IZMIR BIOMEDICINE AND GENOME CENTER

STATUS AND NEEDS ASSESSMENT FOR RARE AND UNDIAGNOSED DISEASES WITH RESEARCH AREA STAKEHOLDERS: SURVEY AND WORKSHOP REPORT

RareBoost
ERA-CHAIR PROJECT

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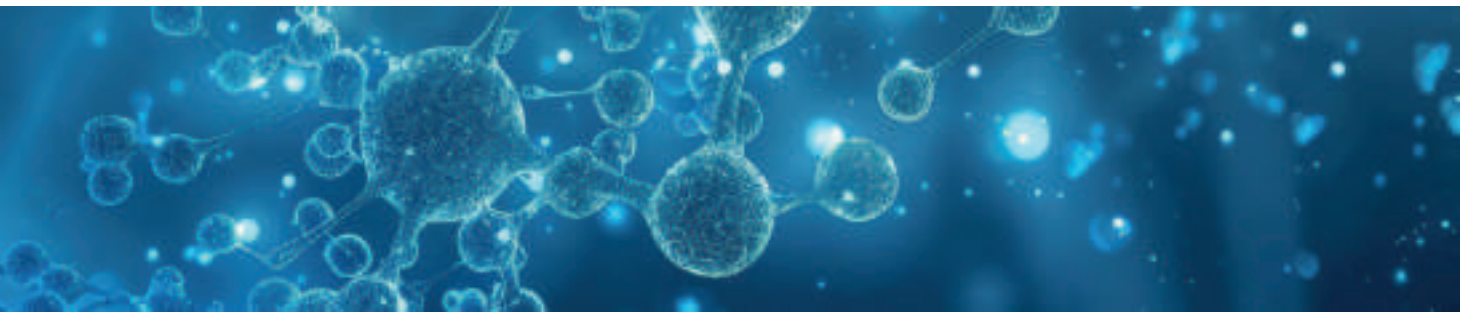
CONTENTS

EDITOR 1
ASSISTANT EDITORS 1
CONTRIBUTORS 3
CONTENTS 5
TABLE OF FIGURES 6
TABLE OF TABLES 6
ABBREVIATIONS 7
INTRODUCTION 8
1. RARE DISEASES 9
1.1. OVERVIEW RARE DISEASES 9
1.2. INTERNATIONAL AWARENESS OF RARE DISEASES 9
1.3. VARIOUS ACTIVITIES CONDUCTED IN OUR COUNTRY ON RARE DISEASES 10
2. RARE AND UNDIAGNOSIS DISEASES NEEDS ASSESSMENT SURVEY 12
2.1. QUESTIONS AND ANSWERS 12
2.1.1. QUESTIONS ABOUT PERSONAL INFORMATION 14
2.1.1.1. Gender Information 14
2.1.1.2. Age Distribution 14
2.1.1.3. Professional Information 14
2.1.1.4. Area of Expertise 15
2.1.1.5. Subspecialty 15
2.1.1.6. Post-specialization time 15
2.1.1.7. Institution (Affiliation) Information 16
2.1.1.8. Status of Conducting Activities in the RD Area Activities Conducted if the Answer is “Yes” 16
2.1.1.9. Status of Conducting Activities in the RD Area and Responses Given If the Answer is “No” 17
2.1.2. QUESTIONS ABOUT GENERAL INFORMATION AND EXPERIENCE 18
2.1.2.1. Frequency of Encountering RD 18
2.1.2.2. Frequency of Encounters During the Follow-Up of Patients Diagnosed with RD 18
2.1.2.3. Conditions and Rates of Regular Follow-up of Patients 19
2.1.2.4. Conditions of Regular Follow-up of Patients (Reasons if the answer is “No”) 19
2.1.3. QUESTIONS ABOUT THE CHALLENGES ENCOUNTERED AND THE DIAGNOSIS PROCESS 20
2.1.3.1. Most common challenges in the management of rare and undiagnosed diseases 20
2.1.3.2. Status of referral of patients to another center/ Reasons if the answer is “yes”/ Information the facility if the answer is “no”. 21
2.1.3.3. Presence of an Interdisciplinary Center or Council in the Institution and Distribution of Answers (Yes/No/Don’t Know) 22
2.1.3.4. Access to Resources on RD Diagnosis and Distribution of Different Resources Used by Subject 23
2.1.4. QUESTIONS ABOUT PATIENT CARE, SUPPORT OF PATIENTS AND PATIENTS’ RELATIVES 24
2.1.4.1. Support for Patients’ Needs in Diagnosis and Post-Diagnosis Processes and Locations to Get Support If the Answer is “Yes” 24



2.1.4.2. Patients in Accessing Special Care and Treatments for Patients and Proportional Distribution of These Difficulties 24
2.1.4.3. General Awareness Level 25
2.1.4.4. Improvement of Awareness Level 26
2.1.5. QUESTIONS ABOUT RESEARCH AND EDUCATION 26
2.1.5.1. Status of being present as an executive or researcher in a scientific research within the scope of RD and, if the answer is "Yes", the scope of the study 26
2.1.5.2. Status of receiving training on RD 27
2.1.5.3. Information on how and from which source one is informed about the latest developments on RD 28
2.1.5.4. Attitude Towards Sharing the Data Obtained from the Samples Evaluated in the Research 28
2.1.5.5. The Nature of the Challenges Encountered in Scientific Studies in the Field of RD and Orphan Drugs in Türkiye 30
2.1.6. QUESTIONS REGARDING ECOSYSTEM STAKEHOLDERS AND COOPERATION 30
2.1.6.1. Frequency of Collaboration with Other Healthcare Professionals in RD Diagnosis 30
2.1.6.2. Information about institutions and organizations contacted regarding RD 31
2.1.6.3. Awareness on Supporting RD Research and Treatment Processes as Government Policy 31
2.1.6.4. Information on Policy Changes or Improvements in the RD Area 31
3. SUGGESTIONS 33
3.1. RESEARCH STUDIES IN DIAGNOSTIC PROCESSES 34
a) Developments in Diagnostic Processes in the World and in Europe 34
b) Studies and Development Areas Regarding Diagnostic Processes in Our Country 35
i) Improvement Steps Regarding Diagnostic Processes 36
ii) Human Resources, Infrastructure and Financing Needs in Diagnostic Processes 36
3.2. RESEARCH STUDIES IN TREATMENT PROCESSES 39
a) Developments Regarding Treatment Processes 39
b) Necessary Developments for the Improvement of Treatment Processes in Türkiye 39
3.3. AWARENESS AND EDUCATION ACTIVITIES 41
a) Trainings to be Implemented in Türkiye 41
b) Content of Educational Materials and Guides on Diagnosis and Treatment of RD 42
i) For Physicians and Healthcare Professionals 42
ii) For Patients and Their Relatives 44
3.4. DEFINITION OF THE ECOSYSTEM AND COOPERATION POSSIBILITIES 45
a) Industrial Contribution of Pharmaceutical Companies 46
b) Angel Investor and Orphan Drugs 47
4. CONCLUSION 47
5. REFERENCES 50

TABLE OF FIGURES

Figure 1: Distribution of survey participants according to their professional field 14
Figure 2: Distribution of survey participants according to their areas of expertise 15
Figure 3: Distribution of survey participants according to the institutions they work for 16
Figure 4:distribution of activities carried out in the field of rd in the institutions of the survey participants. 17
Figure 5: General awareness distribution. 26
Figure 6: Scope of the studies in which the participants worked as administrators or researchers in scientific research within the scope of RD. 27
Figure 7: Distribution of sources through which survey participants are informed about developments in RD. 28
Figure 8: Attitudes towards sharing sample data used in research 29
Figure 9: Group titles in the workshop 34

TABLE OF TABLES

Table 1: Occupations of the participants who responded to the question “how often do you estimate that you encounter rare and undiagnosed patients? 18
Table 2: Most common challenges in the management of rare and undiagnosed diseases 20
Table 3: Distribution of institutions where participants do not need to refer their patients to other centers work 22
Table 4: Distribution of institutions worked according to interdisciplinary center or council presence* 22
Table 5: Difficulties encountered by patients in accessing special care and treatments for patients 25
Table 6: Challenges encountered in scientific studies in the field of rd and orphan drugs in türkiye 30
Table 7: Occupational distribution according to the frequency of cooperation with other healthcare professionals in diagnosing RD 31
Table 8: Participant responses and number of participants regarding policy changes or improvements in the field of rare and undiagnosed diseases 32

ABBREVIATIONS

EU	Europe Union
USA	United States of America
AIFD	Association of Research-Based Pharmaceutical Companies
R&D	Research and Development
Asrid	Advocacy Service for Rare and Interactable Diseases
CORD	Canadian Organization for Rare Disorders
ERA	European Research Area
EURORDIS	European Organisation for Rare
GC	Good Clinical
GMP	Good Manufacturing Practice
HTA	Health Technology Assessment
IRDiRC	International Rare Diseases Research Consortium
IBG	Izmir Biomedicine and Genome Center
İSTisNA	Istanbul Solution Platform for Undiagnosed and Rare Diseases
RD	Rare Disease
NICE	National Institute for Health and Care Excellence
NORD	National Organization for Rare Diseases
OMIM	Online Mendelian Inheritance in Man
ORPHANET	The Portal For Rare Diseases And Orphan Drugs
RUDiP	Rare and Undiognosed Disease Platform
SMA	Spinal Muscular Atrophy
STK	Civil Society Organisation
TUBITAK	Scientific and Technological Research Council of Turkey
TUSEB	Presidency of Turkish Health Institutes
YÖK	The Council of Higher Education

INTRODUCTION

This report covers the scope, results, recommendations and presentations of the workshop titled “Status and Needs Assessment Workshop for Rare and Undiagnosed Diseases with Research Field Stakeholders”, which was carried out within the scope of the RareBoost ERA Chair project supported by the European Union H2020 program, implemented by Izmir Biomedicine and Genome Center, in the context of Rare Diseases.

A total of 68 people, including experts, public officials and representatives of non-governmental organizations, attended the Workshop held on December 22, 2023.

The questions and other necessary information about the workshop and the survey conducted within this scope can be accessed from the **“ Workshop “** and **“ Survey “** headings in the News and Events tab at https://rareboost.ibg.edu.tr .

1. RARE DISEASES

1.1. OVERVIEW OF RARE DISEASES

Depending on the criteria determined by different countries, some diseases are considered "rare" and all of these "rare" conditions are collectively called Rare Diseases (RD)[1] . Although RD are called "rare" according to their frequency of occurrence, when we look at the general population, it is understood that the condition has a different feature. For example, approximately 25-30 million individuals in the United States (US) and approximately 30 million individuals in the European Union (EU) suffer from RD [2,3] . When the number of patients mentioned is evaluated together with their families, it is clear that this number will increase several times. When we look at the data of OMIM (Online Mendelian Inheritance in Man) , which is one of the most reliable databases where human diseases are cataloged, it has been reported that there are around 7000 identified RD. In a study published in 2019, information from ORPHANET, another database, was evaluated and it was reported that there were 6172 RDs[4,5] . According to the mentioned study, 71.9% of these diseases are of genetic origin and 69.9% have childhood onset [4].

Approximately 35% of deaths in the first year among live births are due to RD-related conditions[6]. Another important data is that 1/3 of children born with a RD die before the age of five [7]. The 149 diseases identified among RD correspond to 4.2% of all groups and, as such, have a frequency of 1-5/10,000 in the society. 84.5% of RD include 5304 diseases and their frequency is less than 1/1,000,000 [4].

1.2. INTERNATIONAL AWARENESS OF RARE DISEASES

RDs are generally a heterogeneous group of diseases and occur at different rates geographically in various regions of the world [4]. In addition, they have a low prevalence, which causes the lack of information about the disease and the insufficient number of experts on the subject, making access to these experts limited and difficult [8]. Considering the information explained above, it is understood that the fight against these diseases poses a serious problem for patients and their families, as well as a burden for the social/health policies of states.

In order to overcome the problems and increase social awareness, RD associations or organizations operating with different structures have been established in various countries. Some of them are striving to expand their power and effectiveness by forming umbrella organizations.

Brief information about different efforts is given below in chronological order.

In this context, the first studies carried out started in the USA. In the last quarter of the 20th century, RD awareness activities began with various associations established by patients and their relatives, which were local at that time. With the effective efforts of NORD (National Organization for Rare Diseases), which was established afterwards, public opinion was created and the law, also known today as the Orphan Drug Act , was adopted in 1983[9,10]. NORD currently includes more than 300 communities and provides legal, educational, scientific, etc. services on RD. It carries out its activities as the strongest and largest umbrella organization in its field, carrying out studies on many subjects[11].

In the EU, the first steps on RD were taken approximately a quarter of a century later than the USA. The first example in this context can be given as EURORDIS (European Organization for Rare Diseases), which was established in 1997. EURORDIS has set the goal of conducting RD-related studies and developing orphan drugs to be used in the treatment of these diseases. As a non-profit, non-governmental organization, EURORDIS either supports all these processes or provides support by being involved in the processes. EURODIS, like NORD, is an umbrella organization with its structure representing 894 RD patient organizations from 72 different countries (https://www.eurordis.org/about-eurordis). Apart from these, CORD (Canadian Organization for Rare Disorders) in Canada (http://www.raredisorders.ca/about-cord/) and ASrid (Advocacy Service for Rare and Interactable Diseases) in Japan.
Incurable Diseases Defense Service (https://asrid.org/en) and India's ORDI (Organization for Rare Diseases India) (https://ordindia.in) organizations also discuss national priorities on similar issues. They organize various studies taking this into account.

As a result of the coming together of RD organizations under the leadership of the USA and the EU, briefly mentioned above, in 2011, IRDiRC (International Rare Diseases Research Consortium) was established with the cooperation of NIH (National Institutes of Health) from the USA and the European Commission (http://www.irdirc.org/about-us/history/). IRDIRC facilitated the organization of international congresses attended by specialized scientists and researchers in the field of RD. These were held in April 2013 (Ireland), November 2014 (China), February 2017 (France), October 2023 (Canada) and December 2023 (Online)
(https://irdirc.org/activities/irdirc-conferences/). Various scientific articles in which the outcomes of the congresses were presented and discussed were also published simultaneously [12-14].

1.3. VARIOUS ACTIVITIES CONDUCTED IN OUR COUNTRY ON RARE DISEASES

Our country is trying to contribute, within its means, to the studies on RD that are carried out on international platforms mentioned above. Previously, studies on RD were carried out in Türkiye in an unorganized fashion, but these were mainly through well-intentioned individual initiatives of scientists interested in the subject. Following these initiatives, Türkiye began to officially participate in studies on RD. For example, our country contributes as a partner to the formation of ORPHANET, which also serves as a non-profit internet portal supported by the EU Commission, where information on RD and Orphan Drugs is compiled. As stated in the report published in January 2023, where ORPHANET members and supporting countries were presented, Prof. Uğur ÖZBEK, Prof. İlhan SATMAN and Head of Autism and Special Needs Department of the Ministry of Health, Prof. Onur Burak DURSUN from Türkiye has been authorized as ORPHANET Türkiye National Team.
(https://www.orpha.net/pdfs/orphacom/cahiers/docs/GB/Orphanet_Network_MB_members.pdf).
Many associations, which are deeply involved with the real problems regarding RD, are the material and spiritual advocates of this issue, organize various events to raise awareness. These associations, which initially worked independently of each other, came together and established the Rare Diseases Network. Today, they have brought together 16 different associations in this network and continue their work with the power gained from this unity (https://www.nadirhastaliklaragi.org.tr/uyeler). Another positive development in our country is that RD Day events are organized regularly, just like in many other countries. Thanks to these events, awareness about RD is raised in a wide segment of the society. These events are held regularly in many cities across the country in universities and hospitals of different levels, on the last day of

February every year. The impact of these awareness activities, carried out throughout the society, has shown itself in many areas. For example, in some scientific project application calls opened by TUSEB recently, RD issue is directly reported as a priority. Scientific calls opened in 2019 and 2020 and titled "Individual and Transformational Medicine Field Applied Project Collaboration Call" (calls numbered 2019-BT-01 and 2020-BT-02) are examples of these.

Another initiative; "ISTisNA – Istanbul Tanısız ve NAdir Hastalıklara Çözüm Platformu– Istanbul Solution Platform for Undiagnosed and Rare Diseases" supported by the Ministry of Industry and Technology and Istanbul Development Agency can be given as an example. This platform was created by Prof. Uğur ÖZBEK, in order to minimize the effects of social and physical disadvantages caused by rare and undiagnosed diseases. It was implemented as a project led by Prof. Uğur ÖZBEK, jointly carried out by Acıbadem Mehmet Ali Aydınlar University, Istanbul University Aziz Sancar Experimental Medicine Research Institute and the Health Institutes of Türkiye (TUSEB). In line with the aim of raising awareness about RD to a wide audience, the project brought together participants from different stakeholders. These are: Istanbul Provincial Health Directorate, Istanbul University-Cerrahpaşa Neurological Sciences Institute, Health Sciences University, Turkish Spastic Children Foundation, Izmir Biomedicine and Genome Center, Istanbul University Clinical Research Excellence Application and Research Center. The supporters of the mentioned project are: Association of Research-Based Pharmaceutical Companies (AIFD), Boğaziçi University Life Sciences and Technologies Application and Research Center, Hacettepe University Genomics and Rare Diseases Application and Research Center, Istanbul University - Bioinformatics Department, Rare Diseases Network. The total budget of the project was determined as 12,984,174.74 TL. The unity of such a large audience in the context of a specialized subject is undoubtedly a good and successful example of the dimensions that awareness has reached.

The "RareBoost" project, which has been approved and supported by Izmir Biomedicine and Genome Center (IBG) within the scope of the EU Horizon 2020 "ERA Chair" program implemented in 2020 and led by Prof. Uğur ÖZBEK, is carried out with the aim of transforming IBG into an international center of excellence in RD research and innovation.

Within the scope of the project, which has a budget of approximately 2.5 million Euros, a 'Rare and Undiagnosed Diseases Platform' (IBG- RUDiP) was established in IBG (https://www.ibg.edu.tr/research-programs/groups/ibg-rare- diseases/). 17 faculty members who contribute to this platform conduct research on subjects such as RD diagnosis, modeling, and developing possible treatment options with a multidisciplinary approach. In this context, researchers will be involved in or carry out numerous national and international collaborations. In line with the aforementioned objectives, the RareBoost project purpose to organize a patient advisory council focused on RD, a seminar series, a needs assessment workshop on orphan drugs, and to facilitate the learning of the subject by large masses by organizing joint events with various student clubs.

As one of the activities of the mentioned project, a comprehensive workshop was conducted with 68 participants including experts on the subject, public officials and representatives of different non-governmental organizations, and a survey was conducted in parallel.

2. RARE AND UNDIAGNOSIS DISEASES NEEDS ASSESSMENT SURVEY

Considering the above-mentioned issues, the " Status and Needs Assessment Survey for Rare and Undiagnosed Diseases with Research Area Stakeholders" , including four main groups (Researcher, Clinician, Clinician-Researcher, Healthcare professionals) , was prepared and shared with the stakeholders.

The main purpose of conducting the survey was to determine the awareness about RD based on the reality of our country, to report the problems from the stakeholders in the specified groups from their own perspectives, and finally, to present the situation in writing to all stakeholders, especially the decision makers, after defining the solution suggestions for the future.

The situation after the survey was discussed with the contribution of the relevant parties at the "Situation and Needs Determination Workshop for Rare and Undiagnosed Diseases Research Field Stakeholders", held within the scope of the RareBoost ERA Chair project under the management of Izmir Biomedicine and Genome Center, and the report in question was produced.

Below, the survey questions, responses, and suggestions based on feedback from participants will be detailed. However, to briefly state here, the main audience consists of people whose awareness of the subject is expected to be relatively higher than other interested parties. The most important contribution of this is that the findings of a specific community that has the opportunity to have direct contact with individuals diagnosed with RD and their families contain clearer information about objective conditions.

2.1. QUESTIONS AND ANSWERS

The questions asked to the survey participants are listed under headings below. While preparing these questions, determining the demographic information of the participants, their expertise and their level of awareness on the subject were determined as the primary objectives.

Questions asked under the heading "Personal Information" in the survey:

1. Gender information,
2. Age distribution,
3. Professional information,
4. Area of expertise,
5. Subspecialty,
6. Post-specialization time,
7. Affiliated institution/organization,
8. Status of activities in the field of RD in participants' institutions,
9. If the answer is "Yes", the activities carried out,
10. If the answer is "No", reasons:

Questions asked in the survey under the heading "Difficulties Encountered and Diagnostic Processes":

1. The most common challenges in RD management,
2. The need for the referral of patients to other centers,
3. If the answer is "Yes", the reasons and the distribution of these reasons,
4. If the answer is "No", the institutions where the participants who gave this answer work,
5. The presence of an interdisciplinary center or council in the institution where the participant work,
6. Distribution of the answers given (Yes/No/Don't know),
7. Access to resources on RD diagnosis and distribution of different resources used according to their subjects,

Questions asked in the survey under the heading "Patient Care, Support of Patients and Their Relatives":

1. Support for patients' needs during diagnosis and post-diagnostic processes,
2. If the answer is "Yes", types of support ,
3. Challangesencountered by patients in accessing specialized care and treatments for patients and the proportional distribution of these challanges,
4. General awareness level,
5. Improved level of awareness,

Questions asked in the survey under the heading "Research and Education":

1. Participation as a researcher or principal investigator in a scientific research within the scope of RD,
2. If the answer is "Yes", the scope of the study information,
3. Status of receiving training on RD,
4. How and from what source the participant was informed about the latest developments regarding RD,
5. Attitude towards sharing the data obtained from the sample obtainedin their research,
6. Challenges encountered in scientific studies in the field of RD and orphan drugs in Türkiye,

Questions asked in the survey under the title "Ecosystem Stakeholders and Cooperation":

1. Frequency of collaboration with other healthcare professionals in diagnosing RD,
2. Information about institutions and organizations contacted regarding RD,
3. Awareness of supporting RD research and treatment processes as government policy,
4. Information on policy changes or improvements in the RD area,

The above questions are detailed under the headings below.

2.1.1. QUESTIONS ABOUT PERSONAL INFORMATION

2.1.1.1. Gender Information

The first question of the survey, Gender Information, Age and Occupation Information, aimed to determine the demographic distribution. In this context, according to the answers given by a total of 363 participants, 65.84% of the respondents were women and 33.88% were men. One person among the participants did not want to indicate their gender (0.28%). According to the answers to the first question, it was determined that women participated approximately twice as much as men. It can be considered that women are more interested in issues directly related to social awareness in the survey, as in many other areas.

2.1.1.2. Age Distribution

All participants (363 people) answered the age question. Responses given according to age range, from youngest to oldest: 7 people (1.93%) in the 18-24 age range, 35 people (9.64%) in the 25-29 age range, 108 people (29.75%) in the 30-39 age range, 111 people (30.58%) in the 40-49 age range, 64 people (17.63%) in the 50-59 age range, 38 people (10.47%) in the 60 and over age range.

When the age ranges were examined, it was determined that people between the ages of 40-49 and 30-39 constituted the majority of the participants, with a rate of 30.58% and 29.75%, respectively. This situation revealed the density of individuals in active working life and participants corresponding to the age range of specialist education.

2.1.1.3. Professional Information

In response to the question about their occupational information, participants reported that they fell into one of four main groups. i) Researcher, ii) Clinician, iii) Researcher-Clinician and iv) Healthcare Professionals. (Figure 1)

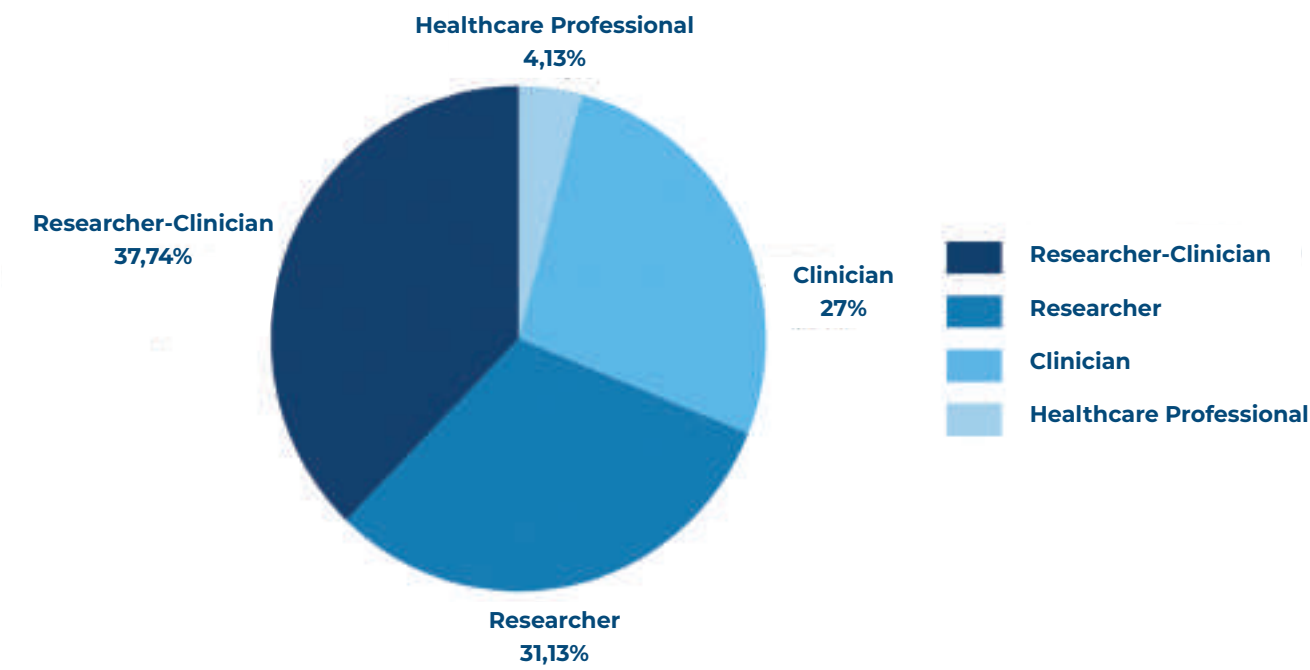


Figure 1: Distribution of survey participants according to their professional field

2.1.1.4. Area of Expertise

According to the answers given in the survey, the majority of participants working in the RD field are experts in the field of Child Health and Diseases (39%) and Biology-Genetics (26%) (Figure 2). Again, it is seen that more than half of the participants work at the University and/or University Hospital (University Hospital: 50.14%; University-Research Institute/Center: 29.48%; State Hospital/ Training-Research Hospital: 16% ,80) (Figure 3).

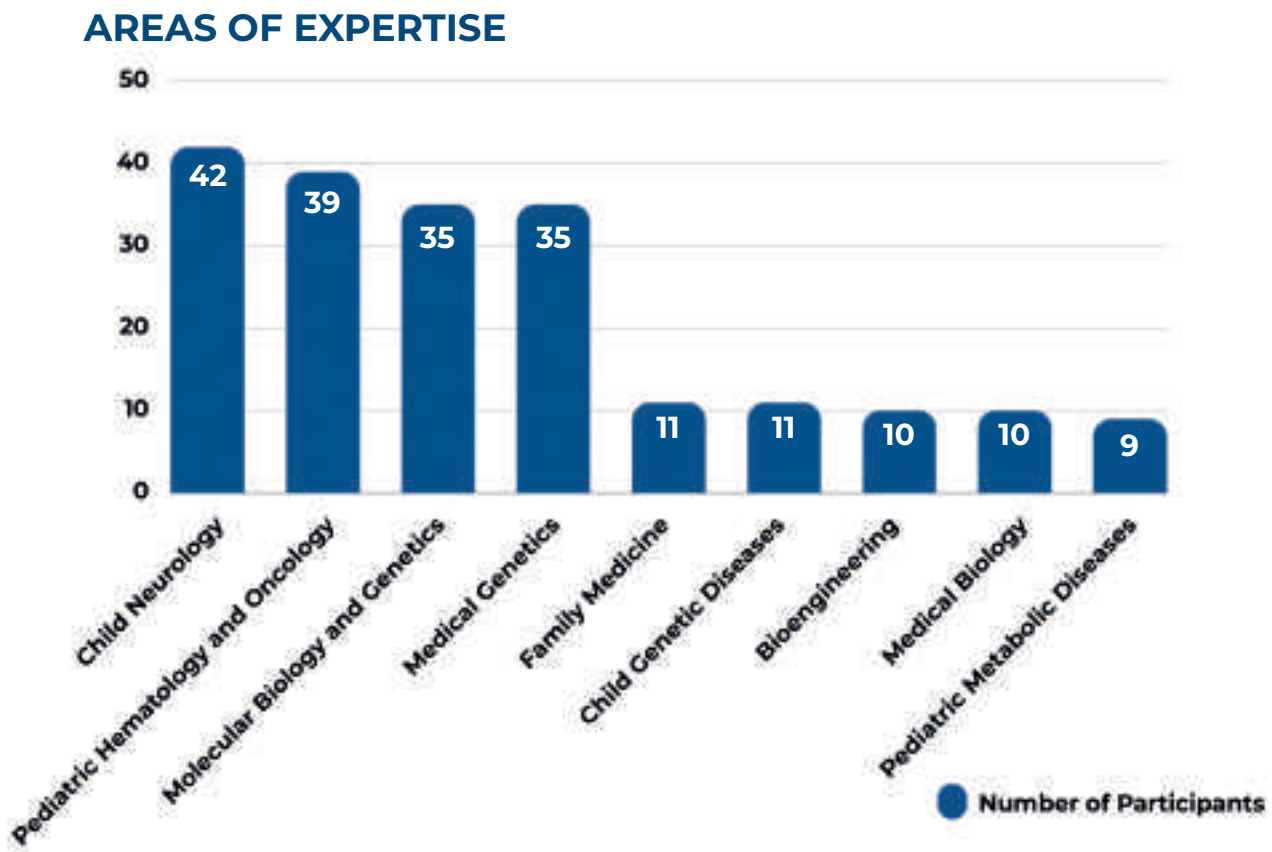


Figure 2:Distribution of survey participants according to their areas of expertise

2.1.1.5. Subspecialty

47.93% of the participants stated that they had a subspecialty, and 52.07% stated that they did not have a subspecialty. These rates show that those who have subspecialty and those who do not participate in the survey at equal rates. Considering the number of subspecialists in the total physician population, it is considered an understandable fact that these rates are approximately equal.

2.1.1.6. Post-specialization time

In this question, participants were asked to indicate their working period in the field of expertise, including the "Assistantship/Specialization or PhD" period.
Examination of the survey participants' working hours in their field of expertise shows that there is a group of participants who are experienced and have been working in the field of rare and undiagnosed diseases for a long time. When the answers given are sorted by taking into account the duration of experience, they are as follows: The rate of those with more than 15 years of experience is 40.77%, the rate of those with 11-15 years of experience is 16.53%, the rate of those with 6-10 years of experience is 16.80%, the rate of those with 1-5 years of experience is The rate of those with less than 1 (one) year experience is 21.49% and the rate of those with less than 1 (one) year experience is 4.41%.

In particular, the fact that the majority of the participants (40.77%) stated that they have been working in their field of expertise for more than 15 years suggests that they have in-depth knowledge and experience in this field. This emphasizes the importance of knowledge and expertise in the field and reflects the potential to contribute to the quality of research, treatment and management studies in this field.

2.1.1.7. Institution (Affiliation) Information

Participants were divided into six groups according to their affiliations based on their responses. (Figure 3).

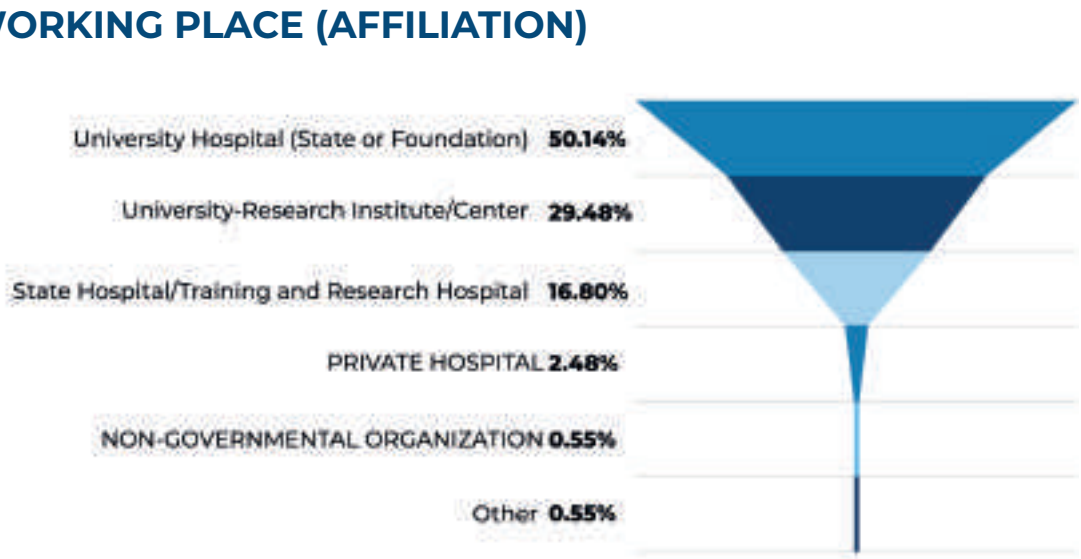


Figure 3:Distribution of survey participants according to the institutions they work for

2.1.1.8. Status of Conducting Activities in the RD Area and Activities Conducted if the Answer is "Yes"

Of the 363 participants who answered the survey question, 293 (80.72%) stated that "activities in the field of RD (diagnosis, follow-up, treatment and research, etc.)" were carried out in their institutions, and 70 (19.28%) stated that it was not done.

According to the survey results, the high rate of those who answered "Yes" (80.72%) indicates that the majority of the participants are familiar with the activities and studies on RD.

Participants who reported that "activities are carried out in the field of RD" in their institutions were asked what these activities were and the answers given by 284 of 293 participants who had the opportunity to mark more than one option are summarized below;

- Category 1: Diagnostics and genetic tests for RD (233 people)
- Category 2: Treatment and management of patients with RD (199 people)
- Category 3: Participation in RD research and clinical trials (190 people)
- Category 4: Education and training on RD for healthcare professionals (118 people)
- Category 5: Collaboration with patient associations / non-governmental organizations and support networks (79 people) (Figure 4).

These results indicate that institutions and stakeholders are active in researching, diagnosing, and managing RD. The prominence of the most basic activities, especially the application of diagnosis and genetic tests, shows that the focus is on the diagnosis and treatment processes of RD, while participation in research and educational activities are also important.

These data highlight the need for stakeholders working in the field of RD to collaborate and adopt a multifaceted approach. It also reveals the importance of collaborating with patient associations and non-governmental organizations to support patients and their families.

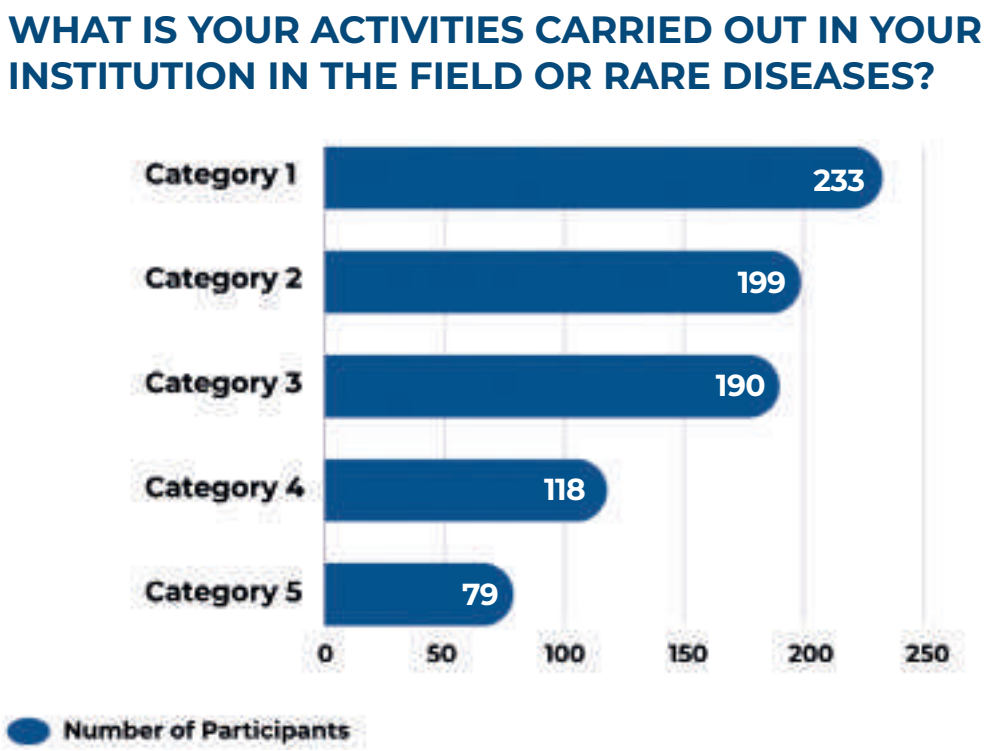


Figure 4:Distribution of activities carried out in the field of RD in the institutions of the survey participants.

Responses included in the categories are provided in the text.

2.1.1.9. Status of Conducting Activities in the RD Area and Responses Given If the Answer is "No"

Participants (70 people) who reported that "activities in the field of RD (diagnosis, follow-up, treatment and research, etc.)" are not carried out in their institutions were asked why these activities could not be carried out (with the opportunity to choose more than one category) and the answers given by 67 participants (number of people who responded) are summarized below;

- Category 1: I have to make a referral due to insufficient examinations (27 participitants)
- Category 2: Does not cover my area of expertise (25 participitants)
- Category 3: I have no contact or knowledge with centers conducting clinical research / studies (17 participants)
- Other (10 participants)

In the "Other" option, an area has been created where participants can make explanations. Participants chose the other option respectively; limited data, incomplete laboratory infrastructure, patients not being referred to their institutions, lack of a specialized unit in their hospitals, forgetting patient information due to the large number of patients, having to refer patients due to the high costs of examinations in private hospitals, and not enough specialists to serve chronic patients.

2.1.2. QUESTIONS ABOUT GENERAL INFORMATION AND EXPERIENCE

2.1.2.1. Frequency of Encountering RD

Within the scope of the survey, a question was asked to clinicians, researchers-clinicians and healthcare professionals (250 people): 'How often do you estimate that you encounter individuals with rare and undiagnosed diseases?' 237 participants answered the question. Analysis results show that participants mostly (49.79%) encounter between 11 to 50 rare and undiagnosed patients per year. This shows that healthcare professionals encounter rare patients intensively, RD has an important place in healthcare services, and that they are not as rare as they think. However, some participants (3.38%) stated that they had never encountered rare or undiagnosed patients. Additionally, no one among the participants encountered more than 50 cases per year. These data highlight the need for greater awareness and resources in the healthcare system regarding the diagnosis and management of RD.
Within the scope of the survey, the professions of the participants who answered the question "How often do you estimate that you encounter rare and undiagnosed patients" are shown in Table 1.

Table 1: Occupations of the participants who responded to the question "How often do you estimate that you encounter rare and undiagnosed patients?

	Rarely (1-2 times a year)	**Sometimes** (3-10 times a year)	**Often** (11-50 times a year)	**I never encounter**
Clinician	17	30	42	5
Researcher-Clinician	18	37	74	2
Healthcare Professional	4	5	2	1

2.1.2.2. Frequency of Encounters During the Follow-Up of Patients Diagnosed with RD

Within the scope of the survey, participants in the professional groups of clinicians, researchers-clinicians and healthcare professionals were asked how often they encountered these cases during the follow-up period after the first evaluation.

Most participants who answered the survey question encountered rare and undiagnosed cases "sometimes (3-10 times a year)". This shows that those working on rare and undiagnosed diseases come into regular contact with these cases. It also revealed that there was a significant proportion (34.18%) of cases encountered "frequently (11-50 times a year)". These data make

visible the conclusion that the majority of participants (71.73%) encountered an average of three or more rare and undiagnosed cases per year during the follow-up period. Additionally, of the 15 participants who selected the "I do not follow" option, eight are researchers-clinicians, six are clinicians, and the remaining one is a healthcare professional. The areas of expertise of these participants are listed below:

- Clinical Pharmacy
- Oral, Dental and Maxillofacial Radiology
- Pediatric Intensive Care (Child Health and Diseases)
- Algology
- Gynecological Oncology Surgery (Gynecology and Obstetrics)
- Anesthesiology and Reanimation
- Medical Pharmacology
- Medical Biology
- Family Medicine
- Medical Genetics
- Ear Nose Throat Diseases
- Medical Biochemistry
- Intensive Care

2.1.2.3. Conditions and Rates of Regular Follow-up of Patients

Within the scope of the survey, participants in the clinician, researcher-clinician and healthcare professional groups were asked whether they could follow up their patients regularly. 164 of the 237 responding participants (69.20%) stated that they could follow up their patients regularly. This shows that the majority of survey participants have the opportunity to effectively follow up their patients regarding rare and undiagnosed diseases. 30.80% of the participants stated that they could not follow up their patients regularly. A separate question area was opened for these participants and they were asked to indicate why they could not follow up their patients.

2.1.2.4. Conditions of Regular Follow-up of Patients (Reasons if the answer is "No")

In the question asked to 73 participants who stated that they did not follow up their patients regularly, 72 participants stated why they could not follow up their patients. In line with the answers, the fact that the option "I refer them to advanced centers" is the most frequently selected answer (44.44%) shows that the participants refer their patients to more appropriate units/centers because they do not have sufficient infrastructure and expertise on the subject. Additionally, approximately one-third (38.89%) of the respondents stated that they were unable to follow up with their patients because the patients stopped following up. These data suggest that reasons such as the long duration of diagnosis of rare and undiagnosed diseases, the lack of treatment for many of them, and the inability to reach specialists may be effective in patient follow-up, and point to important problems that need to be solved for patient follow-up.

In the "Other" option, an area has been created for participants to make explanations, and it is stated that they cannot follow up their patients due to reasons such as having completed their rotations, not having referral authority, not being able to follow up patients due to their branch, or providing only laboratory services.
These responses reflect the main challenges and limitations faced in the follow-up of rare and undiagnosed diseases.

2.1.3. QUESTIONS ABOUT THE CHALLENGES ENCOUNTERED AND THE DIAGNOSIS PROCESSES

2.1.3.1. Most common challenges in the management of rare and undiagnosed diseases

Challenges in RD management are summarized in Table 2. Other questions asked under this heading and their answers are detailed below.

Table 2:Most common challenges in the management of rare and undiagnosed diseases

WHAT ARE THE MOST COMMON CHALLENGES YOU FACE IN MANAGING RARE AND UNDIAGNOSED DISEASES?		
A	**Research Studies in Diagnostic Processes**	**Number of Participants**
	Access to private testing and the economic burden of testing fees	197
	Limited resources, inability to access examinations and diagnostic tests	181
	Length of time for diagnostic tests to be completed	144
	Ability to access existing genetic tests, but not access advanced enzyme analysis, metabolic testing or functional tests	1
	Lack of infrastructure	2
B	**Research Studies in Treatment Processes**	
	Medicines not available in Türkiye	1
C	**Awareness and Academic Studies**	
	Sustainability in sample collection and patient communication (in terms of additional requirements and oversight)	93
	Limited awareness of RD among healthcare professionals	91
	Inability to clarify the diagnosis in disease groups with high clinical diversity	75
	Loss of time due to not being able to perform the main tests due to a different preliminary diagnosis	47
	Difficulty communicating with patient relatives	38
	Failure to provide patient consent	23
	Difficulty in convincing the family as a result of the family receiving incorrect/incomplete diagnosis or treatment as a result of incorrect/incomplete genetic counseling and evaluations by different departments.	1
D	**Defining the Ecosystem and Developing Collaboration Possibilities**	
	Insufficient access to resources due to the patient's socioeconomic status	166
	Lack of collaboration between researchers	124
	Lack of a central information system regarding access to tests and testing centers	117
	Insufficient communication between complementary centers	61
	Uncertainty of the clinic/unit where undiagnosed patients should be followed up	44
E	**Topics Questioned in the Survey but Not in the Form of an Additional Session in the Organized Workshop, Therefore Potentially in Need of an Additional Workshop**	
	Relevant branch physicians cannot be found in every geographical region	63
	Limitation of examination time (insufficient time interval to evaluate diagnostic clues)	54
	Insufficient number of specialist physicians or difficulty in reaching a physician	46
	Lack of a social health system to improve regular follow-up for RD	1

Based on the answers given by 316 participants, the most common difficulties encountered in the management of rare and undiagnosed diseases include difficulties in accessing specialized tests, limited resources, prolonged periods to obtain diagnostic test results, insufficient access to resources due to the socioeconomic status of the patient, a lack of collaboration and a lack of a centralised information system that provides access and testing.

The information obtained has highlighted the problems and obstacles in the management processes of rare and undiagnosed diseases. Factors such as patients' socioeconomic status and limited resources negatively affect the diagnosis and treatment processes of patients.

Access to special tests and the prolonged test completion times delay the accurate/rapid diagnosis and treatment of diseases. The lack of a central information system and lack of cooperation lead to problems in the coordination of health services and follow-up of patients.

These conclusions emphasize the need to develop more effective policies and practices for the management of rare and undiagnosed diseases, manage resources more effectively, and increase coordination in health services. If the difficulties encountered in the diagnosis and treatment processes of patients are minimized, better results can be achieved.

2.1.3.2. Status of referral of patients to another center/ Reasons if the answer is "yes"/ Information on the facility if the answer is "no".

Within the scope of the survey, participants in the professional groups of clinicians, researchers-clinicians and healthcare professionals were asked whether they should refer their patients to other centers. The answers given by the 229 respondents show that the number of centers where the clinical evaluation and examinations necessary for the diagnosis of RD performed is limited. The majority of the participants (75.98%) stated that they felt the need to transfer their rare patients to other centers (public/private) for diagnosis. This situation emphasizes that centers and resources specialized in the diagnosis and treatment of RD are limited and the need for centers providing services in this field is important. However, some participants (24.02%) stated that it was not necessary to refer patients to other centers. This answer has led some experts to consider RD in their own institutions or fields of study. It may indicate that they can perform the necessary clinical evaluations and examinations for diagnosis or that they think the diagnosis and treatment services provided are sufficient.

These data highlight the need for a more comprehensive approach at the national level for the diagnosis and management of RD. Steps such as increasing the number of specialized centers for the diagnosis of RD, encouraging the training of health professionals in the field of RD, and developing coordination mechanisms that will facilitate patient access to diagnosis and treatment will contribute to increasing the quality of service in this area.

The number of participants who answered no and the types of institutions they worked for are listed in Table 3.

Table 3:Distribution of institutions where participants do not need to refer their patients to other centers work

	NO
University Hospital (Public or Foundation)	38
State Hospital / Training-Research Hospital	9
Private Hospital	2
University - Research Institute / Center	6

2.1.3.3. Presence of an Interdisciplinary Center or Council in the Institution and Distribution of Answers (Yes/No/Don't Know)

Within the scope of the survey, participants in the clinician, researcher-clinician and healthcare professional groups were asked about the existence of an interdisciplinary council in their center. Approximately half of the 229 participants (43.23%) who answered the question declared that there was an interdisciplinary council in their center, while the other half (45.85%) reported that there was no such council. This shows that the multidisciplinary approach for the management of RD has not yet been properly implemented in all health centres. Considering that some of the survey participants (10.92%) do not have knowledge on this subject, it becomes clear that some health professionals do not have sufficient information about the organizational structure of the centers where they work. This clearly shows that there is a lack of information sharing and cooperation.

These data demonstrate the critical need to establish and strengthen multidisciplinary teams in the assessment and treatment of RD. This approach may contribute to providing more comprehensive treatment and care to patients and improving health outcomes.

The number of participants / institution types according to the answer options of the survey question are listed below (Table 4).

*Table 4: Distribution of Institutions Worked According to Interdisciplinary Center or Council Presence**

	YES	NO	I DON'T KNOW
University Hospital (Public or Foundation)	77	54	17
State Hospital /Training-Research Hospital	13	37	4
Private Hospital	2	4	1
University - Research Institute / Center	7	8	2
Non-Governmental Organization (Association, Foundation etc.)	0	1	1

*One participant who answered "No" to the question did not specify his institution.

Based on these data, we see that the existence of interdisciplinary councils for the management of RD is generally more common in academic institutions such as university hospitals and teaching-research hospitals. The majority of participants working in these institutions stated that interdisciplinary councils existed. On the other hand, in other institutions, such as public hospitals, private hospitals and research institutes, such councils are less present or do not exist at all. This situation shows the lack of a multidisciplinary approach to the management of RD in these institutions and fewer opportunities for collaboration. It thus becomes clear that efforts should be made to promote interdisciplinary collaboration in these institutions and ensure a more effective approach to the management of RD.

2.1.3.4. Access to Resources on RD Diagnosis and Distribution of Different Resources Used by Subject

Within the scope of the survey, participants in the clinician, researcher-clinician and healthcare professional groups were asked whether they had access to resources for the diagnosis of RD. The responses we received from the 229 participants who answered the question indicate that the majority of survey participants (77.29%) have access to resources for diagnosing RD. On the other hand, approximately one quarter do not have access to these resources.

This information shows that access to examinations/tests used to diagnose RD is restricted or limited for some healthcare professionals. Commentary arising from the response underlines the need to increase or make available resources for the diagnosis and management of RD. This development will help healthcare professionals and researchers improve the diagnosis and treatment processes of RD.

Based on the answers given in this field, specific questions were additionally asked to the participants to mark more than one option.

Based on the above data, it can be observed that survey participants were able to access a variety of resources for diagnosing RD. 147 people who answered the question “Yes” reported that they had the opportunity to direct patients to relevant places for tests that were not available in their centers. Additionally, some participants (73 people) stated that they benefited from the examinations provided by the Ministry of Health and that they were able to access resources within the scope of projects (55 people) or with pharmaceutical company-based supports (54 people).

This diversity reflects alternative sources used to diagnose RD. This information not only expresses the health system’s desire to provide more comprehensive and accessible resources for the diagnosis of RD, but also reveals the need for policies and support mechanisms to be developed for researchers and healthcare professionals to have easy access to these resources.
Within the scope of the same question, it was also determined that 52 of the survey participants experienced various difficulties in accessing the resources necessary for the diagnosis of RD. These are respectively; i) Insufficiency of examinations in the institution (44 people), ii) Insufficiency of examinations performed within the scope of general health insurance (33 people) and iii) Lack of family insurance (9 people). The results show that there are difficulties in accessing the resources required for the diagnosis of RD and patient-related restrictions. They also point out that health policies and systems need to be improved to overcome these problems and provide all individuals with fair access to necessary diagnoses and examinations.

2.1.4. QUESTIONS ABOUT PATIENT CARE, SUPPORT OF PATIENTS AND PATIENTS' RELATIVES

2.1.4.1. Support for Patients' Needs in Diagnosis and Post-Diagnosis Processes and Locations to Get Support If the Answer is "Yes"

Among the survey participants who gave answers to the questions asked under this heading, regarding support for the needs of patients in the diagnosis and post-diagnostic processes: The rate of participants who selected "Yes" was 38.73%, the rate of participants who selected "No" was 21.59% and the rate of participants who chose "I have no information" was 39.68%. This situation suggests that support services related to RD are not sufficient. It can be considered that there are certain limitations in accessing resources that will help patients and their families cope with the difficulties they encounter during the diagnosis and treatment processes. These data emphasize the need to establish more comprehensive support systems in the management of RD and to improve existing systems.

Based on the answers given in this area, specific questions were asked to the participants and they were asked to choose more than one option.

Details of the support stated by the 122 participants who answered "Yes" are summarized below; i) Follow-up/genetic counseling (110 people), ii) Private branch outpatient clinics (81 people), iii) Rehabilitation (72 people), iv) Communication with representatives (34 people). When the responses are examined, it is seen that the survey participants provide various support services to meet the needs of RD patients during the diagnosis and post-diagnostic processes. The most frequently mentioned support service is "follow-up/genetic counselling", followed by "specialty outpatient clinics" and "rehabilitation" services. Additionally, "communication with representatives " was identified as an important source of support.

In this regard, it can be said that patients and their families struggling with RD need different support services to address the challenges they face. The data emphasize that RD-related health services should be provided with a multidisciplinary approach and in an integrated manner with different support services. Thus, by responding to the needs of patients and their families more effectively, their quality of life will be improved.

2.1.4.2. Patients in Accessing Special Care and Treatments for Patients and Proportional Distribution of These Difficulties

The answers given under this heading are compiled in Table 5.

Table 5: Difficulties encountered by patients in accessing special care and treatments for patients

	Number of Participants
Families are worn out or overwhelmed by the process	181
Lack of access to new treatment methods	178
Insufficient/non-coverage of treatment or special education expenses by insurance	156
Delays in treatment due to lack of awareness and expertise	140
Lack of access to medicines and lack of active communication channels for this purpose	136
Difficulty in reaching a specialist physician and therefore irregularity in follow-up	136
Geographical barriers	109
The following physician cannot allocate enough time to the patient	93
I don't know	33
Other	1

Response rate: 84.57%

Analyzing the responses, it appears that there are several gaps and challenges in accessing specialized care and treatments for RD. Families being worn out or overwhelmed by the process is the most frequently cited challenge, followed by lack of access to new treatment methods and inadequate coverage of treatment costs by insurance. In addition, other challenges such as lack of awareness and expertise, difficulty in accessing medicines, geographical barriers and difficulty in reaching a specialist physician are also marked at a very high rate. This highlights the importance of access to specialized healthcare professionals for the diagnosis and treatment of RD.

The responses received show that there are deficiencies and difficulties in the management and treatment of RD, and that more resources should be used with a multidisciplinary effort to overcome these difficulties. It also reveals the need for more support and guidance services to meet the needs of patients and their families.

Additionally, those who selected the "Other" option were asked to explain the difficulties they encountered. One participant said, "We have to admit patients coming from far away for examinations, we do not have enough beds. "Generally, there is a lack of special units for socioeconomic and psychological support."

2.1.4.3. General Awareness Level

The question "How would you rate the general awareness of RD?" was asked to the participants. The answers to the question showing the awareness dimension are summarized in the chart below. The most answered option in this question, which will evaluate the general awareness in RD, is the answer "low", marked by 153 participants. 79 people preferred the medium option, 59 preferred the very low option, 13 preferred the high option, and three preferred the very high option. High and very high options are the least marked options (Figure 5).

GENERAL AWARENESS

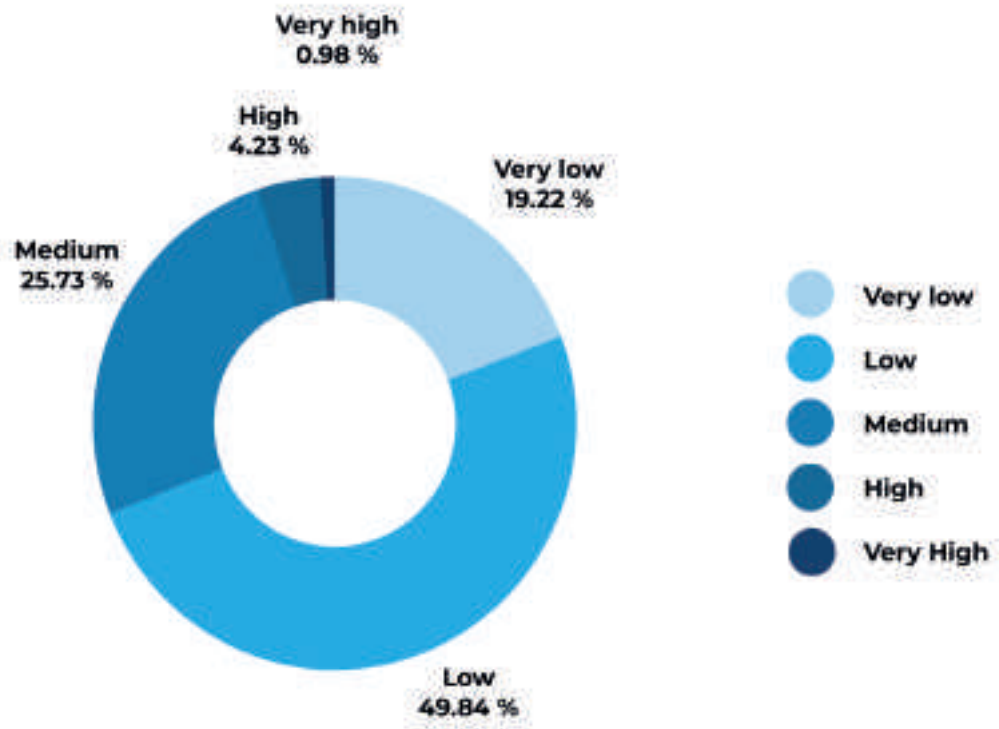


Figure 5:General awareness distribution.

Based on these data, it can be concluded that the general awareness of RD is low. In this context, it is understood that RD is not well known in society in general and the level of awareness should be increased. This highlights the importance of education and information programs regarding RD. Increasing awareness about RD in society may contribute to patients' access to accurate/ rapid diagnosis and treatment.

2.1.4.4. Improvement of Awareness Level

The rate of those who answered this question is 84.57%. Based on the responses, it can be said that the level of awareness about RD has shown a positive increase. The rate of participants who stated that their awareness level had improved was determined as 61.24%, and the rate of participants who thought that it had not improved was 12.70%. 26.06% of the participants selected the "Not sure" option. The fact that the opinions of the participants in this group were unclear in the context of the question asked, or that some participants thought that there was no improvement, shows that even if the efforts to recognize RD and increase its awareness in society have positive effects, these efforts should continue and be strengthened.

2.1.5. QUESTIONS ABOUT RESEARCH AND EDUCATION

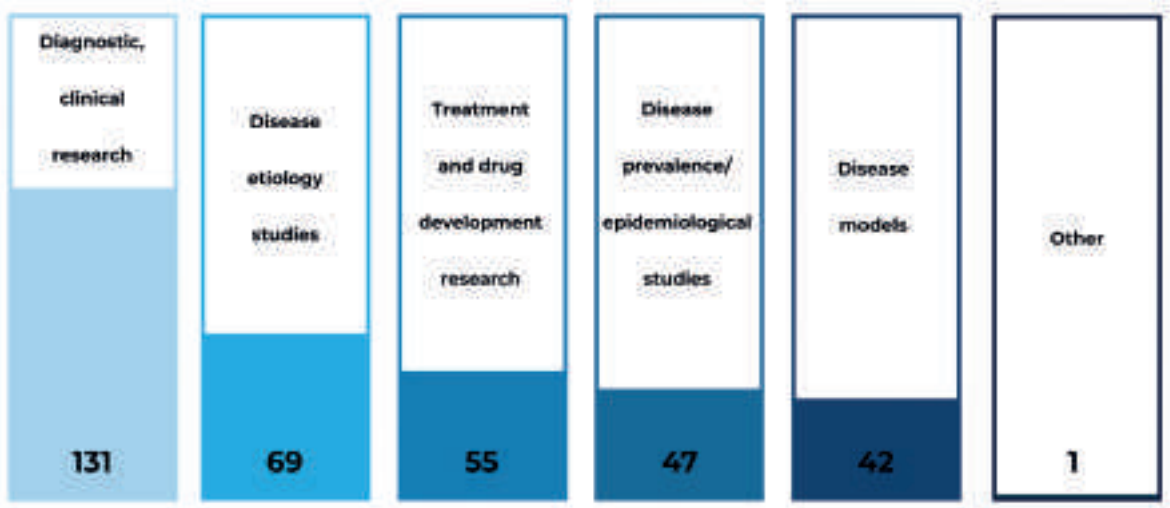
2.1.5.1. Status of being present as an executive or researcher in a scientific research within the scope of RD and, if the answer is "Yes", the scope of the study

It appears that a significant portion of the survey participants take an active role in research on rare and undiagnosed diseases. The number of participants who answered "Yes" (178 people) was higher than those who answered "No" (129 people). This shows that research and studies

in this field are supported and carried out by a wide participant base. However, the fact that approximately half of the participants did not participate in research on rare and undiagnosed diseases revealed that more studies in this field should be encouraged for researchers, clinicians and other relevant stakeholders.

A new question has been opened for the 178 people who answered "Yes" in this field. Responses to this question are summarized in Figure 6;

IF YES;



Number indicate the number of participants.

Figure 6: Scope of the studies in which the participants worked as administrators or researchers in scientific research within the scope of RD

Response Rate: 100%

Participants appear to perform diagnostic studies and clinical investigations most frequently. The participant who gave the 'other' answer declared that he was conducting a study on the economic burden of diseases.

2.1.5.2. Status of receiving training on RD

It is seen that a significant number of the participants in the survey received training on the identification of RD during their education or career. More than half of the participants (203 people) received such training, which may indicate that awareness of the identification and management of RD has increased. However, it is also noteworthy that 104 participants (33.88%) stated that they did not receive training. This situation shows that training on the identification and management of RD should be provided to a wider audience and awareness should be increased. If educational institutions and health institutions include RD-related topics in their training programs, the dissemination of knowledge and skills in this area can be ensured.

2.1.5.3. Information on how and from which source one is informed about the latest developments on RD

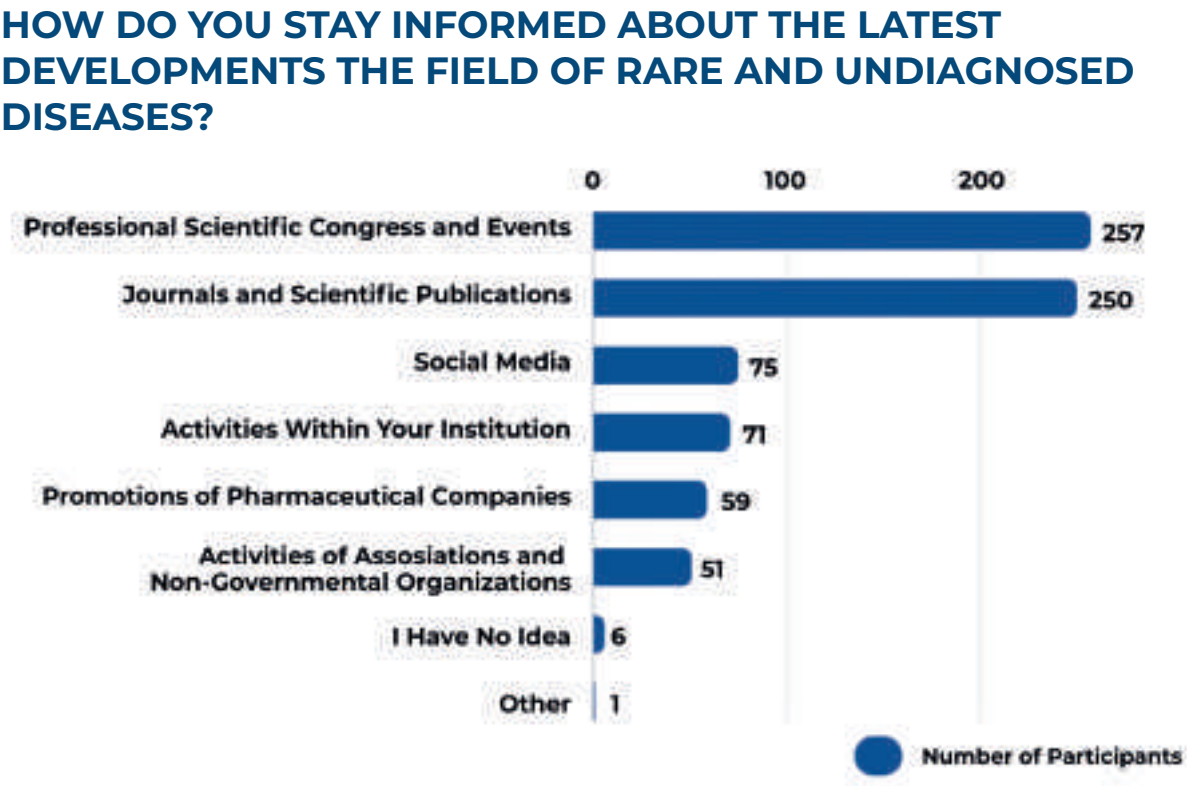


Figure 7:Distribution of sources through which survey participants are informed about developments in RD.

Response rate: 84.57%

Based on these data, we can see that survey respondents use a variety of sources to stay informed about the latest developments in the RD field (Figure 7). In this question, where more than one option can be selected, the most commonly used sources include professional scientific congresses and events (257 participants) and journals and scientific publications (250 participants). This suggests that participants attach importance to scientific sources to stay professionally current and informed of the latest research on RD.

In addition, association and non-governmental organization events (51 participants), in-house events (71 participants), social media platforms (75 participants) and promotions of pharmaceutical companies (59 participants) also stand out as important sources where the latest developments regarding RD can be followed.

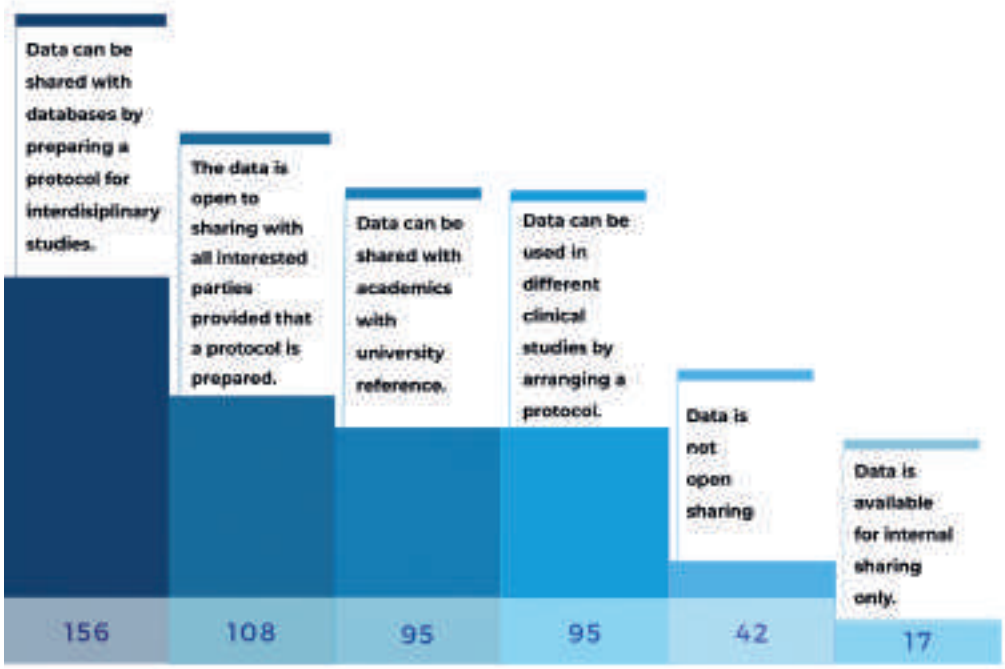
However, considering that there were six participants who selected the “No idea” option, it can be thought that some people have difficulty accessing current information about RD or are not interested in this issue.

A participant who chose the Other category mentioned the source he was aware of as “EU funds”.

2.1.5.4. Attitude Towards Sharing the Data Obtained from the Samples Evaluated in the Research

Under this heading, participants were able to choose more than one option. The answers given are listed below.

WHAT IS YOUR ATTITUDE TO SHARING THE DATA OBTAINED FROM THE SAMPLES YOU USE IN YOUR RESEARCH?



Number indicate the number of participants.

Figure 8:Attitudes towards sharing sample data used in research

Response rate: 82.09%

298 participants were able to select more than one option and it is seen that the majority of the participants have a positive attitude towards sharing the data obtained from the sample used in their research.

In particular, the majority of the participants stated that the data can be shared with all researchers through the database for interdisciplinary studies by organizing a protocol, with academicians with university reference, or can be used in different clinical researches by organizing a protocol. The high rate of these responses shows that data sharing has the potential to foster scientific collaboration and research progress.

However, some of the participants stated that the data was only available for internal sharing or that the data was not open for sharing. This shows that some researchers adopt a more restrictive approach and have concerns about data sharing. Therefore, it is important to establish a policy regarding data sharing and disseminate this policy among researchers.

2.1.5.5. The Nature of the Challenges Encountered in Scientific Studies in the Field of RD and Orphan Drugs in Türkiye

The answers given to the questions under this heading are compiled in Table 6 below.

Table 6: : Challenges encountered in scientific studies in the field of RD and orphan drugs in Türkiye

	Number of Participants
Insufficient public and private sector support for research in the field of RD	212
Lack of dialogue, collaboration and data sharing	183
The small patient group makes research difficult	181
Insufficient investment in orphan drugs	147
Lack of awareness in the field of RD	124
Lack of disease code and data	111
Researchers' lack of interest in studies on RD	92
Difficulty in ethics committee approval of drug studies, especially in the pediatric age group	74
Insufficient information resources in the field of RD	45
Other	1

Response rate: 81.54%

The answers given by 296 participants to this question, where more than one option can be selected, can form an important basis for understanding the difficulties encountered in the research and treatment of RD and developing solutions. It suggests that steps such as greater collaboration and resources between the public, private sector and non-governmental organizations, strengthening communication between researchers and raising general awareness can greatly help overcome these challenges.

2.1.6. QUESTIONS REGARDING ECOSYSTEM STAKEHOLDERS AND COOPERATION

2.1.6.1. Frequency of Collaboration with Other Healthcare Professionals in RD Diagnosis

Responses to the question "How often do you collaborate with other healthcare professionals in the diagnosis of RD?", answered by 297 participants, highlight the importance of a multidisciplinary approach to the diagnosis and management of RD.

The number of participants collaborating on a daily (72 participants) or monthly level (77 participants) shows how widespread the multidisciplinary approach is, while the number of participants rarely (103 participants) or not collaborating at all (45 participants) indicates that collaboration in this field is further encouraged.

The distribution of the answers given according to institutional information is shown in Table 7.

Based on the answers given by the participants, the professional groups of the participants who have collaborated and are currently collaborating are shown in the table below:

Table 7: Occupational distribution according to the frequency of cooperation with other healthcare professionals in diagnosing RD

	Researcher	Clinician	Researcher–Clinician	Healthcare Professional
I've never done this before.	26	11	5	3
I collaborate daily.	10	23	39	0
I collaborate monthly.	18	21	37	1
I collaborate rarely.	28	29	42	4

2.1.6.2. Information about institutions and organizations contacted regarding RD

The responses given by 297 participants to the question "How often do you collaborate with other healthcare professionals in the diagnosis of RD?" highlight the importance of a multidisciplinary approach to the diagnosis and management of RD. The number of participants who collaborate daily (72 participants) or monthly (77 participants) shows how common the multidisciplinary approach is, while the number of participants who rarely (103 participants) or never collaborate (45 participants) shows that collaboration in this area should be encouraged more.

2.1.6.3. Awareness on Supporting RD Research and Treatment Processes as Government Policy

297 participants responded to the question "Do you have any information about any government policies or initiatives that support rare and undiagnosed disease research and treatment processes, patients and their relatives?" and 89 participants responded yes. In addition, it was determined that a significant percentage of participants, 70% (208 participants), did not have information on this subject. In this context, it can be concluded that the awareness of RD-related policies and supports should be increased among the wider community.

2.1.6.4. Information on Policy Changes or Improvements in the RD Area

"What should be the policy changes or improvements in the field of rare and undiagnosed diseases?", to which 290 out of 363 participants responded and more than one option could be selected. In line with the question, it shows that policy changes or improvements should be made by increasing funding support, especially at national and international levels, establishing more effective follow-up systems for patients, developing guidelines and strategies, increasing

funding for research projects and encouraging cooperation between healthcare institutions. In line with the answers received from the question, it becomes clear in which areas the most improvements need to be made.

Table 8 below compiles the participants' suggestions.

Table 8: Participant responses and number of participants regarding policy changes or improvements in the field of rare and undiagnosed diseases

	Number of Participants
Increasing national/international funding support) or (supporting the number of drugs, advanced investigations, research projects)	215
Establishment of follow-up systems for rare patients	199
Development of national RD strategies and guidelines	184
Expanding the scope of prenatal screening	158
Increasing funding support for RD research	154
Ensuring more efficient communication between healthcare practitioners and legislators for legal regulations	148
Increasing collaboration between healthcare institutions and researchers	141
Development of improved insurance coverage for diagnosis and treatment	109
Providing/Increasing incentives for pharmaceutical companies to develop orphan drugs	99
Increasing support for patient support organizations and awareness campaigns	62
Expanding telemedicine and telehealth services	47

Response rate: 79.89%

3. SUGGESTIONS

As part of the "Status and Needs Assessment Workshop for Rare and Undiagnosed Diseases Research Area Stakeholders", 68 people attended the event hosted by the IBG to discuss various challenges related to the diagnosis, treatment and awareness of RD.

The participants consisted of healthcare professionals, public officials and representatives of non-governmental organizations. At the beginning of the workshop, general information was given to all participants by Prof. Uğur ÖZBEK, and after this information, the participants were divided into groups to discuss four main topics. These topics were: "Research Studies in Diagnostic Processes", "Research Studies in Treatment Processes", "Awareness and Education Studies" and "Definition of the Ecosystem and Collaboration Possibilities" (Figure 9).

Figure 9: Group titles in the workshop

Each group held 45-minute meetings under the management of moderators appointed for each main topic. During the group discussions, first the participants took turns in putting forward their individual opinions on the topic, ideas were exchanged among the group members, and then all opinions and suggestions were delivered to the moderator. Next, all group members were directed to the next moderator and the table to discuss the other topics. With this rotation method, each group had the opportunity to share their opinions on all main issues.

3.1. RESEARCH STUDIES IN DIAGNOSTIC PROCESSES

Under this heading, a "recommendation report" was prepared, compiling the common opinions of all participants in four groups. Under the first main heading, two subheadings emerged based on the agreed items in the information received from all groups.

a) Developments in Diagnostic Processes in the World and in Europe
b) Studies and Development Areas Regarding Diagnostic Processes in Our Country

a) Developments in Diagnostic Processes in the World and in Europe

When the opinions and suggestions in this subheading are evaluated together; it has been reported that epidemiological studies have been conducted in the world in general and in Europe in particular to determine the frequency and distribution of RD and to better understand the effects of these diseases. The reason for this is that, thanks to the research mentioned, it has been stated that it is possible to determine how frequently diseases are seen in certain populations, and based on this information, health services can be planned more rationally, and subsequently, the allocation of public/private resources can be based on more objective foundations.

As a consensus, most RD are of genetic origin, and therefore genetic research is essential for understanding the causes and mechanisms of diseases. According to the meeting proposal notes, it is thought that genetic research conducted within the scope of RD can be used to identify genetic changes underlying diseases, develop gene therapies and direct personalized medical treatments.

In addition to the genetic research mentioned, it has been stated that conducting clinical research to improve diagnosis and treatment methods for RD in parallel is important in terms of evaluating the effectiveness and reliability of new diagnostic tests and treatment options. Another outcome suggested at the workshop was that RD is a global problem, thus requiring cooperation across borders and requiring cross-country coordination. In this context, several initiatives have already been mentioned at the international level to promote collaboration and knowledge sharing between researchers, clinicians, health policymakers and other stakeholders. When all these factors were evaluated together, it was taken as a common decision that RD studies would be the most effective way to improve diagnostic processes and possible treatment options, provide better care to patients and increase the quality of life of individuals suffering from RD.

b) Studies and Development Areas Regarding Diagnostic Processes in Our Country

Under this heading, a question arose within the scope of "What are the studies conducted in the diagnosis processes in our country and in which areas can developments be made?".

A consensus was reached on the answer to this question, in which all participants expressed their opinions quite intensely, and gave examples, especially from SMA (Spinal Muscle Atrophy) disease, as a common suggestion. These examples include; the social awareness on SMA and the mandatory pre-pregnancy screening made possible, and the improvement of health policies on this specific issue in our country show how important it is in the fight against RD.

Thanks to this orientation on SMA, carriers will be determined in advance, and this will bring Türkiye closer to developed world standards. The decision taken is also important in terms of showing that our country complies with international norms in the diagnosis and treatment of RD. The final word on this subject is as follows: "These and similar developments show that Türkiye is taking steps forward in the fight against RD and adopting patient-focused health policies. Continuing such practices can help increase the quality of life of individuals diagnosed with RD and reinforce their trust in the health system."

Deficiencies and areas that need improvement in the diagnostic processes of RD in Türkiye have been determined in line with the opinions of expert participants, and these issues are listed under the following two main headings.

i. Improvement Steps Regarding Diagnostic Processes
ii. Human Resources, Infrastructure and Financing Needs in Diagnostic Processes

i) Improvement Steps Regarding Diagnostic Processes

As a result of the consensus of all participants in four groups, a total of nine different suggestions emerged under this heading.

Recommendation 1: *Establishing a structure for the diagnosis and treatment processes of RD in Türkiye*

In this context, it is proposed to establish a central management and an infrastructure that will include all stakeholders, regardless of the public, private sector and universities. In this way, it will be possible to develop diagnostic studies more quickly by collecting information in a single pool.

Recommendation 2: *Specialized regional centers should be established for different diseases*

In this context, "Regional centers in Türkiye should be selected and specialized for different RD , and cooperation should be made through the coordination of these centers." has been suggested.

Recommendation 3: *Planning multidisciplinary studies and increasing their number*

For studies carried out within the scope of RD, it is recommended to receive support from a multidisciplinary scientific board/council. It has also been reported that, if necessary, studies on model organisms should be conducted.

Recommendation 4: *Participatory legislation should be prepared with relevant stakeholders (person, service provider, payer, supplier, industry, rule maker, decision maker).*

Recommendation 5: *A holistic approach (holistic view) should be brought to the service, starting from primary care to the relevant department at the university.*

Recommendation 6: *The financing provided by general health insurance is not sufficient. A new financing and repayment model should be developed.*

Recommendation 7: *Protocols should be made to universities for budget transfer and national / international funding support for R&D.*

Recommendation 8: *The applicability of data flow with a correct method should be increased. (Digital infrastructure/system, sharing, artificial intelligence/machine learning support, security)*

Recommendation 9: *It has been stated that progress can be made in the diagnosis of RD , starting from consanguineous marriage and family screening.*

ii) Human Resources, Infrastructure and Financing Needs in Diagnostic Processes

Various strategic recommendations have been presented in the areas of human resources, infrastructure and financing for the effective management of rare and undiagnosed diseases.

Recommendation 1: *Technological Infrastructure Must Be Provided.*

It was mentioned that it is necessary to provide technological infrastructure in order to prioritize the problems in the diagnosis processes and then to eliminate the problems that arise during the diagnosis processes. In this context, it is emphasized that Artificial Intelligence technologies, which are a current approach and have the opportunity to be applied in many different fields,

can also be used in the diagnosis and treatment processes of rare and undiagnosed diseases. It has been stated that these technologies can improve the diagnostic process and also make great contributions to issues such as data analysis and disease prediction.

Recommendation 2: *An Intervention Plan Should Be Created for Screening Results.*

Another suggestion is to improve and develop the screening tests routinely applied in our country, thus creating an intervention plan for the screening results. A common opinion has been expressed that predetermining treatment and intervention plans based on screening results can increase the effectiveness of these processes and ensure that patients receive timely and appropriate treatment.

Recommendation 3: *Plans Should Be Made to Increase Awareness and Health Literacy.*

As widely accepted, educating the public on general health issues is critical for early diagnosis and prevention of diseases. In this context, it has been suggested that organizing educational campaigns with broad participation about RD and disseminating awareness activities may be effective in this process. Participants described this situation as "increasing health literacy".

Recommendation 4: *Diagnosis and Treatment Protocols Should Be Developed.*

It has been suggested that up-to-date and agreed-upon standard protocols should be developed to improve the diagnosis and treatment processes of rare and undiagnosed patients.

Recommendation 5: *Clinical Research Legislation Should Be Created.*

To provide a legal framework for clinical research on rare and undiagnosed diseases, it has been proposed to establish a "Clinical Research Legislation".

In this context, it has been stated that regulations that encourage cooperation with the health industry can ensure the expansion of clinical research and the rapid and accessible introduction of innovative treatments to the market.

Recommendation 6: *Nationalization Should Be Ensured.*

Testing by people who are not competent in the services received from domestic or international centers, makes control difficult and may sometimes lead to erroneous results.

There was consensus on the need to strengthen the local and national health infrastructure. Achieving this would improve quality control and ensure independence.

It was also mentioned that if nationalization is achieved, foreign dependency can be reduced to a minimum level and this will contribute positively to the country's economy.

Recommendation 7: *Patient-Focused Trainings Should Be Planned.*

It has been suggested that patient-focused training should be planned by determining appropriate methods together with relevant non-governmental organizations and patient associations. In this way, patients' awareness will be increased and their opinions will be obtained in all areas, as active rather than passive actors of the process.

Recommendation 8: *Pre-Graduation Education Programs Should Be Updated.*

It has also been suggested to make curriculum updates that define threshold values at the knowledge/skill level in the Council of Higher Education (YÖK) Core Education Program for all health professions before graduation; and to develop various (modular face-to-face or distance) education programs in the Continuing Education Centers of universities.

Recommendation 9: *Post-Graduation Trainings Should Be Institutionalized.*

Professional development programs and evaluations conducted at regular intervals not only support career development by keeping the knowledge and skills of health professionals up to date, but also ensure the provision of high standards of health care. In this context, it has been stated that institutionalizing and regularly conducting orientation/adaptation/in-service training may be beneficial. In addition, the idea of conducting periodic proficiency exams (every 3-5 years) and introducing certification and scoring for health professions has been suggested.

Recommendation 10: *Compliance with International Standards Should Be Ensured.*

It has been stated that the adoption of successful international practices can improve the quality of health services in our country. In this context, it has been suggested that international good practice examples should be scanned and those deemed suitable should be integrated into our country and institutional relations should be implemented with European Reference Networks.

Recommendation 11: *Exchange Programs Should Be Supported.*

Parallel to the 10th Recommendation, the necessity and benefits of our country's physicians and researchers going to different countries with various foreign exchange programs (Erasmus etc.), gaining international experience in their specific fields and especially taking a direct role in bringing good practice examples to our country were stated.

Recommendation 12: *Free Screening Commitment Should Be Provided.*

It has been proposed to introduce a free screening commitment for some reimbursed drugs and medical devices. Thus, early diagnosis rates and accessibility of health services can be increased. It was agreed that this situation would bring positive results for both patients and the country's economy.

Recommendation 13: *Refunds for Unsuccessful Treatments Should Be Examined.*

Examples from the USA and Europe, where the fee collected from the patient is refunded if the treatment of rare and undiagnosed diseases is not successful, should be examined. After examining the process in detail, the application conditions in our country should be analyzed.

Recommendation 14: *Rapid Approval and Economic Evaluation Should Be Made.*

It was emphasized that approvals should be rapid in the payment process for orphan drugs, and it was stated that this accelerates patients' access to innovative treatments. To concretize the proposal, the example of NICE (National Institute for health and Care Excellence) from the UK was given and it was suggested that similar to NICE, innovative treatments should first be given rapid approval and then economic evaluation (HTA) should be carried out.

Recommendation 15: *Alternative Reimbursement Models Should Be Developed.*

It was mentioned that alternative reimbursement models should be developed and diversified instead of only a single reimbursement model in RD; it was stated that in this way, the treatment processes of diseases will be financially supported and patients' access to treatment will increase.

3.2. RESEARCH STUDIES IN TREATMENT PROCESSES

Under the second main heading, participants shared their opinions and suggestions about the innovations in current treatment processes and the developments required for the improvement of treatment services in Türkiye, regarding the topics "Developments regarding treatment processes" and "Developments necessary for the improvement of treatment processes in Türkiye".

a) Developments Regarding Treatment Processes

Under this heading, the participants particularly discussed the gene therapy option and generally agreed on the situations mentioned below. In line with the common opinion of the workshop participants, it was stated that the developments observed in the field of gene therapy in Türkiye have strengthened our country's technological infrastructure in the field of health, and this has brought our country to a parallel level with other developed countries. Gene therapy is a relatively innovative approach that has significant potential in the treatment of RD . They declared that the developments in this direction, which show the increase in the scientific and technological potential in our country, show Türkiye's progress towards becoming a country based on high technology in the health sector. In addition, it was emphasized that it could improve patient quality of life by allowing the development of more effective and personalized solutions compatible with the concept of personalized medicine in the treatment of RD.

b) Necessary Developments for the Improvement of Treatment Processes in Türkiye

In this session, the social and economic dimensions of treatment processes in the RD field were discussed in detail. In this context, participants stated that cost problems and reimbursement problems by the Social Security Institution (SSI) are common in targeted treatments. It has been emphasized that drugs used in the treatment of RD are rarely approved by SSI. It has been reported that there are serious problems in the reimbursement of the drugs that patients need to use during the treatment process. In addition to the fact that the developments in this field are not at the expected level, it has been stated that it is difficult for patients to financially access the new technologies developed.

Participants stated that there was a lack of cooperation in the RD treatment process due to insufficient communication networks, and that in addition to this situation, training and developing technology could not be adequately followed. The participants' opinions and suggestions on these issues were collected under 11 headings.

Recommendation 1: *A National Registration and Data Management System should be established.*

In line with the opportunities offered by developing technology, it has been suggested to create a special registration and data management system for RD. It has been stated that this system will enable effective monitoring of national disease prevalence and can play an important role in planning appropriate treatment processes.

Recommendation 2: *Patient-Focused Treatment Processes Should Be Initiated.*

After target definition was made according to disease prevalence, the need to initiate appropriate treatment processes was emphasized. In this context, it is recommended to plan patient-oriented trainings and create content that will increase health literacy.

Recommendation 3: *Patient-Focused Treatment Processes Should Be Initiated.*

It has been stated that expanding diagnosis and treatment centers for RD will contribute to patients' faster and more accurate diagnosis and access to treatment.

Recommendation 4: *NGO Support Should Be Increased.*

It has been stated that the supports of non-governmental organizations (NGOs) have the potential to play an important role in the treatment processes of RD and it was emphasized that these supports should be increased.

Recommendation 5: *Implementation of Certified Health Services*

It is recommended to obtain international certificates such as Hospitilized examination (art-Cell), GC, GMP in hospitals and laboratories and to conduct research in accordance with these standards.

Recommendation 6: *Nationalization and Encouragement of Domestic Production*

It was suggested by all participants that there should be nationalization in the RD field in Türkiye. As a justification for this, considering the access problem and high cost of drugs procured from abroad, a consensus was reached that domestic production should be encouraged. In addition, instead of sending biological samples abroad, it is recommended to develop the infrastructure to carry out tests and analyses at the local level and within our country's own resources.

Recommendation 7: *R&D Studies and Patented Products Should Be Increased.*

It was stated that the findings obtained from the studies should be evaluated on a more professional level and researchers should take initiatives regarding patent processes during and after the R&D processes.

Recommendation 8: *Technological Infrastructure Should Be Strengthened.*

The importance of integration into the European Reference Networks System for the development of technological infrastructure was mentioned. In this context, an agreement was reached on supporting the technological infrastructure with artificial intelligence applications, including the E-pulse system in this process, and using user-friendly interfaces in patient registration systems.

Recommendation 9: *Clinician-Researcher Communication and University Collaborations Should Be Increased.*

It has been stated that there is a need to develop cooperation between researchers focusing on rare and undiagnosed diseases and physicians who have direct contact with patients. In the same context, it has been put forward as a recommendation that universities should ensure and improve cooperation both within the institution and with other institutions.

Recommendation 10: *Legal Regulations and Policies Should Be Developed.*

It was emphasized that legal regulations and health policies should be developed to meet additional needs in treatment processes.

Recommendation 11: *Specialized Centers Should Be Established.*

The importance of prevention, early diagnosis, genomic and functional approaches for the effective management of RD was emphasized, and in this regard, the roles that specialized centers and tertiary hospitals should play in the process were emphasized. It has been reported that increasing the capacities of the mentioned centers in both quantity and quality and providing the most appropriate infrastructure will provide patients with access to better diagnosis and treatment.

3.3. AWARENESS AND EDUCATION ACTIVITIES

Workshop participants had the opportunity to discuss and shape education and awareness studies and cooperation development activities in the "Awareness and Education Activities" session. In this session, it was emphasized that there is a lack of education in various fields in Türkiye and it was stated that educational practices in this field should be increased due to the lack of awareness, especially at the diagnosis stage. Participants pointed out the importance of including experts in the field for the diagnosis phase, as well as professions in supporting roles such as psychologists, lawyers, social workers, developmental psychologists and dietitians due to the characteristics of some diseases, within the scope of in-service training.

Questions were asked to the participants under three basic headings ("What are good international education practices? Which trainings are compatible with Türkiye?", "Which trainings are needed? What should the training contents be?" and "What integrations should be there if there will be distance education?") and in this direction, all two subheadings emerged according to the agreed items in the information received from the groups.

a) Trainings to be Implemented in Türkiye
b) Content of Educational Materials and Guides on Diagnosis and Treatment of RD

i. For Physicians and Healthcare Professionals
i. For Patients and Their Relatives

a) Trainings to be Implemented in Türkiye

Participants stated that the training offered in Europe for the diagnosis and treatment of RD should be integrated into Türkiye. Full agreement has been reached that these trainings should be sustainable, open to improvement and aimed at raising awareness among patients, their relatives and healthcare professionals.

Suggestions within the scope of training that can be implemented in Türkiye during the session are stated below:

Recommendation 1: *Türkiye should be integrated into European Union's Orphanet Portal.*

Recommendation 2: *Continuing Education Centers should be established.*

Recommendation 3: *R&D studies should be increased in universities.*

It has been declared that in order for R&D studies to continue in universities, funding support (TUBITAK, TUSEB, etc.) and subject-specific research budgets should be increased.

Recommendation 4: *Integration into Erasmus Programs Should Be Provided.*

The importance of integrating into various international programs, especially the Erasmus program, and thus increasing the knowledge of researchers and developing international collaborations was emphasized.

Recommendation 5: *Reference Centers should be established.*

The necessity of establishing reference centers for the diagnosis and treatment of RD was mentioned, and it was stated that the establishment of specialized centers was necessary in this context and that patients could be directed to the relevant areas more quickly and appropriately.

It was also stated that the establishment of reference centers would ensure the continuation of the process in a holistic manner.

Recommendation 6: *Social Responsibility Projects should be developed.*

It has been stated that it is necessary to implement Social Responsibility Projects in order to inform not only healthcare providers, researchers and patient relatives, but also individuals in general about the many layers that make up society, about the nature of rare and undiagnosed diseases.

Recommendation 7: *Training modules in Turkish should be created within the scope of Orphanet.*

There was a consensus among the participants on the issue of creating training modules in Turkish so that it is easier to follow the studies and developments in Europe on rare and undiagnosed diseases and that all stakeholders (patients, relatives, researchers, physicians, etc.) can follow up-to-date and reliable sources on the subject.

b) Content of Educational Materials and Guides on Diagnosis and Treatment of RD

Within the framework of training activities, it was reported that training programs for both healthcare professionals and patients/patient relatives were planned and some of them were implemented.

It has been stated that the trainings must be organized specifically for different communities, taking into account the characteristics of that group, and that it is necessary to meet the needs, knowledge levels and expectations of each community. In this context, participants were asked to share their opinions on the processes of creating trainings and disease guides for the relevant target communities.

i) For Physicians and Healthcare Professionals

There is a consensus that training for physicians and other healthcare professionals should include technical and detailed information. The scope of these trainings were suggested to include topics such as new treatment methods, diagnostic techniques, ethical issues and communication skills with the patient. It has been stated that such training will increase healthcare professionals' access to current information, improve their professional skills and increase their ability to provide higher quality healthcare services. In this context, various suggestions have emerged regarding the content of the materials and guides for training physicians and healthcare professionals, based on the common views of the participants.

Recommendation 1: *Principles of Excellence in Science, Education and Applications Should Be Provided.*

It has been suggested that the concepts of good science, better education and best practice should be given importance and training should be provided within this scope.

Recommendation 2: *Importance Should Be Given to Communication-Focused Trainings.*

It was stated that importance should be given to patient approach and communication with the patient in the trainings.

Recommendation 3: *Creating and Updating Guides*

It has been reported that relevant guidelines should be created for a diagnosed disease. In addition, it is recommended that both educational content and disease guides be updated at regular intervals.

Recommendation 4: *A Multidisciplinary Approach Should Be Adopted in Education.*

It has been reported that a multidisciplinary approach should be adopted in determining the subjects of the training and preparing the content.

Recommendation 5: *Educational Resources Should Be Localized.*

It was emphasized that it is important to localize foreign-sourced educational contents by taking into account the reality of our country, and it was suggested that studies be carried out on this subject.

Recommendation 6: *Online Trainings Should Be Organized.*

It was recommended to provide online options for training and to make disease guides available online.

Recommendation 7: *Institutional Cooperation Should Be Established in Education.*

It was emphasized that fundamental decision-making institutions such as the Ministry of National Education and the Ministry of Health should also be involved in the preparation of educational contents. In this context, it has been stated that it is important for these institutions to keep up-to-date with RD.

Recommendation 8: *RD-Focused Trainings Should Be Implemented within the Faculty of Medicine and Related Institutes.*

It has been stated that training on RD should be given especially to medical students. It has been suggested that the education programs in faculties should be updated accordingly and that expert staff should be created in these fields. It was also emphasized that the opening of postgraduate programs on RD should be encouraged.

Recommendation 9: *Supporting Personnel Training Should Be Organized.*

It was suggested that special training programs be organized for auxiliary and technical personnel so that these personnel can take an active role in the management of RD.

Recommendation 10: *Economic and Treatment Aspects of RD Should Be Considered in Educational Contents.*

During the preparation of the training programs presented as suggestions above, it was suggested that all aspects of the economic implications of Rare and Undiagnosed Diseases and the treatment process should be explained in detail.

Recommendation 11: *Risk Reports Should Be Prepared for Consanguineous Marriages.*

Since rare and undiagnosed diseases are detected at a relatively high rate in the children of individuals who have consanguineous marriages, it has been recommended that risk reports be prepared to include individuals who have married in this way and that they be updated at regular intervals.

Recommendation 12: *Family Medicine Should Be Activated as Primary Care for Rare and Undiagnosed Diseases*

It has been suggested that family medicine should be considered as the first step in dealing with rare and undiagnosed diseases, and that this perspective should be taken into account in training and guide contents.

ii) For Patients and Their Relatives

It has been stated that trainings should be organized specifically for different target communities and adjusted to meet the needs, knowledge levels and expectations of each community. In particular, it has been suggested that topics such as symptoms of diseases, treatment options, care methods and access to resources should be emphasized in training for patients and their relatives. Finally, it was emphasized that such training can increase the ability of patients and their relatives to cope with the disease, support their compliance with treatment, and enable them to benefit from health services more effectively.

Recommendation 1: *Monitoring International Patient Associations and Taking them as a Model*

The idea of examining the educational activities of patient associations operating around the world, especially in Europe, and taking them as an example was put forward.

Recommendation 2: *Studies should be carried out to raise public awareness and disseminate accurate information.*

The idea of preparing basic information training for RD was emphasized. It has also been stated that the effects of television programs and social media on people should be used correctly. It has been discussed that people who are not experts on the subject are giving misleading information to the public on television and social media, and examples of Celiac disease have been given. It was stated that the mentioned issue would cause serious problems in terms of public health, and in order to prevent this situation to some extent, it was emphasized that there should be participation in TV programs in a way that provides accurate information about RD.

Recommendation 3: *RD and Awareness Days should be organized.*

It was recommended to raise awareness of both healthcare professionals and patients/patient relatives by organizing RD Days. It has also been suggested to organize Awareness Days in all affiliated educational institutions in cooperation with the Ministry of National Education.

Recommendation 4: *Guides and Brochures Should Be Published.*

It was recommended that the Ministry publish guides and brochures regarding RD and organize their delivery to their addressees. A common opinion has been expressed that these resources can provide information to the society.

Recommendation 5: *Planning Child Simulation Trainings Supported by Pedagogical Approaches*

It has been stated that encouraging children to receive education on the relevant subject in simulation centers for children, who are the largest population suffering from rare and undiagnosed diseases, can be an effective method. It was mentioned that it is important to use special pedagogical approaches for the education of children in simulation centers. As a consensus, it is generally accepted that educational programs should be appropriate to the age and developmental level

of children. Although these trainings have a positive side in that they can help children get used to clinical environments and understand medical procedures by enabling them to gain experience in the field of health, if the simulation is misperceived or negative experiences are experienced, negative perceptions such as fear may occur in children, and therefore it is important to use special pedagogical approaches for training in simulation centers.

Recommendation 6: *Information Appropriate to Education Level Should Be Provided.*

It has been stated that information transfer should be made taking into account the education level of the patient/patient's relatives.

3.4. DEFINITION OF THE ECOSYSTEM AND COOPERATION POSSIBILITIES

Identification of the ecosystem and collaboration opportunities in the diagnosis and treatment process of RD are created with a multidisciplinary approach. RD generally focus on a small number of patients, and knowledge and expertise regarding these diseases is not at the desired level. Therefore, the collaboration of a number of different stakeholders is required to combat RD and create an effective ecosystem in this regard. Workshop participants exchanged ideas for the purpose of "Defining the Ecosystem and Collaboration Possibilities" in this session.

Recommendation 1: *Raising Awareness*

Active participation of the society and increasing public awareness are vital in the fight against RD. For this purpose, information sharing should be increased and support networks should be strengthened through different platforms such as patient groups, patient associations, volunteer groups and social media.

Recommendation 2: *Establishing Multidisciplinary Collaborations*

A suggestion has been made that collaborations should be handled with a multidisciplinary approach; to get support not only from patients, relatives and healthcare providers, but also from psychologists and sociologists in education and awareness activities.

Recommendation 3: *Education of Health Professionals*

Education and awareness of healthcare professionals regarding RD is an essential step to improve diagnosis and treatment processes. In this context, it was emphasized that faculties of medicine, dentistry, pharmacy and health sciences and other health institutions and vocational training programs should be developed, thus the importance of training personnel specialized in the diagnosis and management of RD.

Recommendation 4: *Encouraging R&D Activities and Supporting Innovation*

It has been suggested that R&D activities should be encouraged and innovation should be supported simultaneously, together with inter-university collaborations in the fight against RD. It has been stated that this will mean the discovery of new treatment methods and possible drugs, the development of genetic diagnosis technologies and advances in the field of personalized medicine.

Recommendation 5: *Encouraging Participation in Clinical Trials*

It has been reported that easy access to clinical trials for the treatment of RD can significantly improve patients' lives. Therefore, the importance of facilitating clinical trial processes, encouraging patient participation in these trials, and facilitating access to treatments has been emphasized.

Recommendation 6: *Increasing the Role of the Private Sector in the Treatment of RD*

It was emphasized that rare and undiagnosed diseases are a large area that cannot be left to the monopoly of the public sector, and therefore the participation of the private sector in the development of drugs and treatments for the treatment of RD is important.

Recommendation 7: *The Role of Government and Regulators*

It was stated that the government and regulatory institutions (Ministry of Health and TUSEB) should play an active role in policy making and regulation processes in combating RD. As a suggestion in the same scope, it was mentioned that these institutions should take the lead in issues such as facilitating access to treatment, improving the quality of health services and directing research funds.

Recommendation 8: *Financial Sustainability and Collaborations*

The importance of the government's cooperation with the Presidential Strategy and Budget Directorate was emphasized. It has been stated that RD have a high financial burden on the health system and that in order to maintain the continuity of the system, it is necessary for the SSI in particular, as well as NGOs, to work together on this issue.

Recommendation 9: *International Collaborations*

Although the prevalence of RD varies between countries, it is clear that the condition is a public health problem at the global level. For this reason, RD often transcends the borders of a country and international collaborations appear as a necessity rather than a necessity. Taken together, the importance of international cooperation in areas such as sharing information and data between countries, developing joint research projects and sharing resources is emphasized.

In this session, workshop participants also shared important information on the concepts of "Industrial contribution of pharmaceutical companies" and "Orphan Medicine with Angel Investors".

a) Industrial Contribution of Pharmaceutical Companies

Recommendation 1: *Support should be sought from healthcare professionals working in pharmaceutical companies.*

The contributions of pharmaceutical companies to the RD field are significant, and employees in this field generally have a broader perspective and knowledge than the rest of society. For this reason, it has been stated that the information and services provided by healthcare personnel working in pharmaceutical companies, especially during the diagnosis phase, clearly contribute to the correct diagnosis and effective management of RD , and it has been put forward as a common recommendation that support should be received from these employees.

Recommendation 2: *Tests used in the diagnosis of RD can be accessed through pharmaceutical companies.*

The idea presented as the suggestion in this title is as follows: "Pharmaceutical companies can contribute significantly to improving the diagnostic processes of diseases and enabling patients to reach more effective treatments quickly, with the support they provide in the development, financing and dissemination of diagnostic tests and analyzes of RD."

Recommendation 3: *Collaborations should be established between pharmaceutical companies, healthcare institutions and healthcare professionals.*

It was stated that increasing the collaboration between pharmaceutical companies, health institutions and health personnel could enable more effective results to be achieved in the fight against RD. It was also emphasized that these collaborations are important for improving the quality of life of patients and reducing the burden of RD.

b) Angel Investor and Orphan Drugs

RD are generally considered conditions that affect a small number of people and have limited treatment options. It has been stated that the reason for this is that the return on investment in orphan drugs is relatively low and they are not commercially attractive. Participants offered the following suggestion to overcome this situation. In the process of developing Orphan Drugs, which are not deemed suitable for investment by major industries, the contributions of people called Angel Investors who provide financial support to entrepreneurs come into play. Angel investors not only provide financial support to entrepreneurs involved in RD , but also access to a wide network of industry experience and contacts. This allows new therapeutic approaches to be developed and commercialized, as well as providing access to critical resources such as consultancy and industry connections. They can also help foster innovation and progress by giving more attention to long-term and high-risk projects.

4. CONCLUSION

On December 22, 2023, the “Workshop on Determining the Situation and Needs for Rare and Undiagnosed Diseases Research Area Stakeholders”, was held within the scope of the RareBoost ERA Chair project supported by the European Union H2020 program and carried out within the Izmir Biomedicine and Genome Center. The workshop was held with the aim of raising awareness on this issue, and included 68 people, including researchers, physicians, and NGO representatives, who are direct interlocutors of RD research.

In the workshop, topics were discussed, ideas were exchanged, and various suggestions were presented in the context of the Rare Diseases Survey, which was previously presented to the relevant parties and answered by 363 participants.

Above, both the survey questions and answers given, as well as the workshop topics and suggestions offered, are detailed. In the workshop, where many suggestions were presented based on the reality of our country, the actions of both decision makers and experts in the academy, the pharmaceutical industry and NGOs to raise awareness on the subject were revealed, and what needs to be done was listed in order of priority. It has been stated that these outputs can help those interested in studying RD in drawing a road map. The topics discussed in the context of the workshop also include the titles within the scope of the “Rare Diseases Health Strategy and Action Plan 2023-2027” prepared by the Ministry of Health of the Republic of Türkiye.

Workshop participants and survey respondents represented a broad group. Looking at the results reported in the presented report, there are similar problems and solution suggestions identified among both workshop and survey participants regarding RD.

What is particularly noteworthy among these is that despite the abundant research conducted and the activities carried out throughout our country to increase social awareness, the desired level of knowledge has still not been achieved. Again, as an important and noteworthy point, the age range of researchers focusing on RD has been determined as a situation that needs to be considered. It was determined that the survey participants' awareness of RD was at its maximum level, especially in the 30-50 age range (219 out of 363 participants were in this age range). Since the 30-50 age range coincides with the age range for both the necessary specialized education and socially active work, it is understandable that these individuals' awareness of RD is higher than other age ranges . However, it is clear that in order to keep the interest of younger and older age groups alive in the subject, education, training activities, etc must be carried out with increasing momentum. The most important outcome of the presented report is that the problems are generally similar across different stakeholders. This situation is the fact that if the solution proposals are implemented, the demands of many segments will be resolved at once.

The workshop suggestions were compiled as four main items and some sub-items, as detailed above. One of the four main items was 'Research Studies in Diagnostic Processes' (this item was divided into two as "in the World and Europe" and "in Türkiye". Then, the sub-item regarding the recommendations in Türkiye included two more items. These were: i) Improvement steps regarding diagnostic processes and ii) Human resources, infrastructure and financing needs in diagnostic processes). The participants made a general comment about diagnostic processes "in the World and in Europe" and provided a summarized suggestion. The participants presented nine different suggestions as "improvement steps" on the subject "diagnostic processes in our country" and 15 suggestions under the title of "human resources, infrastructure and financing needs". The first nine of the suggestions were; the establishment of a superstructure for the diagnosis and treatment processes of RD, the establishment of specialized centers, the implementation of multidisciplinary studies, the preparation of relevant legislation, the holistic focus of health services (from primary care to university hospitals), the adequacy of the financing provided by health insurance, the development of national or international R&D collaborations in universities, the establishment of digital data infrastructure systems and finally, the implementation of family screenings, especially in cases of consanguineous marriages. The other 15 articles offer concrete suggestions that also include quite technical details. Among these were; providing a technological infrastructure that includes artificial intelligence technologies, creating intervention plans for screening results, implementing awareness training, developing diagnosis/treatment protocols, creating clinical research legislation, turning to national resources, providing patient-centered training, providing regular pre-graduation training for healthcare professionals, institutionalizing post-graduation training, providing an international equivalence mechanism, supporting exchange programs for experts in the field, making free screening tests possible, bringing the option of refunds in case of unsuccessful treatments to the agenda, ensuring rapid approval of orphan drugs, and developing alternative reimbursement models.

This situation shows that the participants are aware of global developments, that the deficiencies detected in our country are known in parallel with this, and that solution proposals are put forward in the light of this information.

A general evaluation under the title of "Research Studies in Treatment Processes", which is another of the main items, is compiled under the subtitle of "Developments Regarding Treatment Processes". Following this general evaluation, under the subheading "Necessary Developments for the Improvement of Treatment Processes in Türkiye" specific to our country, participants made 11 different suggestions, including the establishment of a national RD registration and data management system, initiation of personalized treatment processes, expansion of RD-

based diagnosis/treatment centers, increase in NGO support, implementation of certified health services, nationalization and encouragement of domestic production in parallel, increase in R&D studies and patented products, strengthening of technological infrastructure, improvement of interaction between scientific stakeholders, implementation of legal regulations, establishment of specialized centers. When these suggestions are examined in general, it is determined that, similar to the situation in the first main item, the participants have a grasp of the general picture in Türkiye and put forward various reasonable ideas to eliminate its shortcomings. Under the other main item, "Awareness and Education Studies", two subheadings were determined and the suggestions were listed under these headings. The first of these was the title "Trainings to be Implemented in Türkiye" and seven sub-suggestions were put forward within this scope. In order these were; the coordination of EU and Türkiye systems, the establishment of continuous education centers, the increase of R&D activities at universities, the active participation in similar activities, especially the Erasmus program, the establishment of reference centers, the implementation of social responsibility projects and the creation of Turkish education modules within the scope of ORPHANET.

Another subheading was determined as "Content of Educational Materials and Guides Regarding Diagnosis and Treatment of RD" and this item contained two different groups of suggestions as "Towards physicians and healthcare professionals" and "Towards patients and their relatives". 12 suggestions were presented for healthcare professionals and six suggestions were presented for patients/relatives. The suggestions presented for healthcare professionals were as follows; adopting the concepts of good science, better education and best practice, increasing the importance given to communication-focused trainings, creating application-oriented guides, conducting training in a multidisciplinary manner, localizing training resources specific to Türkiye, organizing online trainings, establishing institutional collaborations in education, carrying out RD-focused trainings within the body of medical faculties and relevant institutes, organizing trainings for assistant personnel, teaching the economic dimensions of RD treatment in these trainings, preparing risk reports for consanguineous marriages and activating primary health care services for all RD patients. The items listed for patients/relatives included; monitoring global patient associations and taking them as models, conducting studies to access accurate information, organizing RD awareness days, publishing targeted guides and brochures, planning child simulation trainings from a pedagogical perspective, and providing information appropriate to the level of education of patients/relatives.

Under the last main item, "Defining the Ecosystem and Collaboration Possibilities", nine different suggestions were presented that included general suggestions and were similar to the items above. In addition to these, suggestions on the "Industrial Contribution of Pharmaceutical Companies" were presented with three sub-items. The suggestions presented for pharmaceutical companies were grouped under the titles of receiving professional support about RD from people working in these companies, providing access to tests used in RD diagnosis through pharmaceutical companies, and developing cooperation between pharmaceutical companies and healthcare professionals. As a final sub-item, the suggestion of receiving support from people or institutions called "angel investors", similar to examples abroad, was presented within the scope of the Workshop.

Finally, in this context, conducting meetings similar to this workshop where all stakeholders come together, and conducting similar surveys with different groups or similar groups but with more participants will directly increase RD awareness.

5. REFERENCES

1. Richter T, Nestler-Parr S, Babela R, Khan ZM, Tesoro T, Molsen E, et al. Rare Disease Terminology and Definitions-A Systematic Global Review: Report of the ISPOR Rare Disease Special ınterest Group. Value Health. 2015;18(6):906-14

2. Whicher D, philbin S, Aronson N. An Overview of the ımpact of Rare Disease Characteristics on Research Methodology. Orphanet J Rare Dis. 2018;13(1):14.

3. Fernandez-Marmiesse A, Gouveia S , Couce Ml. NGS Technologies as a Turning point in Rare Disease Research, Diagnosis and Treatment. Curr Med Chem. 2018; 25(3):404-32.

4. Wakap SN, lambert DM, Olry A, Charlotte Rodwell C, Gueydan C, lanneau V. Estimating Cumulative point prevalence of Rare Diseases: Analysis of the Orphanet Database. Eur J Hum Genet. 2020;28(2):165-73.

5. Amberger JS, Bocchini CA, Schiettecatte F, Scott AF, Hamosh A. OMıM.org: Online Mendelian Inheritance in Man (OMIM®), an online catalog of human genes and genetic disorders. Nucleic Acids Res. 2015;43:789-98.

6. Dodge JA, Chigladze T, Donadieu J, Grossman Z, Ramos F, Serlicorni A, et al. The importance of rare diseases: from the gene to society. Arch Dis Child. 2011;96(9):791-2.

7. Wright CF, Fitzpatrick DR, Firth HV. Paediatric Genomics: Diagnosing Rare Disease in Children. Nat Rev Genet. 2018;19(5):253-68.

8. Huyard C. How did uncommon disorders become ‘rare diseases’? History of a boundary object. Sociol Health ılln. 2009;31(4):463- 77.

9. Herder M. What is the purpose of the Orphan Drug Act? PloS Med. 2017;3:14(1):e1002191.

10. Wellman-Labadie O, Zhou Y. The US Orphan Drug Act: rare disease research stimulator or commercial opportunity? Health policy. 2010;95(2-3):216-28.

11. Putkowski S. National Organization for Rare Disorders (NORD): providing advocacy for people with rare disorders. NASN Sch Nurse. 2010;25(1):38-41.

12. Dawkins HJS, Draghia-Akli R, Lasko P, Lau LPL, Jonker AH, Cutillo CM, et al. progress in Rare Diseases Research 2010-2016: An IRDiRC perspective. Clin Transl Sci. 2018;11(1):11-20.

13. Cutillo CM, Austin Cp, Groft SC. A Global Approach to Rare Diseases Research and Orphan Products Development: The international Rare Diseases Research Consortium (IRDiRC). Adv Exp Med Biol. 2017;1031:349-69.

14. Austin Cp, Cutillo CM, lau lpl, Jonker AH, Rath A, Julkowska D, et al. Future of Rare Diseases Research 2017-2027: An ıRDiRC perspective. Clin Transl Sci. 2018;11(1):21-7.

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