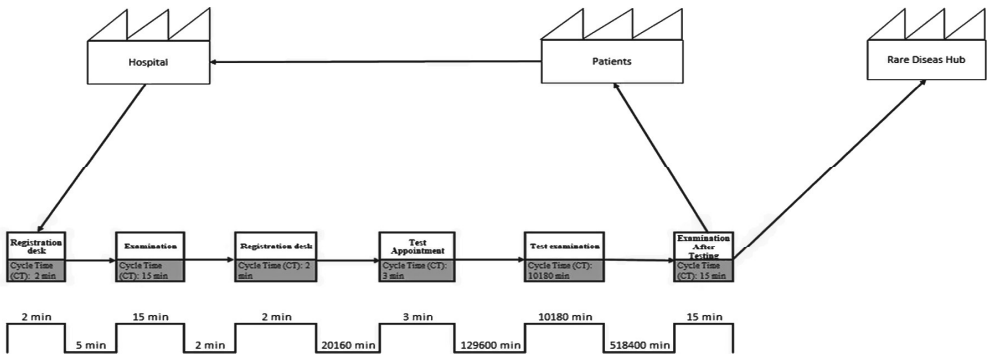

Fig. 7. Cystic fibrosis patients future flow

5 Concept Analysis

5.1 Concept Generation and Concept Selection with AHP Technique

The Analytic Hierarchy Process (AHP) is a structured technique for organizing and analysing complex decisions. In this study, evaluated options are website, app, new hub, department of hospital. When choosing from the options, different criteria are considered which affect not only cost but also the sustainability of hub. Also, articles that is about hospital location selection are considered. We have identified 3 main criteria as an efficiency, feasibility and ease of communication and 7 other sub-criteria beneath them.

The top of the hierarchy is goal of the analysis and then multi criteria that consist of several factors. The last level is the alternatives. The weights of the criteria is calculated by the dual evaluation method.

Step 1. Develop the weights for the criteria by
- developing a single pair-wise comparison matrix for the criteria
- multiplying the values in each row together and calculating the n^{th} root of said product
- normalizing the aforementioned n^{th} root of products to get the appropriate weights
- calculating and checking the Consistency Ratio (CR)

Step 2. Develop the ratings for each decision alternative for each criterion by
- developing a pair-wise comparison matrix for each criterion, with each matrix containing the pair-wise comparisons of the performance of decision alternatives on each criterion
- multiplying the values in each row together and calculating the n^{th} root of said product
- normalizing the aforementioned n^{th} root of product values to get the corresponding ratings
- calculating and checking the Consistency Ratio (CR)

Step 3. Calculate the weighted average rating for each decision alternative. Choose the one with the highest score.

The weights obtained by comparing each criterion are indicated. Then, the scores of the positions were determined by collecting the data obtained by multiplying the weight of the criteria for each position by the weight of that criterion. In accordance with this scoring, new hub establishment has the most consistent results.

5.2 Framework for the Selected Concept

Technically it is possible for Turkey to establish a rare diseases hub from the constructional, administrative and technological levels. However, the lack of knowledge of the healthcare personnel cannot be underestimated in this case, because the hub will work by their helps as well. Firstly, a training design should be considered for physicians. Secondly, conferences for the patients should be organized and interactions with the physicians is aimed to be increased during the pathway. From the technological

perspective, data analysis tools can be used to develop the pathway estimations with the each entered data. Later on, if the budget is enough, new technological implementations can be considered.

Since the health budget for the 2019 is still argued at the Grand National Assembly of Turkey, the budget estimation for rare diseases implementations is unknown as well. However, EU health budget plan for 2021–2027 period for ERN is € 413 million. In other words, Europe will allocate this money only for 30 million rare disease patients living in EU [2]. The health budget according to Grand National Assembly estimations was 33.583 billion Turkish lira for 2018 period. The rare diseases hub will be located under Health Institutes of Turkey, whose budget is 53 million Turkish lira in Turkey. Another finding showed that there is a test made at birth for PKU and cystic fibrosis patients, and there is plan for SMA test but the budget is not given for any of them [1].

In Turkey, currently there is no decisions or estimated budgets for such a project. A rare diseases hub as a patient flow guider should be created under the Ministry of Health with necessary budget amount to be calculated. Looking at legal structure of health sector in Turkey shows us that only rare diseases section is only mentioned under the Medical Social Services Unit. Since there is no legal documentation for rare diseases in Turkey, EU legislations will be offered to use.

6 Conclusions and Future Work

There are 4 main parts executed on this study to design a rare disease patient flow in Turkey. These parts are the literature review, the field analysis, value stream mapping implementation and concept analysis for future studies.

The results of this study can be collected on 3 main points, which are informing the community, the health personnel and the rule makers, which are Ministry of Health and government authorities. Informing the society and increasing the public awareness about rare diseases is one of the key points. The world rare diseases day on the last day of February is for that aim a good option to increase the awareness. Commercials, social media postings and videos should be increased. This can be done via including public communications technical personnel on the rare diseases hub. Especially training the healthcare staff and the rule makers are very important as they significantly contribute to the decision making and technological application part. A rare diseases hub will be a starting point for collection of all genetic information and evaluation of them to develop the national understanding on rare diseases. It will also serve as a research centre as it will have the collected rare diseases patients data. All in all, the biggest lesson learned from study was that, this rare diseases field should not only be studied by medicine and genetics & bioengineering students, but also by the management and computer engineering students as well. In that way, different perspectives can be considered for the most effective patient flows.

This study aimed to execute the first analysis on the rare diseases patients in Turkey. Taking this as a key resource, it is suggested that a detailed analysis and a feasibility plan for the rare diseases hub to be carried out. Furthermore, to raise awareness of the community, technological solutions and social media platforms could

be used to promote the importance of rare diseases case. The world rare disease day on the end of February is the best opportunity serving to this issue.

As a conclusion, necessary training programs for the doctors and other healthcare personnel should be strictly planned to increase their knowledge level about rare diseases. Besides, comprising a rare diseases expertise for geneticists and doctors would increase the effectiveness of rare diseases hub, and contribute to Turkish health sector by enabling researchers to develop treatment options inside the country.

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