RARE DISEASES FEDERATION

2nd Rare Lives and Rare Diseases Summit

26 March 2026 Bilkent Hotel - Ankara / TÜRKİYE

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SUMMIT REPORT

FOREWORD

The second Rare Lives and Rare Diseases Summit, hosted by the Rare Diseases Federation and organized in collaboration with the relevant ministries and institutions, particularly the Ministry of Health of the Republic of Türkiye, was successfully held on 26 March 2026 at the Bilkent Hotel in Ankara.

The Summit commenced with opening remarks by Prof. Dr. Nurullah OKUMUŞ, Deputy Minister of Health; Prof. Dr. Necdet ÜNÜVAR, Member of the Presidential Health Policy Board and Rector of Ankara University; Prof. Dr. Nuri AYDIN, Rector of Istanbul University-Cerrahpaşa and President of the Association of University Hospitals; Osman Nuri ERDEM, Director General of Plans and Programs at the Presidency of Strategy and Budget; Assoc. Prof. Dr. Muhammed Emin DEMİRKOL, Director General of Public Health at the Ministry of Health; and Deniz ATAKAY, President of the Rare Diseases Federation. The Summit featured four separate panel sessions and a special workshop. Bringing together more than 250 participants representing relevant public institutions, universities, industry organizations, and civil society organizations, the 2nd Rare Lives and Rare Diseases Summit provided a platform for important speeches and presentations that will help guide the development of effective and sustainable policies in this field.

This report has been prepared for the benefit of interested stakeholders by presenting summarized versions of selected speeches and presentations delivered at the Summit, with the aim of strengthening the foundation for collaboration and collective action in the field of rare diseases.

We extend our sincere gratitude to all contributors and participants who supported the Summit, where rare diseases were addressed through a shared sense of responsibility and where a value-based, inclusive, and sustainable policy approach was strongly advocated through the active engagement and contributions of all stakeholders.

RARE DISEASES FEDERATION

CONTENTS

PANEL – 3

FINANCING AND REIMBURSEMENT PRACTICES IN RARE DISEASES

(Türkiye and Global Perspectives)

Moderators:
Prof. Dr. Zafer ÇALIŞKAN / Faculty Member, Hacettepe University
Attorney Güneş UYAR / Secretary General, Rare Diseases Federation

Speakers:
Osman Nuri ERDEM / Director General of Plans and Programs, Presidency of Strategy and Budget
Ayşegül GÜNBEY ÖZTEK / Head of the Department of Overseas Health Services, General Directorate of General Health Insurance, Social Security Institution (SSI)
Prof. Dr. Fulya İlgin GÖNENÇ / Dean, Faculty of Law, Medipol University
Osman ŞAHİN / Senior Engagement Manager, FrontierView

PANEL – 4

PREVENTIVE MEDICINE AND SOCIAL PRACTICES IN RARE DISEASES

(Genetic and Newborn Screening Programmes)

Moderators:
Prof. Dr. Mehmet GÜNDÜZ / Ankara Bilkent City Hospital
Deniz ATAKAY / President, Rare Diseases Federation

Speakers:
Prof. Dr. Fatih ÖZALTIN / Director, HUGEN (Hacettepe University Center for Genome Sciences and Rare Diseases Research and Application)
Dr. Rahşan ÇINAR / Unit Coordinator, Department of Child and Adolescent Health, Directorate General of Public Health, Ministry of Health

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OPENING SPEECHES


İSTANBUL ÜNİVERSİTESİ
1453
GAZİ ÜNİVERSİTESİ
1926
HACETTEPE
ÜNİVERSİTESİ
Prof. Dr.

Prof. Dr. Nurullah OKUMUŞ
Deputy Minister of Health

The Individual, Social and Economic Burden of Rare Diseases

Distinguished participants, first of all, I would like to express my gratitude for this valuable organization. In fact, there are many issues to discuss in this field. As we always emphasize, the term "Rare Disease" is insufficient to describe this picture; it would be much more accurate to define the current situation as "Rarely Occurring Multiple Diseases."

Social Impact and the Chronic Nature of the Process

Although these diseases are individually rare within society, when viewed as a whole, we are faced with the reality that one in every 12 to 20 people is affected by a rare disease. It is now well established in the literature that approximately 5% to 7% of the world's population is affected by diseases within this group. Therefore, we are talking about an enormous issue that directly concerns a very large segment of society.

The most fundamental characteristic of these diseases is that a large proportion of them are inscribed in our genes; in other words, they are, so to speak, part of our destiny. Moreover, these are not temporary health problems that can be overcome within a few days; they are lifelong, chronic, and progressive in nature. Even when faced with a short-term illness, we find much to tell, but believe me, the depth of rare disease stories that span an entire lifetime, both for individuals and their families, is too great to fit into novels or encyclopedias

Challenges in Diagnosis and Treatment

The struggle against rare diseases, their diagnosis, and their follow-up are all extremely difficult. Since even the slightest delay in diagnosis can trigger lifelong damage, every second is critical. Today, while our hopes have increased with many options such as gene therapies, personalized approaches, and enzyme replacement therapies, we continue to face two fundamental challenges:

1. The clinical effectiveness of some treatments has not yet been fully proven.
2. Economic Burden: Costs have now reached unimaginable levels. In a case file I recently reviewed, the price of a single dose was USD 4.4 million. When recurring annual doses are taken into account, these figures become almost impossible to bear not only for individuals but also for governments and even the strongest healthcare systems. This issue is a shared and pressing concern for all of us.

Access to Information and the Problem of "Invisibility"

Accessing information in this field is equally challenging. Families often express their helplessness by saying, "We have been left alone with a disease whose name we had never even heard before." Since these disease names are largely unknown to the general public, our patients and their families are unfortunately overlooked and, in a sense, rendered "invisible."

When left untreated, these individuals may be pushed to the margins of society both physically and socially, becoming a silent population unable to make their voices heard. Breaking down these barriers is not only a medical obligation for us but also a humanitarian duty. During the long and arduous social journey that begins at the moment of diagnosis, families are forced to struggle not only with the disease itself but also with the prejudices of even those closest to them. This situation points to an area in which we must develop social solutions very rapidly.

Early Diagnosis:

A Struggle to Change a Destiny or a Choice

Yes, because rare diseases are written into our genes, we can speak of a reality that may be described as "destiny." However, being left helpless in the face of these diseases is not our destiny. The most fundamental characteristic of rare diseases is that treatment and management become possible when they are diagnosed early. Therefore, our foremost duty as the Ministry of Health and as healthcare administrators is to ensure early diagnosis of these diseases and uninterrupted access to treatment.

Screening Programs: From Pre-Marital Screening to Newborn Screening

We continue to expand our early diagnosis spectrum with each passing day. We are not limiting ourselves to the newborn stage alone.

- **Pre-Marital and Pregnancy Screening:** We can now identify risks at a much earlier stage through pre-marital screening programs. We have implemented these practices with determination both in our country and around the world.
- **Directorate General of Public Health Initiatives:** Our heel-prick blood screening, vision screening, and hearing screening programs continue with great success.
- **Newborn Critical Congenital Heart Disease Screening:** This program, which we launched recently, operates through the use of the "Pulse Oximeter" method. Through this simple yet life-saving intervention, we save the lives of our babies and prevent chronic complications before they even begin.

Impact on National Health Indicators and Mortality Rates

Rare diseases that are not diagnosed early lead to severe disabilities, chronic health problems, and, unfortunately, loss of life. For this reason, early diagnosis efforts are not merely an individual healthcare service; they are a vital factor that directly affects infant and neonatal mortality rates and, consequently, our national health indicators.

One of the most fundamental indicators of a country's level of development and prosperity remains its infant mortality rate. Thanks to the effective screening and monitoring programs we have implemented over the past 20 years, Türkiye has achieved a remarkable transformation:

- **Under-Five Mortality Rate:** While it stood at around 40 per thousand twenty years ago, we have succeeded in reducing it to 10.9 per thousand today.
- **Infant Mortality Rate:** It has declined from 31.5 per thousand to 8.9 per thousand.

Major Transformation in Neonatal Indicators

I am a pediatrician and also a neonatology specialist. Therefore, these figures are not merely statistics for me; each one represents a child whose life has been saved and who has been given the chance to hold on to life. In the early 2000s, our neonatal mortality rate was approximately 17 per thousand. Today, through the Ministry's strong healthcare infrastructure and effective initiatives, this figure has been reduced to around 5 per thousand. Of course, we are not satisfied with this achievement alone. Our goal is to surpass even the standards of the developed world and provide every baby with the healthiest possible start in life.

Technological Vision and Domestic Treatment Strategies

Breathtaking Technological Developments

Today, truly breathtaking developments are taking place in the fields of biotechnology, informatics, and information systems. We observe this progress particularly clearly in the pharmaceutical industry, especially in the areas of personalized treatments and gene therapies. We encounter new methods almost every day. The chronic nature of rare diseases and their need for solutions tailored directly to specific target populations have made this field one of the primary focal points of the global pharmaceutical industry.

We Must Not Be Those Who "Circle Around"; We Must Be Those Who "Sit Beside"

By their very nature, rare diseases require an absolutely multidisciplinary approach. I would like you to imagine the following picture: Place our patient and their family at the center; around them is a vast circle consisting of healthcare systems, physicians, social service professionals, civil society organizations, and pharmaceutical companies. Everyone is moving within a cycle around that center.

However, at the very center stands an individual desperately waiting for support and a ray of hope. Our primary duty is not merely to revolve around that person like components of a system. Our responsibility is to step out of that circle, sit beside the patient, stand alongside them, and truly help carry that heavy burden. We should regard technology and informatics as valuable tools only insofar as they serve this purpose.

Combating the Exploitation of Hope and the Potential for Domestic Production

The intensity of efforts in the field of rare diseases unfortunately sometimes brings with it situations that deeply concern us. One of our greatest sensitivities is the presentation of methods whose effectiveness has not yet been clinically proven as if they were a "certain hope" for families. May God spare everyone from such a test; however, when you find yourself in such a situation, you gain a much clearer understanding of how a family or an individual searching for something to hold on to will grasp every opportunity that appears before them.

Our fundamental duty as scientists and healthcare administrators is to provide our citizens with the most appropriate, most effective, and most cost-effective treatment. When we examine the basic structure of certain medicines that are valued at millions of dollars today, we see that they actually consist of simple enzyme structures or just a few amino acids. The academics and researchers in our country possess every capability necessary to develop these treatments. We are working with all our strength to make these high-cost therapies available to every individual at much more accessible costs.

Strategic Steps and a Call for Cooperation

With the strong support of our Minister, we have begun our production efforts on gene and enzyme therapies within TÜSEB. However, as you will appreciate, this is not a burden that we, as the Ministry, can shoulder alone.

I would like to make a call here to our civil society organizations, associations, and federations: Please do not come to us solely as the representative of a single disease. We undoubtedly want to reach every disease and every individual; however, for a stronger basis of cooperation, we need to join hands and act with an integrated strategy together with our universities and research centers. If we do not develop our own gene and enzyme therapies through our own domestic capabilities, after a while, the sustainability of this enormous economic burden will become impossible.

Sustainable Payment Models and Scientific Determination

Performance-Based Payment and Regulation Strategy

Regarding high-cost treatments, countries such as the United States, France, and the Netherlands have now begun to apply much stricter criteria. These countries are transitioning to "Risk-Sharing" or "Performance-Based Payment" models. In short, they say: "I will cover the cost of this treatment, but I will make this payment only if the treatment provides the targeted benefit."

As a country, it has now become a necessity for us to transition to this system as well. On one side, we have our families who have a right to treatment and are waiting with hope; on the other side, there is the reality that this sincere hope and public resources must not be exploited. As the Ministry of Health, our most critical duty is to apply our regulatory role without compromise and to deliver clinically proven treatments to our citizens as quickly as possible.

Integrated Coordination Power

The support of our scientists, universities, and civil society organizations is of vital importance in bringing these processes to success. As I stated before, we do not want to revolve around you; we want to sit beside you. However, the way to achieve this is through full coordination and joint action. Rare diseases are not merely a health problem;

they are a multi-stakeholder and integrated issue extending from education to employment, from social support to legal rights.

On Disinformation and Heel-Prick Blood Screening Debates

Before concluding my remarks, I would like to touch upon an issue that has recently been occupying all of our time and energy unjustly. On the one hand, our esteemed professors are setting aside their own work and supporting us in the light of science; on the other hand, we are encountering an unusual resistance whose source we cannot understand. Unfortunately, an opposition to "heel-prick blood screening" is now being added to opposition to vaccination.

We are following with alarm the irrational claims written by certain groups organized on social media and addressed to our Minister, Prof. Dr. Kemal Memişoğlu. Claims with no scientific basis whatsoever are being put forward, such as "Why are the reproductive points on newborn babies' heels being punctured?" or "According to reflexology, the heel area represents the reproductive organs; are you damaging children's future functions?"

Unwavering Determination in the Light of Science

The tragicomic aspect of this issue is that there is not a single scientific study or piece of literature supporting these claims. Even if you were to consult the most advanced artificial intelligence tools or medical databases available today, you would find no evidence whatsoever, because this claim is entirely fictitious.

We pay no attention to those who attempt to place obstacles in our path through such unfounded statements, nor to the harsh language used or threats of compensation claims. We have only one priority: preventing even a single baby from becoming disabled or losing their life due to a rare disease. Guided by science, we will continue our screening programmes with the same determination.

Let me add a technical note as well; the name of this programme is the "Heel-Prick Blood Screening Programme." However, we are not obliged to collect the sample specifically from the heel; what matters is that the specimen is obtained and incorporated into the system in the healthiest possible manner.

The Reality of Heel-Prick Blood Screening and Vaccination in the Light of Scientific Evidence

Why Is Heel-Prick Blood Preferred?

I would like to clarify a technical issue that has generated public interest: Why heel-prick blood? In fact, if blood is already being drawn from a newborn through venous access in a clinical setting, our healthcare personnel can simply transfer a drop from that syringe onto the screening card. Blood obtained through venous sampling is, in fact, highly advantageous in terms of causing less pain, providing more reliable results, and carrying a lower risk of hemolysis (the breakdown of blood cells).

However, establishing venous access for every newborn prior to discharge requires significant expertise and an invasive procedure. By contrast, collecting blood from the heel is a method that can be easily performed by any trained healthcare professional, provides the fastest results with minimal intervention to the infant, and, because of this practicality, is accepted as the standard method worldwide. In my view, producing absurd claims such as "damage to reproductive points" based on this practice is not merely ignorance but deliberate propaganda. As scientists, it is our fundamental responsibility to warn our citizens against such misinformation.

Vaccine Hesitancy and the Principle of "Overall Benefit"

We encounter similar unfounded claims in vaccine hesitancy as well. Statements such as "They are changing our genes" or "The preservatives inside are harmful" are not compatible with scientific facts. We should not forget that even the simplest syrups or tablets we use every day contain preservatives to ensure shelf life and stability.

With every medical intervention, even with the simplest medicine, there is always a theoretical risk of allergic reactions or anaphylaxis. However, in our scientific evaluations, we always consider the principle of "overall benefit." Vaccines represent one of the greatest achievements in the history of humanity. Guided by science and evidence, we will continue to move forward with determination on the path we know to be right in order to protect our children from preventable risks.

A Comprehensive Fight Against Disinformation

The addition of "heel-prick blood screening opposition" to vaccine opposition is a matter of deep concern for us. At this point, our universities, associations, and scientists all have major responsibilities. However, our most critical stakeholders are the media and broadcasting organizations. The media, which represents the most direct route to reaching society, must help educate the public and continue communicating these scientific facts tirelessly. On every platform, we must emphasize that each screening programme we conduct serves as an insurance policy for public health through the life-saving benefits it provides.

Our Hopes for the Future Continue to Grow

Before concluding my remarks, I would like to share an observation. When I think back to my residency years, approximately 15–20 years ago, rare diseases were not nearly as prominent on our agenda as they are today. When the first associations began to be established, there were even those who struggled to understand the significance of these efforts.

However, at the point we have reached today, the high level of awareness that has developed both within society and the scientific community gives us great strength. The fact that rare diseases are no longer "invisible" and have become one of the principal agenda items of both the state and the scientific community is the greatest assurance that we will achieve far more beneficial and successful outcomes in the future.

I hope that this Summit will lead to beneficial outcomes, and I extend my gratitude to everyone who contributed to its organization. Stay well.

Prof. Dr. Necdet ÜNÜVAR
Rector of Ankara University,
Member of the Presidential Health Policies Board

Rare Diseases: A Reality Greater Than It Appears

My dear friend, Deputy Minister of Health Prof. Dr. Nurullah Okumuş, esteemed rectors, President of the Rare Diseases Federation Ms. Deniz Atakay, distinguished representatives of the Presidency of Strategy and Budget, our respected directors general, esteemed professors, and valued participants; I greet you all with my sincerest respect and affection. I would like to begin my remarks by expressing how pleased I am to be with you at this strategic summit organized by the Rare Diseases Federation.

The Widespread Impact of What Is Considered "Rare"

As our distinguished speakers before me have also emphasized, what we define as "rare" is, in fact, not rare at all when viewed from a societal perspective. In Türkiye alone, we are talking about a reality that directly affects at least 7 million people. This issue, which directly or indirectly concerns millions of citizens and carries a significant economic and social burden, is not only a challenge for our country but a shared problem across the world. For this reason, rare diseases constitute an area that must remain continuously on the agenda and be addressed from multiple dimensions.

Ankara University's Visionary Approach

As Ankara University, we regard rare diseases as both an academic and a humanitarian priority. We continue our efforts in this field with determination. When I assumed the rectorship in August 2020, while still serving as President of İVEK, this issue was brought to our attention. When Ms. Burcu, the Chair of our Rare Diseases Commission, introduced the matter to me, we decided to act immediately on behalf of our university without losing any time.

Academic Structuring and Research Centre

Although rare diseases also affect the adult population, they primarily fall within the field of paediatrics. Indeed, our Deputy Minister Prof. Dr. Nurullah Okumuş has devoted considerable effort to this field as a paediatrician himself.

During this process, we consulted with Prof. Dr. Tanıl Kendirli, Chief Physician of Cebeci Hospital, and identified experts within our university who had developed expertise in this area.

We subsequently met with Prof. Dr. Fatma Tuba Eminoğlu, who had gained experience through training in centres in Belgium and the United Kingdom during the tenure of our previous rector, and discussed the process in detail. We rapidly took the necessary steps to establish a research centre dedicated to rare diseases at Ankara University and transformed this scientific infrastructure into an institutional entity.

Türkiye's First and Only Independent Rare Diseases Centre

We quickly implemented this decision and not only established a unit but also built its physical infrastructure. Today, I can proudly state that Ankara University has established one of the few centres in Türkiye dedicated to rare diseases with its own independent building. One floor of our two-and-a-half-storey building has been allocated to a Phase I Centre, while the remaining one and a half floors are devoted entirely to the Rare Diseases Centre. Although five or six universities in Türkiye have centres in this field, Ankara University is home to the only centre exclusively dedicated to rare diseases within a standalone building.

The Social Dimension and Public Perception

Rare diseases often enter the media agenda through tragic stories. We frequently encounter them in images of children in wheelchairs appealing for medication during visits by our President, touching the public's sense of compassion. Yet there is also an enormous medical and economic dimension to this issue. Our physicians know well that, for example, while partial success may be achieved in SMA Type 1, the probability of success in Type 2 is considerably lower. Nevertheless, a public perception can emerge suggesting that every medication should be provided under all circumstances. At our university, we did not approach this matter solely from a medical perspective or as an issue confined to academic publications. Above all, this is a profound social issue.

Integrated Scientific and Advisory Board

In order to address the matter in all its dimensions, we did not limit our Scientific and Advisory Board to healthcare professionals alone. We brought together public sector representatives, civil society organizations, communication experts, and individuals from various disciplines. We believe that rare diseases are multifaceted issues with social, economic, and societal dimensions. We view this not merely as a problem of today but as a challenge whose solutions will shape tomorrow, and we approach it with a holistic perspective.

The Power of Being Complementary

I would particularly like to emphasize the concept of *mütemmim*—that is, complementary elements that complete one another. The pandemic taught us the critical importance of this concept in a painful way. Before the pandemic, WHO capacity assessments ranked countries such as the United States, the United Kingdom, and France at the top, while Türkiye was placed 21st. However, when the crisis arrived, we saw that those major countries struggled to access even the most basic protective equipment, including masks.

This experience demonstrated that systems can survive only when complementary elements come together and operate through strong coordination. The field of rare diseases is perhaps the area to which the concept of *mütemmim* is most applicable. Economy, healthcare, academia, media, and civil society—every institution capable of shaping public understanding, from bureaucrats to opinion leaders, must act as a single body.

I consider gatherings such as this extremely valuable because they help sustain this collective awareness. I thank everyone who contributed to this event and extend my respectful greetings to all of you.

Prof. Dr. Nuri AYDIN
Rector of Istanbul University-Cerrahpaşa,
President of the Association of University Hospitals

Rare Diseases in the Context of Medical Discoveries and Scientific Responsibility

Honourable Minister, esteemed rectors, and distinguished participants; it is a great pleasure to be with you today on the occasion of the Rare Diseases and Rare Lives Summit. I would like to sincerely thank the Rare Diseases Federation for organizing this meaningful event. Everything that is rare in life is inherently valuable; however, when it comes to health, rarity also brings with it a significant responsibility and high-cost treatment processes that must be carefully managed.

Historical Legacy and the Process of Disease Identification

Rare diseases sometimes emerge as newly identified conditions entering the medical literature for the first time. In this regard, I would like to commemorate Prof. Dr. Hulusi Behçet, one of the great sources of pride for my institution, Cerrahpaşa. The disease he identified, Behçet's disease, was also considered a rare disease in its early years. It should not be forgotten that the prevalence of a disease may vary according to geography; a condition that is extremely rare in one country may constitute a much more common health issue in another region.

Technological Advances: A Double-Edged Sword

The rapid development of genetic testing technologies has significantly increased the discovery and identification of rare diseases. However, this development is, so to speak, a "double-edged sword." While it enhances our diagnostic capabilities, it also triggers a process that is highly complex and sensitive to manage. In particular, the emergence of methods whose efficacy has not yet been fully proven, treatments with limited benefit, or off-label applications requires us to exercise great caution. The fact that this field has become such a focal point for the pharmaceutical industry and the wider healthcare sector makes it imperative that we conduct scientific research on a much more rigorous and robust foundation.

Comprehensive Social Awareness

We should not view rare diseases solely as an area confined to laboratory data and medical interventions. This issue is as much a social phenomenon as it is a medical one. Ensuring that individuals living with rare diseases can find their place in society, are not excluded, and benefit from increased public awareness is just as critical as the treatment process itself. I sincerely believe that this valuable gathering will make significant contributions both to scientific progress and to social awareness, benefiting our sector and, most importantly, our patients. I would like to extend my gratitude to everyone who contributed to its organization.

Osman Nuri ERDEM
Director General of Plans and Programmes,
Presidency of Strategy and Budget

Technological Transformation and Sustainable Management Strategies

Honourable Minister, esteemed Rectors, esteemed Directors General, our valued professors, and distinguished participants; I greet you all with respect and esteem. The breathtaking developments we are witnessing in medical science and digitalization are today placing many opportunities that could not even have been imagined in the past at the service of humanity. This broad technological spectrum, ranging from gene and cell therapies to artificial intelligence applications, is now a powerful source of hope for many diseases that were once considered impossible to treat.

Proper Management of Opportunities and Global Challenges

These developments are, of course, extremely pleasing for us; however, the proper management of these opportunities is just as critical as the discovery of the technologies themselves. Indeed, opportunities that are not properly managed may also bring with them costs and structural challenges that are difficult to manage. The question of what strategy should be used to manage this process is a priority agenda not only for our country but for the entire world, and it emerges as an area that requires all stakeholders to work in full coordination.

Personalized Medicine and Social Impact

Today, medical science is becoming increasingly personalized, evolving from standard practices toward individualized solutions. Although rare diseases may appear to have low prevalence on an individual basis, when considered collectively, they constitute an enormous field that directly affects a very large segment of society. It is not possible for a picture of this magnitude to be neglected or overlooked from a managerial perspective.

New-Generation Cooperation Models

All these scientific and technical developments clearly demonstrate that the public and private sectors must move beyond traditional patterns and develop new and sustainable models. In our strategic planning and programming processes, the need for these new-generation models is becoming more evident with each passing day.

On this occasion, I would like to extend my gratitude to everyone who contributed to the creation of such a productive environment for communication and discussion. I respectfully greet you all.

Assoc. Prof. Dr. M. Emin DEMİRKOL
Director General of Public Health, Ministry of Health of the Republic of Türkiye

Rare Diseases from a Public Health Perspective: Prevention, Screening and Continuous Education

Honourable Minister, esteemed Rectors, distinguished Directors General, and valued academics from across Türkiye; I greet you all with respect and affection. Today, we have gathered to address rare diseases—conditions that may have a low prevalence but exert profound effects on individuals, families, and society—through a holistic approach. Rare diseases are not an area limited solely to curative services; rather, we must manage this process as a whole through early diagnosis, preventive healthcare, and strong social support mechanisms.

The Power of Screening Programmes in Early Diagnosis

Genetic and newborn screening programmes, in particular, are among our most critical public health services, enabling diseases to be identified before clinical symptoms emerge and directly improving quality of life. As the Ministry of Health, we successfully implement numerous screening programmes within this framework. However, I would especially like to emphasize that rare diseases are not solely the responsibility of the Ministry of Health. Together with the Presidency of Strategy and Budget, our other ministries, civil society organizations, and academics present here today, we must embrace this issue with the spirit of a national mobilization.

The "Healthy Türkiye Century" Vision

In line with the "Protective, Development-Oriented and Productive Health Model" and the "Healthy Türkiye Century" vision put forward under the leadership of our Minister, we continue to strengthen effective prevention, high-quality screening, and follow-up processes. We are currently conducting nationwide screening programmes for six different diseases with great success. Beginning in the newborn period and reinforced through premarital screening programmes, these processes enable the early detection and effective monitoring of diseases. This entire operation is carried out under the guidance of our scientific committees and the coordination of our Directorate General through a vast network spanning all 81 provinces of Türkiye.

Field Experience and Family Medicine Training

From a public health perspective, we regard citizens living with rare diseases not merely as "rare" but as among the most "valuable" members of our society. In order to reflect this understanding in practice, we have launched a comprehensive educational initiative for family physicians. Since November, we have completed six months of face-to-face and digital training programmes that combine professional knowledge with real-world field experience.

In accordance with the instructions of our Minister, we will dedicate one month of this year entirely to training focused on rare diseases and paediatric disorders. All family physicians and primary healthcare personnel across Türkiye will update their knowledge through this professional development programme, which includes pre-tests, post-tests, and digital follow-up processes. Conducted with the support of our esteemed academics, this awareness initiative will significantly enhance our success in achieving early diagnosis in the field.

I believe that this productive symposium will strengthen the links between early diagnosis, treatment, and awareness, and I would like to express my gratitude to all stakeholders who have contributed to this effort.

Deniz ATAKAY
President of the Rare Diseases Federation

A Rare Solidarity for a Shared Future

Honourable Minister, esteemed Rectors, Directors General, representatives of patient associations, valued stakeholders, academics, and dear supporters; on behalf of the Rare Diseases Federation, I greet you all with affection, respect, and an enduring sense of hope. No matter how much experience we gain or how much we achieve, we can never overcome the excitement we felt on the very first day whenever we stand at this podium. Today, we are gathered not merely to hold a meeting, but to share a common life, shoulder our responsibilities together, and, most importantly, develop solutions collectively.

Rare Lives with Widespread Impact

Every rare life embodies a profound struggle and a silent effort to endure. We know very well that although the names of these diseases may be rare, their impact on individuals and families is anything but rare. These families face barriers not only in accessing diagnosis and treatment, but also in every aspect of life—from education and employment to social acceptance and legal rights. All too often, these individuals are pushed to the margins of society, confronted by barriers that are sometimes physical and sometimes rooted in attitudes and perceptions.

An Integrated Human Rights Struggle

At this point, we would like to underline one reality in the strongest possible terms: rare diseases are not merely a subcategory of the healthcare system. These lives stand at the intersection of education, nutrition, social policy, and employment—in other words, at the crossroads of all public policies—and therefore constitute a matter of human rights. As a federation, we believe that the future should be built not only in hospitals but also in classrooms, offices, and every aspect of social life, in a healthier and more inclusive manner.

Our Achievements and Vision for the Future

Over the past year, we have witnessed encouraging progress. Rare lives have become more visible within education,

meaningful success stories—albeit limited in number—have emerged in employment, and rare diseases have even found representation in television dramas, contributing to public awareness. However, we must take these achievements further. During the panels we will hold today, we will discuss with experts how communication and coordination can be strengthened and which new support models can be implemented. I kindly ask you to remain with us throughout the day and guide us through your ideas and contributions.

A Call for a Change in Mindset and National Policy

When patient organizations, public institutions, academia, and the private sector come together around the same table, solutions become not only possible but also sustainable. We seek to initiate a transformation in mindset. Rather than asking solely, "What is the Ministry of Health doing?", we choose to take a step further and ask, as all stakeholders, "What can we do for rare diseases within national policy?" As a federation, we are ready to contribute in every possible way on the ground.

Every contribution you make today may directly change a child's educational journey or improve a family's quality of life. Let us think together and create together for a more inclusive Türkiye. Because through effective partnership, individuals living with rare diseases will not be "lost lives," but rather "realized potential."

I would like to thank everyone who is working toward the establishment of a value-based and inclusive system.

RARE DISEASES FEDERATION

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PANELS

PANEL-1

NATIONAL ACTION PLAN AND HEALTH POLICIES FOR RARE DISEASES

MODERATORS

Prof. Dr. Onur Burak DURSUN
University of Hvealth Sciences
(Member of the Rare Diseases Scientific Committee)

Gülnur GÖKMEN
Rare Diseases Federation

SPEAKERS

Dr. Murat GÜLŞEN
Head of the Rare Diseases Department, General Directorate of Health Services (SHGM)

Prof. Dr. Çiğdem Seher KASAPKARA
Faculty Member, Gazi University

Esra MUŞ
Head of the Department of Standards and Accreditation, General Directorate of Health Information Systems, Ministry of Health

Dr. Murat GÜLŞEN
Head of the Rare Diseases Department, Ministry of Health,
General Directorate of Health Services (SHGM)

Rare Diseases Action Plan and Health Policies

Overview of Rare Diseases and Key Statistics

Rare Diseases

- Affect fewer than 1 in 2,000 individuals
- Approximately 5–8% of the population is affected by one of the rare diseases (millions of people worldwide)
- Approximately 5–6.4 million people in Türkiye
- Mostly of genetic origin
- Difficult to diagnose
- Limited treatment options and restricted access
- High mortality and disability rates

With regard to the characteristic features of rare diseases, we know that they are largely of genetic origin. The difficulty of diagnostic processes, the complexity of treatment protocols, and, unfortunately, the high rates of mortality and disability are among the most fundamental and critical characteristics that distinguish this group from other disease categories.

The data you see in the table are part of a dynamic process. Many new diseases that have not yet been named or phenotypically differentiated continue to be identified, and we closely monitor these scientific developments in real time.

On the Concept of "Orphan Diseases"

I would also like to touch upon the term "orphan disease," which is frequently used in the literature to describe rare diseases. However, I must open a parenthesis here; the true concept of "orphanhood" originally referred to patients who, in the early 1900s, remained in the corners of clinics and were effectively left without support because no treatment options existed.

Today, however, the picture is changing. As symbolized in the visual, these individuals are no longer alone within the crowd. Thanks to the growing influence of civil society organizations, the establishment of strong support mechanisms, and the development of our healthcare systems, we are moving further away from this sense of "orphanhood" with each passing day. Increasing public awareness and the growth of patient associations are enabling us to move forward on this path with far greater confidence and determination.

Department of Autism, Intellectual Special Needs and Rare Diseases

The Department of Autism, Intellectual Special Needs and Rare Diseases was established on 10 January 2020. Our Department serves as the primary counterpart for civil society organizations in the fields of autism and rare diseases and functions as a strategic unit that plans and implements activities by considering healthcare, education, and social service needs. Since its establishment, the projects carried out by our Department have progressed in alignment with the findings and recommendations of the separate Grand National Assembly of Türkiye (TBMM) Research Commissions established for both fields. We continue our activities within the framework of the Rare Diseases Action Plan and the Second Autism Action Plan. Both scientific evidence and international examples, as well as needs identified in the field, clearly demonstrate the necessity of such a department. It represents a holistic and systematic transformation in Türkiye's approach to individuals with special needs and citizens living with rare diseases.

In fact, developments progressed in a more simultaneous and mutually reinforcing manner than we had anticipated. The two critical reports displayed on the screen, both dated March 2020—the TBMM Research Commission Report No. 199 examining difficult-to-treat diseases such as ALS, SMA, DMD, and MS, and Report No. 200 addressing developmental disorders such as Down syndrome and autism—reached their final form shortly after our Department was established. This provided a significant advantage for us. The alignment between the establishment of our Department and the findings of this comprehensive parliamentary field study further clarified the roadmap before us.

To summarize the roadmap of our healthcare system regarding rare diseases, as emphasized by our Minister and our Director General in their opening remarks, our primary focus is on prevention and early diagnosis strategies.

J Pharm Bioallied Sci. 2010 Oct-Dec; 2(4): 290–299.
doi: 10.4103/0975-7406.72128
PMCID: PMC2996062
PMID: 21180460

Orphan drug: Development trends and strategies

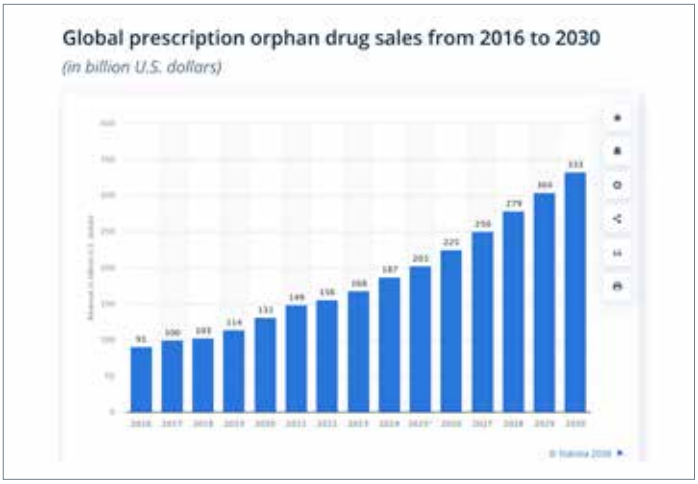
Aarti Sharma, Abraham Jacob, Manas Tandon, and Dushyant Kumar

Abstract

The growth of pharma industries has slowed in recent years because of various reasons such as patent expiries, generic competition, drying pipelines, and increasingly stringent regulatory guidelines. Many blockbuster drugs will loose their exclusivity in next 5 years. Therefore, the current economic situation plus the huge generic competition shifted the focus of pharmaceutical companies from the essential medicines to the new business model — niche busters, also called orphan drugs. Orphan drugs may help pharma companies to reduce the impact of revenue loss caused by patent expiries of blockbuster drugs. The new business model of orphan drugs could offer an integrated healthcare solution that enables pharma companies to develop newer areas of therapeutics, diagnosis, treatment, monitoring, and patient support. Incentives for drug development provided by governments, as well as support from the FDA and EU Commission in special protocols, are a further boost for the companies developing orphan drugs. Although there may still be challenges ahead for the pharmaceutical industry, orphan drugs seem to offer the key to recovery and stability within the market. In our study, we have compared the policies and orphan drug incentives worldwide alongwith the challenges faced by the pharmaceutical companies. Recent

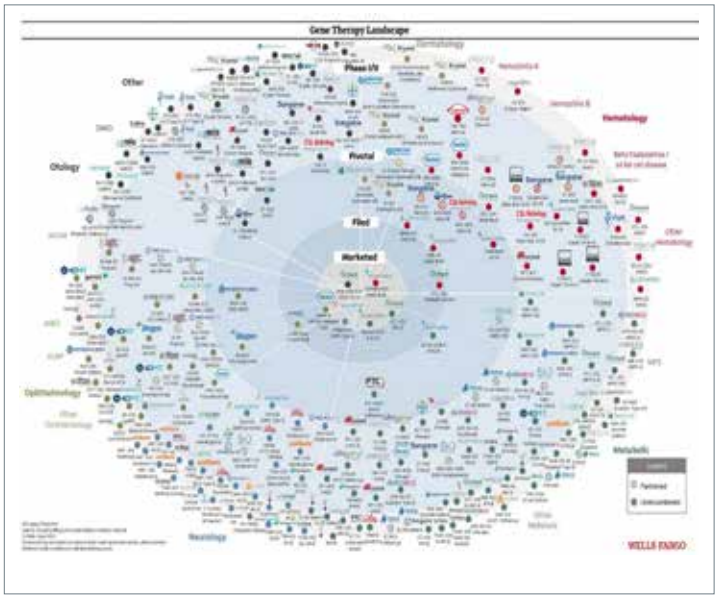
To understand the scientific and economic evolution of this field, the literature reveals a truly striking transformation. This study from 2010, displayed on the screen, serves almost as a documentary record of the sector's evolution.

As highlighted in the publication, we observe that major pharmaceutical companies increasingly shifted their focus toward the orphan drug field as a means of compensating for revenue losses. In a sense, the global pharmaceutical industry's interest in this niche area has been driven not only by medical necessity but also by a strategy aimed at maintaining market stability. Consequently, many of the treatment alternatives we discuss today are rooted in this macroeconomic and scientific shift that gained momentum beginning in the 2010s.



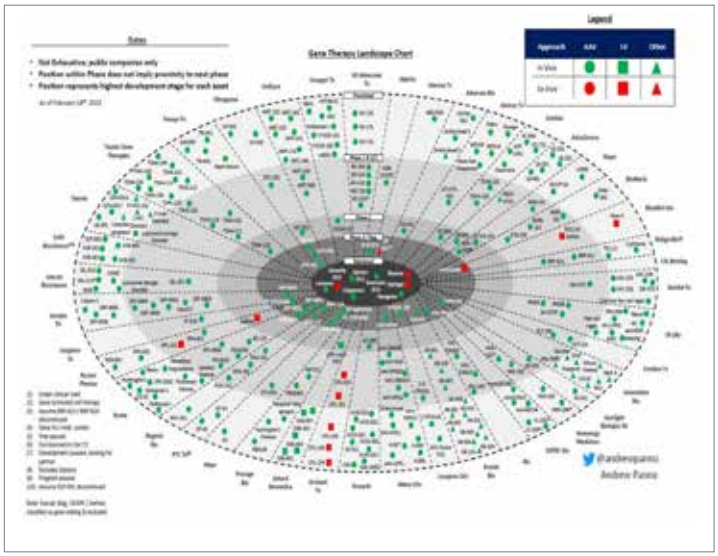
When we examine the global economic landscape, we can clearly see the extraordinary pace at which the rare disease market has expanded. According to the current market research data presented on the screen, prescription orphan drug sales, which stood at approximately USD 91 billion in 2016, have surpassed the USD 200 billion threshold as of 2025.

2021 Gene Therapies



2023 Gene Therapies

- More than 115 companies
- More than 350 clinical studies

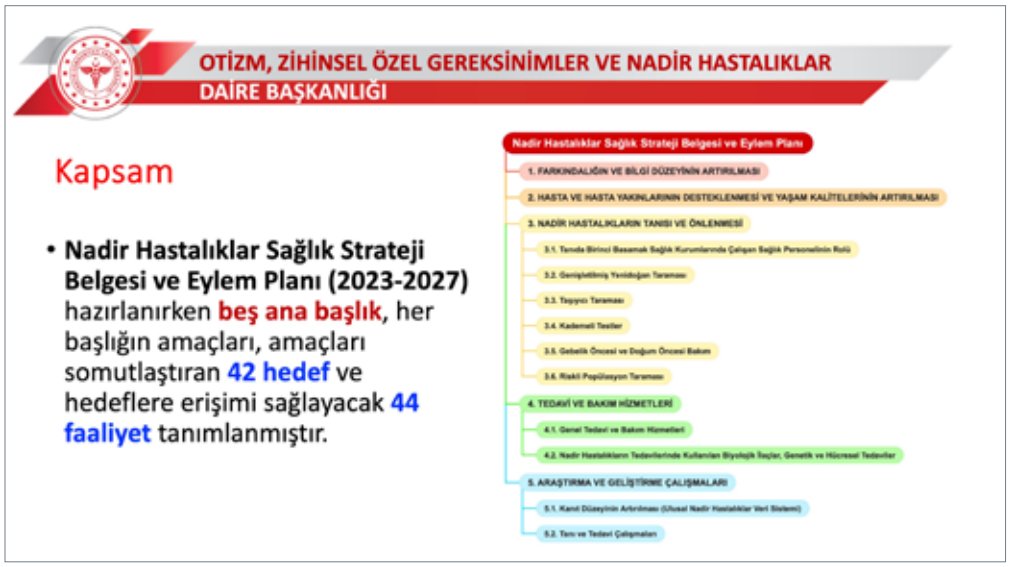


Looking at the global landscape, I would say that we are standing on the threshold of a revolution in gene therapy. This broad-spectrum Gene Therapy Landscape presented on the screen clearly demonstrates the vast scale and diversity of ongoing activities in the field.

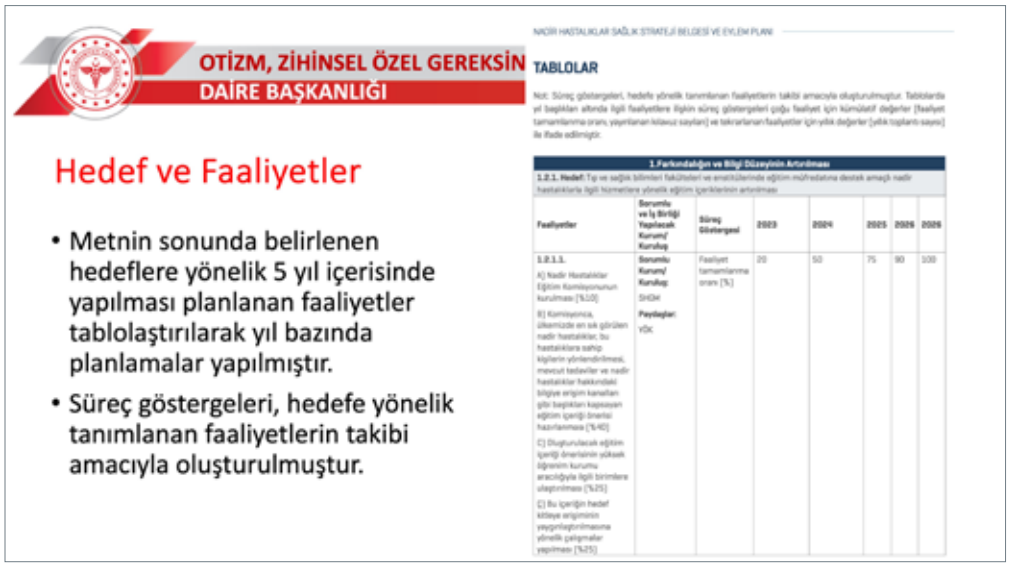
National Rare Diseases Action Plan

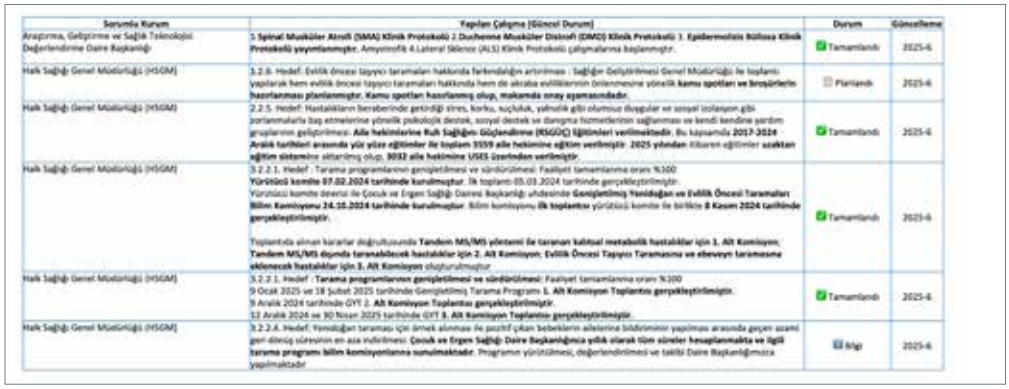
When our Department Presidency was established, we clearly recognized that the greatest deficiency before us was the absence of an overarching strategic document that would govern the entire process, namely a comprehensive Action Plan. To fill this gap, we rolled up our sleeves and began by meticulously examining successful examples from around the world.

While preparing the document whose covers you see on the screen; we consolidated previous drafts, international reports, and the valuable opinions of our sector representatives into a single framework. The primary objective of this plan, which is currently accessible through our website in both Turkish and English, is to establish a strong organizational structure and a sustainable foundation for awareness.



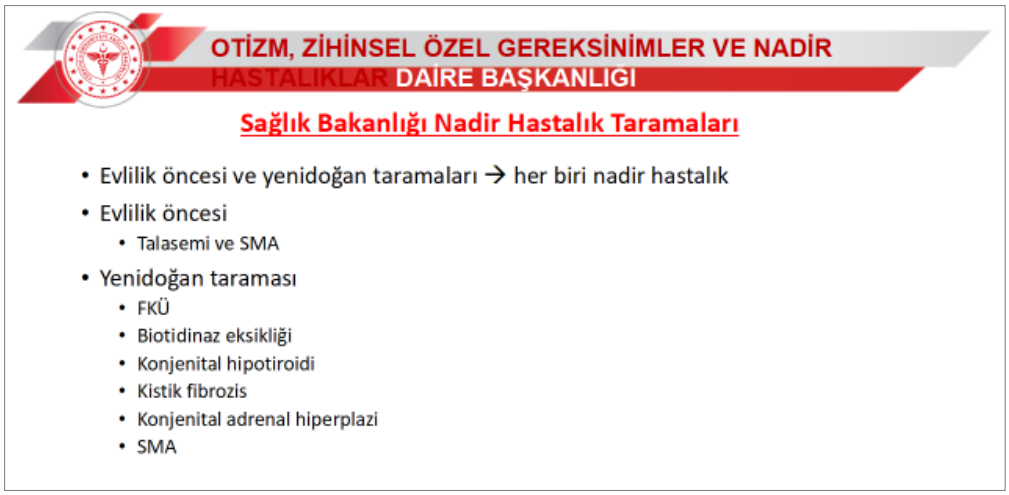
We built the backbone of the Rare Diseases Health Strategy Document and Action Plan covering the years 2023–2027 upon five main pillars that complement one another. This structure is not merely composed of general statements; it encompasses 42 carefully developed objectives and 44 concrete activities that will enable us to achieve those objectives.





Monitoring and Evaluation

Perhaps the most critical phase of our Action Plan is the "Monitoring and Evaluation" process, through which we assess the extent to which the objectives defined on paper are reflected in practice. Within the scope of the plan, we have individually defined every step to be taken in the short, medium, and long term, together with the responsible parties and stakeholders.



Screening Programmes and "Well-Being"

Looking more closely at screening programmes, I can say that each component of both our premarital screening programmes and our newborn screening programmes is, in essence, part of the fight against rare diseases.

Our primary objective here is not merely to treat a disease, but to ensure that a child reaches the highest biological and social potential possible—in other words, a complete state of well-being. For us, the measure of success is building a future in which healthy generations can thrive.

PGT and Genetic Services

It is also worth mentioning PGT (Preimplantation Genetic Testing), one of the most technologically advanced and promising components of our prevention strategies, namely selective reproductive services. As the Ministry, we continue our efforts uninterruptedly to expand the availability of these advanced genetic services within the public healthcare system for many rare diseases, particularly blood disorders.

Specialized Units

With regard to specialized units, if we are to make an honest observation, if we were to ask any citizen on the street today, "What is a rare disease?", the answer would most likely, without exception, be "SMA." Although our activities may at times appear to be concentrated in that direction due to the strong public awareness and perception surrounding SMA, our actual objective is to expand service units in a manner that encompasses all rare disease groups.

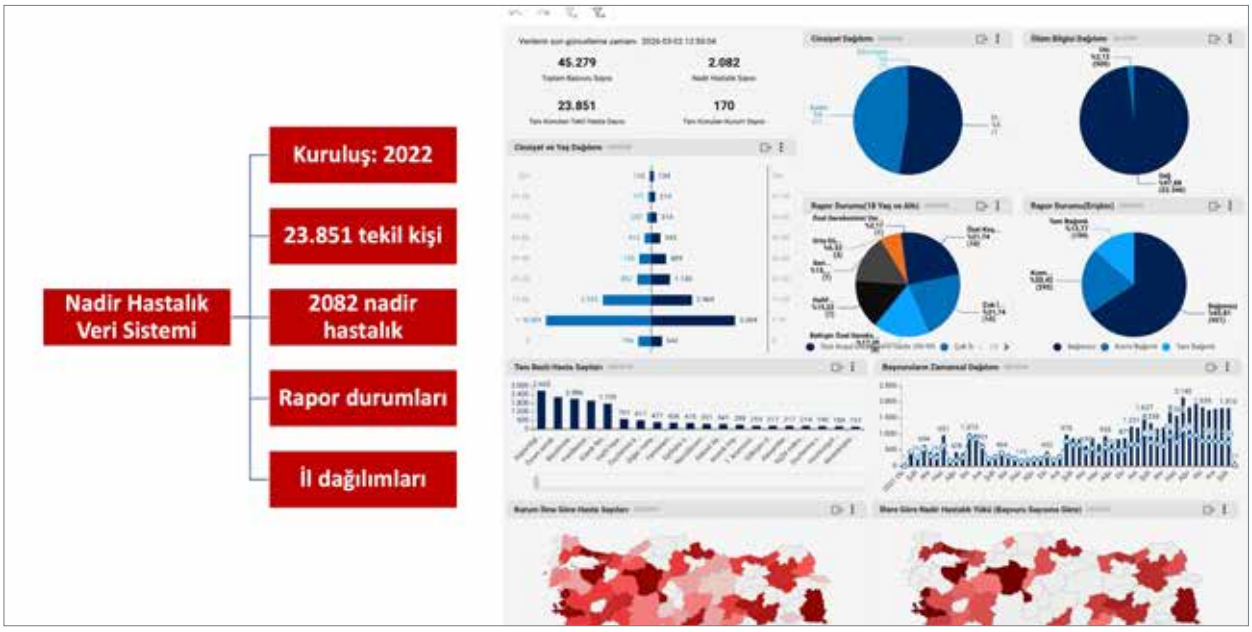
Development of Criteria for Rare Disease Centres of Excellence

- The criteria continue to be developed in collaboration with TÜSKA.
- Rare Diseases Sub-Working Areas:
  - Rare Neuromuscular Diseases Centre of Excellence Sub-Working Group
  - Metabolic Diseases Centre of Excellence Sub-Working Group
  - Rare Eye Diseases Centre of Excellence Sub-Working Group
  - Rare Respiratory Diseases Centre of Excellence Sub-Working Group
  - Congenital Malformations and Rare Cognitive Developmental Disorders Centre of Excellence Sub-Working Group

Centres of Excellence and Specialization Efforts

Rare diseases constitute a vast and highly complex field that cuts across almost every medical specialty. For this reason, it is neither technically feasible nor efficient for a single centre to address all specialties with the same level of expertise. Recognizing this reality, we worked extensively with TÜSKA (Turkish Health Services Quality and Accreditation Institute) in order to accelerate our efforts and establish genuine specialization.

Through this specialization approach, each patient group will have the opportunity to receive treatment at centres possessing the deepest expertise and the most advanced technologies in their respective fields. Our objective is to give real substance to the concept of "excellence" and provide our patients with services that meet international standards.



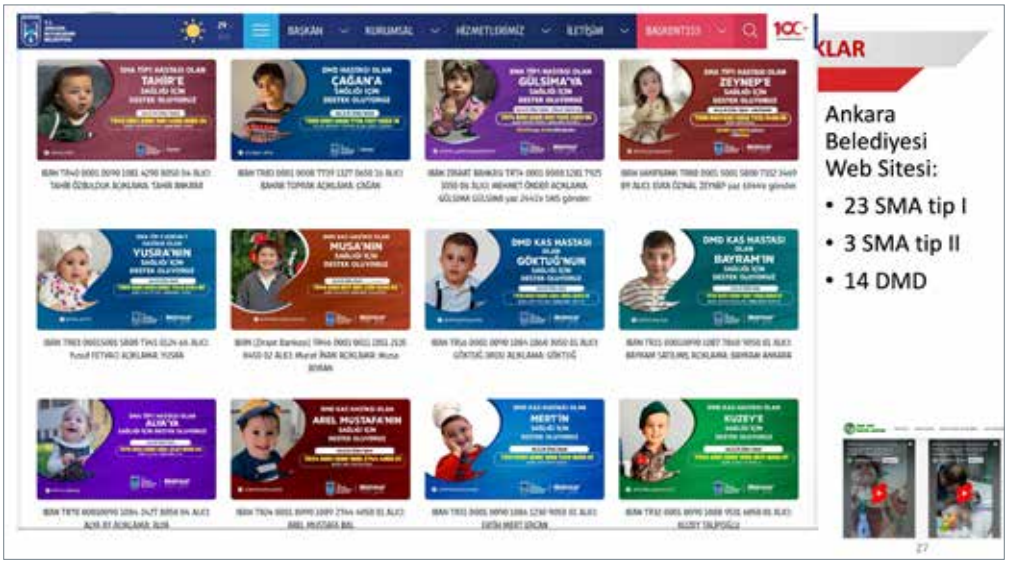
Nadir Disease Data System and the Coding Challenge (ICD vs. Orphanet)

The Rare Disease Data System, one of the most critical projects we have undertaken in collaboration with the General Directorate of Health Information Systems, essentially represents our digital memory and our capacity to develop evidence-based policies. Through this system, which we established in 2022, we are currently able to track 23,851 unique individuals and 2,082 different rare diseases within our database.

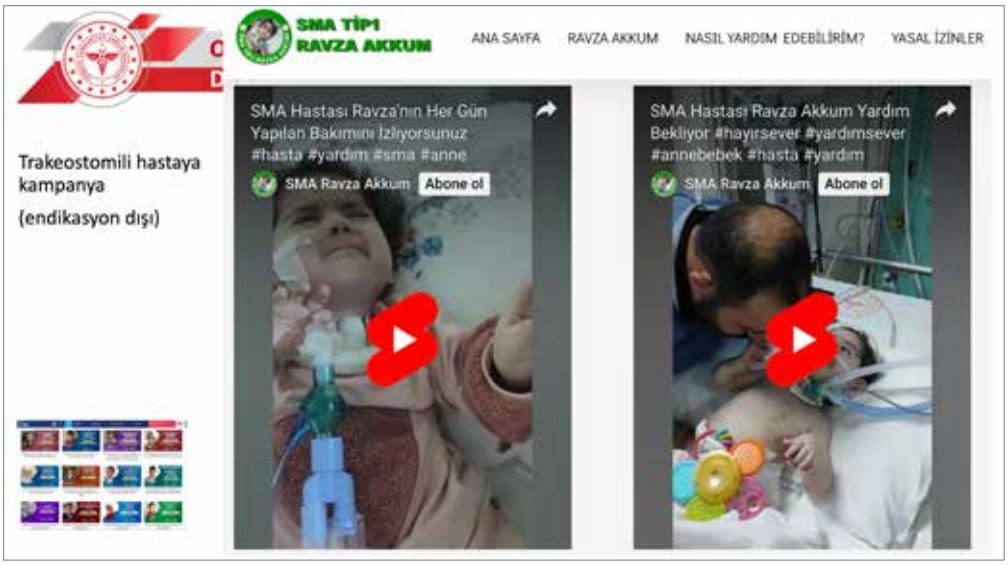
Our work on guidelines, protocols, clinical indicators, and other research and publication activities constitutes the scientific standardization component of our efforts.

SMA Clinical Quality Indicators

As a Ministry, we aim to measure the quality of our services in the field of rare diseases not only through quantitative metrics, but also through concrete data and high standards. We implemented the first and most comprehensive example of this vision through the Indicator Cards for the Spinal Muscular Atrophy (SMA) Health Condition, published in February 2025.



Donation campaigns authorized by governorates are an issue that we approach with particular sensitivity and that directly interacts with our health policies. When we review the website of Ankara Metropolitan Municipality and the related announcements, we observe that a large number of active campaigns are being conducted. We continue to closely monitor the ethical and medical dimensions of these processes in a manner that minimizes the hardships experienced by our families.



Scientific Evidence and Treatment Comparisons

Grounding discussions on medicines and treatment options in scientific evidence is of great importance for both our patients and the public. As a Ministry, our primary objective is to ensure that every patient gains the fastest possible access to the most appropriate and scientifically proven treatment, without having to embark on a separate search for it.

Legal Processes and Ethical Concerns

The legal and ethical dimensions of donation campaigns represent one of the areas where scientific realities and public conscience most frequently intersect. This situation once again demonstrates the need to align not only medical practices, but also legal and ethical standards in the management of rare diseases with scientific evidence.

The Vital Importance of Early Diagnosis

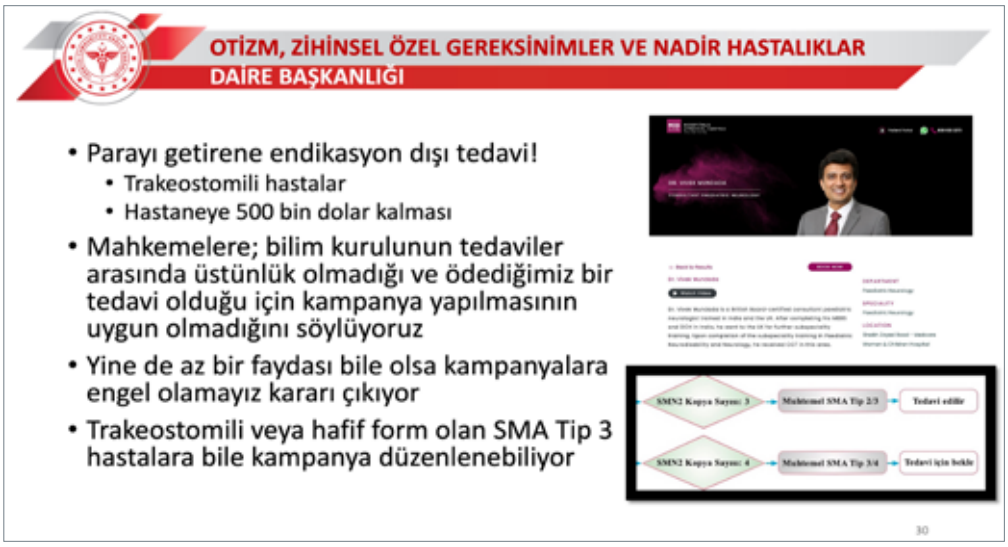
At the heart of our Action Plan and the entire strategy we are implementing lies a single reality: in rare diseases, early diagnosis is not merely an advantage—it is life itself. True success is achieved when treatment can be delivered before symptoms even emerge, that is, before neurological or organ damage begins. This is precisely where the Newborn Screening Programme becomes our strongest line of defence.

Unethical Practices Abroad

A campaign conducted by a physician in Dubai using a Turkish mother in promotional materials is perhaps the clearest indication that the issue has moved beyond its medical dimension and evolved into a commercial and ethically questionable matter.

Our priority is to ensure that the hopes of our families and the compassion of our citizens are not exploited by such unethical commercial operations. Without departing from the principles of science and medical ethics, we will continue to stand by our patients through the most accurate and honest approaches available.

The position adopted by pharmaceutical companies in this process is not merely a commercial choice; it is also an



ethical responsibility. It is unacceptable for a company to take the position that, "The physician has prescribed it; the rest is none of my concern." Companies must also operate effective oversight mechanisms to determine whether a medicine is genuinely being requested for a valid medical indication or whether it is being sought for a patient group that falls entirely outside approved criteria.

SMA Tip	Frekans	Şiddet	Başlama Yaşı	Motor Fonksiyon Durumu			Semptomlar	Beklenen *SMN2* Kopya Sayısı	Yaşam Süresi
				Oturma	Ayakta Durma	Yürüme			
0	<%1	Şiddetli	Prenatal	✗	✗	✗	Şiddetli Hipotoni	1	<1 ay
I	%60	Şiddetli	0–6 ay	✗	✗	✗	Solunum Yetersizliği	1,2,3	<2 yıl
II	%20-30	Orta	<18 ay	✓	✗	✗	Solunum Komplikasyonları Tekerlekli sandalye ihtiyacı	2,3,4	>25 yıl
III	%15	Hafif	>18 ay	✓	✓	Destekli veya Desteksiz	Kas Güçsüzlüğü	3,4,5	Normal
IV	<%1	Hafif	>5 yaş	✓	✓	✓	Yavaş ilerleyen Kas Güçsüzlüğü	≥4	Normal

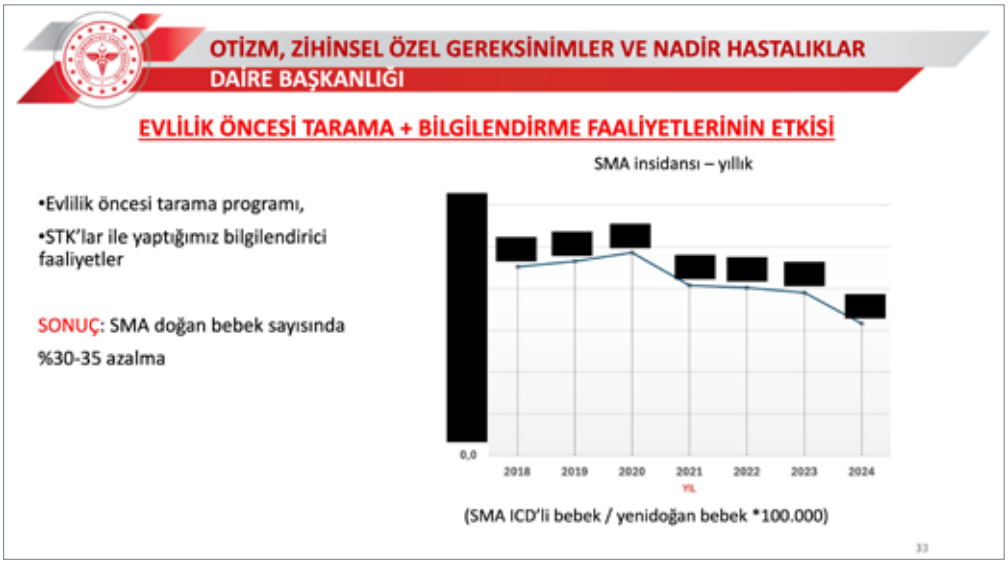
SMA Type 1 and Post-Treatment Development

SMA Type 1 is one of the most severe forms among rare diseases; however, the treatment outcomes achieved by Türkiye in this field represent a medical breakthrough. As a result, in light of scientific evidence and real-world outcomes, there is currently no unmet treatment need for SMA in our country. Naturally, as new medicines are developed and applications are submitted by pharmaceutical companies, these alternatives will also be incorporated into our treatment portfolio following approval by institutions such as the Turkish Medicines and Medical Devices Agency (TİTCK) and the Social Security Institution (SGK).

These findings once again demonstrate the critical importance of the principle of "early diagnosis and rapid intervention," which I emphasized at the very beginning of our strategy.

Delphi Consensus Report and Early Diagnosis

The Delphi Consensus Report is a relatively recent and highly influential document for the scientific community. Prepared with the participation of approximately 30 specialists from neuromuscular disease centres in countries such as Germany, Austria, and Switzerland, the report provides critically important insights into the management of rare diseases.



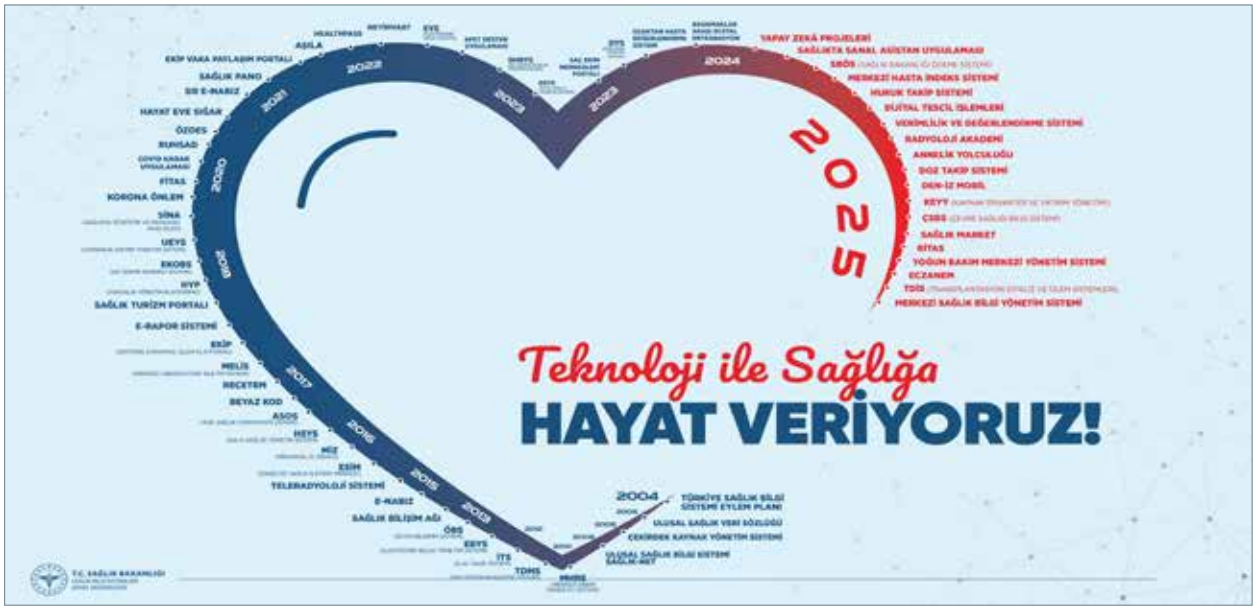
The Tangible Impact of Screening Programmes

We have now arrived at the most crucial part of our presentation—the real-world impact of all the strategic efforts we have undertaken. Alongside our premarital and newborn screening programmes, the extensive awareness-raising activities conducted in collaboration with civil society organizations are permanently transforming the rare disease landscape in Türkiye today.

The graph displayed on the screen, entitled "The Impact of Premarital Screening and Awareness-Raising Activities," represents the most tangible evidence of this achievement.

Esra MUŞ
Head of the Department of Standards and Accreditation,
General Directorate of Health Information Systems, Ministry of Health

Health Information Systems and the Rare Diseases Data Infrastructure



As you know, as a General Directorate, we implement numerous projects that bring Türkiye's digital health infrastructure to international standards. As can be seen from the heart-shaped technology roadmap displayed on the screen, since 2013 we have been managing a vast ecosystem ranging from e-Nabız and Teleradiology to Hayat Eve Sığar, which proved its effectiveness during the pandemic, and the Artificial Intelligence projects we are discussing today.

In a field such as rare diseases, where data is of vital importance, we work in very close collaboration with the General Directorate of Health Services and all our other stakeholders. Today, I will try to explain, from a technical perspective, how we have transformed this rare and valuable data into an infrastructure that is more standardized, measurable, and actionable.

National Health Data Dictionary and Terminology Harmonization

The most critical component forming the foundation of our Action Plan and defining the backbone of our digital architecture is the National Health Data Dictionary (USVS). As you can appreciate, it is impossible to manage such a vast ecosystem unless terminology harmonization is achieved in health data—that is, unless systems are enabled to communicate in the same language.

Through this dictionary initiative, we established a hierarchical pool of terms and data sets that serve as a reference for all information systems across our healthcare institutions. Following the implementation of the USVS, we configured a reference server that technically operationalizes these standards: the Health Coding Reference Server (SKRS).

Through the coding and classification systems incorporated within the SKRS:

- **Nationwide Reference:** All hospitals and software systems use the same set of codes when recording a diagnosis or procedure.
- **Interoperability:** When data is transferred between different institutions, the accuracy and semantic integrity of the information are preserved.
- **Precision in Rare Diseases:** The technical infrastructure serves as our greatest asset in overcoming the coding challenges mentioned in previous presentations and in enabling more refined and meaningful data collection.

In summary, we created the alphabet of our digitalization journey through this dictionary and reference server. As a result, every data entry made anywhere in Türkiye is transformed into meaningful and processable information within our central system.

National Rare Diseases Data System

In response to the request of the relevant General Directorate and in alignment with the objectives set forth in the National Action Plan, we have built our goal of establishing a National Rare Diseases Data System on this foundation.

Rare Diseases: ICD-10 vs. ICD-11

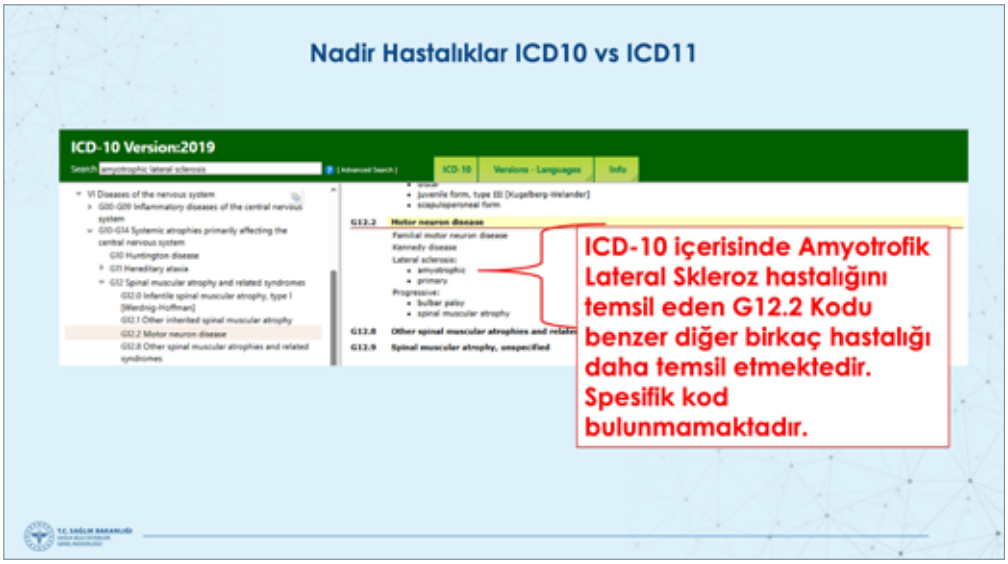
Under the general ICD (International Classification of Diseases) classification approach, for a disease entity to be included in the classification system, it is generally expected to affect a sufficient number of individuals and constitute a significant public health concern. While advances in technology have expanded these possibilities, the structure of ICD-10 has not fully kept pace with these developments.

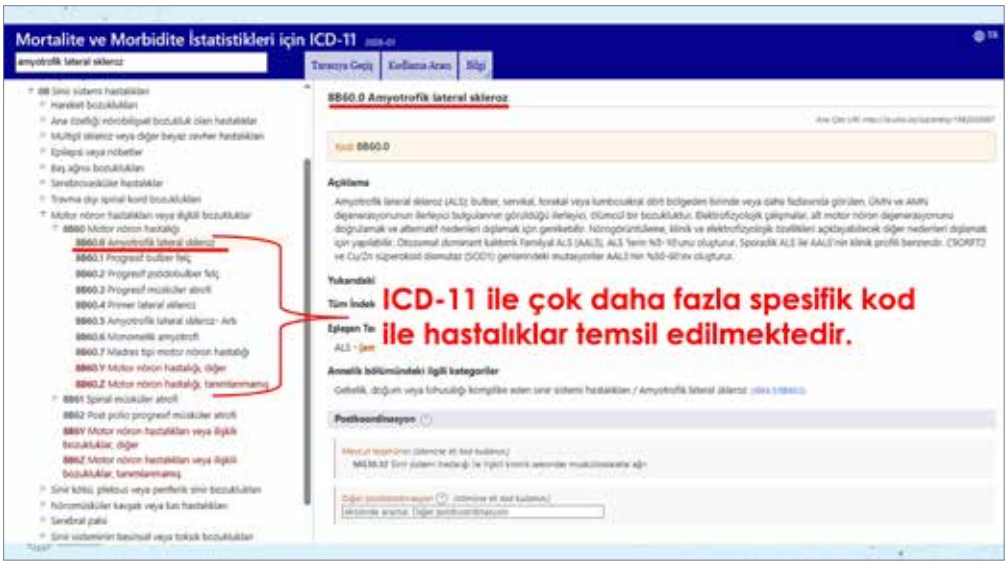
Although some rare diseases are included in ICD-10, many are not. A large number of rare diseases are collectively represented under non-specific code categories. At present, approximately 5,500 rare diseases are represented in ICD-11. Although an exact figure is not available for ICD-10, it is estimated that only about one-tenth of this number is represented as rare diseases within the ICD-10 framework.

Transition from ICD-10 to ICD-11 and Associated Challenges

One of the most prominent and challenging topics currently on our agenda is the transition to ICD-11. Those working on the technical side will know that ICD-11 is not merely a "code list"; it represents an entirely different philosophy. As a country, we have become accustomed to using coding systems as traditional lists. However, with ICD-11, the World Health Organization (WHO) is changing this approach.

The organization now seeks diagnoses to be processed, transmitted, and managed on a concept-based basis through a standardized API and service infrastructure. When viewed from the perspective of rare diseases, it is evident that the current ICD-10 structure has become outdated. Although some rare diseases are included within ICD-10, the vast majority are not defined in the system, which is directing us toward more current and disease-specific frameworks.





As you know, under the current ICD-10 system, many rare diseases are collectively represented under non-specific general code categories. This situation makes it more difficult to ensure data accuracy.

ICD-11 and Coding Precision

Let us take the code G12.2 as an example. While this code simultaneously represents several different diseases with similar characteristics, it unfortunately does not provide a specific sub-code for one of those conditions. This presents a challenge not only for you during the diagnostic process but also for us in the course of data analysis.

Rare Diseases: ICD-10 vs. ICD-11

While ICD-10 represents the rare diseases it contains through simple definitions, ICD-11 offers the ability to describe these diseases in much greater detail through the use of post-coordination.

In addition to being a disease classification system, ICD-11 also incorporates functions for searching and identifying the appropriate disease within its structure. In other words, ICD-11 has a software dimension that maintains and manages the network of relationships embedded within the system.

ICD-11 Transition Timeline and the Turkish Version

The Turkish version of ICD-11 is currently accessible. Our translation refinement and enhancement efforts continue without interruption. We are highly receptive to all feedback and suggestions coming from the field regarding this process.

Deputy Minister of Health Dr. Şuayip Birinci has set a very ambitious and relatively short timeline for the transition to ICD-11. Therefore, close collaboration will be essential to ensure that neither you on the clinical side nor we on the technical side encounter unnecessary difficulties.

We may choose to initiate this process through pilot hospitals or proceed on a specialty-by-specialty basis. We remain open to all recommendations and suggestions regarding the most effective approach.

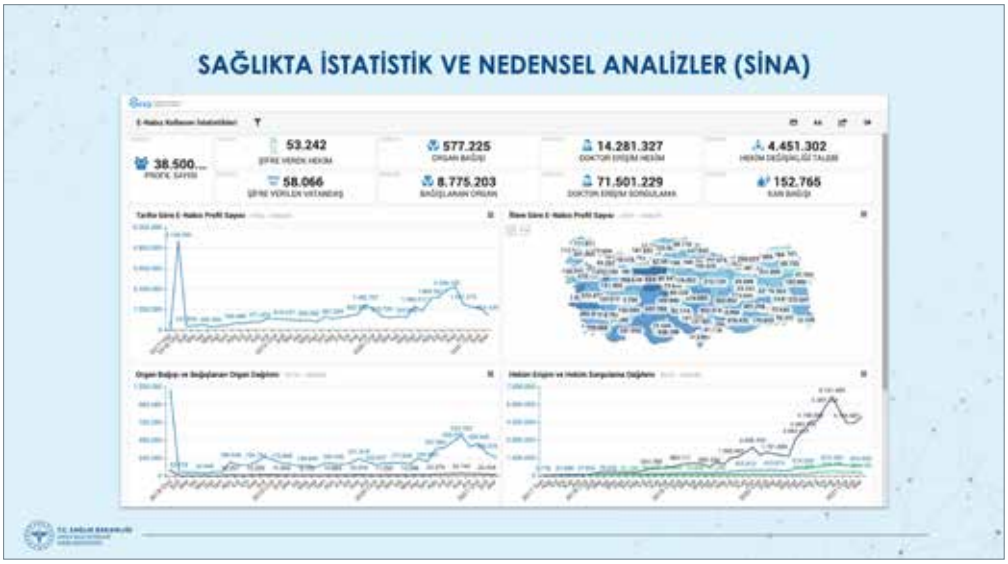
Data Architecture Flow: From AHBS to SINA

So, what do we do once we receive this data?

1. Data Source: Standardized data packages are transmitted to us through the Family Medicine Information System (AHBS) at the primary care level and through the Hospital Information Management System (HBYS) in hospitals.
2. Database: These data are standardized through our processes and entered into our relational databases.
3. Analysis and Reporting: In the final stage, the data are reported through SINA (Health Statistics and Analysis), the Ministry's data dictionary and decision-support platform. I assume there is probably no one among you who is unfamiliar with or does not use e-Nabız.

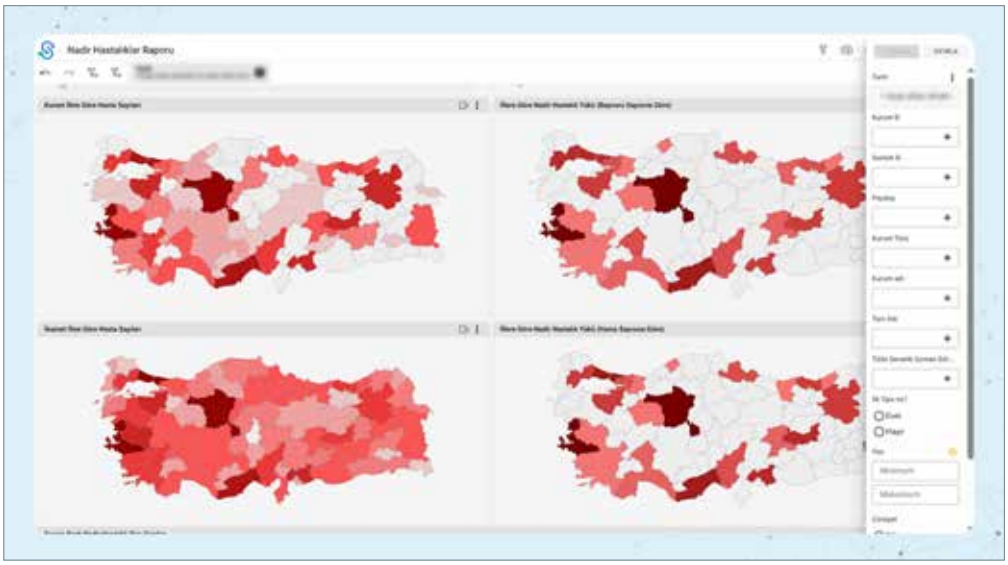
Once this data cycle is completed, we will be able to develop our rare disease policies not on the basis of assumptions, but on the basis of real-time and real-world data generated through this digital infrastructure.

The statistics generated through e-Nabız, one of our flagship applications, and the integrations we have established with more than 63,000 healthcare facilities are not merely part of an internal Ministry process. We operate within a vast data-sharing network that encompasses all of our stakeholder institutions.



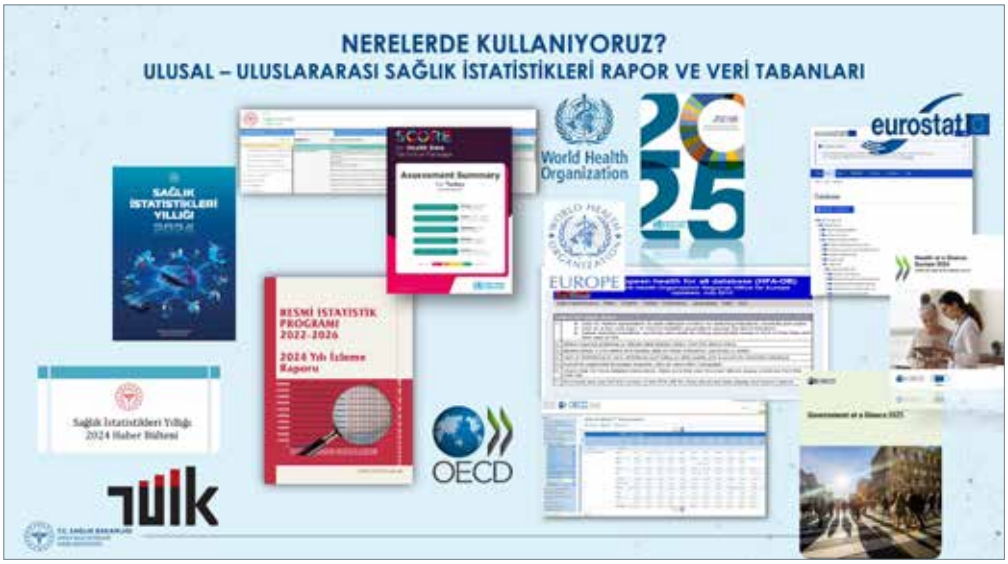
SINA: From Data to Policy

The name of our decision-support platform is inspired by the great physician and scholar Avicenna (Ibn Sina): SINA (Health Statistics and Analysis). Through this platform, we present data at different authorization and reporting levels to our Minister, Deputy Ministers, General Directors, and Provincial Health Directors.



Rare Diseases Report

Within SINA, we have a dedicated Rare Diseases Report dashboard. The figures displayed are for illustrative purposes and may not be current; however, the underlying logic of the system is clear: we are able to monitor the nationwide distribution, clustering, and trends of rare diseases in real time.



Global Data Sharing and the Health Statistics Yearbook

Using these data, we work together with the Department of Health Statistics to produce the Health Statistics Yearbook, as well as various bulletins and publications. We provide data to stakeholder institutions such as the OECD, Turkish Statistical Institute (TurkStat), and the World Health Organization (WHO), and we respond to their surveys and data requests. As a result, our country is able to achieve strong performance in digitalization indices.

Prof. Dr. Çiğdem Seher KASAPKARA
Faculty Member, Gazi University

Clinical Research in Rare Diseases and the Gazi University Phase 1 Center

Although rare diseases are defined as conditions affecting fewer than 1 in 2,000 individuals, when considered collectively they constitute a substantial portion of medicine; therefore, they are not truly "rare" at all. In Türkiye, in particular, we encounter these diseases frequently due to the high rate of consanguineous marriages. We know that approximately 5–6 million people in Türkiye are affected by a rare disease.

The Vital Role of New Treatment Research

One of the most difficult moments for a physician is having to tell a patient's family that treatment is not yet available for certain rare diseases. Sharing that sense of helplessness and emotion with them is an immense burden for us as well. This is precisely where new treatment research and clinical studies become critically important.

Gazi University Phase I Clinical Research Center

As Gazi University, we have taken a significant step in this field. Our center, established in 2018 and inaugurated in 2022 under the name of our esteemed professor Prof. Dr. Alev Hasanoğlu, houses the Departments of Metabolism and Genetics. It is a highly advanced facility with substantial technical capabilities, enabling not only Phase II and Phase III studies but also the most critical stage of research—Phase I clinical trials.

- **Our esteemed colleague** Prof. Dr. Fatih Süheyl Ezgü, who unfortunately could not be with us today, devoted tremendous effort to the establishment of this center. Likewise, Prof. Dr. Leyla Tümer, Head of the Department of Metabolism, made invaluable contributions. Although I have worked with this team for many years, I have officially been part of this strong group for the last six months and am proud to do so.
- **Gene Therapy Studies:** More than twenty clinical studies are currently ongoing at our center, encompassing all phases of clinical research, including Phase II and Phase III trials, as well as gene therapy studies for adult patients with conditions such as GM1 gangliosidosis and phenylketonuria (PKU).

Challenges in Clinical Research and the Need for Data

To address your question, the greatest obstacle we face in conducting these studies is our inability to reach, in practice, the number of patients that should theoretically be available. As Ms. Esra noted, there should not actually be such a thing as an "insufficient number of patients" in our country. Yet we are unable to reach patients, and patients are unable to access early treatment opportunities. The most important reason for this is that ICD-10 codes do not cover all 8,000 rare diseases. With the current ICD-10 structure, we can accurately identify only around 500 diseases.

Example: Phenylketonuria and the Coding Problem

Under the ICD-10 system currently in use, there is a single main code assigned to phenylketonuria (PKU). However, numerous distinct subtypes exist within this category. Each of these subgroups has markedly different clinical courses and treatment approaches.

For example, while a specific code exists for classical phenylketonuria, cases with phenylalanine levels above 2 mg/dL are generally grouped together under the broad category of hyperphenylalaninemia. Yet this category encompasses numerous genetically and metabolically distinct disorders, each characterized by different pathophysiological mechanisms and treatment requirements. These include various BH4 deficiencies and enzyme defects, each representing a separate clinical entity.

This situation makes it difficult to match patients with the correct subtype diagnosis and, consequently, impedes access to disease-specific treatments. Indeed, clinical management may differ even among individuals with similar phenylalanine levels. For instance, some patient groups within a certain range may not require treatment, whereas patients within the same range who have BH4 metabolism-related subtypes—such as HPR deficiency or PTPS deficiency—require different and highly specific pharmacological therapies.

Ethical Challenges in Clinical Research and Follow-up Criteria

If we continue to enter these diseases into the system under broad, non-specific codes, we are unable to identify the appropriate patients either for our research studies or for early access to investigational and novel therapies.

By contrast, if specific systems such as Orphanet (ORPHA) codes are utilized, even the rarest subtypes can be identified within the system. This would enable us both to establish more precise diagnoses and to create robust data pools for clinical research. When patients are categorized as diagnosed, undiagnosed, or under investigation, it becomes possible to identify diseases whose names are often difficult even to pronounce.

The translation of all disease names into Turkish and their incorporation into the database is of immense value for the research community. The problem of "insufficient patient numbers" can cause clinical studies to fail before they even begin. Reaching the required patient numbers is particularly critical in phase studies. We know that these patients exist in our country, yet we cannot reach them because of shortcomings in the data system. This not only prevents patients from accessing new treatments but also weakens the statistical power of studies conducted with

limited patient populations. For this reason, I believe that the implementation of ICD-11 and ORPHA coding systems can provide an effective solution.

Natural History Studies and Drug Development

One of the greatest deficiencies in the field of rare diseases is the limited number of Natural History studies. To evaluate the effectiveness of a treatment, we must first understand how the disease progresses when left untreated. However, because data are fragmented and data sharing between centers remains limited, managing these processes is often challenging.

Ethical Challenges and the Placebo Dilemma

One of the most sensitive issues encountered in clinical research concerns ethical considerations:

- **Placebo Use:** Many rare diseases are fatal in their natural course. In such cases, assigning an inactive treatment (placebo) to a group of patients raises serious concerns for both families and physicians. Patients may be reluctant to participate in a potentially life-saving study due to fears of being assigned to the placebo arm. We may not even be aware of patients receiving treatment at other centers. As a result, patients may be unable to reach us and may lose the opportunity for early treatment access.
- **Lack of Biomarkers:** For some rare diseases, objective measures that allow assessment of disease progression and treatment response are not available. This creates a significant limitation, particularly in clinical follow-up and the evaluation of therapeutic effectiveness.

For example, in diseases such as Fabry disease, biomarkers exist that allow monitoring of treatment response. Biomarkers such as lyso-Gb3 make it possible to track both disease progression and treatment effectiveness on an ongoing basis.

However, the absence of such biomarkers in many rare diseases makes it difficult to evaluate treatment efficacy objectively. This creates significant uncertainty in both clinical decision-making and in treatment access and reimbursement processes.

Ethical Processes and Patient Safety

Even setting aside the challenges associated with obtaining ethical approvals, it is essential that all processes be conducted transparently and in full compliance with ethical principles. Rare disease research involves particularly vulnerable and fragile patient populations.

Therefore, safeguarding patient rights, obtaining fully informed consent, and ensuring that all research and implementation processes adhere to the highest ethical standards are regarded as fundamental requirements.

SURVEY

"DEFINITIVE COORDINATION" IS ESSENTIAL FOR A NATIONAL SUPPORT MECHANISM

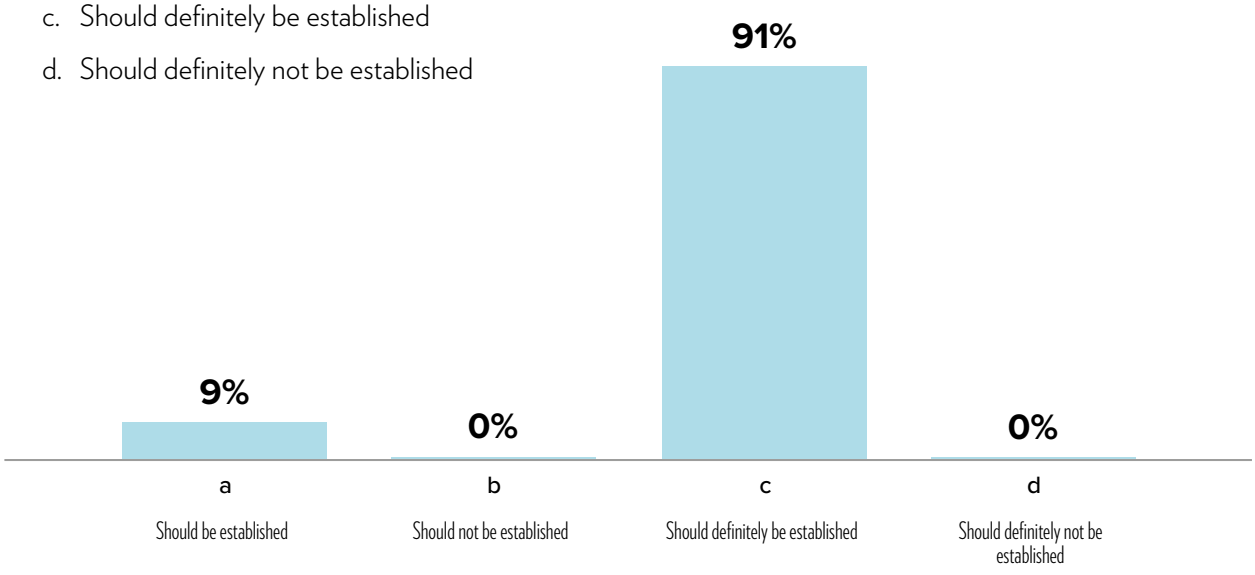
Nearly all participants (91%) emphasized that inter-institutional coordination must definitely be established in order to strengthen the Rare Diseases Action Plan and ensure the effective implementation of national support mechanisms. When combined with the 9% who selected the option "should be established," 100% of participants demonstrated complete consensus on the necessity of coordination.

These findings reveal a shared understanding that, in a complex and multi-layered field such as rare diseases—which simultaneously involves health, finance, labor, and social services—isolated institutional efforts are insufficient. This unanimous support for coordination demonstrates that institutional integration is regarded as the only viable path to ensuring that action plans move beyond paper-based commitments and evolve into functional and accountable national mechanisms.

Overall, the distribution of responses indicates that the success of the Rare Diseases Action Plan is contingent upon the establishment of a strong, continuous, and collaborative framework that enables institutions to work beyond their individual mandates and boundaries.

1. Should there be inter-institutional coordination as part of a national support mechanism aimed at strengthening the Rare Diseases Action Plan?

a. Should be established
b. Should not be established
c. Should definitely be established
d. Should definitely not be established



PATIENT ASSOCIATIONS ARE EMPHASIZED AS "ACTIVE STAKEHOLDERS" IN DECISION-MAKING MECHANISMS

A large majority of participants (72%) stated that patient associations should definitely serve as active stakeholders in decision-making and policy development processes, particularly in relation to rapid problem-solving and coordination mechanisms. When combined with the 23% who responded that they "should" be involved, a total of 95% of participants support the direct involvement of patient associations in policy-making processes.

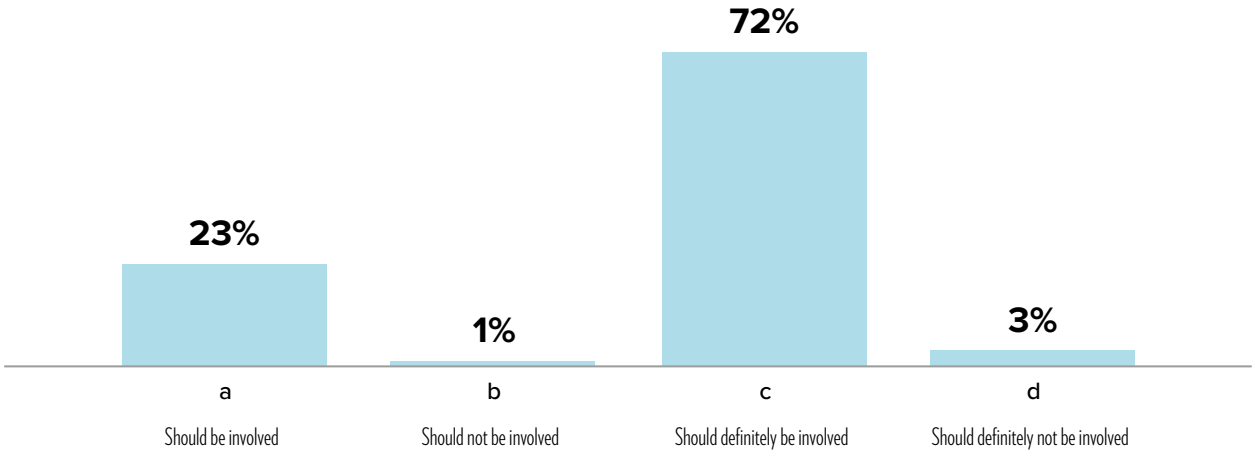
These findings demonstrate that, in a field such as rare diseases—where patient experience and insights from the field are of critical importance—patient associations are viewed not merely as supporting organizations, but as strategic stakeholders and architects of solutions. This strong consensus among participants highlights the need for the expertise, guidance, and lived experience of patient organizations to ensure that bureaucratic decision-making processes remain aligned with realities on the ground.

Only 4% of respondents expressed a negative view ("Should not" or "Definitely should not"). This limited proportion reflects the strength of confidence in a participatory governance model across the ecosystem and underscores a clear desire to move away from traditional, closed decision-making structures toward a modern and inclusive multi-stakeholder approach.

Overall, the findings suggest that an effective rare disease policy can only be achieved if patient associations are granted an active role at the decision-making table through formal and institutionalized representation.

2. Should patient associations serve as active stakeholders in decision-making and policy processes in order to facilitate rapid solutions and coordination?

a. Should be involved
b. Should not be involved
c. Should definitely be involved
d. Should definitely not be involved



Balancing Institutional Identity and Independence in NGO–Government Collaboration

Participation in Decision-Making Mechanisms and Consensus

It was observed that there is broad consensus regarding the inclusion of civil society in the rare disease ecosystem. However, the most critical question raised was how this participation should be structured. It was noted that a delicate balance exists between the state's responsibility to preserve the independence of civil society organizations and its need to protect its own institutional processes from excessive external influence.

Preserving Independence and the Risk of Functional Loss

Drawing on the literature and past experiences, it was emphasized that organizations that maintain excessive proximity to decision-makers or lose their institutional independence risk gradually losing their function as civil society representatives. This could weaken the role of NGOs as a bridge between society and public institutions.

Bureaucratic Perspectives and the Necessity of Institutionalization

Departure from Institutional Structures and Political Risks

It was observed that the occasionally cautious attitude within bureaucratic circles toward NGO participation stems from previous examples that lacked institutional structure. Particular attention was drawn to initiatives that began solely through digital communication groups and later evolved into political platforms without developing a formal institutional identity, creating distortions within the system. Therefore, it was stated that civil society participation should be conducted through organizations with clearly defined institutional identities rather than through individual or uncontrolled processes.

A Vision of Partnership in Solutions

It was emphasized that the primary objective is to position NGOs not merely as entities that make demands, but as "solution partners" that contribute to the sustainability of the system. It was concluded that participation in decision-making processes should take place within a transparent, accountable, and scientifically grounded institutional framework, thereby strengthening both public institutions and civil society.

Exchange of Ideas and Future Outlook

Dialogue-Oriented Development

It was stated that future initiatives will be shaped within a platform where diverse viewpoints can be discussed freely and evaluated through collective wisdom. The goal, it was emphasized, is not to impose any particular perspective but rather to create an open environment for dialogue in order to establish the most effective model of collaboration.

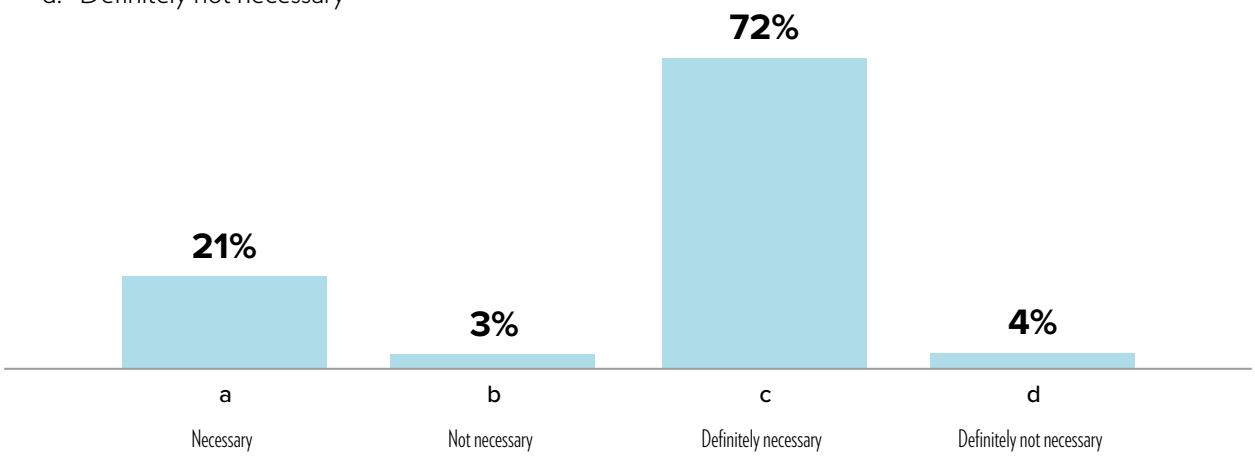
DIGITAL INTEGRATION: A "CRITICAL" REQUIREMENT FOR THE FUTURE OF PATIENT REGISTRY SYSTEMS

A large majority of participants (72%) stated that the integration of digital platforms within the patient registry system is absolutely necessary. When the 21% who indicated that it is "necessary" are also considered, a total of 93% of participants agree that digitalization and interoperability between systems are indispensable requirements.

Overall, the findings indicate that an effective patient follow-up mechanism can only be established through an integrated ecosystem in which all digital platforms are capable of communicating with one another.

3. Is the integration of digital platforms necessary within the scope of the patient registry system?

a. Necessary
b. Not necessary
c. Definitely necessary
d. Definitely not necessary



Data Security, Coordination, and Access Challenges in Rare Diseases

Data Accuracy and Systemic Risks

Although the majority of respondents indicated that integration is "definitely necessary," it was noted that the minority who responded "not necessary" raised important concerns regarding data security, improper integration, and bureaucratic processes. In this context, it was emphasized that inaccurate data entry could lead to misguided health policies, while the limitations of ICD coding systems and the challenges of accurate coding in busy clinical settings remain significant concerns.

Lack of Coordination and Delays in Access to Treatment

It was stated that there are significant shortcomings in directing rare disease patients to the appropriate centers following diagnosis, and that existing appointment systems are insufficient to meet this need. Consequently, the establishment of coordination centers and "Centers of Excellence" was identified as critical. Delays in treatment access due to slow bureaucratic processes were reported to contribute to the progression of patients toward irreversible clinical conditions.

In addition, it was emphasized that rare diseases must be accurately defined, that areas such as mitochondrial diseases should be prioritized within action plans, that specialized units should be established within university hospitals, and that NGOs should be involved in decision-making mechanisms. Across all these processes, speed, coordination, and effective data management were highlighted as being of vital importance.

Identification, Academic Capacity, and Digital Guidance in Rare Diseases

Coding Systems and Data Classification

Accurate identification and classification form the cornerstone of rare disease management. While the transition to ICD-11 is being guided through academic expertise, the integration of alternative systems such as the ORPHA codes used within the Orphanet framework is considered a critical tool for achieving more precise disease identification. The effective use of these data is regarded as a prerequisite both for increasing the visibility of rare diseases within the healthcare system and for conducting accurate statistical analyses.

Academic Structures and Centers of Excellence

The need for a systemic transformation to enhance research capacity within academia was emphasized. Under the current structure, expecting academics to conduct research while carrying heavy clinical workloads was considered unsustainable. It was suggested that protected research time and dedicated incentive mechanisms should be established within Centers of Excellence. To preserve Türkiye's valuable human capital, it was proposed that the balance between intensive clinical duties and academic productivity be restructured at a systemic level.

Smart Referral Systems Through e-Nabız and Reference Centers

The concept of a digital guidance system capable of directing families to the appropriate center as soon as a diagnostic suspicion arises was brought to the agenda. It was stated that the e-Nabız infrastructure is technically ready to support such intelligent notification systems; however, due to concerns regarding data security and social sensitivities (such as the risk of misinformation), identity-verified models should be preferred. By enabling diagnostic data to flow directly to designated Reference Centers, the objective is to ensure that patients can rapidly access the most qualified specialist regardless of their geographic location. To achieve this goal, encouraging data entry into the Rare Diseases Registry System and strengthening cooperation with civil society organizations were identified as strategic priorities.

PANEL-2

EARLY DIAGNOSIS AND INNOVATIVE SOLUTIONS IN RARE DISEASES

MODERATORS

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Medical Director, Rare Diseases, Sanofi Eurasia

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Akdeniz University – President of the Turkish Society of Pediatric Genetics

International Perspective on Rare Diseases: The Importance of the Multi-Stakeholder Framework

ERDERA NMG
NATIONAL MIRROR GROUP TÜRKİYE

ERDERA and International Collaborations

Launched in September 2024, ERDERA (European Rare Diseases Research Alliance) is the European Rare Diseases Research Partnership under the Horizon Europe programme. This international initiative brings together more than 170 organizations from 37 countries, and Türkiye is among the stakeholders of this strategic project.

National Mirror Groups and Global Integration

Within the scope of the "Capacity Building and Alignment" work package of this international structure, National Mirror Groups are being established. The primary objectives of these groups are to collect comparable data in national rare disease research, generate high-quality knowledge, and establish strong synergy among stakeholders.

National Mirror Group and the Multi-Stakeholder Collaboration Structure

The "National Mirror Group" (National Mirror Group), which has brought us together today and enables all these processes to be carried out through collaborative cooperation, is in fact composed of a very broad range of stakeholders.

ERDERA Thematic Pillars and Strategic Objectives

The activities carried out under the ERDERA framework are primarily structured around the following three strategic areas:

- **Evidence and Knowledge Hub:** Standardization of data collection processes and establishment of a comprehensive knowledge hub.
- **Capacity and Capability Development:** Strengthening the competencies of the human resources working in the field of rare diseases and enhancing the technical infrastructure.
- **Policy Dialogue:** Designing and managing sectoral policy processes and establishing the organizational building blocks required for these processes.

Strategic Alignment and Working Groups

The fundamental vision of this roadmap is to align the objectives of the "Türkiye Rare Diseases Action Plan (2023–2027)" with those of the "National Capacity Alignment (Work Package 23)" under the ERDERA project. In order to increase researcher awareness and maximize stakeholder engagement through collaboration among public institutions, academia, and NGOs, five main working groups have been established:

1. **Information and Evidence Group:** Establishment of a rare diseases information and evidence hub.
2. **Capacity Building Group:** Expansion of research capacity and the sectoral talent pool.
3. **Policy and Dialogue Group:** Raising awareness of orphan drugs and establishing a sustainable dialogue platform for policy development processes.
4. **NGO and Awareness Group:** Coordinating the activities of civil society awareness centers.
5. **Network and Collaboration Group:** Structuring national and international research networks dedicated to rare diseases.

Group 1: Rare Diseases Information and Evidence Hub

The Working Group 1, in which I am also actively involved, has a multi-stakeholder structure consisting of civil society organizations, relevant units of the Ministry of Health, universities, and professional associations. The group's main areas of activity are as follows:

- Thematic Research: Conducting targeted research to analyze gaps in diagnosis and treatment access processes and in the field of health economics.
- Financial Model Proposals: Developing strategic recommendations for the establishment of an "Innovative Treatment Fund" specific to rare diseases.

- Policy Support: Publishing annual research briefs for decision-makers and policymakers.
- Academic Collaboration: Promoting interdisciplinary interaction among academic institutions.

Expected Outputs and Strategic Gains

The following tangible outcomes are expected as a result of the activities of Working Group 1:

- Academic Literature: Producing dynamic and up-to-date academic publications on access to diagnosis and the challenges encountered throughout this process.
- National Repository: Establishing a comprehensive national data repository to be made available to policymakers and ERDERA partners.
- Academia–Policy Interaction: Strengthening the link between academic knowledge and policy development processes, independently of existing reform proposals.
- Global Integration: Increasing the visibility of academic research clusters between Türkiye and Europe by aligning Türkiye's rare diseases roadmap with ERDERA objectives through the Information and Evidence Hub.

Group 2: Rare Diseases Capacity and Capability Development Project

Our capacity-building activities are carried out on the basis of strong collaboration established with Rare Diseases Research Centers and the Council of Higher Education (CoHE). In line with the strategic decision taken last year to introduce rare diseases as a compulsory subject across all universities and to increase awareness, we have initiated active educational processes within our faculties.

The main activities carried out within this scope are as follows:

- Integration of Educational Modules: Incorporating rare diseases modules into undergraduate, graduate, and Continuing Medical Education (CME) curricula; expanding the use of e-learning and multidisciplinary learning methodologies.
- Motivation of Young Researchers: Implementing capacity-building projects within student communities and academic institutions; institutionally supporting student clubs and interdisciplinary workshops.
- Awareness Activities: Increasing public and academic awareness through the traditional Rare Disease Day activities.

Interdisciplinary Talent Pool and Networking Objective

The primary outcome of this project is the establishment of a "Multidisciplinary Talent Pool" dedicated to rare diseases. Rare diseases constitute a multidisciplinary field directly related to numerous specialties, ranging from pediatrics and obstetrics to oncology and genetics.

Our objective is to bring together student clubs across the country under an academic mentorship umbrella, establish a strong network in which participants are aware of one another's activities, and achieve lasting and tangible outcomes through this multidimensional approach.

Group 3: Orphan Drug Awareness and Policy Dialogue Platform

Our "Orphan Drug Awareness and Policy Dialogue Platform" working group has been structured to increase information sharing on orphan drugs and to develop sustainable policy dialogues. This platform brings together key stakeholders, including health economists, patient organizations, the Ministry of Health, TITCK (Turkish Medicines and Medical Devices Agency), and AIFD (Association of Research-Based Pharmaceutical Companies), where highly productive brainstorming activities are being conducted.

The group's main working principles and objectives are as follows:

- **Neutral Platform for Dialogue:** Establishing a transparent and impartial communication environment among all stakeholders on sensitive issues such as access to medicines and cost management.
- **Academic Approach:** Conducting scientifically grounded discussions, rather than directly imposing reforms, through academic roundtable meetings on technical areas such as pricing and reimbursement processes.
- **Knowledge Generation and Publications:** Creating an institutional memory for the process by preparing academic publications, policy briefs, and informational documents on the issues discussed.
- **Global Representation and Awareness:** Raising public awareness regarding barriers to medicine access and promoting Türkiye's vision in the field of rare diseases more effectively on international platforms.

This multi-stakeholder communication model provides strategic value in managing complex processes and developing a shared understanding.

Group 4: Civil Society Engagement and Awareness Center (Nadir-Ses)

Our fourth working group aims to strengthen civil society engagement and public awareness under the umbrella of "Nadir-Ses." Bringing together numerous patient and patient-relative organizations, particularly the Rare Diseases Federation, this structure seeks to reinforce these organizations' communication with public authorities and their roles in educational processes.

Areas of Activity of "Nadir-Ses"

- **Education and Capacity Building:** Coordinating workshops organized within the ERDERA project and training workshops for patient advocates.
- **Awareness and Communication:** Organizing nationwide campaigns, storytelling initiatives, and various patient-centered activities. (The meeting we are holding today is also a concrete reflection of this vision.)

Strategic Objective: A Culture of Advocacy. The primary objective of this group is to build a structured advocacy capacity. Through national campaigns to be organized annually, we aim to ensure that the real-life experiences of patients and their families are shared with scientific committees, thereby fostering a common and meaningful "rare disease narrative" culture between care providers and care recipients.

Group 5: Rare Diseases Research and Collaboration Networks

Our fifth and final working group focuses on research and collaboration activities aimed at increasing the international visibility of rare disease studies in Türkiye and achieving full integration with the European Union ecosystem. With TÜBİTAK, academic units, and research centers playing active roles, our primary priority is to represent Türkiye's capabilities on a global scale.

Strategic Focus Areas and Activities

- Project Support and Information Sharing: Encouraging participation in Horizon Europe and ERDERA projects and regularly informing stakeholders about newly opened calls and funding opportunities.
- Institutional Matchmaking: Building bridges between national and international research institutions to facilitate the development of joint projects.
- Strategic Development Modules: Integrating datasets generated through the Türkiye Genome Project, scientific studies in the field of medical genetics, and contributions from relevant associations into research processes.

Final Vision and Outputs. The primary objective of this group is to strengthen national research collaborations based on local capacity and maximize stakeholder communication in scientific conferences and publication processes. In the long term, our goal is to position Türkiye among the leading countries shaping strategies in cross-border rare disease research.

Case Analyses and Health Economics-Focused Publications

In the coming period, we plan to identify 2 or 3 specific diseases that are treatable and preventable as our focal areas, taking into consideration the views of NGOs as well. Our primary objective is to develop comprehensive publications on these diseases, whose treatment feasibility, cost-effectiveness, and contribution to quality of life are supported by health economics data. In doing so, we will present a clearer picture of both the survival journeys of individuals living with rare diseases and the economic dimensions of the process.

Our Working Team and Areas of Expertise

Our distinguished academics and experts play critical roles in ensuring the successful implementation of this process.

Three-Year Strategic Plan

Our ultimate objective is to publish a strategic plan covering the next three years, ensure data integration with the Türkiye Genome Project, and establish a sustainable foundation for the rare diseases ecosystem through structured mentorship programs.

The meaningful anecdote you shared has been revised as follows as a professional and impactful closing paragraph that complements the technical content of the presentation with a human success story:

A Local Success Story: From Prenatal Diagnosis to the Genetic Future

Finally, I would like to share a valuable anecdote illustrating how theoretical work translates into real-world impact. Our efforts in the field of perinatology, which began approximately 15 years ago with more limited local resources and have now evolved into a fully professional structure, are in fact the product of 20 years of accumulated experience. Within Akdeniz University, through the collaboration of our Departments of Pediatric Genetics, Medical Biology, and Genetics, the data support of our Ministry of Health, and the dedication of our stakeholders, we have achieved a success story that serves as a model for the Antalya region.

Prof. Dr. F. Duygu ÖZEL DEMİRALP
Head of the Biotechnology Institute, Health Institutes of Türkiye (TÜSEB)

TÜSEB Vision: The National Genome Project and Innovative Therapeutic Approaches

The Rare Diseases Group within our National Genome Project is one of our highest-priority strategic units. Through the contributions of İBG, our council within Bilkent City Hospital, and our stakeholder centers, we have achieved a 30% direct and 30% indirect diagnostic success rate in rare diseases using next-generation sequencing (NGS) technologies.

For the remaining 40% group, we are further deepening our efforts through:

- **Advanced Technology:** We are introducing Long-Read sequencing technologies.
- **Trio Analyses:** Through trio analyses involving the proband (index patient), mother, and father, as well as family studies that include living siblings, we are mapping gene frequencies specific to Türkiye.
- **Scope:** Although we are still at the beginning of the journey with our current volume of 12,000 samples, we have already started generating data-driven insights.

Premarital Screening and Diagnostic Initiatives

In coordination with the relevant departments of our Ministry of Health, we aim to elevate our premarital screening programs to the highest technological level. The technical planning and implementation framework of our project, which will simultaneously screen multiple gene regions, have already commenced. Together with our Ministry units, we hope to share encouraging developments regarding the expansion of this screening program with the public in the near future.

A New Era in Cell and Gene Therapies: GMP and CAR-T

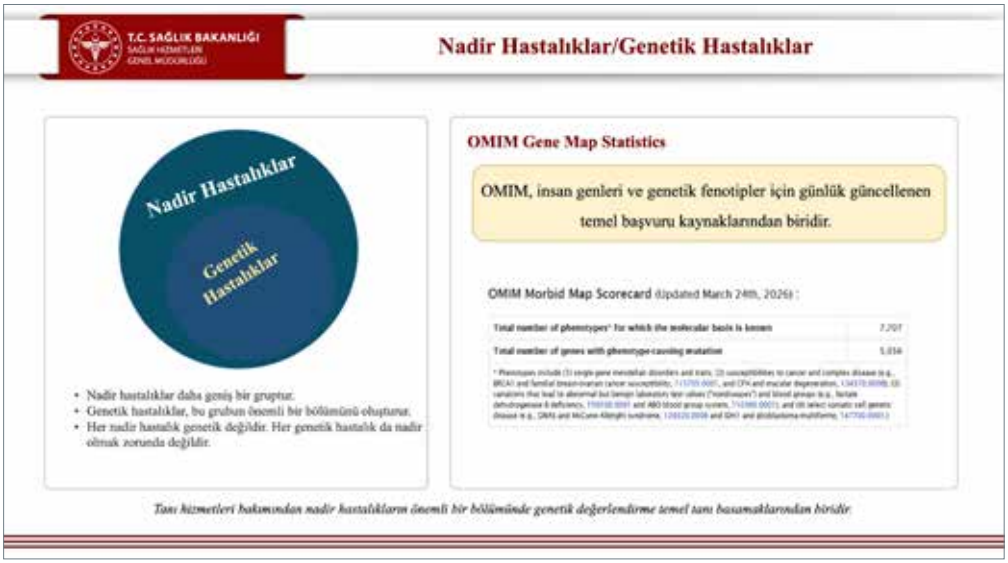
Our fundamental objective is to transform genetic diseases from being regarded merely as a "destiny" into conditions that can be managed through advanced technological interventions. In this regard:

- **GMP Manufacturing Activities:** We have initiated GMP-compliant manufacturing activities at our center located within Etlik City Hospital under the auspices of TÜSEB.
- **Immunotherapy:** In addition to the CAR-T cell therapies that we currently apply for certain types of leukemia and lymphoma, we will soon introduce these therapies for Multiple Myeloma and rare diseases in the pediatric population.
- **R&D Achievements:** We have successfully completed our innovative CRISPR project on mesothelioma. This represents the most recent example of our research capacity in rare oncological cases.

I would like to extend my gratitude to the Rare Diseases Federation, the relevant departments of our Ministry, and TÜBİTAK. These knowledge-sharing platforms, which we continue to expand each year through new projects, constitute the strongest assurance of our future tangible achievements.

Dr. İbrahim KARAKUŞ
Head of the Department of Examination and Diagnostic Services
General Directorate of Health Services, Ministry of Health

Strengthening Diagnostic Services in Rare Diseases



Examination and Diagnostic Services in Rare Diseases: An Institutional Approach

In order to clarify the conceptual confusion surrounding rare and genetic diseases, we refer to both international and national databases:

- **Database Analysis:** There are more than 8,000 defined entities within the Health Coding Reference Dictionary (SKRS) system. According to current OMIM (Online Mendelian Inheritance in Man) data, there are approximately 7,700 diseases with identified molecular bases and phenotypes.
- **Scope of the Challenge:** The current landscape demonstrates that we are addressing an extremely broad group of diseases encompassing thousands of different phenotypes and molecular foundations.

Healthcare Service Policy and Strategic Priorities

Addressing such a vast group of diseases requires not only a diagnostic process but also a comprehensive healthcare policy extending from early diagnosis to treatment, rehabilitation, and long-term follow-up.

Our primary priority on the diagnostic services side is to ensure that "the right test is performed at the right time for the right patient." We continue to take concrete steps within our service policies to accelerate access to early diagnosis and to support subsequent treatment processes through this success in early diagnosis.

Access to Services and Key Challenges in Diagnostic Processes

The service delivery capacity of our current system and the challenges encountered can be summarized under the following headings:

- **Regional Accessibility:** At present, there are no significant regional disruptions in access to services. Specialists within our public healthcare system are able to provide broad access to diagnostic services, including through outsourced service procurement mechanisms.
- **Delays in Diagnostic Processes:** Although access channels are available, diagnostic processes may still fall short of the desired speed, resulting in delays.
- **Access to Appropriate Tests:** There remain deficiencies that need to be addressed in accessing the most appropriate specific tests for a given clinical presentation.

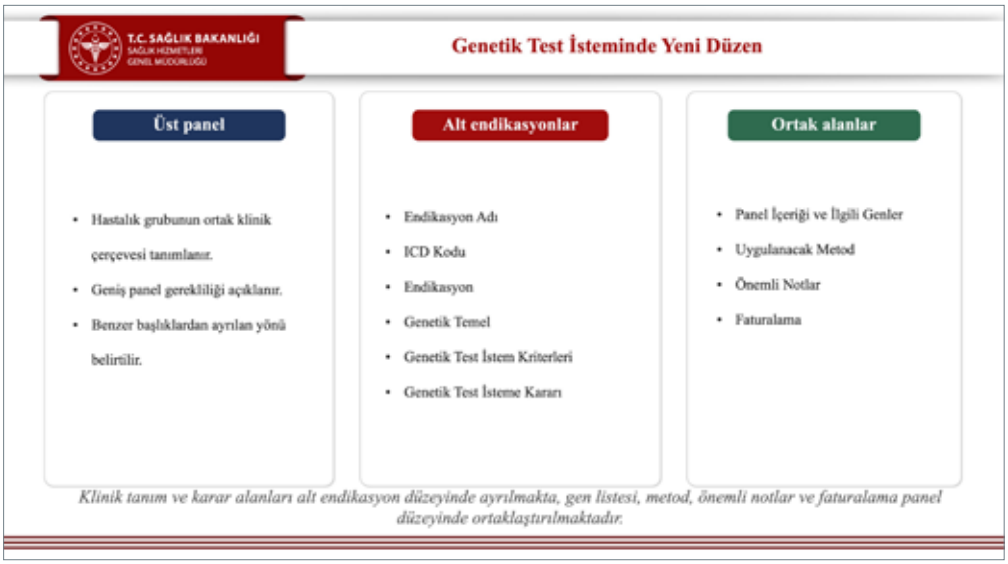
Our efforts to overcome these bottlenecks, standardize diagnostic processes, and increase test diversity continue at full pace.

Clinical Evaluation and the Structuring of the Genetic Services Network

Medical geneticists and pediatric genetic specialists play a critical role in integrating clinical findings with genetic evaluation processes. Significant efforts are being made to ensure proper workforce planning and the strategic positioning of diagnostic centers.

Data Standardization and Revisions to SUT Coding

In previous years, we encountered serious systemic challenges in recording and analyzing rare diseases. In particular, the "reaction-based" definitions used within the Health Implementation Communiqué (SUT) made it difficult to collect clinical data in a comprehensive and coherent manner.



Structural Transformation of SUT Codes and Expert Commissions

To improve data quality and make diagnostic processes more specific, we have phased out the previous SUT codes and transitioned to a new disease- and phenotype-based approach. To facilitate the technical management of this process, we have integrated the concepts of "upper panel," "sub-indication," and "common area" into our system.

To support this structural transformation, approximately 55 different working groups have been established. These groups include medical geneticists, pediatric genetic specialists, and clinicians from relevant specialties working together.

Smart Decision Support Systems and Test Ordering Algorithms

In the next phase of the process, coordinated work will be carried out with the Standards and Accreditation Department of the General Directorate of Health Information Systems. Our primary objective is to establish test ordering criteria within a data-driven and auditable framework.

System Oversight and the Panel-Based Approach

- **Automated Oversight:** The system will incorporate a control mechanism that prevents the ordering of panels that are not appropriate for the patient's clinical phenotype.
- **Cost-Effectiveness:** Disease groups with similar phenotypes will be evaluated under a single umbrella through a panel-based approach, based on cost-effectiveness analyses.

Clinical Workflow Based on Measurable Criteria: In the new system, clinical presentations must be supported by measurable and clearly defined parameters before an appropriate testing decision can be made. The following criteria will serve as the basis:

- Laboratory and biochemical parameters,
- Radiological and nuclear medicine imaging results,
- Physical examination findings and detailed family history.

Standard Diagnostic Protocol: A flexible and comprehensive approach will be adopted, including WES (Whole Exome Sequencing) analyses whenever required by the clinical presentation. In summary, our new operational workflow will follow the sequence:

Clinical Finding → Measurable Criterion → Strategic Testing Decision → Standardized Reporting

Methodological Standardization and Alignment with International Guidelines

The establishment of diagnostic methodologies will be based on rational and scientific standardization rather than individual preferences. From NGS (Next-Generation Sequencing) analyses to CNV analyses and MLPA confirmations, all methods are intended to be implemented at the same high standard across all centers.

Reporting Standards and Quality Assurance

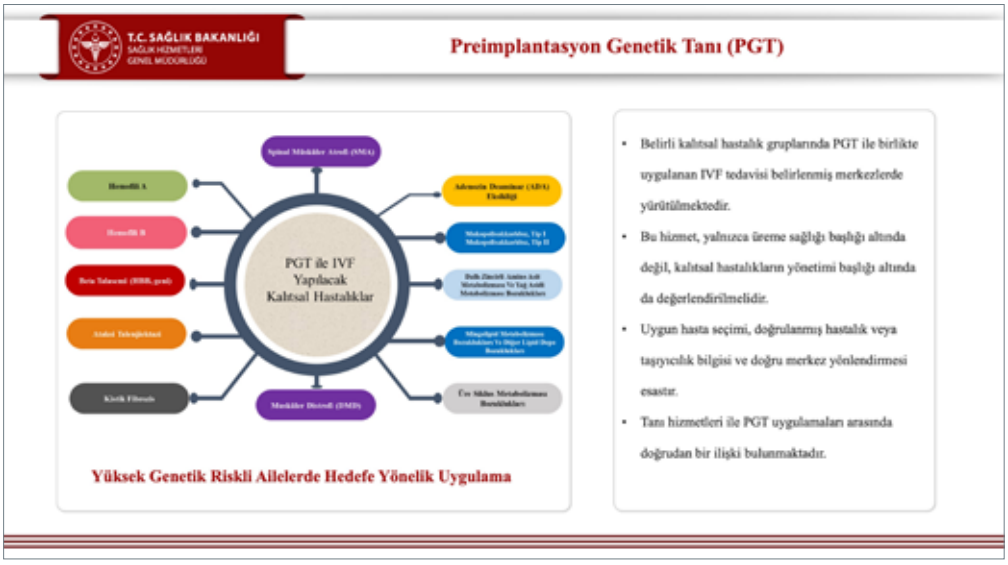
A comprehensive standardization initiative has been completed for the reporting stage, which constitutes the final

link in the genetic diagnostic process, in order to ensure that data are correctly interpreted by physicians. As of last week, this framework has been disseminated to the field. Reports generated through different techniques, including NGS, Real-Time PCR, QF-PCR, and Microarray, have now been standardized under ten core reporting categories.

Standard Report Content and Components: Prepared with the contributions of our distinguished genetics specialists, these standardized reports include the following critical elements:

- **Analysis Methodology:** Clearly specifying the technical details of the method employed.
- **Technical Limitations:** Transparently sharing the scope and potential limitations of the methodology used.
- **Legal Framework:** Standardizing mandatory statements required by legislation.
- **Clinical Interpretation:** Providing expert guidance by correlating analytical results with the patient's clinical presentation.

Through this standardization, reports issued by Genetic Diseases Diagnosis and Evaluation Centers have become clear, reliable, and high-quality decision-support documents for clinicians throughout Türkiye.



Expansion of PGT (Preimplantation Genetic Testing) Services and Strategic Steps

PGT (Preimplantation Genetic Testing), integrated into IVF (in vitro fertilization) processes, plays a critical role in preventing rare diseases and ensuring the continuation of healthy generations. Pursuant to the legal regulations introduced in 2018, PGT services were incorporated into the scope of the Health Implementation Communiqué (SUT) as of 2021.

Data Integration with the Türkiye Genome Project and Variant Mapping

Under a new initiative launched by our General Directorate of Health Information Systems, we aim to standardize data flow between the Türkiye Genome Project and our Genetic Diseases Diagnosis and Evaluation Centers. The primary focus of this project, which is currently nearing completion, is the full integration of clinical data with large-scale NGS (Next-Generation Sequencing) datasets.

The Türkiye Genome Project: The Data Engine of Future Medical Technologies

The Türkiye Genome Project is one of our most valuable initiatives and holds strategic importance for our nation's healthcare vision, serving as a true "incubation center." Achieving its full potential depends on being continuously nourished by real-world clinical data and on integrating patient data from our genetic diagnostic centers into the system.

Breakthrough Areas in Next-Generation Treatments and Technologies

If clinical and genomic data are accurately matched and managed through a systematic workflow, significant advances will be achieved in the following fields of advanced medicine:

- **Advanced Treatment Options:** Personalized medicine approaches and targeted treatment protocols.
- **Gene and Cell Therapies:** Stem cell applications, gene therapy options, and tissue engineering studies.
- **Advanced Technology and Nanomedicine:** Nanomedicine applications, mRNA-based next-generation technologies, and theranostic (combined diagnostic and therapeutic) approaches.
- **Research and Innovation:** Developing effective solutions for domestic pharmaceutical and diagnostic kit development through the proper utilization of data.

Conclusion and Vision

The standardization of these data and their incorporation into the system through scientific discipline will pave the way for Türkiye to become not only a regional but also a global leader in healthcare technologies. When we successfully combine the right data with the right technologies, we believe that we will rapidly advance toward producing sustainable and nationally driven solutions for rare diseases and all other genetically based health challenges.

Prof. Dr. F. Tuba EMİNOĞLU
Director of the Rare Diseases Application and Research Center, Ankara University

A Model of Academic Excellence: ANAMER

The Rare Diseases Application and Research Center (ANAMER), established within Ankara University, has a modern infrastructure spanning 1,200 square meters and was realized through the collaboration of the Presidency of Strategy and Budget of the Republic of Türkiye, the university, and the private sector. Our center offers a new model aimed at developing sustainable solutions to rare disease challenges worldwide within the university ecosystem.

Our Multidimensional Areas of Activity and Mission

The fundamental operating principle of ANAMER is not limited to scientific research alone but seeks to transform the process into a social and academic mobilization:

- **Capacity Building:** Training qualified professionals specialized in the field and conducting regular seminars and workshops for healthcare professionals.
- **Public Awareness:** Active collaboration with student communities, organization of nationally recognized congresses, and public information activities.
- **Interdisciplinary Collaboration:** Managing project development processes through a broad interdisciplinary team ranging from chemists and basic scientists to pediatric specialists and genetics experts.

Innovative Medicines and Gene Therapies

We closely monitor, discuss, and actively participate as researchers in numerous international studies on innovative drug development processes, particularly gene therapies in the field of rare diseases. At this point, our most critical priority is "early diagnosis," the single most important factor determining treatment success. Since it is not possible to reverse the process once organ damage has occurred, we focus all our efforts on accelerating diagnosis.

Key Projects: Newborn Screening and Reference Values

Among the more than 30 projects currently underway, two strategic initiatives are of particular importance:

1. **Heel-Prick Blood Screening and Prevalence Assessment:** Within the nationwide newborn screening program we are conducting across Türkiye, we have reached 15,000 households.
2. **National Enzyme Reference Ranges:** Using data obtained from 5,000 households, we have established enzyme reference ranges specific to the Turkish population.

Why Is This Important?

Our primary objective is to determine which rare diseases are more prevalent in specific regions of our country and, in particular, to diagnose treatable diseases before clinical symptoms emerge. By sharing the experience gained from these pilot studies with healthcare policymakers, we contribute to the development of nationwide screening programs and help ensure that children receive treatment before symptoms appear.

Digital Transformation in Diagnosis: Artificial Intelligence and Algorithmic Navigation

To minimize the diagnostic odyssey, which represents the greatest obstacle in the diagnosis of rare diseases, we have developed four core artificial intelligence models at Ankara University using clinical data accumulated over the past ten years.

- **e-Nabız Integration and Strategic Collaboration:** To enhance the performance of our algorithms through machine learning, we signed a tripartite Memorandum of Understanding with the Ministry of Health and Sanofi. Within this framework, we integrated our system with the e-Nabız infrastructure and began analyzing data within a broader ecosystem.
- **Early Warning System:** The primary objective of the project is that when symptoms are entered at the primary care level, the system analyzes all available examinations, identifies risks through its algorithm, and automatically transmits an alert to the relevant specialist units.
- **Clinical Validation:** The clinical and analytical validations of these navigational algorithms and diagnostic kits are meticulously carried out within our ANAMER center.

The Data Treasure of the Future: Biobanking and Biological Material Management

We place great importance on biobanking activities to better understand the biological foundations of diseases and to map variant frequencies specific to our country:

- **Biological Archive:** Subject to comprehensive ethics committee approvals, we store all biological materials related to rare diseases in accordance with established standards and conduct advanced research on these materials.
- **Academic Depth:** This field provides a rich research environment for master's theses, doctoral dissertations, and specialty training projects, thereby contributing to the development of highly qualified human resources.

Industrial Collaboration and Clinical Research

Although the field of rare diseases remains a niche segment in Türkiye, we aim to elevate it to an industrial scale through projects supported by TÜSEB and TÜBİTAK. Our primary goal is to increase our participation in national and international clinical studies and to develop sustainable, competitive solutions together with all stakeholders. We continue to expand our collaboration networks to ensure that these efforts gain visibility on a global scale and that Türkiye becomes a center that delivers solutions.

Assoc. Prof. Dr. Büşranur ÇAVDARLI
Faculty Member, Ankara Bilkent City Hospital
(Turkish Society of Medical Genetics)

A Revolution in Medical Genetics: From Molecular Diagnosis to a Healthy Future

As medical geneticists, we are a discipline that dedicates its entire professional effort to rare diseases and approaches rare cases across all specialties as a whole. Our field represents a generation that has personally witnessed the technological revolution in genetics. During our residency years, we could only define diseases phenotypically; today, we have reached the capacity to diagnose nearly all of them at the molecular level.

Türkiye's Public Health Success and Diagnostic Standards

I am proud to state that Türkiye is one of the rare examples in the world, including among European countries, in terms of diagnostic access and public accessibility for rare diseases.

- **Success in Coding Regions:** With our current technologies, we have largely resolved the identification of variations in coding regions (the exome) and the diagnosis of inherited diseases.
- **Advanced Research Models:** For cases with yet undefined phenotypes or more complex genetic mechanisms, the models offered by İBG, ANAMER, and TÜSEB, together with the Türkiye Genome Project, are of vital importance.
- **Multidisciplinary Councils:** Cases that cannot be diagnosed through standard means are brought before multidisciplinary councils established within our institutions, where we seek to elucidate them through functional analyses such as Whole Genome Sequencing (WGS) and RNA studies (transcriptomics).

PGT and Preventive Healthcare Services

As Ankara Bilkent City Hospital, we obtain highly valuable clinical outcomes as an authorized center for PGT (Preimplantation Genetic Testing) procedures.

- **A Tangible Success:** Over the past four to five years, we have helped healthy individuals unaffected by carrier status to be born. Seeing these children visit us today, healthy and thriving, is our greatest source of motivation.

- **Request for Expanded Scope:** Our greatest expectation is to move beyond the current limitation of 14 diseases and 37 genes and to include all rare diseases, which are far too numerous to fit within predefined lists. Preventing severe cases for which we have established the world's first diagnosis depends on this expansion.

Strategic Objective: Family Physician Education and Early Referral

As the Turkish Society of Medical Genetics and the Ministry of Health, we are engaged in comprehensive planning focused on the education of family physicians.

- **Timing Saves Lives:** Identifying a known genetic risk within a family before pregnancy occurs is critical for both ethical and medical management. For example, in diseases such as Huntington's disease, which manifest in adulthood, if individuals are referred to us before conception rather than after becoming pregnant, PGT opportunities can help prevent high-risk pregnancies.
- **Navigation:** Ensuring that our family physicians possess this awareness will enable patients to be referred to medical genetics units at the appropriate time and will ensure that the multidisciplinary approach is fully implemented in practice.

Specialist Dr. Adnan KARAN
Medical Director, Rare Diseases, Sanofi Eurasia

Sanofi: AI-Driven Biopharma Transformation and Regional Leadership

At Sanofi, we combine our more than 100 years of heritage with modern technology, guided by a vision of transforming from a traditional pharmaceutical company into an AI-powered biopharmaceutical company. As a global healthcare leader, we continue to create value within the healthcare ecosystem through our workforce of 80,000 employees across more than 70 countries.

Strategic Focus and Geographic Reach

Within Sanofi's global operations, Türkiye serves not only as a local market but also as the management hub for a vast geographical region:

- **Eurasia Regional Management:** Managed from Türkiye, the Eurasia region represents a strategic corridor encompassing 17 countries across Central Asia, the Caucasus, and the Middle East.
- **A Long-Standing Presence in Türkiye:** Having maintained uninterrupted operations in Türkiye for 67 years, we have become one of the most consistent stakeholders within the national healthcare system.

We continue to expand the value we create through innovation and partnerships in the field of rare diseases by combining our global capabilities with local needs.

Smart Investment and Strategic R&D Priorities

For Sanofi, global scale gains significance only when that potential is transformed into tangible value. At the heart of this value creation is our R&D portfolio, which currently includes more than 80 ongoing projects. Approximately half of these projects consist entirely of new drug or vaccine candidates.

Our Focus Areas:

- Immunology and Rare Diseases
- Neurology and Hematology
- Oncology and Vaccine Technologies

In today's world, we embrace the principle of smart investment, going beyond merely allocating financial resources. By leveraging artificial intelligence, we advance clinical decision-making processes and make diagnosis and treatment pathways more precise and effective.

Next-Generation Technologies in Drug Discovery: Digital Twins and Efficiency

Technological transformation is fundamentally changing traditional drug discovery processes. Through artificial intelligence and machine learning, drug discovery cycles that traditionally required much longer periods are expected to be reduced to as little as 8–10 years. This acceleration is one of the most important factors enabling innovative treatments to reach the right patient at the right time.

A Revolution in Clinical Research Through Digital Twin Technology

This technology, which enables clinical studies to be conducted not only in the real world but also through virtual simulations, is ushering in a new era in drug development:

- **Virtual Simulations:** The effects of a drug candidate on the liver and other organs can be evaluated through digital models, enabling potential adverse effects to be identified before real-world application.
- **Time and Cost Advantages:** Through digital twin technologies:
  - Clinical research timelines can be reduced by 25%.
  - Operational costs can be reduced by 15–20%.
- This increase in efficiency means that new treatments can reach patients much earlier, particularly in fields such as rare diseases where time is critical.

Innovation and Entrepreneurship Ecosystem: PharmUp and Care4Rare

At the center of our innovation strategy lies not only internal R&D but also the startup ecosystem, which creates value through its agility. As Sanofi, we support this ecosystem through two key programs:

- **PharmUp Startup Accelerator Program:** Through this program, launched five years ago, we provide mentoring, training, and global visibility to health technology startups. We have supported dozens of startups and established active collaboration models with several of them.
- **Care4Rare Program:** Fully aligned with the Ministry of Health's National Rare Diseases Action Plan, this program aims to develop innovative projects in early diagnosis, treatment, and care services. Our objective is to build an innovation culture in our country together with all stakeholders.

Early Diagnosis: Overcoming the Eight-Year Delay Through Technology

The greatest challenge in rare diseases is the process referred to in the literature as the Diagnostic Odyssey:

Critical Data: Globally, it takes an average of eight years for an individual with a rare disease to receive an accurate diagnosis. During this period, patients often endure numerous misdiagnoses and unnecessary tests.

Early diagnosis is not merely a medical necessity; it is also:

1. **Quality of Life:** Providing an opportunity for intervention before irreversible damage occurs.
2. **Economic Efficiency:** Significantly reducing repetitive and unproductive costs imposed on the healthcare system.

Türkiye's robust digital health infrastructure (such as e-Nabız) provides one of the most suitable environments in the world for innovative solutions capable of shortening this eight-year period.

Strategic Collaboration and the VisionRare Project

Our strategic collaboration with Ankara University (ANAMER) forms part of a vision that will position Türkiye among the leading countries in digital diagnostics.

- **Algorithmic Diagnostic Power:** We are currently developing an early diagnosis algorithm focused primarily on Gaucher Disease.
- **A Scalable Model:** Once successful, this initiative will not be limited to Gaucher Disease but can be adapted to other lysosomal storage diseases, various rare diseases, and even common diseases.
- **VisionRare:** Through this project, we aim to establish our country as a global reference point in the field of digital diagnosis of rare diseases.

National Integration: A Memorandum of Understanding for Public–University–Industry Collaboration

A strategic partnership structure has been established to scale the digital diagnostic solutions developed with Ankara University (ANAMER) and make them available throughout Türkiye.

Strategic Integration and e-Nabız: The goal is to integrate the developed algorithmic models with the Ministry of Health's digital health infrastructures, including e-Nabız and SINA (Health Statistics and Causal Analysis), which are among the world's most advanced digital health systems. Through this integration, the diagnostic tool will function not only in selected centers but throughout the healthcare system, beginning at the primary care level, as an active monitoring and alert mechanism.

A Triple Alliance: The Memorandum of Understanding signed between the Ministry of Health, Ankara University, and Sanofi represents a milestone in Türkiye's national technological advancement in the field of rare diseases.

Core Vision: For us, early diagnosis is not merely a technical achievement or a medical process; it is a fundamental and inalienable human right. This protocol represents the most concrete and powerful step taken to protect that right and to consign the eight-year delay of the Diagnostic Odyssey to history.

The Key to Healthcare Transformation: Collective Wisdom and Strategic Solidarity

The success of all projects conducted in the field of rare diseases depends on strong collaboration among stakeholders and the ability to build collective wisdom. Transforming Türkiye's robust healthcare infrastructure into tangible value is only possible through complete solidarity and alignment.

A Vision Centered on Solidarity

- **The Critical Key:** The concept of solidarity is the true key to making a difference in the fight against rare diseases.
- **Aligned Objectives:** It is vital that all stakeholders—from the public sector to academia, from the private sector to civil society—work in a synchronized manner toward the common objective of earlier diagnosis and more accurate treatment.
- **Ultimate Goal:** To elevate Türkiye beyond global standards in rare disease management and improve patients' quality of life through a holistic approach.

Serap ÖZKURT KARAÇİÇEK
Market Access, Sustainability and External Affairs Director, UCB Pharma

A Global Perspective: The Need for Systemic Transformation in Rare Diseases

A Global Perspective: Current Status and Policy Requirements in Rare Diseases

Despite technological and policy advances achieved worldwide in the field of rare diseases, approximately 300 million patients continue to face structural barriers in diagnosis and treatment processes. In addition to medical challenges, these individuals must also contend with social isolation and significant financial burdens.

Global Access Barriers and the Time Factor

When examining the efficiency of current systems, the most striking indicator is the time required to access innovative therapies:

- **Access Time:** Across Europe, the average waiting period for access to innovative medicines is 578 days.
- **Critical Impact:** This waiting period of more than 1.5 years represents not merely a chronological loss for an individual living with a rare disease, but also the loss of an opportunity to benefit from treatment and the risk of irreversible clinical consequences.

Policy Vision: A More Inclusive System

For stakeholders united by the belief that "a better system is possible," the primary focus is the restructuring of healthcare policies. Within this framework, the following strategic objectives stand out:

1. **Strong Infrastructure:** Strengthening existing healthcare systems to respond effectively to the complexity of rare diseases.
2. **Inclusiveness:** Adopting a holistic approach that eliminates social and financial barriers.
3. **Openness to Innovation:** Accelerating the integration of innovative therapies and technologies into healthcare systems.

The fundamental challenge in addressing rare diseases is the development of sustainable policies that work in favor of patients by overcoming bureaucratic and operational barriers.

A Global Policy Instrument: The ASPIRE4RARE Platform

Creating sustainable change in the field of rare diseases requires the establishment of structural and measurable systems rather than isolated efforts. Developed with this vision, ASPIRE4RARE represents one of the most concrete global examples of a multi-stakeholder approach.

The Platform's Core Mission and Operating Model

- **Inspiration and Reference:** Analyzing successful global best practices and transforming them into reference points for other countries and healthcare systems.
- **Guidance and Measurement:** Serving not only as a knowledge repository but also as a guidance tool strengthened by measurement mechanisms that assess policy effectiveness.
- **Policy-Level Change:** Identifying bottlenecks within the rare disease ecosystem and providing policymakers with data-driven, actionable, and sustainable recommendations.

Strategic Value: ASPIRE4RARE acts as a strategic bridge that brings together stakeholders across the public sector, academia, and industry, enabling theoretical goals to be translated into measurable and concrete policies.

Methodological Foundations and Global References

ASPIRE4RARE has been structured not merely as a theoretical model but on the basis of globally recognized healthcare policy instruments. Its methodology was inspired by two principal pillars:

- **World Health Organization (WHO) Health System Building Blocks:** The universal standards established by WHO have been adopted as guidance for sustainability and governance.
- **The European Rare 2030 Report:** This comprehensive vision document on the future of rare diseases served as a foundation for defining the project's strategic objectives.

From Theory to Practice: Implementation Modules

Three key components transform the system from a report into a practical and usable tool:

1. **Expert Panels:** The process has been enriched through multidisciplinary expert input and subjected to scientific validation.
2. **Measurable Indicators:** Each module is supported by concrete and trackable performance indicators for evaluating policy success.
3. **Policy Recommendations and Best Practices:** The theoretical framework is reinforced through real-world success stories and specific recommendations for policymakers.

This methodological approach positions ASPIRE4RARE as a dynamic policy instrument supporting data-driven decision-making within the rare disease ecosystem.

Strategic Architecture: The Aspire4Rare Framework

The Aspire4Rare Framework, the platform's most concrete output, has been built upon six key pillars designed to manage the rare disease ecosystem from a holistic perspective.

Critical Dynamics Shaping the Diagnostic Process

1. **Awareness:** As we have discussed throughout these sessions, increasing awareness among both society and healthcare professionals is the first essential step.
2. **Technology and Access to Knowledge:** This involves not only improving diagnostic methods but also ensuring access to expert opinions, including second opinions, through digital platforms.
3. **Social Context:** The way a society, family, or healthcare ecosystem perceives disease is a significant determinant in the diagnostic process.
4. **Dynamic Diagnosis:** In rare diseases, diagnosis is not a process in which a diagnosis is made once and the file is closed. Due to complex disease structures and evolving symptoms, diagnosis is an ongoing process that accompanies the patient throughout life and is continuously updated through new diagnostic methods

5. **Economic Dimensions:** While this is sometimes a sensitive topic, we must openly discuss both the economic burden of innovative diagnostic solutions and treatments, as well as the value they generate.
6. **Standardization:** The most effective means of eliminating differences among institutions and regions and ensuring that diagnosis is conducted at the same level of quality everywhere.
7. **Research and Development:** Scientific advancement remains the only pathway to finding answers for cases and diseases that have remained unresolved to date.

Local Applications of Global Models: Examples from Spain, the United States, and Germany

The Aspire4Rare Framework is designed as a flexible structure that can be adapted to the needs of individual countries. I would like to share three examples illustrating how this flexibility has been applied globally:

- **Spain:** Spain chose to adopt the framework holistically. In updating its regional rare disease plans, the country utilized all framework modules and implemented a broad collaborative process.
- **United States:** The United States chose to apply the framework primarily through the lens of best practices, particularly to address healthcare inequalities and improve access to innovative treatments.
- **Germany:** Perhaps the most striking example is Germany's approach. For the first update of its National Rare Disease Plan in ten years, Germany focused exclusively on the Governance and Leadership module of the framework.

From Strategy to Implementation: The Power of Measurement

Whenever we discuss rare diseases, we all arrive at the same conclusion: collaboration and collective wisdom are the keys to success. We know that Türkiye has established a very strong policy foundation in this field. However, global developments demonstrate that while excellent strategic plans and action documents are developed worldwide, implementation and measurement processes often fail to progress with the same strength and speed.

For this reason, we believe that frameworks such as Aspire4Rare, which provide measurable indicators, are invaluable for enriching existing plans and translating them into action.

Such global frameworks are particularly valuable because they ensure that strategic plans do not remain merely on paper but are implemented in a measurable and accountable manner. Due to time constraints, I had to move through the content rather quickly; however, you may access the global report through the QR code displayed on the screen.

SURVEY

STRONG SUPPORT FOR ESTABLISHING A LEGAL FRAMEWORK FOR DIGITAL HEALTH ASSISTANTS

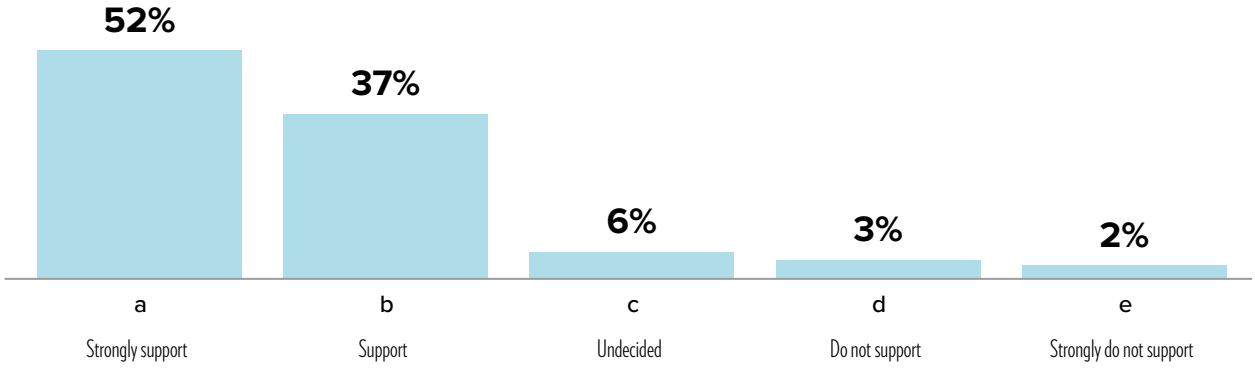
A large majority of participants (89%) support the inclusion of digital health assistants in official protocols and their establishment as a legal requirement in rare disease management. These assistants enable patients and caregivers to become active stakeholders in the management process. The fact that 52% of respondents selected "strongly support" reflects a firm belief that digital solutions should no longer be regarded as an option or an auxiliary tool, but rather as an integral component of standard care pathways.

While the proportion of respondents who indicated that they were undecided remained at 6%, the total proportion expressing a negative opinion was recorded at only 5% ("Do not support" and "Strongly do not support"). This low level of opposition demonstrates that although there may be certain implementation-related concerns regarding the legal and technical infrastructure of digital health tools, the ecosystem is eagerly awaiting regulations in this area.

When the overall distribution is evaluated, it becomes evident that in the future of rare disease management, digital assistants that transform patients from passive recipients into active managers of their own care should be legally defined and fully integrated components of the healthcare system.

4. Do you support the inclusion of digital health assistants in official protocols and their establishment as a legal requirement in rare disease management, given that they empower patients/caregivers through information provision, symptom monitoring, and personalized guidance?

a. Strongly support
b. Support
c. Undecided
d. Do not support
e. Strongly do not support



Digital Systems in Rare Diseases: Physician-Centered Decision Support and Ethical Boundaries

Digitalization as a Decision Support Mechanism

It was emphasized that digital systems and artificial intelligence in rare disease management should be positioned not as structures that replace physicians, but as decision-support mechanisms that provide data to physicians. These systems, which can make significant contributions in areas such as symptom monitoring, literature analysis, and the standardization of clinical processes, were noted to have the potential to reduce the margin of error by providing "check-up"-style reminders to physicians, particularly in busy clinical settings. Furthermore, applications such as epicrisis-based follow-up models, the automation of disease-specific monitoring schedules, and the improvement of patient referral processes through digital algorithms were highlighted as tools that could support uniform quality in healthcare services. The ability of artificial intelligence to analyze extensive data pools and provide physicians with "collective intelligence" was regarded as a strategic advantage capable of accelerating diagnostic and follow-up processes in rare diseases.

Ethics, Legal Responsibility, and Physician Authority

At the same time, it was clearly stated that digital systems can under no circumstances replace medical practice and that ultimate responsibility for diagnosis and treatment must always remain with the physician. It was emphasized that, in cases of medical error, the legal responsibility can rest only with the physician; therefore, positioning artificial intelligence as an independent decision-maker would be ethically and professionally unacceptable. Given the heterogeneous nature of rare diseases and individual patient differences, it was noted that fixed algorithms alone would not be sufficient and that clinical judgment and physician experience must continue to play a decisive role. In this context, digitalization should be integrated through a gradual, controlled, and guidance-oriented approach, positioned as a support layer that strengthens physician–data synergy, and advanced through a sustainable model encompassing all stakeholders.

CAUTIOUS OPTIMISM PREVAILS REGARDING TÜRKİYE'S POTENTIAL IN INNOVATIVE DIAGNOSTIC SOLUTIONS

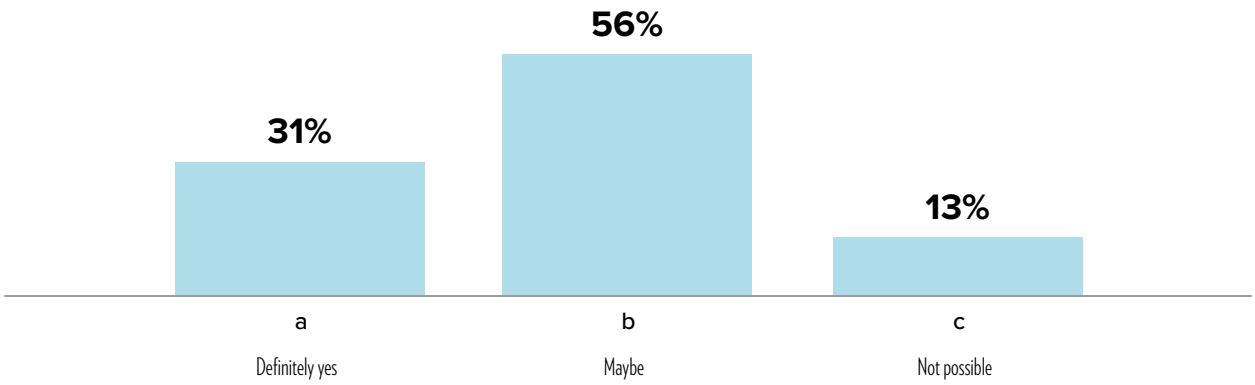
More than half of the participants (56%) adopted a cautious approach by responding "Maybe" when asked whether Türkiye has the potential to serve as a model for other countries in the field of innovative early diagnostic solutions for rare diseases. This figure indicates that Türkiye's considerable potential is widely recognized, while also suggesting that additional milestones must be achieved before this potential can be translated into concrete and sustainable leadership.

The 31% of respondents who expressed full confidence in Türkiye's capabilities by selecting "Definitely yes" represent a strong belief that the country can become a global role model through its healthcare infrastructure, dynamic population, and rapid technological adaptation. This perspective highlights the possibility that, through the right strategic initiatives, Türkiye could become a "center of excellence for solutions" within the rare diseases ecosystem.

When the overall distribution is evaluated, it becomes clear that Türkiye possesses the necessary raw materials—data, expertise, and infrastructure—to develop early diagnostic technologies for rare diseases. However, to establish a globally recognized success story, the country requires a clearer strategic roadmap and more visionary incentives.

5. In your opinion, does Türkiye have the potential and capability to serve as a model for other countries in the field of innovative early diagnostic solutions for rare diseases?

a. Definitely yes
b. Maybe
c. Not possible



Türkiye's Digital Health Strength and Vision for Rare Diseases

Global Leadership and Seamless Data Integration

Türkiye's digital health infrastructure, particularly through systems such as e-Nabız and Teleradiology, stands out as a global model. Thanks to full integration between public and private healthcare institutions, physicians can instantly access patients' historical records, imaging results, and laboratory data through a single interface. This "invisible" infrastructural strength provides a continuity of data that even advanced countries such as Germany and the United Kingdom have not yet fully achieved, thereby modernizing diagnostic processes at remarkable speed.

Strategic Advantage in Rare Diseases and a Future-Oriented Vision

This advanced ecosystem provides Türkiye with a unique strategic advantage in the management of rare diseases, which are inherently difficult to monitor and require a multidisciplinary approach. The current objective is to transform this vast pool of data into meaningful value through the integration of artificial intelligence and clinical algorithms. By combining this technological strength with scientific analytics, Türkiye is advancing toward becoming a global reference point in the diagnosis and management of rare diseases and a national source of digital strength in healthcare.

THE ECOSYSTEM'S DEVELOPMENT AGENDA: LEADERSHIP AND COORDINATION EMERGE AS THE PRIMARY NEEDS

The largest proportion of participants (34%) indicated that inter-institutional coordination is the area most in need of development in the field of rare diseases. This finding reveals that, rather than technical, medical, or financial limitations, the absence of a higher-level governance and coordination mechanism capable of ensuring the harmonious management of existing resources and processes is perceived as the weakest link in the system.

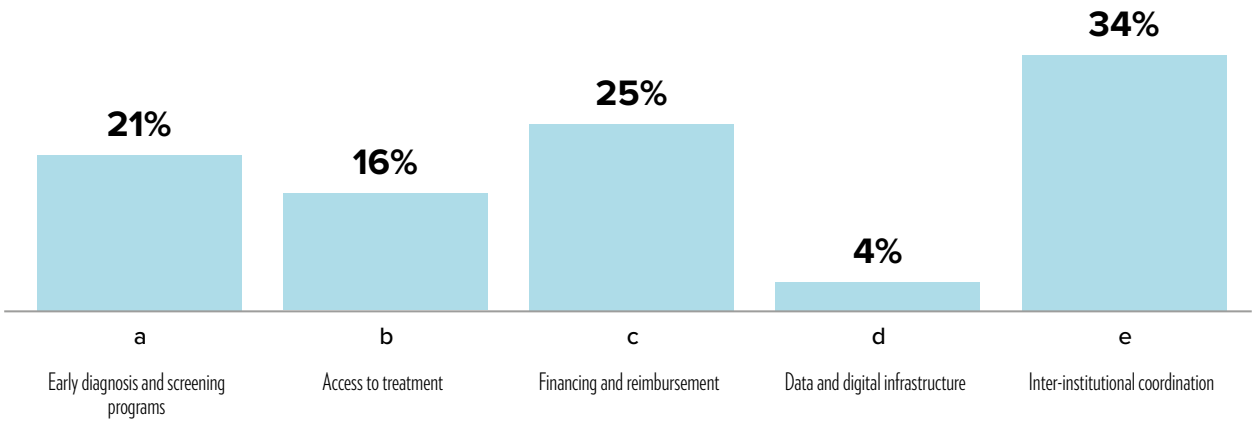
While 25% of respondents identified the financial dimension as a critical barrier and prioritized improvements in financing and reimbursement models, 21% argued that greater emphasis should be placed on early diagnosis and screening programs. This distribution demonstrates that, following coordination, the establishment of a sustainable financial structure and the strengthening of diagnostic infrastructure that enables intervention before disease progression constitute the other major strategic priorities.

The proportion of participants who viewed access to treatment as the primary area requiring development remained at 16%. Notably, the option of data and digital infrastructure was selected by only 4% of respondents. This suggests that data and digitalization are perceived not as an objective in themselves but as tools for achieving broader goals such as coordination and diagnosis, or that the current level of digital capability is viewed as more manageable than other structural challenges.

When the overall distribution is evaluated, it becomes clear that meaningful progress in the field of rare diseases will be achieved not through isolated technological or financial interventions, but through a comprehensive institutional governance reform that connects all stakeholders and processes end-to-end.

6. In your opinion, which area requires the greatest development in the field of rare diseases?

a. Early diagnosis and screening programs
b. Access to treatment
c. Financing and reimbursement
d. Data and digital infrastructure
e. Inter-institutional coordination



PANEL-3

FINANCING AND REIMBURSEMENT PRACTICES IN RARE DISEASES

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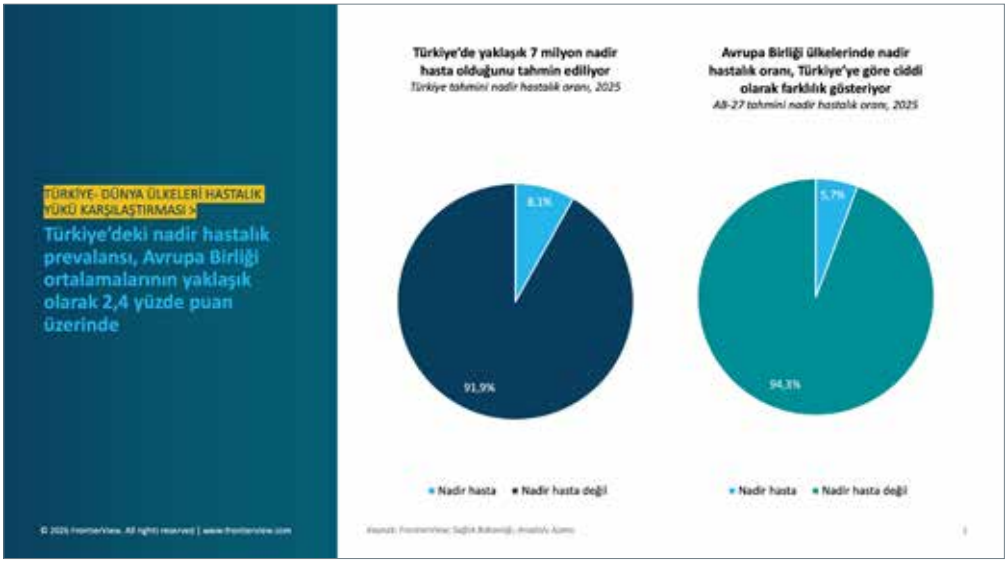
Osman ŞAHİN
Senior Engagement Manager
(FrontierView)

Osman ŞAHİN
Senior Engagement Manager, FrontierView

A Healthcare Policy Approach Developed Through Global Experience

The study I will share with you today constitutes one of four core projects conducted through the collaboration of the Rare Diseases Federation, the Hacettepe University Center for Health Economics and Health Policy Research and Application, and Alexion Pharmaceuticals.

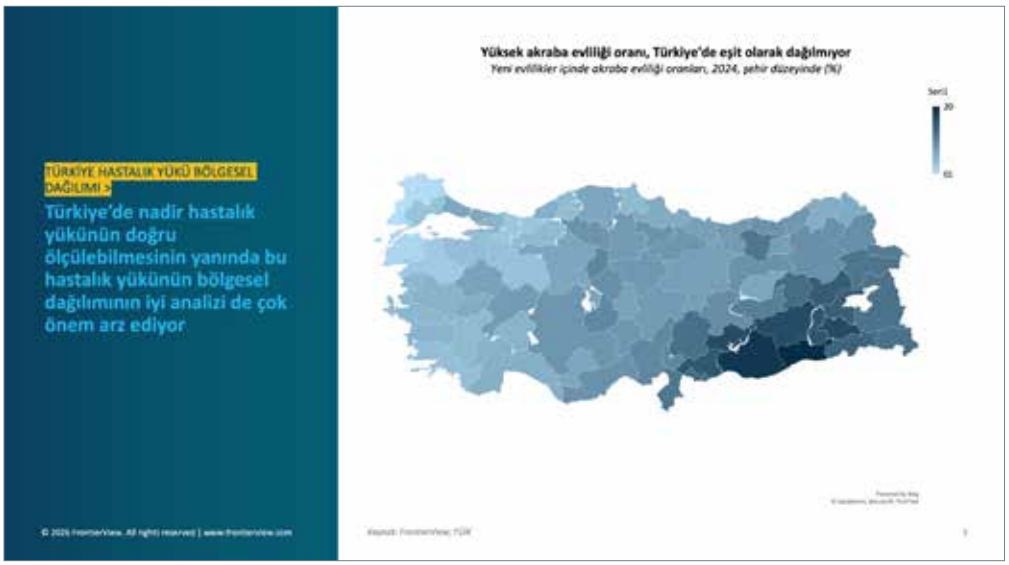


The Prevalence and Importance of Rare Diseases in Türkiye

Rare diseases are, in fact, an important issue for all countries around the world. However, the matter occupies a much more critical position in the context of Türkiye. The primary reason for this is the relatively higher prevalence of rare diseases in our country.

Consider the following: within Türkiye's population of approximately 86 million, it is estimated that around 7 million people are living with a rare disease. In the European Union, by comparison, there is a total population of 456 million across 27 countries, among whom approximately 25–30 million individuals are affected by rare diseases.

When these figures are examined proportionally, a striking picture emerges. We are speaking of a reality in which more than 8 out of every 100 people we encounter on the street are living with a rare disease. From this perspective, it becomes much clearer that rare diseases are not, in fact, all that "rare."



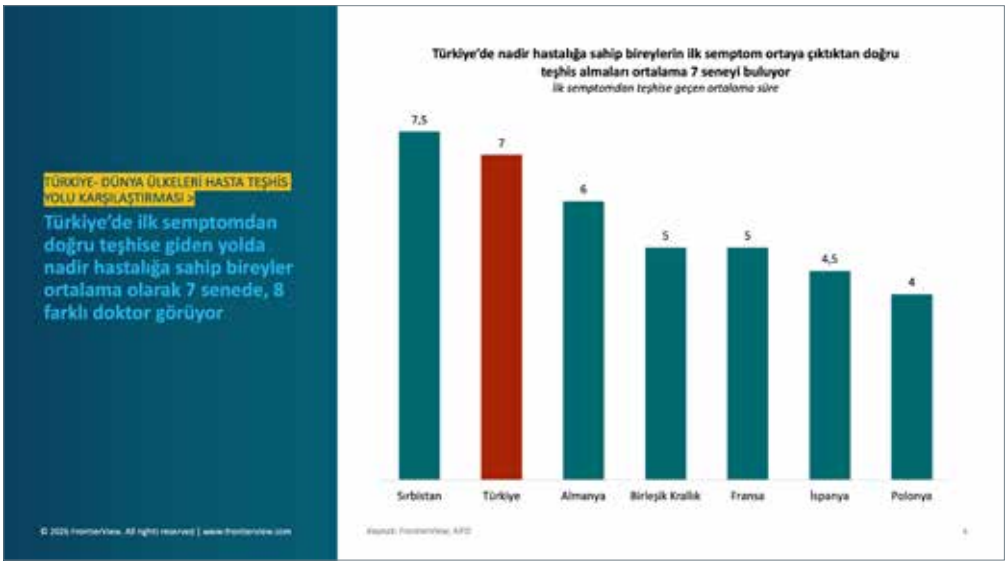
Regional Distribution and Inequalities

The second important point is this: although the prevalence of rare diseases is high in Türkiye, this burden is not distributed evenly across the country. These differences must be taken into account when developing policies, designing funding mechanisms, or planning any type of intervention.

Broadly speaking, we observe that the disease burden increases as one moves from west to east. This concentration becomes particularly pronounced in the Southeastern Anatolia Region.

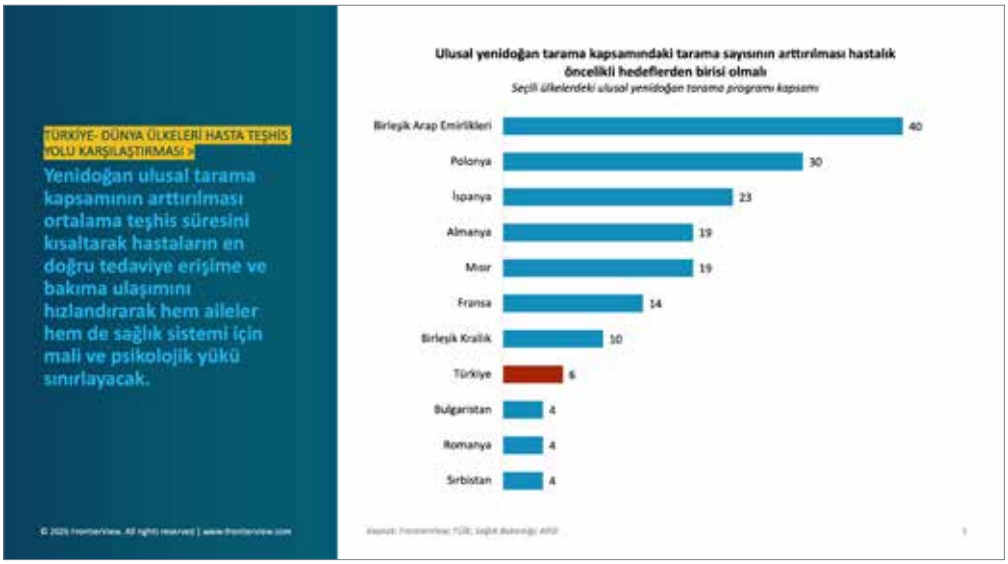
One of the most significant reasons for this is the relatively high rate of consanguineous marriages. When we examine these rates across Türkiye, we see that they reach approximately 22%. Furthermore, the 2024 data published by the Turkish Statistical Institute (TurkStat) support this picture and, in fact, provide an important roadmap for policymakers.

Therefore, we are discussing not only disease burden but also regional inequalities. For this reason, it is of great importance that every policy and financing model developed be structured in a manner that takes these differences into account, remains target-oriented, and is sensitive to regional needs.



Diagnostic Delay and the Multidimensional Burden

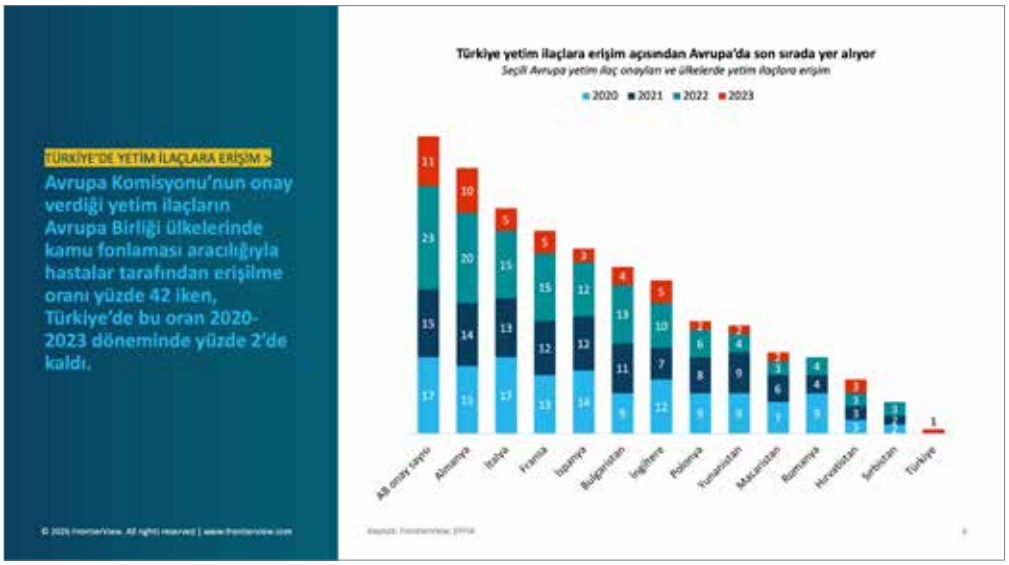
Another critical issue is the diagnostic timeline and the burdens associated with it. In this regard, we must acknowledge a significant loss of time. When comparing Türkiye with Europe, we observe that the average time to diagnosis is approximately five years in Europe, whereas in Türkiye this period can extend to an average of seven years.



The Strategic Importance of Newborn Screening Programs

In fact, this issue has been discussed on many platforms and at numerous panels before. However, there is one highly critical topic that deserves renewed and particular emphasis: national newborn screening programs.

When early diagnosis and treatment opportunities are not available, diseases tend to progress and become more severe over time. This results in substantially higher costs and far more complex healthcare needs, both at the individual level and across the healthcare system.



Current Status and Structural Challenges in Access to Treatment

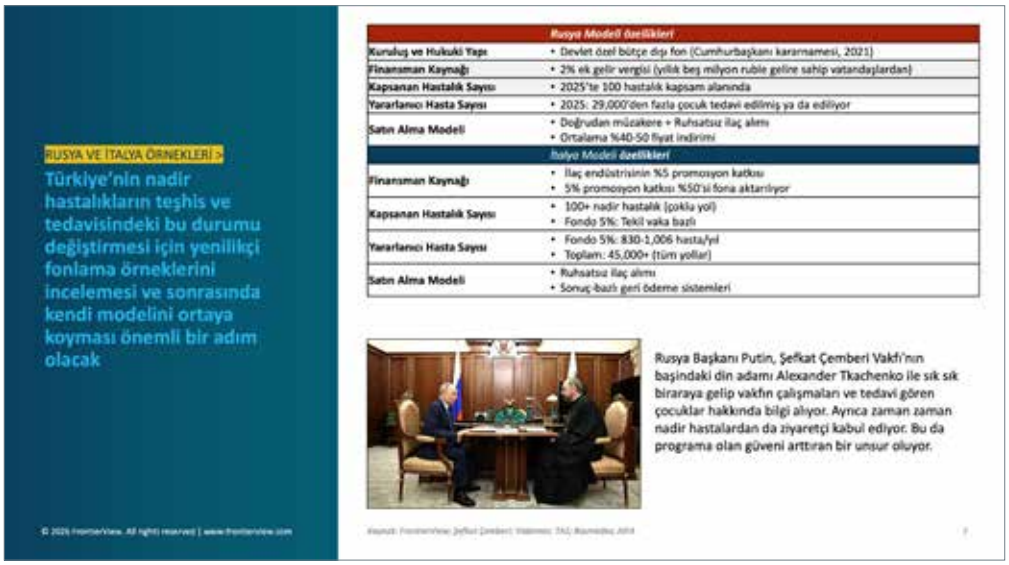
Today, access to treatments for rare diseases in Türkiye remains highly limited. Access is estimated to be at approximately 2%. This figure alone demonstrates the critical nature of the issue.

For example, of the 66 medicines approved by the European Medicines Agency (EMA), only one is fully accessible under the 4A reimbursement scheme, clearly illustrating the bottleneck within the system. There are also cases in which access is provided through the 4C pathway; however, when considering the scale of the burden, it becomes evident that a significant portion of the budget is allocated to rare diseases.

If a substantial share of a budget is directed toward a specific patient population and, despite this, patients are still compelled to pursue legal action in order to gain access to treatment, it must be acknowledged that a structural problem exists.

For this reason, it is not sufficient to evaluate the issue solely through percentage-based indicators. A broader perspective is required, one that examines how the system functions and where bottlenecks occur in a comprehensive manner.

It is precisely at this point that two major models being discussed globally come to the forefront. By exploring these two models, I will attempt to present a framework for how a financing and access structure could be designed for Türkiye. Naturally, a critical part of the process will involve discussing these models in detail, refining them, and, where appropriate, subjecting them to critical evaluation.



Global Models for Rare Disease Financing and Strategic Perspectives for Türkiye

When examining international best practices, one of the leading models developed to address financing and access challenges is Russia's "Circle of Kindness" framework. Established in 2021 through a Presidential Decree, this model combines social solidarity with tax policy through a dedicated fund. Under this system, individuals with annual earnings exceeding 5 million rubles pay an additional 2% income tax. While the standard income tax rate is 13%, it is increased to 15% for this group, and the resulting revenue is allocated directly to the treatment of rare diseases.

Another notable feature of the Russian model is its direct negotiation mechanism for pharmaceutical procurement. Through a centralized structure, the government negotiates directly with pharmaceutical companies, and with the involvement of strong institutions such as the Federal Anti-Monopoly Service, discounts of up to 40–50% are achieved. Thanks to this framework, which continues to expand in scope, more than 29,000 children across over 100 disease groups are currently receiving treatment. One of the most important factors reinforcing confidence in the fund is the fact that the process is monitored directly at the presidential level.

Another successful approach is Italy's AIFA 5% Fund Model. Under this system, pharmaceutical companies contribute 5% of their promotional budgets to a dedicated fund. Half of the fund is used directly to provide patients with access to medicines, while the other half is allocated to research and development (R&D) activities. What makes the Italian model particularly distinctive is its success in applying data analytics to reimbursement decisions. The system does not merely provide access to medicines; through the use of outcome-based payment mechanisms, financing is linked directly to measurable health outcomes.

Drawing on these two models, I believe that a similar structure could be developed for Türkiye. To overcome the current system's most significant bottlenecks—namely, the lack of trust and coordination—a structure operating at the Presidential level may offer a viable solution. Such high-level coordination could function as a form of institutional guarantee, fostering trust among stakeholders while enabling much closer alignment among different institutions.

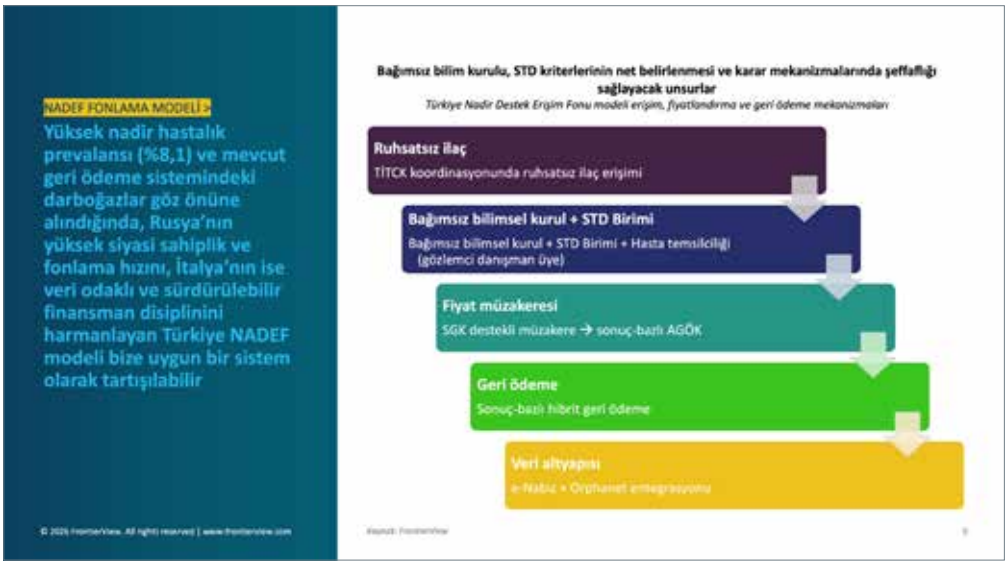
As highlighted during previous panels, one of the most significant challenges within the current system is the lack of trust and coordination. A higher-level structure such as the Presidency could serve as a safeguard for the program, creating confidence while also providing a framework capable of bringing together diverse stakeholders under a common vision.

Financing Models and the Search for Alternative Funding Sources for Türkiye

In high-cost areas such as the treatment of rare diseases, various innovative alternatives may be considered in order to diversify funding sources. Allocating a symbolic share of existing taxes on tobacco, alcohol, or luxury consumption—such as 0.5%—to a dedicated fund could generate substantial resources. Likewise, imposing an additional 1% tax on highly profitable sectors such as banking and games of chance could create a significant funding stream. Furthermore, as seen in the Italian model, contributions derived from pharmaceutical companies' promotional budgets, along with voluntary corporate and individual donations, could become important components supporting this funding pool.

In fact, such mechanisms are commonly used in many countries around the world to promote economic equity. During periods when certain sectors benefit disproportionately from economic fluctuations or macroeconomic developments, additional taxation or dedicated funding mechanisms targeting these sectors are frequently employed. When a particular sector experiences exceptional growth due to favorable economic conditions, directing a portion of that growth toward socially beneficial initiatives—especially critical areas such as rare diseases—would also resonate positively with public sentiment.

Adapting effective international examples to Türkiye's unique dynamics would not only establish a sustainable financing foundation but also strengthen confidence in the system. Therefore, I believe that such instruments should be seriously considered within our national context. Within this overall framework, we foresee the development of a phased model that can be implemented progressively. Let us now take a closer look at the key components and implementation details of this model.



Conditional Licensing and Transparent Governance for Sustainable Access

One of the most critical elements of our system is the provision of conditional access to unlicensed medicines. I deliberately emphasize the term "conditional" because, under the current system, some pharmaceutical companies have effectively adopted a practice of importing medicines without obtaining marketing authorization and, instead of utilizing SSI reimbursement pathways, selling them at full price through court rulings. It is quite clear that this situation is not economically sustainable. Under the new financing model we envisage, if access to a medicine is provided through this system, a fundamental requirement should be that the relevant company submits a marketing authorization application to the Turkish Medicines and Medical Devices Agency (TİTCK) within a defined period—for example, within one year. Such a requirement would strengthen the legal foundation of the system while also enabling long-term planning.

A second key element for the effective functioning of the model is the establishment of an independent scientific committee. The independence of this committee is of vital importance, as its decisions must be based entirely on scientific, objective, and impartial grounds, free from any form of external influence. This structure would both oversee treatment effectiveness and ensure that resources are directed toward the most appropriate cases.

Third, we need a transparent health technology assessment (HTA) process. The treatments to be included within the system and the criteria on which these decisions are based must be clearly defined. In this context, transparency should not be viewed merely as a preference, but as a fundamental principle. The reasons why a particular medicine is prioritized and the criteria it satisfies should be openly known to the public and all stakeholders.

Finally, transparent decision-making mechanisms will serve as the cornerstone of this structure. If we wish society and all stakeholders to have full confidence in the system, decision-making processes must be designed to be as open as possible, and evaluation criteria must be clearly disclosed. Only in this way can we build a trust-based, sustainable rare diseases ecosystem in which all parties have confidence in the fairness of the system.

NADEF: A Strategic Roadmap and Implementation Phases

So, how exactly will this model be implemented? Undoubtedly, it must be acknowledged that this will not be an easy process and will require patience and diligence. However, it is possible to move forward through a phased approach and by taking well-founded steps. For the time being, we may refer to this structure as the Rare Diseases Support Fund (NADEF); naturally, the naming can be further refined as the process evolves.

The first step in its establishment should involve a comprehensive preparation phase. At this stage, a strong framework should be established through a Presidential Decree, followed by the rapid development of the legal infrastructure required to support the model. Once the legal foundation is in place, it is vital that all stakeholders—including patients, physicians, the pharmaceutical industry, the Turkish Medicines and Medical Devices Agency (TİTCK), the Social Security Institution (SSI), and the Ministry of Health—come together and contribute to the process. During this phase, the structure of the independent scientific committee should be clearly defined and funding sources should be finalized. As previously noted, funding streams may be diversified according to need, or the most efficient options may be selected from among the available alternatives.

The next critical stage is the pilot implementation. Rather than launching the system across all disease groups simultaneously, a more effective approach would be to begin with selected rare diseases that require priority attention and urgent intervention. This selection should be based on a detailed analysis specific to Türkiye. Following the achievements and lessons learned from the pilot phase, the scope can be expanded gradually until full-scale implementation is achieved.

The final—and perhaps most important—component of the model is the process of continuous monitoring and evaluation. The performance of the system must be measured on an ongoing basis. Implemented measures, collaborations established with institutions such as ELDERA, and treatment outcomes should be reported regularly. Through the feedback generated by these evaluations, deficiencies within the system should be identified and necessary improvements implemented in real time. Only through such a cyclical approach can we preserve the sustainability of the system while ensuring the most effective use of limited resources.

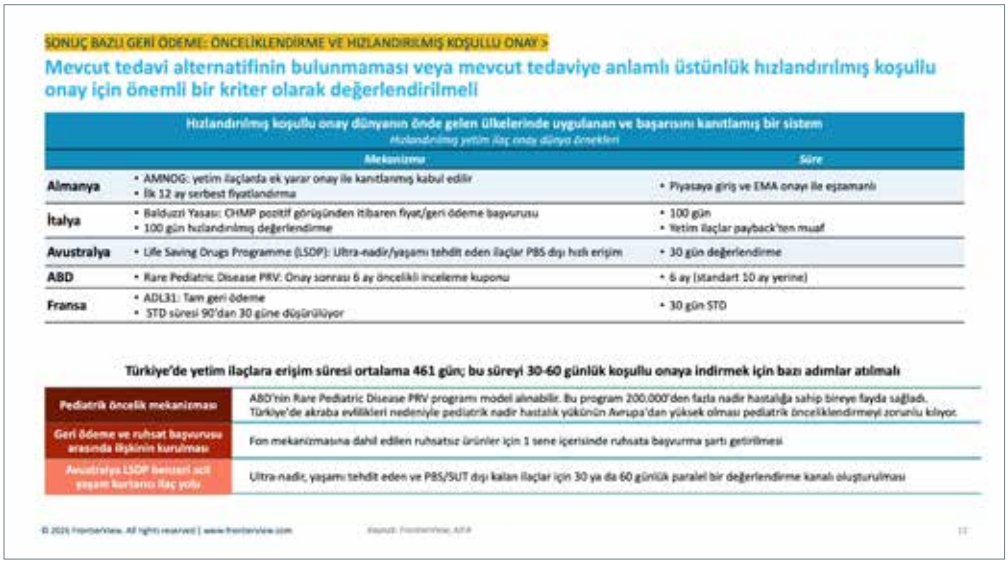
The Heart of the System: Outcome-Based Reimbursement and Risk Sharing

At the heart of this model lies an outcome-based reimbursement mechanism that places both financial sustainability and clinical reality at its core. This approach, which is increasingly being adopted worldwide, ensures that resources are allocated not merely to the medicine itself, but to the tangible benefits generated by that medicine. The structure is built around four main pillars.

The first stage of the system consists of prioritization and an accelerated, conditional approval process. However, several critical questions must be clearly answered at this stage: Is there an alternative to this medicine in Türkiye? Is it more effective than existing treatments? Has this superiority been demonstrated clinically? For an unlicensed medicine or a medicine provided through an early access pathway to be included in the system, this clinical superiority must be clearly established.

One of the second and most important components of the model is risk sharing. A fair structure must be established in which financial and clinical risks are balanced among the government, patients, and industry. The third pillar, evidence generation, serves as a vital bridge for the sustainability of the system. Here, it is essential to go beyond laboratory data and assess how effective treatments are in real-world settings. Clinical trials alone do not tell the entire story; the determining factor is how a treatment performs in real-world data.

The final stage involves a rigorous monitoring and evaluation process. The performance of the system must be assessed on a regular basis, and treatments that fail to demonstrate the expected impact in real-world practice should be promptly removed from the system. Only through such a dynamic oversight mechanism can we ensure that our resources are directed toward the most appropriate and effective treatments.



SONUÇ BAZLI GERİ ÖDEME: ÖNCELİKLENDİRME VE HIZLANDIRILMIŞ KOŞULLU ONAY >

Mevcut tedavi alternatifinin bulunmaması veya mevcut tedaviye anlamlı üstünlük hızlandırılmış koşullu onay için önemli bir kriter olarak değerlendirilmeli

Hızlandırılmış koşullu onay dünyanın önde gelen ülkelerinde uygulanan ve başarısını kanıtlamış bir sistem

Hızlandırılmış yetim ilaç onay dünya örnekleri

	Mekanizma	Süre
Almanya	• AMNOG: yetim ilaçlarda ek yarar onayı ile kanıtlanmış kabul edilir • İlk 12 ay serbest fiyatlandırma	• Piyasaya giriş ve EMA onayı ile eşzamanlı
İtalya	• Balduzzi Yasası: CHMP pozitif görüşünden itibaren fiyat/geri ödeme başvurusu • 100 gün hızlandırılmış değerlendirme	• 100 gün • Yetim ilaçlar payback'ten muaf
Avustralya	• Life Saving Drugs Programme (LSDP): Ultra-nadir/yaşamı tehdit eden ilaçlar PBS dışı hızlı erişim	• 30 gün değerlendirme
ABD	• Rare Pediatric Disease PRV: Onay sonrası 6 ay öncelikli inceleme kuponu	• 6 ay (standart 10 ay yerine)
Fransa	• ADL31: Tam geri ödeme • STD süresi 90'dan 30 güne düşürülüyor	• 30 gün STD

Türkiye'de yetim ilaçlara erişim süresi ortalama 461 gün; bu süreyi 30-60 günlük koşullu onaya indirmek için bazı adımlar atılmalı

Pediatrik öncelik mekanizması	ABD'nin Rare Pediatric Disease PRV programı model alınabilir. Bu program 200.000'den fazla nadir hastalığa sahip bireye fayda sağladı. Türkiye'de akraba evlilikleri nedeniyle pediatrik nadir hastalık yükünün Avrupa'dan yüksek olması pediatrik önceliklendirmeyi zorunlu kılıyor.
Geri ödeme ve ruhsat başvurusu arasında ilişkinin kurulması	Fon mekanizmasına dahil edilen ruhsatsız ürünler için 1 sene içerisinde ruhsata başvurma şartı getirilmesi
Avustralya LSDP benzeri acil yaşam kurtarıcı ilaç yolu	Ultra-nadir, yaşamı tehdit eden ve PBS/SUT dışı kalan ilaçlar için 30 ya da 60 günlük paralel bir değerlendirme kanalı oluşturulması

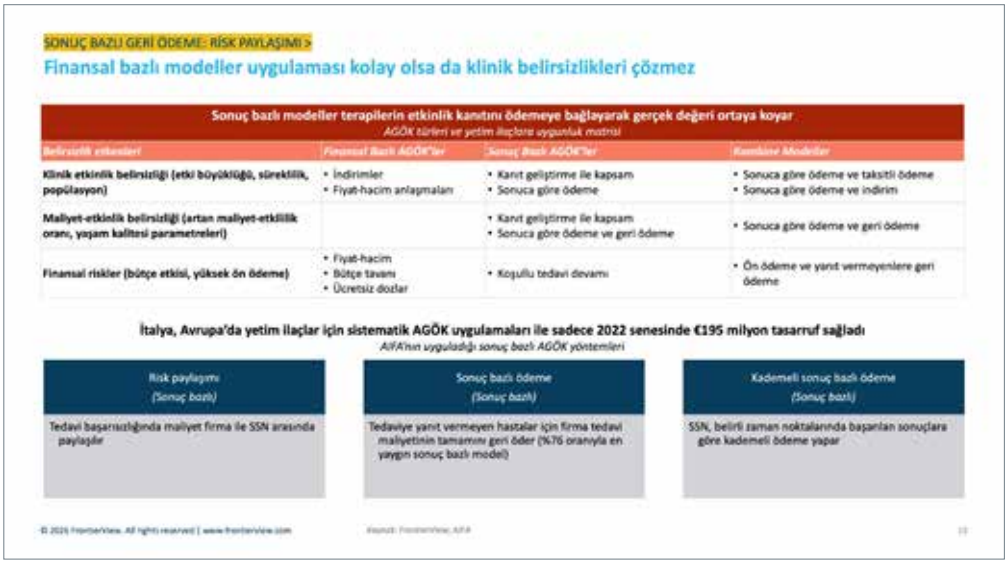
Global Access Timelines and Strategic Objectives for Türkiye

When we examine global practices, we see that the speed at which medicines for rare diseases enter healthcare systems varies across countries; however, the overall trend is toward rapid access. In the United States, for example, accelerated approval pathways are widely utilized. Under the Rare Pediatric Disease program, companies may even receive a six-month Priority Review Voucher following approval, which can be applied to another product, thereby encouraging innovation.

A similar degree of agility can be observed across Europe and other regions. In France, health technology assessments can be completed in as little as 30 days. In Australia, the evaluation process for medicines with no available alternatives takes approximately 30 days, while in Italy the process generally takes around 100 days. In Germany, medicines enter the market with free pricing for the first 12 months, after which permanent pricing is determined through subsequent evaluations.

When we look at Türkiye, unfortunately, the picture is quite different. It is reported that the average time required to gain access to medicines reaches approximately 461 days. We believe that this period should be reduced to reasonable levels, specifically within a range of 30 to 60 days. However, any acceleration initiative must be implemented within a conditional framework. In particular, the connection between reimbursement and marketing authorization processes must not be severed.

Our specific recommendation in this regard is as follows: once a medicine begins receiving funding through the fund structure we aim to establish, the company's marketing authorization application process should be initiated simultaneously and on a mandatory basis. Any medicine benefiting from financial support should be required to obtain marketing authorization in Türkiye within a maximum period of one year. In this way, patients will gain rapid access to treatment while the legal and sustainable foundations of the system are secured.



Risk Management and Outcome-Based Financial Assurance

Our fundamental principle regarding risk sharing is clear and founded on a fair basis: if a medicine genuinely benefits the patient, it should remain within the system; if it does not, it should be removed from the system. In other words, if the medicine works, it should be reimbursed; if it fails to generate a clinical benefit, reimbursement should not be provided. Traditional finance-based reimbursement models, while relatively easy to implement, unfortunately often fail to adequately account for clinical effectiveness. We believe that focusing on outcome-based reimbursement models is essential for managing this risk.

Naturally, it is also important to manage the uncertainties associated with such a model appropriately. For example, in order to address uncertainties regarding a medicine's clinical effectiveness, we can adopt a coverage with evidence development approach. This means that while access to the medicine is permitted, data on its effectiveness continue to be collected. Another important consideration is the balance between cost and effectiveness. The question of whether the benefits generated by a medicine justify the resources expended can only be answered accurately through the analysis of real-world data.

The third and most sensitive issue is financial risk management. To address concerns regarding whether the budget can sustain such a burden, we can deploy robust financial instruments such as conditional treatment pathways, advance payment mechanisms, and next-generation payment models.

Indeed, Italy stands as one of the world's most successful examples of this strategy. By systematically implementing outcome-based reimbursement systems, Italy achieved savings of €195 million in 2022 alone through measures related to orphan medicines. This figure clearly demonstrates that a well-designed risk-sharing model can both deliver meaningful benefits to patients and ensure the efficient stewardship of public resources.

A Data-Driven Future: e-Nabız Integration and Outcome-Based Monitoring

For this model to be sustainable, the most critical element is the generation and effective utilization of real-world data, which will form the backbone of the system. Without a robust data infrastructure, it is impossible to sustain such a financing model. International experience clearly demonstrates this reality. From Türkiye's perspective, however, a major advantage is that the foundations of this infrastructure are already in place. We possess an extremely valuable system such as e-Nabız, for which there are few comparable examples worldwide. If this existing potential is structured effectively, Türkiye can establish a globally recognized model in the field of rare diseases.

The operational framework of the model we propose is based entirely on an outcome-oriented timeline:

- **Initial Stage:** The process begins with negotiations between the SSI and the pharmaceutical company, through a conditional coverage arrangement based on an agreement regarding baseline discounts and outcome-based reimbursement.
- **Six-Month Review:** The effectiveness of the treatment is evaluated for the first time using real-world data.
- **Twelve-Month Assessment:** At the end of the first year, a comprehensive analysis of real-world effectiveness and safety data is conducted.
- **Decision Point (Months 12–15):** If the treatment is found to be clinically effective, a long-term agreement of three to five years is established. However, if the treatment fails to deliver the expected benefit, coverage is terminated and a payback mechanism requiring reimbursement of the amounts paid by the company is activated.

For this structure to function effectively, we believe that three strategic steps must be implemented:

1. Integration of e-Nabız and Orphanet: The e-Nabız system, which we consider a true national asset, should play a central role in the diagnosis, treatment, and monitoring of rare diseases. Integrating financing and monitoring mechanisms into e-Nabız in alignment with international Orphanet coding systems would ensure that every patient and every treatment is monitored according to global standards.

2. Centralized Patient Monitoring System (The Italian Model): A platform similar to Italy's AIFA

Registry System, which has been instrumental in that country's success, should be established in Türkiye. Through a centralized system structured within the SSI, the Turkish Medicines and Medical Devices Agency (TİTCK), or the Ministry of Health, the entire treatment journey of a patient can be recorded from the moment of diagnosis. This would ensure full traceability and enable reimbursement decisions to be based on concrete evidence rather than speculation.

3. Artificial Intelligence-Assisted Patient Identification: One of the highest priorities both in Türkiye and globally is reducing the time required for rare disease patients to receive a diagnosis. As demonstrated in the United Kingdom, the analysis of e-Nabız data through artificial intelligence algorithms could facilitate the early identification of patients who have not yet been diagnosed but already exhibit relevant symptoms. Such a technological initiative would accelerate diagnosis, thereby directly improving treatment outcomes and the efficiency of resource utilization.

Conclusion: A Next-Generation Rare Diseases Ecosystem for Türkiye

The system we propose should be designed under the auspices of the Presidency, founded on trust, committed to financial discipline, and built upon a transparent, multi-stakeholder governance structure. This architecture should be supported by accelerated mechanisms capable of significantly reducing medicine access timelines that currently extend to 461 days, a powerful data infrastructure strengthened by e-Nabız, and decision-making processes based entirely on scientific criteria.

With the implementation of such a structure, the efficient use of public resources will be ensured, expenditures that fail to generate clinical benefit will be prevented, and—most importantly—patients will gain faster and fairer access to life-saving treatments.

Accordingly, the framework presented here is not merely a theoretical policy proposal. Rather, it is a vision for the future—one that overcomes bureaucratic barriers, transforms data into healing, and generates tangible improvements by directly impacting human lives.

Osman Nuri ERDEM
Director General of Plans and Programs
Presidency of Strategy and Budget of the Republic of Türkiye

Financial Balance, Diagnostic Strategies, and Resource Management

We are continuously seeking ways to evolve the system toward a better and more effective structure. Together with your valuable contributions and in collaboration with all relevant institutions, we are shaping our strategic policy documents. In fact, issues such as planning and budgeting are subjects that we have discussed for many years with our stakeholders and with experts such as Professor Zafer, who have been deeply involved in this field.

I would like to reiterate a point that I emphasized during the opening remarks: every individual is rare and valuable. I fully agree with the statement frequently expressed by patient associations that "rare disease patients are not merely statistical figures." However, on the other side of the equation, when the discussion turns to financing, price and cost considerations inevitably play a decisive role. Once this balance is lost, a financing issue that would otherwise be manageable can become far more complex and difficult to address. Therefore, the financing dimension must be approached with great care.

The high prevalence of rare diseases in Türkiye is frequently highlighted, and the role of consanguineous marriages in this picture is undeniable. We know that, for certain diseases, as much as one-quarter of all cases worldwide may be found in our country. Similar patterns can also be observed in countries such as India, where consanguineous marriages are relatively common. However, reducing this situation solely to consanguineous marriages would be an insufficient explanation; diagnosis is equally critical and deserves the same level of attention.

At this point, proper resource allocation is of vital importance. I can state with confidence that Türkiye allocates a share of its healthcare budget to rare diseases and their treatment that is significantly greater than their proportional weight within the broader healthcare system. Although it is difficult to provide a precise definition, an examination of pharmaceutical expenditures shows that more than one-tenth of our medicine spending is directed toward products related to rare diseases.

Naturally, several special mechanisms come into play. In addition to the standard 4A reimbursement list of the Social Security Institution (SSI), there are non-standard channels such as the 4C overseas medicines pathway and payments made through court decisions. The total volume of these channels has reached a scale that cannot be ignored in the financing of rare diseases. When all of these supplementary pathways are considered together—including 4C and court-related processes—I do not agree with the view that Türkiye ranks among the lowest countries in Europe in terms of access to orphan medicines. Of course, our preference would be for such access to occur through more standard and predictable mechanisms.

In conclusion, Türkiye allocates a significant portion of its healthcare resources to this field. Whether that allocation is sufficient or not is a separate matter for discussion. This area is too sensitive to be addressed through simplistic approaches, such as earmarking a fixed percentage of the healthcare budget. In particular, the high costs associated with medicines supplied from abroad and the pressure these costs place on the system must be managed with strategic care.

The Need for Financing Beyond Traditional Insurance Models

I do not believe that direct comparisons between Türkiye and European countries always lead to accurate conclusions. Every country has its own healthcare dynamics, demographic structure, and economic conditions; therefore, evaluations must be made within the context of our own realities. Healthcare is, by its nature, an extremely sensitive domain. If we aim to maximize social benefit, we must establish a very careful balance between price and cost. This balance can only be achieved through coordinated action between the public and private sectors. Otherwise, the system may settle into an inefficient equilibrium far removed from the point at which societal benefit is maximized.

Rare diseases represent an even more concentrated and challenging dimension of healthcare. The fact that a disease affects only a very small segment of society naturally increases research and development costs on a per-patient basis. The limited number of patients drives up the prices of medicines and treatments in this field. Under normal circumstances, society can finance a condition that is "rare" but carries a significant burden through a spirit of social solidarity. However, when we speak of figures ranging from 5 to 7 million individuals, the issue may remain technically "rare," but it ceases to be rare in terms of its aggregate impact.

This situation, often referred to in statistics as the "heavy-tail problem," presents significant challenges from a risk-management perspective. While these diseases are individually rare and situated at the extremes of the distribution, their cumulative impact creates an enormous burden on the system. Risks of this magnitude are often beyond the capacity of private insurers to absorb, while public insurance systems also struggle to maintain sustainability through premium-based financing models alone. Under the traditional insurance framework, premiums collected based on individual risks are insufficient to cover obligations of such magnitude.

Consequently, it is a reality that financing this field exclusively through traditional social insurance mechanisms is extremely difficult. I agree with the view that rare disease financing requires additional and alternative funding sources beyond the classical system. These sources may be supported through taxation on the public side and, although more challenging, through private insurance mechanisms on the private side. Donations and certain forms of co-payment may also form part of the system. In principle, I support the view that orphan medicines and treatments should be addressed through a specialized financing structure that extends beyond the traditional social insurance framework.

Transparent Governance, Social Impact, and Resource Prioritization

I would like to begin by expressing my appreciation for the detailed work and policy proposals developed in the field of rare diseases; my sincere thanks to everyone involved. As emphasized throughout the presentations, increasing transparency, strengthening communication, and ensuring the active participation of all stakeholders are critically important. Ultimately, the issue under discussion is not merely a technical financing matter; it is a sensitive field characterized by multiple dimensions and complex dynamics.

The Challenge of Establishing Rules for Resource Management

Proposals to generate additional resources through mechanisms such as tobacco taxes or income taxes are frequently raised in discussions of healthcare financing. However, determining how such resources should be structured, managed, and allocated is a highly complex issue requiring considerable care. In fact, similar elements

already exist in various forms within our current pricing and reimbursement systems. The central question is where and how every unit of funding should be directed, because these decisions have social implications as well as economic consequences.

Social Impacts and Public Sensitivity

Particularly in the case of diseases affecting children, public perceptions, fundraising campaigns organized through social media, and broader societal sensitivities can directly influence decision-making processes. For this reason, the field extends beyond technical administration and is heavily shaped by social considerations. Even minor shortcomings in expenditure prioritization can result in more harm than benefit. If public authorities depart from fiscal discipline and adopt an approach suggesting that greater flexibility can simply be exercised in certain areas, resources may drift far from their most effective uses.

Appropriate Prioritization and Holistic Impact

Within this framework, we need a management model that emphasizes effectiveness and outcomes rather than fragmented resource allocation. One of the most important outcomes of public–private collaboration should be the ability to establish the right priorities. Determining where to begin and identifying which disease groups or interventions should be prioritized requires a clearly defined framework. Otherwise, the existence of numerous disconnected initiatives within the system will make it impossible to achieve a coherent and comprehensive impact.

The Need for a Systematic and Controlled Structure

My assessment is that additional financing sources beyond the traditional insurance system are essential. In this context, the role of citizen donations within the system may also be considered. In Türkiye, the public sector already assumes a significant share of the burden associated with rare diseases. However, we must also acknowledge that alternative and non-standard payment channels are, at times, utilized in an uncontrolled manner.

We are therefore obliged to make the existing structure more systematic, controlled, and effective. By utilizing our available resources efficiently, we are pleased to evaluate together the models that can deliver the greatest contribution to human life.

Ayşegül GÜNBEY ÖZTEK
Head of the Department of Overseas Health Services
General Directorate of General Health Insurance (GHI), Social Security Institution (SSI)

The Key Role of Financing and Inclusiveness

First of all, I would like to convey the greetings of our Director General of General Health Insurance, Associate Professor Eren Musa. Due to his busy schedule, he is unable to join us today, and I am here on his behalf. Since this morning, I have been following the sessions closely. The perspectives shared by our esteemed professors and industry stakeholders have been extremely valuable; we have also drawn important insights from these discussions and taken note of the actions that need to be considered.

The initiatives carried out by our Ministry of Health, the scientific contributions of academia, and the development of new treatment methods are undoubtedly of great importance. However, we believe that financing is the key element that enables all these valuable efforts to translate into practical outcomes and tangible benefits. It must be clearly stated that regardless of how strong our R&D activities are or how comprehensive our regulations may be, if these efforts are not supported by financing mechanisms, it is not possible to achieve the level of patient access to treatment that we aspire to provide.

In this regard, Türkiye possesses a healthcare system that stands as a global model, with a General Health Insurance (GHI) coverage rate approaching 99%. This represents both a tremendous source of strength and a significant responsibility. Our primary objective is to utilize the financing available to us in the most accurate, effective, and equitable manner possible.

As the Social Security Institution, we assume responsibility for individuals from the moment of conception throughout their entire lives—from medicines and treatment services to preventive healthcare and rehabilitation. To manage this broad scope of responsibility effectively, we continuously update our legislation and implementation practices. In doing so, we work in full coordination with stakeholder institutions such as the Ministry of Health, the Presidency of Strategy and Budget, and the Ministry of Treasury and Finance to ensure that limited resources are directed to the most appropriate areas.

The SSI Perspective: The Current Financial Landscape and New Evidence-Based Processes

The observations presented by Mr. Osman are highly valuable. In fact, a significant portion of the proposed project is already being carried out within the Social Security Institution. However, rather than managing these processes through a separate rare diseases initiative, we address them within a comprehensive healthcare financing framework

that also encompasses oncology and other therapeutic areas. The primary source of funding for these services is the premium income collected under the General Health Insurance system.

Data-driven approaches and outcome-based alternative reimbursement models are not unfamiliar concepts for our institution; we have been conducting detailed analyses in this area since 2016. When we examine the current financial picture, it becomes clear how substantial expenditures related to rare diseases have become:

Scale of Expenditure: According to SSI data, our total healthcare expenditures exceeded TRY 1.3 trillion in 2025.

- **Growth Trend:** Expenditures increased by 70% from 2023 to 2024 and subsequently rose by approximately 40%.
- **Expenditure Distribution:** One-third of total expenditures consists of pharmaceuticals, while the remaining two-thirds cover healthcare services such as diagnostics, assisted reproductive technologies, physical therapy, rehabilitation, and surgical procedures.

Access to Medicines and the Critical Role of the Annex-4/C List

On the pharmaceutical side, we maintain a broad reimbursement network covering both domestically licensed and unlicensed products. As of 2025, approximately 11% of our domestic pharmaceutical budget (Annex-4/A) is allocated to rare disease medicines. Even more strikingly, nearly 80% of the more than 400 medicines included in the Annex-4/C list, which covers medicines supplied from abroad, are used directly for the treatment of rare diseases. In summary, our Annex-4/C list functions almost entirely as a rare diseases medicines list. Since reimbursements are made based on current exchange rates, fluctuations in foreign currency markets increase pressure on our budget, making resource efficiency more critical than ever.

A New Vision for Application and Evaluation Processes

In order to utilize our resources more rationally, we have initiated a new and more rigorous evaluation process, particularly for applications concerning medicines supplied from abroad. We no longer expect companies merely to present their products; rather, we require comprehensive, evidence-based dossiers demonstrating the medicine's effectiveness, clinical superiority, and tangible benefits.

Our expectations in this new era include:

- **High-Quality Data:** Studies supported by concrete evidence generated in real-world practice.
- **Dossier-Based Evaluation:** Submission of detailed data regarding the developed molecules to our commissions.
- **Focus on Effectiveness:** Demonstration not merely of a medicine's existence but of its actual clinical success in patients.

This approach serves both as a governance mechanism that enables our institution to make more informed decisions and as an opportunity for companies to demonstrate the true value of their products. Moving forward, we will continue to institutionalize this process by further clarifying the required documentation and evaluation criteria through detailed procedural frameworks.

Strategic Deadlocks: Company Applications, Public Perception, and Ethical Responsibility

During evaluations conducted by our reimbursement and pricing commissions, we observe that certain medicines that are critically important for patients are not submitted for review by companies despite repeated invitations and clear clinical needs. This situation represents one of the greatest paradoxes in the field of rare diseases.

Corporate Strategies and Public Perception

Some pharmaceutical companies choose not to enter the reimbursement system due to commercial considerations, global market strategies, or Türkiye's pricing policies. However, this decision often creates a public perception that "the government is not providing the medicine."

Let us consider SMA treatment as an example. Today, Türkiye has reimbursed certain medicines since 2017. We have been providing our citizens with treatments for years that are still not reimbursed in several European countries, including Germany and the United Kingdom. Despite this reality, the perception that no treatment options exist is deeply discouraging for those of us who work tirelessly on these issues.

Gene Therapies and Unregulated Processes

Gene therapies such as Zolgensma deserve particular attention. We are aware that substantial fundraising campaigns have been organized by patient organizations and the public to secure access to this treatment. However, there is a striking reality: the company providing this therapy has not submitted an official reimbursement application to either the SSI or the Turkish Medicines and Medical Devices Agency (TİTCK). When companies choose to remain outside the regulatory framework, it weakens the government's negotiating position and places families into an uncontrolled process.

Returning to the System After Treatment Abroad

Another sensitive issue concerns patients who travel abroad in search of treatment. We regard every child as if they were our own. However, there are cases in which substantial sums are raised to finance treatment abroad, only for the expected benefits not to materialize, after which patients return to Türkiye and seek reimbursement through the domestic system. Choosing to pursue treatment abroad without first utilizing the available and evidence-based treatment options in Türkiye can sometimes result in irreversible losses of both time and resources.

Limited Resources and Responsibility to Future Generations

One point must be emphasized clearly: all of our processes are evidence-based. It is not possible, from either a public finance or public health perspective, to reimburse treatments that lack scientific evidence or whose effectiveness remains uncertain.

Our resources are not unlimited. If we expend them today on treatments whose effectiveness has not been proven, we may not have the capacity tomorrow to finance next-generation therapies whose benefits have been definitively demonstrated. This is not merely a challenge for today; it is a responsibility to safeguard the healthcare security of our children and grandchildren. Our objective is to ensure that every unit of funding is directed, in light of the strongest scientific evidence, to the right patient and the most effective treatment.

Data-Driven Monitoring: Patient Follow-Up Forms and Real-World Evidence

Acting under the guidance of science and using our resources rationally is not a matter of choice—it is a necessity for the future of the system. Accordingly, for approximately one and a half years, we have been conducting an extremely valuable initiative aimed at closely monitoring products reimbursed in areas such as rare diseases and oncology.

Patient Monitoring Programs and Transformational Steps

As the General Directorate, we have developed dedicated patient monitoring forms for strategic products included in the reimbursement system. All technical details—including who is responsible for completing these forms and

which clinical data must be entered into the system—have been clearly defined. Through this mechanism, we are now able to monitor patient treatment journeys not only through theoretical data but also through direct real-world evidence.

Although we are only beginning to see the results of this system, I believe it represents a transformative step for Türkiye's healthcare policies. This dataset will enable us to achieve the following:

- **Threshold Analysis:** Establishment of reimbursement thresholds specific to Türkiye based on scientific evidence.
- **Value-Based Reimbursement:** Comparison of treatment costs against the tangible health outcomes they generate.
- **Cost-Effectiveness Analyses:** Clear assessment of the clinical benefits obtained in relation to the resources expended.

Academic and Policy Foundations

Although conducting such analyses may not appear to be the primary responsibility of the SSI, the robust data infrastructure we are building will provide an indispensable foundation for both academic research and high-level policy decisions. Through these monitoring programs implemented specifically for rare diseases, the real-world effectiveness of medicines will no longer be a matter of speculation but will instead be demonstrated through concrete evidence. This will both protect public resources and ensure that our patients receive access to the most appropriate treatments.

Prof. Dr. Fulya İlgin GÖNENÇ
Dean, Faculty of Law, Medipol University

Perspective, Determination, and the Legal Foundation

First of all, I would like to express my pleasure at being part of this valuable platform and having the opportunity to listen to these high-quality discussions conducted in such a sensitive field as rare diseases. I would like to extend my thanks to everyone involved, especially our Federation. As a legal professional who closely follows developments in practice, I must say that the vision presented here today is highly encouraging.

Beyond Regulations: Determination and Approach

While it is certainly important to establish technical regulations in the field of rare diseases, I believe that the real differentiating factors are perspective, determination, and the right approach. It is encouraging to see that such a shift in mindset has begun to emerge in Türkiye. However, for meaningful progress to continue, all stakeholders must move forward with the same level of commitment and alignment.

The Invisible Foundation: Legal Infrastructure

Since this morning, we have discussed in detail access to information, technology, and treatment, preventive healthcare services, diagnostic processes, and the economic dimensions of the issue. However, we have barely addressed the legal infrastructure upon which all these elements must be built. If we are to claim that the system is progressing in a healthy manner, the legal foundation must be discussed just as thoroughly as the financial models.

The relationships among pharmaceutical companies, academia, and civil society organizations can no longer remain solely within the framework of "social solidarity." I believe these collaborations should be redefined through a stronger and more contemporary legal perspective that clearly establishes the rights and responsibilities of all parties involved.

The Triangle of Economics, Health, and Law

As a legal scholar, I can clearly see the inseparable connection between economics, health, and law. Later in my career, I had the opportunity to work on health economics. In the studies I have conducted on disability rights and the right to health since my twenties, gaining knowledge of economics at a later stage actually provided an advantage: it allowed me to shape my aspirations and my perspective on the right to health within a broader rights-based framework, without initially constraining them through financial limitations.

At the point we have reached today, as we discuss financing and reimbursement models for rare diseases, the only force capable of transforming these aspirations into reality, protecting rights, and ensuring the sustainability of the system will be the solid legal framework that underpins these models.

Legal Safeguards, System Trust, and the Deadlock of Court Decisions

The survey results presented in the previous panel actually point to a very fundamental issue of "trust" that deserves our attention. The responses of "maybe" or "definitely disagree" to the question regarding Türkiye's potential in innovative solutions indicate that, despite all the valuable work being undertaken, the field itself has not yet been fully convinced. We must be able to read this picture correctly: what has been done is valuable, but why are we still not sufficiently optimistic?

The primary reason for this pessimism and lack of trust is that the initiatives being undertaken and the rights being offered have not been anchored in a strong legal foundation. Words may fade, but legal texts endure. Today, we are discussing highly valuable projects; however, what will make these projects permanent is transforming them from "well-intentioned practices" into "legal rights." The day we are able to say to patients and their families, "These rights have been secured through this legislation," both confidence in the system and belief in our potential will increase.

Court Decisions Are Not a Reimbursement System

As our speakers have also noted, there is an "access pathway" in Türkiye that is not based on a formal legal framework but has become a practical reality: court decisions. I would like to state this clearly and unequivocally: access to medicines through litigation is not a system; it is merely a method born out of necessity.

Particularly with respect to oncology and rare disease medicines, judicial proceedings have increasingly come to be perceived as an ordinary reimbursement channel. The picture I have observed through the processes that I have voluntarily supported is quite concerning from a legal perspective:

- **Standardized Expert Reports:** We witness expert reports, which should be specific to the case, the patient, and the medicine, being prepared almost as identical copies of one another.
- **Copy-Paste Decisions:** Court decisions themselves have gradually fallen into certain patterns over time and have been shaped by similar approaches, resulting in the judiciary functioning almost like a technical reimbursement commission.

Although this situation may appear to protect the right to health through judicial intervention, it is actually the clearest evidence that the system's own internal mechanisms are not functioning properly. The issue is not merely financing or funding; the issue is designing a comprehensive system that does not force patients to seek remedies through the courts, but instead provides a transparent, predictable, and legally protected framework. We can rebuild trust only through a legal foundation that eliminates arbitrariness and establishes clear rules.

Constitutional Foundations and the Obligation Arising from the "Right to Health"

The fact that the question "Is there a lawyer present?" has rarely been asked at healthcare platforms to date stems from the reality that the field has advanced largely through its own dynamics and technical needs. The progress achieved—from diagnostic processes to the dedicated efforts of civil society—is truly commendable; however, we have now reached a different stage. As has become clear during this session, if a new financing or funding model is to be designed, the inclusion of legal professionals among the architects of that process is no longer a matter of choice but a necessity.

A Constitutional Obligation: "Everyone"

As a legal scholar, I would particularly like to emphasize the word "everyone" in Article 17 of the Constitution. This concept, which emerged through the historical evolution of modern legal systems, encompasses every individual

without any distinction. The right of everyone to develop their material and spiritual existence constitutes the true foundation of all the technical and financial issues we are discussing.

Article 56 of the Constitution further concretizes this framework: the State is under an explicit obligation to ensure the realization of the right to health. The ideal is for healthcare services to be provided at the highest possible level and with full accessibility. Although this is not always easy within existing economic systems, the jurisprudence of the Council of State and judicial decisions have repeatedly affirmed how unshakable this right is as a fundamental human right.

The State's Three Fundamental Obligations

When discussing rare diseases, we are not merely addressing a technical issue; we are discussing how a fundamental human right can be realized in practice. Under human rights doctrine, the State has three fundamental obligations with respect to the right to health:

1. **Respect:** Refrain from interfering with an individual's right to health.
2. **Protect:** Establish legal safeguards to prevent third parties or market conditions from violating this right.
3. **Fulfil:** Put in place the necessary mechanisms, budgets, and systems to ensure that the right can be effectively exercised.

In conclusion, unless we place these three fundamental obligations at the center of our financial models, the structures we establish may appear technically sound, yet remain deficient from both a legal and human perspective. Health economics and public policy can respond to the real needs of society only when they are built upon these constitutional foundations.

From Aspirations to Legislation: A Rights-Based Future

The discussion we are having in this session is, in essence, about how the State will fulfil its obligation to ensure the right to health. The existence of this responsibility is not open to debate; the real issue is determining through which modern methods, transparent models, and legal instruments this obligation will be implemented.

Historical Foundations and the Current Structure

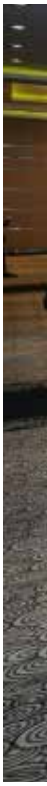
I asked myself: "If I were giving a presentation today, what would be on my slides?" I would probably include the 1928 Law on the Practice of Medicine and Its Branches, the 1930 Public Health Law, or provisions of the 1926 Civil Code. Although this may sound ironic, my purpose would be to remind us of the deeply rooted foundations of our legal system. Yet today, we see an effort to build a much newer and far more complex structure upon these historical foundations. I consider this effort extremely valuable and have great respect for the contributions of all stakeholders involved.

From Good Intentions to Legal Safeguards

However, as a legal scholar, I must offer a word of caution: unless a strong legal foundation and a solid framework of legitimacy are established, much of what is being discussed here risks remaining, unfortunately, at the level of aspiration. Genetic research and medical discoveries are, of course, enduring; the light of science does not fade. However, if access to these scientific advances for individuals living with rare diseases is not defined as a right through written rules, it remains dependent solely on the goodwill of institutions or individuals.

The Highest Level of Consensus: Participation

If we were to conduct a small survey in this room right now and ask, "Should patient organizations be involved in



these processes?", I believe we would obtain one of the highest levels of consensus imaginable. There would likely not be a single person who would answer, "No, it is not necessary." So why is it that we still cannot fully implement in practice something on which we all agree so strongly?

The reason is that we have not yet properly defined, on paper, who the true owners of this process are. Unless it is clearly established how stakeholders will participate in decision-making mechanisms, what authorities they will possess, and what legal guarantees will underpin that participation, the system will remain incomplete.

The issue is not merely the establishment of a fund or the creation of a reimbursement algorithm. The issue is a comprehensive legislative transformation that encompasses all stakeholders in this field and turns rights from requests into law. The State's obligation to fulfil these rights can only be realized through a system in which citizens have clear avenues to seek and enforce their rights, and in which the rules are known in advance.

The Transformation of Civil Society: From Emotion-Driven Advocacy to Evidence-Based Advocacy

As someone who has personally witnessed the evolution of civil society since 1996, I believe this observation is, in fact, a summary of the struggle for rights in Türkiye. The transformation of efforts that were once more emotional and perhaps focused on assistance into a professional, systematic, and evidence-based structure has become the greatest factor strengthening civil society's position at the table with public authorities. Civil society is no longer merely a party that makes demands; it has become a stakeholder that generates solutions through its technical capacity and data resources.

Not 30 Percent Representation, but a Core Role in Decision-Making

What will dispel the uncertainty reflected in the survey results regarding Türkiye's potential is the legitimacy of the new structure that will be established. If a new financing or funding model for rare diseases is to be designed, patients and their families—the true owners of this structure—cannot remain merely figures whose opinions are consulted.

- **Participation Beyond Representation:** That "30 percent" figure you mentioned is not merely a number of seats; it should represent a blocking and guiding power within decision-making, transparency oversight, and strategic planning processes.
- **Transparency and Oversight:** The inclusion of patient associations within this structure would constitute the most natural oversight mechanism for ensuring that every unit of funding is truly directed toward patient benefit.

The Need for "Next-Generation" Legislation That Embraces the Future

The greatest risk in the field of rare diseases and orphan drugs is attempting to solve today's challenges with yesterday's legislation. It is a reality that our healthcare law framework remains fragmented and, in certain respects, lags behind contemporary developments. The regulatory framework we need should possess the following characteristics:

1. **Comprehensive and Flexible:** A framework that provides legal safeguards not only for today's molecules but also for tomorrow's gene therapies and personalized medicine approaches.
2. **Dynamic Rather Than Static:** A vision broad enough to accommodate technological developments that may emerge over the next 10–20 years, including AI-supported diagnostics and biotechnological breakthroughs, without leaving them outside the system.
3. **Legal Assurance:** A structure in which all these processes are transformed from aspirations or institutional preferences into legally guaranteed rights grounded in the constitutional right to health.

The Fund Model and Legal Legitimacy

When evaluating the proposed fund model from this perspective, a structure that both ensures financial sustainability and includes patient associations as core stakeholders could truly position Türkiye as a model for the world. However, the key to such success lies not in technical perfection, but rather in the legal legitimacy of the system and the unwavering place of civil society within it.

Hierarchy of Norms, Fragmented Legislation, and Outdated Provisions

Mr. Osman's proposal for a Presidential Decree (PD) represents a highly practical approach in terms of speed and achieving tangible results. Introduced into our legal system after 2017, Presidential Decrees have created a dynamic regulatory space for the executive branch within the hierarchy of norms. Furthermore, direct ownership of the issue by the Presidency could strengthen public perception and facilitate more decisive implementation.

However, as a legal scholar, I must emphasize that while Presidential Decrees may be ideal for a rapid start, they are insufficient on their own to regulate a multidimensional field such as rare diseases in a comprehensive and lasting manner.

The Misconception of a Single Legislative Instrument

Rare diseases encompass an extensive spectrum, ranging from preventive services and treatment to newborn and adult screening programs. Attempting to address this entire field through a single "Rare Diseases Law" would not be realistic. Each stage involves its own distinct rights and technical requirements:

- **Pre-Marital Processes:** Intersect with family law and property rights.
- **Prenatal Diagnosis and Pregnancy-Related Procedures:** Primarily involve personality rights and principles of medical ethics.
- **Newborn Screening Programs:** Require a careful balance between the State's duty to protect and parental rights.

Each of these areas requires separate, specific, and mutually compatible legal frameworks.

The Civil Code and Outdated "Marriage Restrictions"

While teaching Family Law to my first-year students, I frequently address these very issues, including legal restrictions on marriage. The Civil Code and the Public Health Law of 1930 remain our primary legal references in this area. Yet when we revisit these laws, we find that certain disease classifications and marriage restrictions contained within them are no longer scientifically up to date.

For example, some provisions in the current legislation stipulate the postponement of marriage until certain communicable diseases have been treated. However, the purpose of contemporary screening tests conducted in the context of rare diseases is not to prevent marriage or to declare that individuals "cannot marry." Rather, the objective is to inform couples, identify potential risks, and facilitate access to appropriate medical interventions—such as preimplantation genetic testing (PGT) and assisted reproductive technologies—to support the birth of healthy future generations.

Legal Basis and the Contradiction in Practice

Within the current system, the legal basis for screening tests remains largely confined to the 1930s perspective of "the health of couples intending to marry." However, modern medicine has progressed far beyond the concept of a "barrier to marriage." As the scope of screening expands, our legal foundations must be aligned with contemporary medical realities, including genetic counseling and reproductive rights.

In conclusion, a rapid funding and governance model may indeed be established through a Presidential Decree (PD), and this is valuable. However, in the long term, it is imperative that we recodify the fragmented and outdated legal framework extending from the Civil Code to the Public Health Law in light of modern genetics and the perspective of the "right to health." Screening programs should no longer be treated merely as a "pre-marital procedure," but rather be grounded in law as an individual's fundamental constitutional right to raise healthy generations and to access information.

SMA Screening Programs, the Scope of the Fund, and Data Privacy

Although screening programs for diseases such as SMA represent a medical success, they continue to operate within a legal grey area. Under current legislation, the legal basis for such large-scale screening initiatives has not yet been fully clarified, leaving the system vulnerable to the discretion of individuals or institutions. If a new fund and governance structure are to be established, the following three pillars must be incorporated into the legislation to ensure its effective functioning:

- **Clarification of Proposals:** The medical interventions and needs covered by the system must not be left ambiguous.
- **Stakeholder Definitions:** The powers, responsibilities, and boundaries of decision-makers, supervisors, and implementers must be clearly defined.
- **Financial Principles:** The sources of funding and the criteria governing expenditure must be secured through legal guarantees.

The Scope of the Fund: Preventive vs. Curative Services

One of the most fundamental questions that must be addressed within the proposed financing model concerns the boundaries of the fund itself. Across the world, preventive healthcare services are regarded as primary public services and are financed by the state. If the proposed fund is also intended to cover screening programs, genetic counseling, and preventive medicine, how will these activities be integrated with the state's core responsibilities? Where will the boundaries of curative services (such as pharmaceuticals and surgical interventions) begin and end? Unless this distinction is clearly established, the fund's resources risk being dispersed inefficiently within a short period of time.

The Invisible Threat: Personal Health Data and Privacy

Overshadowed by financial and technical discussions, yet equally critical, is the issue of patient privacy. By their very nature, rare diseases involve highly individualized genetic data. Such data are not merely "records"; they constitute the most private aspect of an individual's identity.

Within any newly established fund and monitoring system, the following issues must be addressed as an integral part of the legal framework:

- Who will have access to these data,
- How the data will be protected,
- The limits of access granted to pharmaceutical companies,
- Compliance with the Law on the Protection of Personal Data (KVKK).

Conclusion: A Sustainable Legal Ecosystem

In summary, the proposed system must not merely be a structure that "has funding"; it must be a structure that "delivers justice." Without a robust and comprehensive legal framework capable of anticipating future technologies, including artificial intelligence and genomic data, any financial achievements will remain temporary. Legal certainty, transparency, and data security are essential prerequisites for sustainability.

SURVEY

THE NEED FOR "REFORM" IN THE CURRENT REIMBURSEMENT SYSTEM IS BECOMING INCREASINGLY APPARENT

More than half of the participants (52%) characterized the current reimbursement and financing system for rare diseases in Türkiye as "Inadequate" (31%) or "Highly Inadequate" (21%). These findings indicate that the existing financial mechanisms face serious structural bottlenecks in ensuring fair and timely access to treatment for patients and that there is a clear need for change capable of restoring stakeholder confidence.

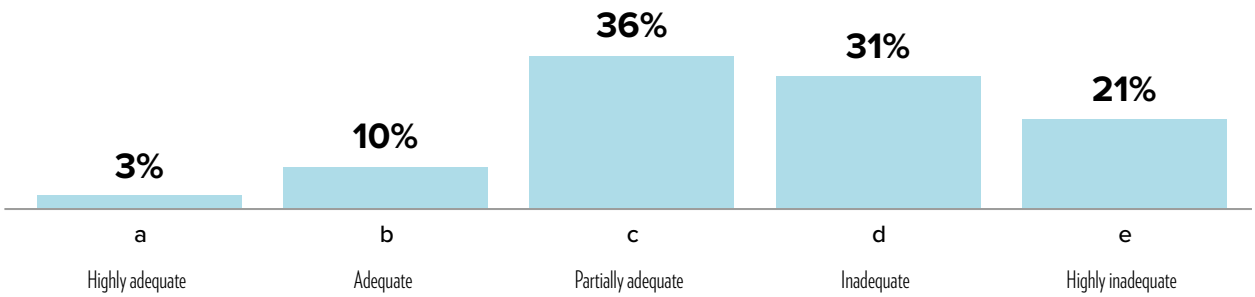
The 36% of respondents who considered the system "Partially Adequate" suggest that although progress has been achieved in certain areas, significant concerns remain regarding the sustainability and scope of existing solutions. The prominence of this "middle category" demonstrates that the system is not entirely dysfunctional; however, it struggles to adapt to the dynamics of innovative and high-cost therapies.

The fact that the combined proportion of respondents who rated the current system as "Adequate" or "Highly Adequate" remained at only 13% confirms that satisfaction with the financing model is confined to a very limited segment. This low percentage reinforces the widely held view within the sector that overall budgetary discipline and the current Social Security Institution (SSI) reimbursement criteria are insufficient to address the exceptional and challenging financial landscape associated with rare diseases.

When the overall distribution is considered, it becomes evident that moving beyond traditional approaches to rare disease financing and designing more flexible, equitable, and accessible "special reimbursement models" capable of safeguarding patients' right to treatment has become a necessity.

7. Is the current reimbursement and financing system for rare diseases in Türkiye adequate in ensuring timely and equitable access to treatment for patients?

a. Highly adequate
b. Adequate
c. Partially adequate
d. Inadequate
e. Highly inadequate



NATIONAL RARE DISEASE FUND: STRONG EXPECTATIONS FOR FINANCIAL SECURITY

A significant majority of participants (66%) support the establishment of a National Rare Disease Fund in Türkiye. The substantial proportion of respondents (43%) who stated "Strongly support" reflects a firm conviction that the high cost burden associated with rare diseases should be separated from general budget allocations and addressed through the creation of a dedicated and sustainable financial pool.

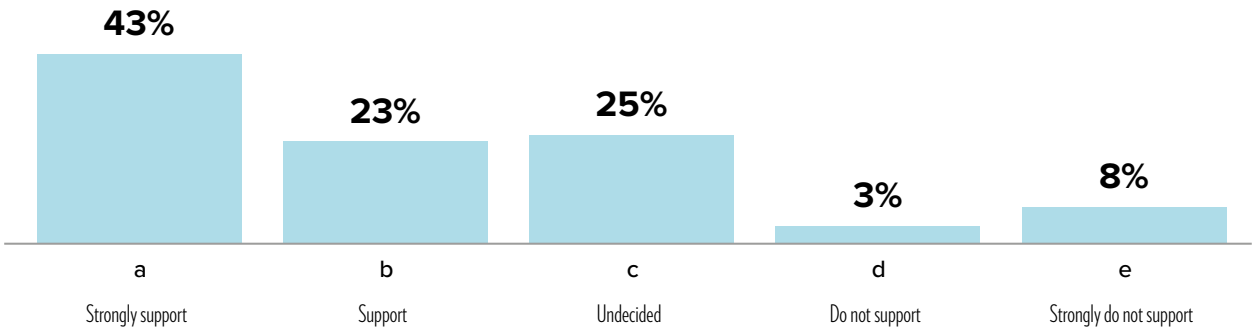
As a noteworthy finding, 25% of participants responded "Undecided." This figure highlights the need for greater clarity regarding operational details, including how the fund would be managed, what its funding sources would be, and how spending priorities would be determined. The relatively high level of uncertainty suggests that while the sector acknowledges the need for a dedicated fund, it requires more concrete information regarding the transparency and functioning of such a mechanism.

The proportion of respondents expressing opposition to the establishment of the fund was recorded at 11% ("Do not support" and "Strongly do not support"). Concerns among this group may stem from potential bureaucratic burdens associated with a new financial structure or possible integration challenges with the existing system. However, this level of opposition is not sufficient to alter the overall positive trend toward the creation of the fund.

When the overall distribution is evaluated, it becomes evident that a "National Fund" model designed to strengthen the financial dimension of rare disease policy in Türkiye is viewed by a large portion of the ecosystem as a key part of the solution. At the same time, it is clear that the successful implementation of such a model will require a trustworthy, transparent, and thoroughly detailed planning process.

8. Do you support the establishment of a National Rare Disease Fund in Türkiye?

a. Strongly support
b. Support
c. Undecided
d. Do not support
e. Strongly do not support



Preventive Approaches to Rare Diseases and the Ethical-Legal Framework

Prioritization in Health Economics: Prevention First, Treatment Second

It has been emphasized that the fundamental vision of health policy should be to "diagnose and prevent at birth" rather than treat diseases after they have developed. The financing needs of expanded newborn screening programs have been defined as a public health and ethical priority that should take precedence over high-cost treatment funds. It has been argued that the success of a healthcare system should be measured not by the number of patients treated, but by the "rate of disabilities prevented." Preventive medicine has been identified as the most rational approach from the perspectives of both medical ethics and sustainable health economics.

Consanguineous Marriages: Legal Boundaries and the Ethics of Responsibility

It has been noted that imposing a legal prohibition on consanguineous marriages is constrained by fundamental human rights principles and the provisions of the Civil Code. In this context, the importance of incentive-based and awareness-raising models, rather than prohibitive legal measures, has been emphasized. While state support for medical alternatives such as Preimplantation Genetic Testing (PGT) is regarded as a strategic step, more radical approaches—such as requiring couples who disregard risk warnings to contribute to treatment costs—have been opened for discussion within the framework of "the best interests of the child."

It has been stated that the ultimate solution lies not in prohibitions, but in sociocultural awareness, education, and institutional collaborations capable of transforming public understanding and social consciousness.

DEMAND FOR "TOP-LEVEL OWNERSHIP" AND "UNIFIED LEADERSHIP" IN FUND GOVERNANCE

The largest proportion of participants (43%) argued that the proposed National Rare Disease Fund should be established under a joint Presidency–Ministry of Health structure. This preference reflects a holistic approach advocating that the fund should be supported by the highest level of political authority (the Presidency) while being managed through technical and medical expertise (the Ministry of Health).

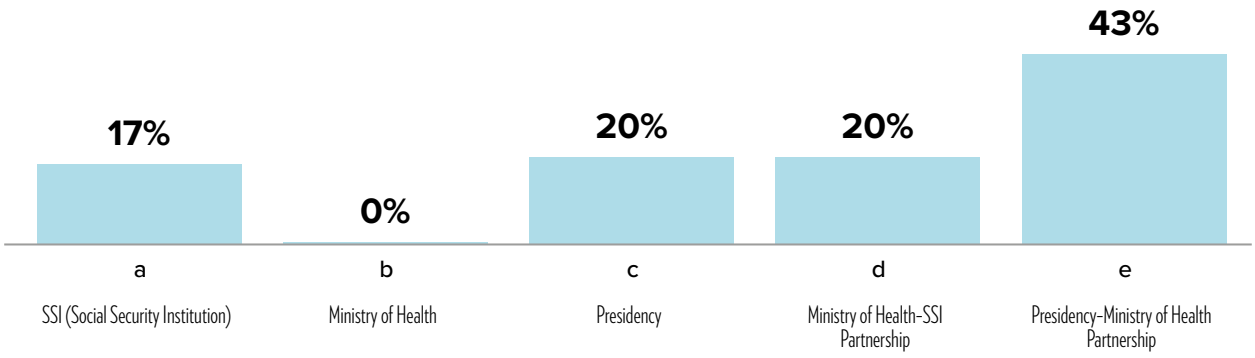
The equal level of support for governance models under the Presidency alone (20%) and a Ministry of Health–SSI Partnership (20%) further reinforces participants' desire to see either a clear "central authority" or a strong framework for inter-institutional cooperation at the heart of the solution. By contrast, only 17% considered a structure operating solely under the Social Security Institution (SSI) to be appropriate, while no participants supported establishing the fund exclusively within the Ministry of Health (0%).

These findings send a clear message that managing a high-cost and strategic area such as rare diseases extends beyond the individual authority boundaries of existing bureaucratic institutions (SSI or the Ministry). Participants directly associate the success of the fund with the oversight of the highest decision-making authority and the combined operational capacity of the relevant public institutions.

When the overall distribution is evaluated, it becomes evident that any future fund should be designed not merely as a financial mechanism, but as a "high-level governance model" supported by the vision of the Presidency and capable of transcending traditional institutional hierarchies.

9. Which institution would be the most appropriate to oversee the governance structure of a potential National Rare Disease Fund?

a. SSI (Social Security Institution)
b. Ministry of Health
c. Presidency
d. Ministry of Health–SSI Partnership
e. Presidency–Ministry of Health Partnership



Sustainable Financing and a Domestic Production Strategy for Rare Diseases

Multi-Stakeholder Governance and Financial Visibility

It has been emphasized that the reimbursement and pricing processes for rare diseases are currently managed through a multi-stakeholder structure comprising the Presidency of Strategy and Budget, the Social Security Institution (SSI), the Ministry of Health, and the Ministry of Treasury and Finance. For the success of this model, defining rare diseases as a distinct category within the broader healthcare system and allocating resources specifically to this area are considered essential prerequisites for financial sustainability.

Strategic Resource Management and Expanding Domestic Capacity

To strengthen the financial framework, it has been proposed that rather than relying on a single funding source, tax-based models, diversified financing mechanisms, and investments in clinical research should be pursued simultaneously. Two primary levers have been identified to facilitate the organic growth of resources allocated to rare diseases: prioritization through a clearly defined set of reimbursement criteria and the expansion of domestic production capacity. It has been stated that the success of the system depends not on the amount of money spent, but on the extent to which that expenditure is supported by a strategic vision for research, development, and production.

PANEL-4

PREVENTIVE MEDICINE AND SOCIAL PRACTICES IN RARE DISEASES (Genetic and Newborn Screening Programs)

MODERATORS

Prof. Dr. Mehmet GÜNDÜZ
Ankara Bilkent City Hospital

Deniz ATAKAY
President, Rare Diseases Federation

SPEAKERS

Prof. Dr. Fatih ÖZALTIN
Director, HÜGEN
(Hacettepe University Genome Sciences and Rare Diseases Application and Research Center)

Specialist Dr. Rahşan ÇINAR
Unit Supervisor, Department of Child and Adolescent Health
General Directorate of Public Health, Ministry of Health of the Republic of Türkiye

Deniz ATAKAY
President, Rare Diseases Federation

Preventive Approaches and a Holistic Financing Model

The issue of financing and funding was discussed in detail during the previous panel. However, I would particularly like to emphasize that the issue is not merely about allocating resources to innovative therapies. We would like this fund to be designed as a comprehensive structure encompassing preventive medicine, preventive approaches, public awareness, education, and effective communication. In fact, this is a shared expectation among all of us.

Innovative solutions and therapies are undoubtedly of great importance. However, our primary responsibility is not only to advocate for access to existing and innovative treatments but also to implement measures that will reduce, as much as possible, the likelihood of new children being born with preventable rare diseases. In other words, we must adopt not only a therapeutic perspective but also a preventive one.

Being solution-oriented is the key issue here. It is not enough to manage existing challenges; we must also prevent future ones from arising. For this reason, strengthening preventive healthcare services should be one of the most fundamental priorities of the system.

You may have seen the rare diseases exhibition outside. That exhibition depicts, in essence, a "country of rare diseases." It contains diagnosis, treatment, and hope; but it also reflects loss, despair, and loneliness. Yet when we listen to the discussions taking place here today, it is possible to see that meaningful progress is being made toward changing this picture. Personally, I believe that we have achieved very important gains today.

From this perspective, I would like to state clearly that, as a representative of a federation that approaches this issue from a newborn-health perspective, we must first and foremost focus on ensuring that children begin life in the healthiest possible way. Accordingly, I would like to emphasize that implementing newborn screening programs on the broadest possible scale is one of the most concrete and effective steps that can be taken in this field.

Prof. Dr. Mehmet GÜNDÜZ
Ankara Bilkent City Hospital

Concerns Regarding Preventive Healthcare, Screening Programs, and the Scope of the Fund

The primary reason I may appear hesitant about the proposed fund stems from certain concerns regarding how it will be structured. Will preventive healthcare services be included within this framework? Will there be a research and development component? If the fund is designed solely around innovative therapies and reimbursement mechanisms, then the issue must be viewed from a different perspective. My main concern relates to how the process will be managed.

At present, discussions appear to be focused largely on treatment and reimbursement. However, the preventive healthcare dimension, as well as awareness and education efforts, are equally important. When these aspects are not adequately addressed, the reality of out-of-pocket healthcare expenditures emerges directly before us.

Looking at 2024, out-of-pocket healthcare expenditures reached approximately TRY 500 billion. Consider, for example, an infant only a few months old, born into a family in which three cousins share similar genetic conditions. The child presents with symptoms such as spasticity and hypotonia and is referred to various centers, yet no diagnosis can be established. In such a case, a genomic sequencing analysis is required to reach a genetic diagnosis. Today, the cost of such testing is approximately USD 1,000, equivalent to around TRY 40,000–45,000.

Given income levels and household budgets in Türkiye, such an expense represents a significant source of uncertainty for many families. When healthcare expenditures increase by as much as 40% of a household budget, this is defined as a "catastrophic health expenditure." Therefore, a financing approach focused solely on treatment may deepen rather than solve the problem.

What we have emphasized from the very beginning is the need to strengthen preventive healthcare services. Within this framework, newborn screening programs play a particularly critical role. As someone involved in coordinating these efforts, I can say that six diseases are currently included in the screening program. Conditions such as Cystic Fibrosis and Congenital Adrenal Hyperplasia have been incorporated. However, progress beyond this point has been difficult, and the inclusion of additional diseases in the screening program is proceeding quite slowly. The scope of screening must be expanded.

We must move diagnosis to the earliest possible stage. In fact, we should not limit this process solely to the postnatal period; the development of prenatal screening programs is equally important. This would enable us not only to

identify existing patients earlier but also to reduce the risks that families may face in the future.

When we turn to the reimbursement landscape, a different picture emerges. It has been stated that the proportion of Social Security Institution (SSI) spending allocated to rare disease treatments has reached 12%. However, last year only a single infusion/emulsion-based therapy was added to the reimbursement system. The absence of any additional new therapies entering the system is concerning.

This compels us to ask a fundamental question: Are we failing to manage our resources effectively, or are we failing to manage the disease itself? Most likely, deficiencies exist in both areas. We must manage both the disease burden and our limited resources in a far more effective and balanced manner.

I view rare diseases as a public health issue. They should be approached from this perspective, and an action plan should be developed accordingly. In this regard, I consider the coordination structure under the Presidency to be extremely valuable. Through the establishment of a high-level council and expert guidance, it will be possible to define clearer rules and priorities.

The risks are particularly high in regions where consanguineous marriages are common. In these areas, recessive gene carriage represents a serious concern, and concrete measures must be taken to address it. Just yesterday, a family came to me regarding Tay-Sachs disease and said, "Doctor, we looked into it and were told that nothing can be done." Our role should be to intervene before families ever reach that point.

To be frank, consanguineous marriage is not the sole determining factor. When one examines the genetic pool in Türkiye, the carrier risk remains relatively high even among individuals from different cities. In other words, this is a risk that concerns everyone.

For this reason, the course of action is clear: screening programs must be expanded without delay, and carriers must be identified at an early stage. Rather than directing all resources solely toward treatment, we must place greater emphasis on preventive healthcare services.

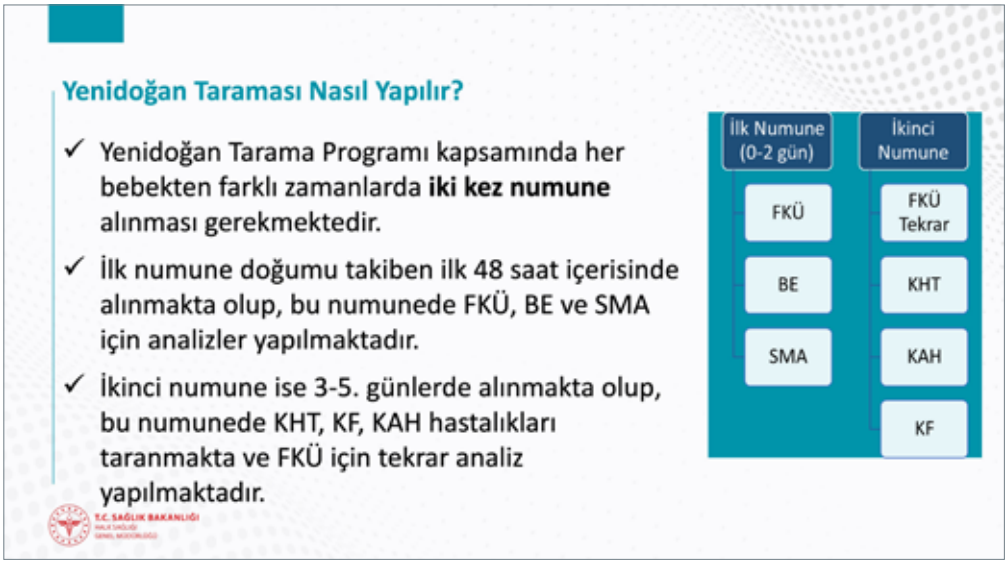
This is particularly important because the world is advancing rapidly, from small-molecule therapies to gene-editing technologies. To keep pace with these developments, we must first focus on the right priorities.

Specialist Dr. Rahşan ÇINAR
Unit Coordinator, Department of Child and Adolescent Health
General Directorate of Public Health, Ministry of Health

Newborn Screening Program and Premarital Screening Program

Our department carries out numerous initiatives under the frameworks of childhood and premarital screening programs. As our Minister and Director General mentioned during the morning sessions, a wide range of activities are currently underway. I would like to focus specifically on the latest developments concerning the Newborn Screening Program.

As you know, six diseases are currently screened on a routine basis. I would particularly like to emphasize the following point regarding the process: samples are currently collected twice from every newborn. Different diseases are analyzed from the first sample and the second sample.



I highlight this specifically to raise awareness because, under our current circular, if the first sample is collected before the infant has been adequately fed, a repeat blood sample is often referred to as a duplicate collection. However, this does not fully reflect the current practice. Within the scope of the Newborn Screening Program, two samples must be collected from every infant at different time points.

Our screening tests are conducted in the Ministry's Newborn Screening Laboratories, one located in Istanbul and the other in Ankara. If any suspicious findings are identified through these analyses, we rapidly contact the family through family physicians, arrange for a repeat sample if necessary, or refer the infant to the appropriate specialist centers.

When we examine our screening rates, we have maintained a success rate of approximately 97% in recent years. Annual referral and patient statistics are also available on our website. According to the data published there, we identify approximately 17,000 suspected cases each year, and nearly 5,000 of these are directed toward definitive diagnosis and treatment processes.

To manage this process, we utilize a robust web-based module. This module functions as an integrated platform connected with multiple systems, including birth notification systems, the newborn hearing screening program, and the Family Medicine Information System (AHBS) used by family physicians. Through this platform, provincial health directorates and authorized healthcare personnel in hospitals with high birth volumes are able to monitor the process in real time.

The monitoring mechanism within our system operates with a very high level of rigor. For example, if a report has been created for an infant in the Birth Notification System but Newborn Screening has not yet been performed, the system immediately generates a list of such infants for our review. Similarly, if an infant has completed hearing screening but has not yet had a heel-prick blood sample collected, the case appears on a separate list of "infants who have undergone hearing screening but have not yet had a heel-prick blood sample collected."

In addition, while each infant's results are automatically displayed through the family physician's software interface, families can also access these results through e-Nabız, particularly via the mother's profile. Within the web module we use, there are alert lists represented by different colors, including:

- Infants under follow-up,
- Referred infants,
- Infants requiring repeat sampling,
- Infants whose samples have not yet reached the laboratory.

These lists are reviewed every morning by our provincial directorates, and each infant is followed up individually. I should emphasize that a great deal of effort is invested behind the scenes by a dedicated team working on this process.

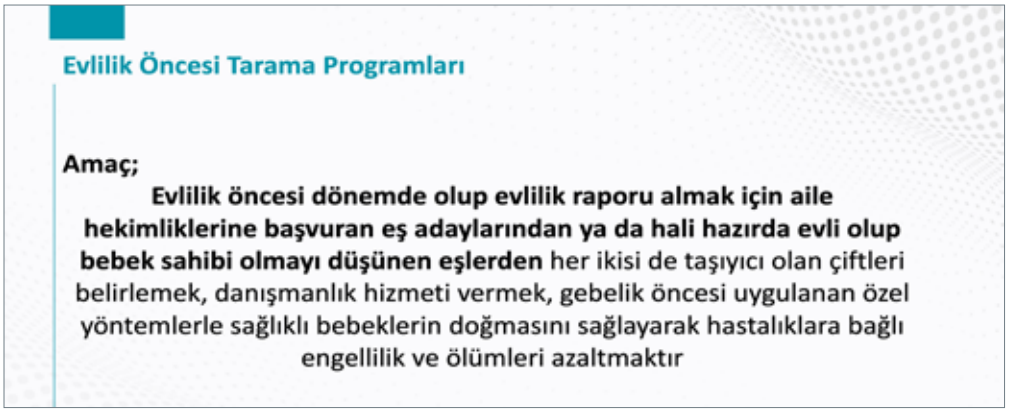
In the past, before integration with e-Nabız, we only contacted families when a suspicious finding was identified or when a repeat sample was required. Families whose results were normal were not informed of the outcome. Today, thanks to this integration, all families are able to view their results through e-Nabız.

Occasionally, physicians contact us because they are unable to locate the results in e-Nabız. There is a small technical detail involved here: during the newborn period, the infant may not yet have an individual Turkish identification number or a personal e-Nabız profile. For this reason, results are currently provided through the "My Tests" section of the mother's profile. Families can easily access screening results there.

As our Minister noted earlier this morning, there has unfortunately been an increase in screening refusals in recent years. Looking at data from 2024 and 2025, we can clearly see that this trend is directly affecting our overall screening rates.

So how frequently do we encounter these refusals, and on what grounds? When we review comments on social media, incoming emails, and petitions submitted through CİMER, we encounter a surprisingly widespread range of misconceptions and misinformation. Families contact us claiming that heel-prick blood samples are being sent abroad, that our genes are being manipulated, or that children are being labelled as ill and made dependent on medication. Some even refuse screening on the grounds that it allegedly threatens newborns' physical and mental well-being, damages reproductive organs, carries a high risk of infection, or that the blood is being sold abroad by the state for financial gain. Others cite highly implausible claims, such as the search for "blue blood," as reasons for refusing screening.

This is precisely why awareness is so critical. To combat this misinformation, we worked with experts to develop dedicated educational videos for each screened condition. These videos have been uploaded to our websites for both healthcare professionals and the general public and shared with all relevant stakeholders. Anyone who wishes can access and benefit from these resources. We have also prepared a dedicated video addressing consanguineous marriage and incorporated it into the system.



However, we know that simply uploading videos to a website does not create awareness on its own. We are also carrying out a comprehensive, multi-faceted effort in the field:

- **Directorate of Religious Affairs:** In order to increase participation in premarital screening programs, we requested support in emphasizing the importance of these programs during Friday sermons, particularly by addressing male audiences. Fortunately, they have been very supportive in this regard.
- **Ministry of Interior:** We are working to ensure that every couple visiting marriage registration offices receives this information. Couples are reminded that they should visit their family physician and undergo these screenings, and that failing to do so may lead to difficulties during official procedures.
- **Ministry of Family and Social Services:** We are incorporating information on these screening programs into premarital education initiatives offered to prospective spouses.

Through this interinstitutional collaboration, we aim to identify rare diseases at the earliest possible stage and to eliminate the misconceptions that persist within society.

Our educational activities are not limited to digital platforms; we are striving to integrate them into every aspect of daily life. We have incorporated these screening programs extensively into educational activities provided both

to women planning a pregnancy and to those who are already pregnant through antenatal classes. We address the importance of newborn and premarital screening programs through every available media channel, ranging from health-focused television programs to lifestyle and entertainment shows. Most recently, the topic received dedicated attention on Ebru Şallı's television program.

To increase the impact of these efforts, we are currently working on integrating these messages into the storylines of popular television series. As we emphasized yesterday, the Ministry of Health is making a substantial effort in this area; however, if we are truly seeking societal awareness, we must act collectively.

Raising awareness among public sector employees is also one of our priorities. For this purpose, we have developed a training module through the Presidential Human Resources Office's Distance Learning Gateway (CBİKO). In the near future, all public employees will be required to complete this training. Is this sufficient on its own? In my opinion, no. Whether among public employees or patient organizations, these awareness initiatives must continue through collaboration and be sustained over time.

I would also like to briefly address the operation of our premarital screening program. Couples applying to family physicians for a marriage health report, as well as married couples planning to have children, first receive counseling and are then referred for screening services. Within this framework, we conduct screening for both hemoglobinopathies and Spinal Muscular Atrophy (SMA) carrier status.

To provide some figures, the hemoglobinopathy screening program was launched nationally in 2018, while the SMA carrier screening program reached nationwide implementation on 27 December 2021. We have currently established regional laboratories for SMA screening in Adana, Antalya, and Eskişehir. Together with our central laboratory in Ankara, we are operating through four major centers and are continuing efforts to expand this number to eight. Samples from all 81 provinces are collected and processed through these centers. An important detail is that the SMA screening program begins by collecting a sample from the prospective male partner in each couple.

In the SMA screening process, testing starts with the sample obtained from the male partner. As mentioned, analyses are conducted meticulously at both our regional laboratories and our central facility. Hemoglobinopathy screening, on the other hand, is carried out through public health laboratories located in every province.

I would particularly like to emphasize that identifying carrier status in a couple does not constitute a barrier to marriage. However, when carrier status is detected, we provide comprehensive counseling. If couples wish, we direct them to specialized options such as Preimplantation Genetic Testing (PGT) before pregnancy to help them have a healthy child and to prevent the birth of affected infants. In addition, we have expanded access to adult screening test results through e-Nabız.

Expanded Newborn and Premarital Screening Programs

Looking ahead, both the 12th Development Plan of the Presidency and the Ministry of Health's Strategic Plan include provisions aimed at increasing the number of diseases covered by screening programs. Our Rare Diseases Strategy Document and Action Plan also contain concrete objectives related to expanding screening programs and strengthening awareness activities.

We have undertaken an extensive preparation process for the Expanded Newborn Screening Program. Pilot studies and workshops were conducted in previous years, and most recently, in 2024, a steering committee was established for this initiative. Shortly thereafter, we formed a comprehensive Scientific Commission for both newborn and premarital screening programs. Through the subgroups established within this commission, we completed the technical evaluations necessary to determine which diseases should be included in the screening framework.

At the current stage, we have submitted our final report, including the proposed diseases and all associated technical details, to the relevant authorities. We are now awaiting implementation instructions. In the meantime, we are not standing still; we continue to strengthen our laboratory and software infrastructure for the expanded screening program and are working intensively to ensure that the system is fully prepared for implementation.

Prof. Dr. Fatih ÖZALTIN
HÜGEN Director

The Real Challenge in Rare Diseases: Coordination or Prevention?

First of all, I would like to sincerely thank all participants who have stayed with us and listened attentively until this hour. We have had a very intensive day filled with discussions that were, at times, quite lively. Frankly, I wish the panels had been more focused on questions and answers so that we could have developed a more concrete roadmap from these discussions. Each topic truly deserves extensive debate.

For future meetings, I would like to suggest a more interactive format, with greater emphasis on discussion, questions and answers, and tangible outcomes.

One observation I have made is that every institution does an excellent job of presenting its own work, and there is clearly a tremendous amount of effort being invested. I have no objection to that. However, the reality remains that the burden of rare diseases in Türkiye has not diminished. This indicates that something is still missing. In particular, there appears to be a significant challenge regarding coordination.

Everyone is undertaking valuable initiatives within their own sphere, but there is still a lack of sufficiently strong communication, a shared language, and a culture of collaborative action across institutions. As a result, the impact of these efforts in practice remains limited.

For hours we have been discussing financing—funds, resources, and various models. However, in my view, the fundamental question is this: if affected children are not born in the first place, then such an enormous financing burden would not arise. Therefore, the question of "What can we do to prevent the birth of affected children?" should have been discussed much earlier and with much broader participation.

Once a child is born, refusing treatment is not an option. That child must receive treatment, and the necessary resources must be found. The child did not choose to be born. The situation may have arisen because of an oversight, a deficiency, or a weakness within the system. Regardless, there is an innocent individual at the center of this issue, and we all have a responsibility to defend that child's rights.

We can say that our infrastructure is strong, our systems are advanced, and e-Nabız functions effectively. All of that may be true. However, if the child ultimately cannot access treatment, then these statements have little meaning in practice. That is why we must return to the same question: How can we prevent these children from being born with disease?

The rate of consanguineous marriage remains high in our society. This is a reality. We know that the majority of rare

diseases are genetic, although it is important to remember that not all of them are. There are rare diseases caused by infections, and there are oncological rare diseases as well. Patients affected by these conditions also have the right to access treatment.

However, in genetic disorders particularly, our population structure contributes to a higher prevalence of recessive diseases, which are most often encountered during childhood. At the same time, there are also genetic diseases that emerge during adulthood. In other words, this is a broad and highly complex issue.

For that reason, it is impossible to address the problem from a single perspective. Each topic deserves detailed discussion in its own right.

Without prolonging my remarks, I would like to emphasize that the ideal solution is, of course, the prevention of consanguineous marriages. Significant steps are needed in both public awareness and legislation in this area. More importantly, however, we must leave this meeting with a practical and actionable plan.

I believe a very practical step could be taken by creating a "Genetic Disease Risk Assessment Checklist." Couples receiving premarital counseling could complete this assessment, allowing for evaluation of potential hereditary genetic or metabolic disease risks.

Based on the results, couples could be assigned a risk score. If that score exceeds a predetermined threshold, the state could routinely offer Whole Exome Sequencing (WES) or the more cost-effective Clinical Exome test.

In reality, integrating such an approach into the existing system would not be difficult. Just as phenylketonuria screening has become a standard practice today, these tests could similarly become a routine component of healthcare services.

Such a model would allow resources to be used in a more targeted manner while providing an opportunity to prevent disease before it emerges in high-risk families.

When discussing costs, it is useful to consider concrete figures. We often say that whole genome sequencing costs approximately USD 1,000 in commercial laboratories, but clinical exome testing has already fallen to the range of USD 500–600. Through public procurement and negotiated pricing, this figure could potentially be reduced to around USD 400. Within our own scientific projects, we are able to perform whole genome sequencing at approximately USD 500.

Now let us compare these figures with treatment costs. As one of our colleagues mentioned yesterday, a single medication used in rare diseases can cost around USD 1 million. This means that the cost of treating a single patient could instead finance whole genome sequencing for 2,000 individuals at USD 500 per test, or for 1,000 individuals at USD 1,000 per test.

If carrier status can be identified in either parent from the outset, the necessary precautions can be taken in advance. Disease can potentially be prevented before birth. This is a far more appropriate approach, both from a humanitarian and an economic perspective. We are not talking about interfering in people's lives; we are talking about providing informed choices. Through methods such as Preimplantation Genetic Testing (PGT), couples can make well-informed decisions.

We are not saying, "Do not get married." Of course they should marry. However, if a consanguineous marriage is planned, the associated risks should be understood and appropriate precautions should be taken. The objective is to prevent the birth of affected children.

Today, we possess extremely powerful technologies, and costs have fallen dramatically. Five or ten years ago, discussing such figures would have been unimaginable. Today, exome sequencing can be performed for approximately USD 300–400, allowing us to map a family's genetic risk profile. Once those risks are identified, appropriate genetic counseling can be provided, and couples can manage the process through options such as PGT.

This is the aspect we should be discussing more extensively. Once a child is born, there is no turning back; treatment becomes the only option. Treatment is both costly and challenging. Nevertheless, access to treatment is a fundamental right, and the state cannot simply claim that resources are unavailable.

Moreover, this is not a challenge unique to Türkiye. These therapies are expensive worldwide. The same discussions are taking place in the United States and across Europe. No one is suggesting unlimited spending; rather, the focus is on finding ways to make these costs more sustainable.

Accordingly, we must develop a solution tailored to our own realities while addressing this global challenge. Whether a fund is established, how it is governed, and which institution oversees it are all matters open to discussion. However, the first requirement is a solid legislative framework. No model can be sustainable without a clear legal foundation.

At the same time, effective resource allocation requires a strong coordination mechanism. A clearly mandated body operating under the Ministry of Health is essential. Within this structure, three core units should work together:

- **Planning Unit:** Responsible for strategy development and policy formulation.
- **Implementation Unit:** Responsible for translating decisions into practice.
- **Data Analysis Unit:** Responsible for collecting, analyzing, and continuously monitoring data and system performance.

In addition, the pathway following diagnosis must be clearly defined. Which center will the patient attend? Where will treatment be delivered? Who will make treatment decisions? All of these elements must be specified. To achieve this, Reference Centers and Centers of Excellence should be established.

Any financing model that is created should operate through these centers rather than through fragmented decision-making processes. Individual institutions should not independently decide to initiate treatment. Diagnostic and treatment decisions should be approved through designated centers, and funding should be allocated accordingly. Only through such a structure can resources be managed both efficiently and equitably.

Frankly, establishing such a system is not impossible. The only requirement is a genuine commitment to focus on the issue and to work in a systematic and determined manner.

CONCLUSION

Türkiye possesses a highly qualified workforce and a robust health data infrastructure, exemplified by systems such as e-Nabız. If this potential is combined with a sound legal framework, experience gained through pilot implementations, and strategic human resource planning, the burden of rare diseases can be reduced significantly and sustainably. More importantly, achieving positive outcomes in the field of rare diseases—as in all areas—requires a value-based approach focused on healthy generations and increased public awareness. In this regard, alignment, cooperation, and coordination among all relevant institutions and stakeholders are of critical importance.

This workshop has provided a valuable platform for collaboration among stakeholders, helping to share and alleviate the treatment-related and social responsibilities associated with rare diseases and rare lives.

As we look forward to coming together again at the 3rd Summit in 2027, we would like to extend our sincere thanks to everyone who contributed to this meeting and reiterate our commitment, together with all participants and stakeholders, to following up on and advancing the outcomes generated through these discussions.

Deniz ATAKAY
President, Rare Diseases Federation

RARE DISEASES FEDERATION

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