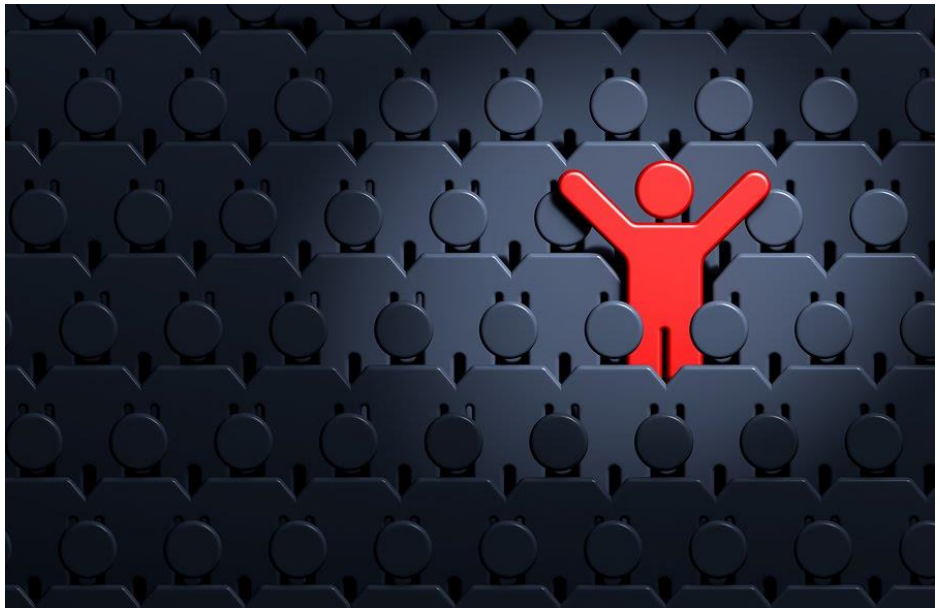
European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

NBS of INHERITED METABOLIC DISEASES AS A SYSTEM TODAY AND IN THE FUTURE

MAURIZIO SCARPA,
Coordinator MetabERN
Regional Coordinating Center for Rare Diseases,
University Hospital Udine, Italy

WHY NEWBORN SCREENING?

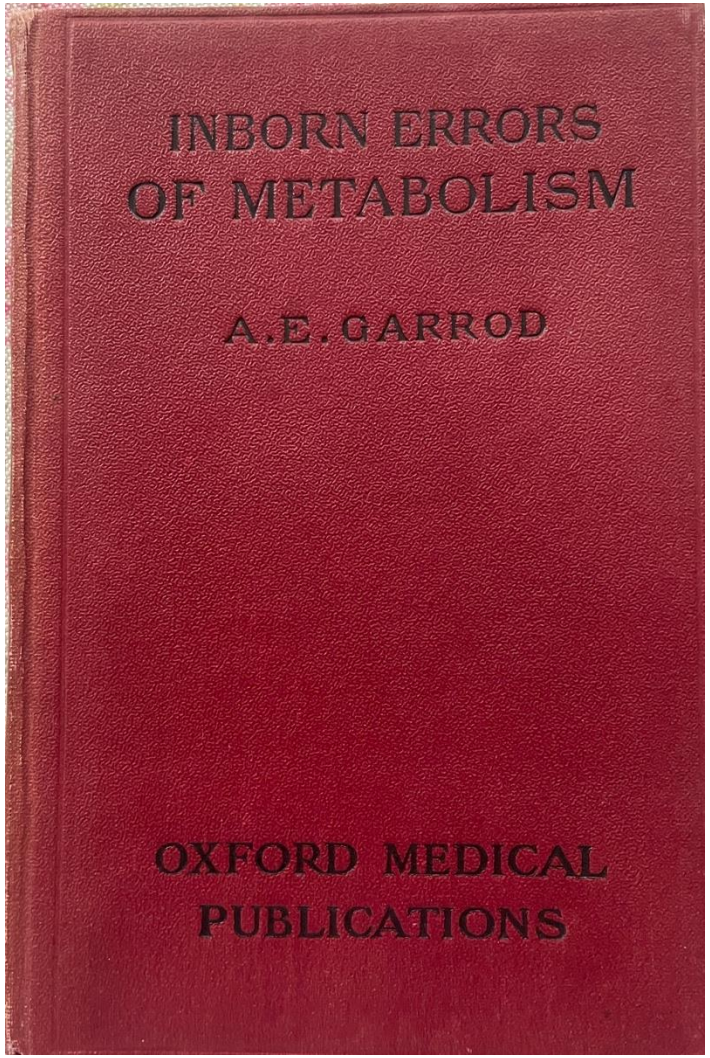
- Rare diseases are common ! – individually these disorders are rare (with fewer than 1:2,000 people affected) but with more than 9,000 rare disorders described, collectively they are common and affect more than 30 m of our people in the EU
- The best outcome can be achieved if they are recognised early in life and proper treatment begins before the child is damaged
- This is also often the most cost effective way to diagnose and treat these conditions avoiding a long and difficult journey for the family
- So how do we detect the conditions early when they are often unfamiliar, even to the well trained family doctor?
- Firstly raise awareness but more practically and if there is a good, simple and inexpensive test – test shortly after birth before the baby shows any sign of the disease

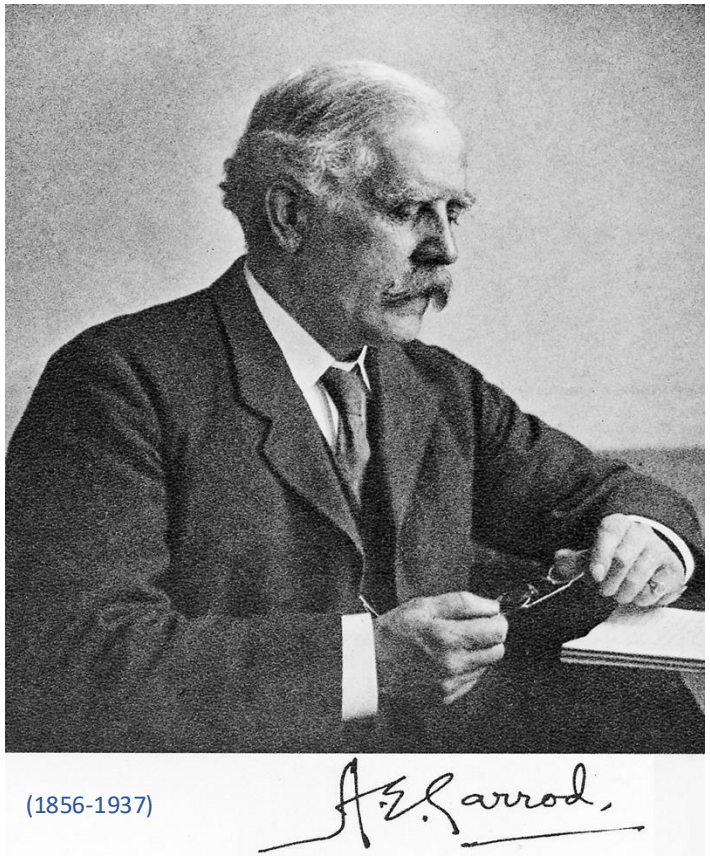


European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

INBORN ERRORS OF METABOLISM

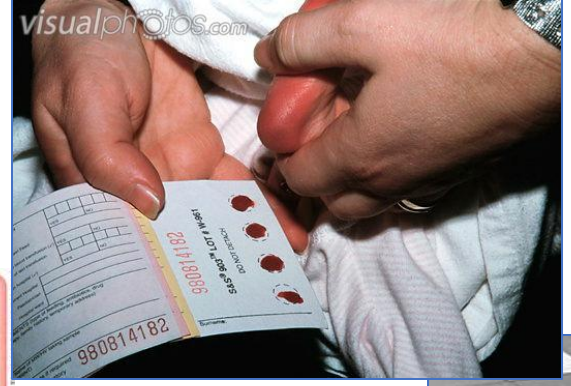
- Name proposed by Sir ARCHIBALD GARROD in 1908
- Observations about 4 disorders, with recurrence in families:
  - Alcaptonuria, Pentosuria, Cystinuria and Albinism
- Investigated urine chemistry as a reflection of systemic metabolism and disease
- In 1923 he wrote his best known work:
  - „INBORN ERRORS OF METABOLISM“

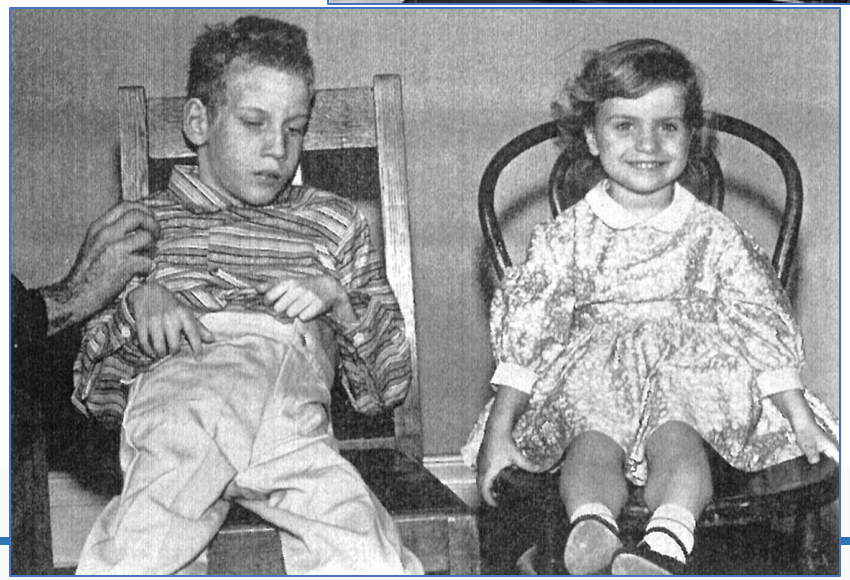


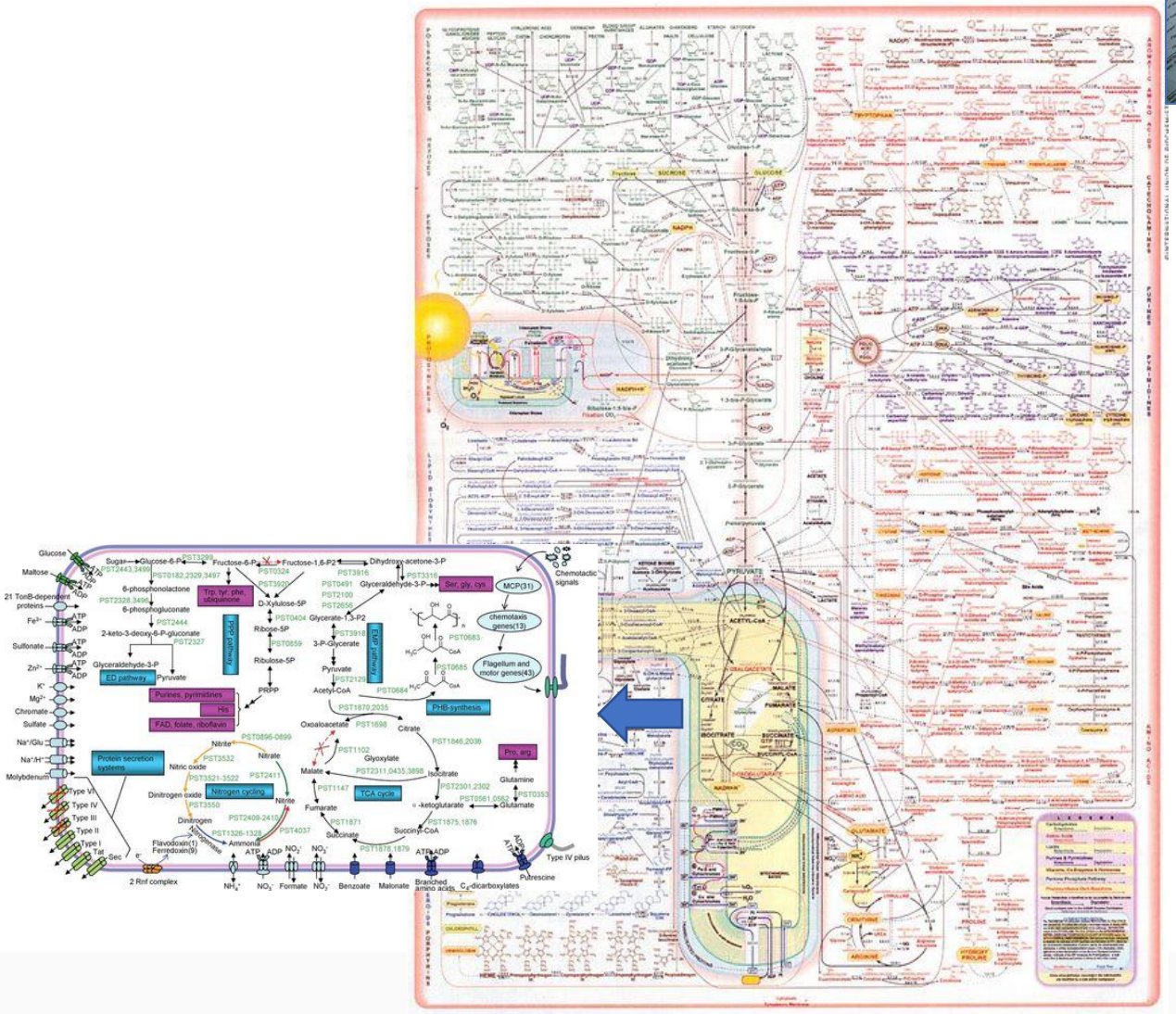


(1856-1937)

METABOLISM TODAY
>1400 diseases





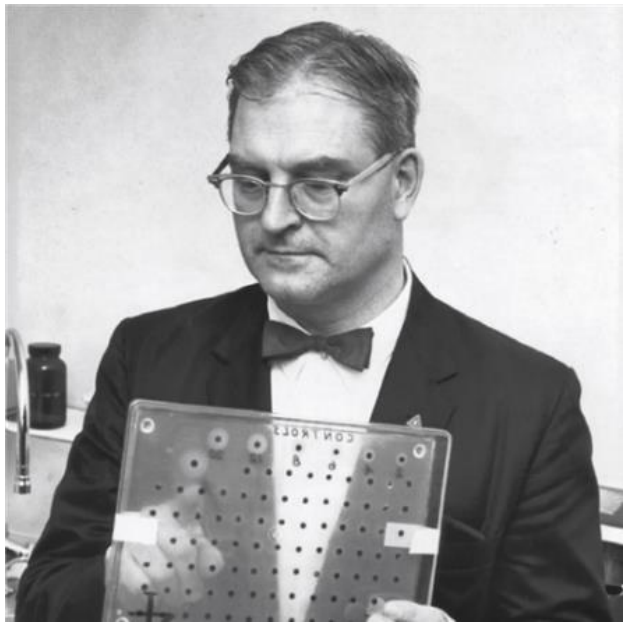


European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

WE HAVE MUCH TO CELEBRATE !

- 2023 marked 60 years since Dr Robert Guthrie described a test to detect phenylketonuria (PKU) shortly after birth
- Since then it is estimated that worldwide approximately 750 million babies have been screened and more than 60,000 children with PKU have benefited from this life changing intervention
- It did not stop with PKU, first conditions one by one and then, one generation on, MS/MS in the mid -1990's
- Today almost 70,000 babies are identified and treated each year as a result of NBS
- This led many around the world to describe newborn screening as: **'One of the major Public Health Advances of the 20th Century'**
- So where are we now in Europe?



screen4rare

ISNS International Society for Neonatal Screening

Kindly from J.Bohnam, ISNS

DESPITE THIS SUCCESS WE NEED TO BE CAREFUL

- Of course as in most of medicine, there is a balance and sometimes difficult choices to make
- The patients/families believe themselves to be well and this gives us a particular burden of responsibility
- "All screening programmes do harm; some do good as well, and, of these, some do more good than harm…." *Gray, BMJ (2008) 336:480*
- More screening does not mean better screening
- Screening which is well organised and delivered as a carefully monitored programme linked to structured treatment is most effective and brings most success

HISTORICAL CONTEXT

- Newborn screening began in the 1960s with the introduction of tests for phenylketonuria (PKU). Over the decades, advancements in biochemical methodologies, such as tandem mass spectrometry (MS/MS), have allowed for the expansion of screening panels to include numerous IMDs. Currently, NBS programs vary significantly across countries, with some employing extensive biochemical testing while others have begun integrating genetic testing.

TRADITIONAL SCREENING METHODS

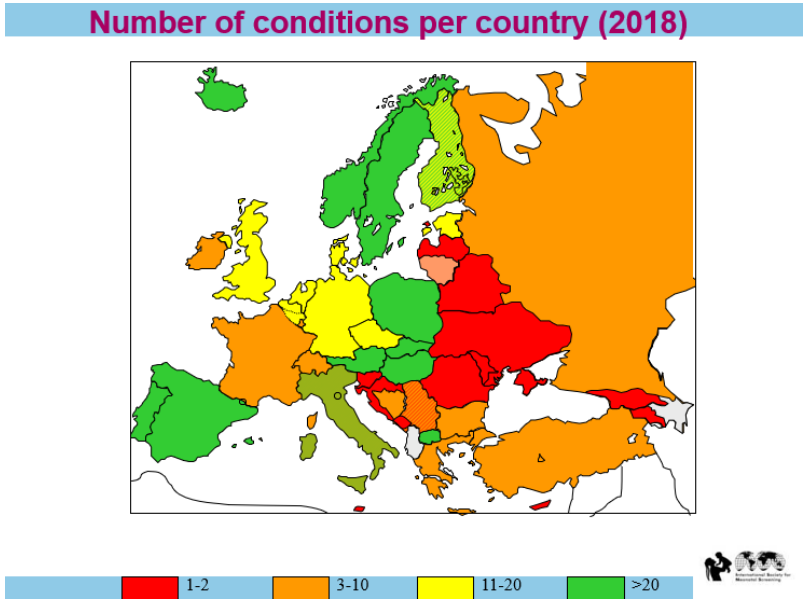
- **Biochemical Assays**: These methods measure specific metabolites in dried blood spots to identify metabolic disorders.

- **Tandem Mass Spectrometry**: A widely adopted technology that allows simultaneous analysis of multiple metabolites, improving efficiency and reducing costs.

- **Genetic Analysis:** a relatively new technology applied to mass testing allowing simultaneous analysis of genes up to WGS, improving efficiency but still with elevated costs

WHERE ARE WE IN EUROPE?

- The conditions that we have chosen to screen
  - *Neonatal Screening in Europe Revisited: An ISNS Perspective on the Current State and Developments Since 2010 J. Gerard Loeber et al (*Int. J. Neonatal Screen. 2021, 7, 15. https://doi.org/10.3390/ijns7010015
  - Still shows considerable variation in practice both in the way that newborn screening is conducted and the number of conditions screened.
  - *Number of conditions* 2 - 48 conditions screened in different countries in Europe



- The way in which we conduct screening

Day of sampling	24h – 120h
Sampling to analysis	1-2d, to 30d
Screening is optional or compulsory	30 optional, 17 compulsory
Informed of the outcome of screening	30 No, 10 Yes
Consent to storage	34 – No, 10 - Yes

Difference
Difference
Difference

Kindly from J.Bohnam, ISNS

European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

NEWBORN SCREENING AS A FULLY INTEGRATED SYSTEM TO STIMULATE EQUITY IN NEONATAL SCREENING IN EUROPE

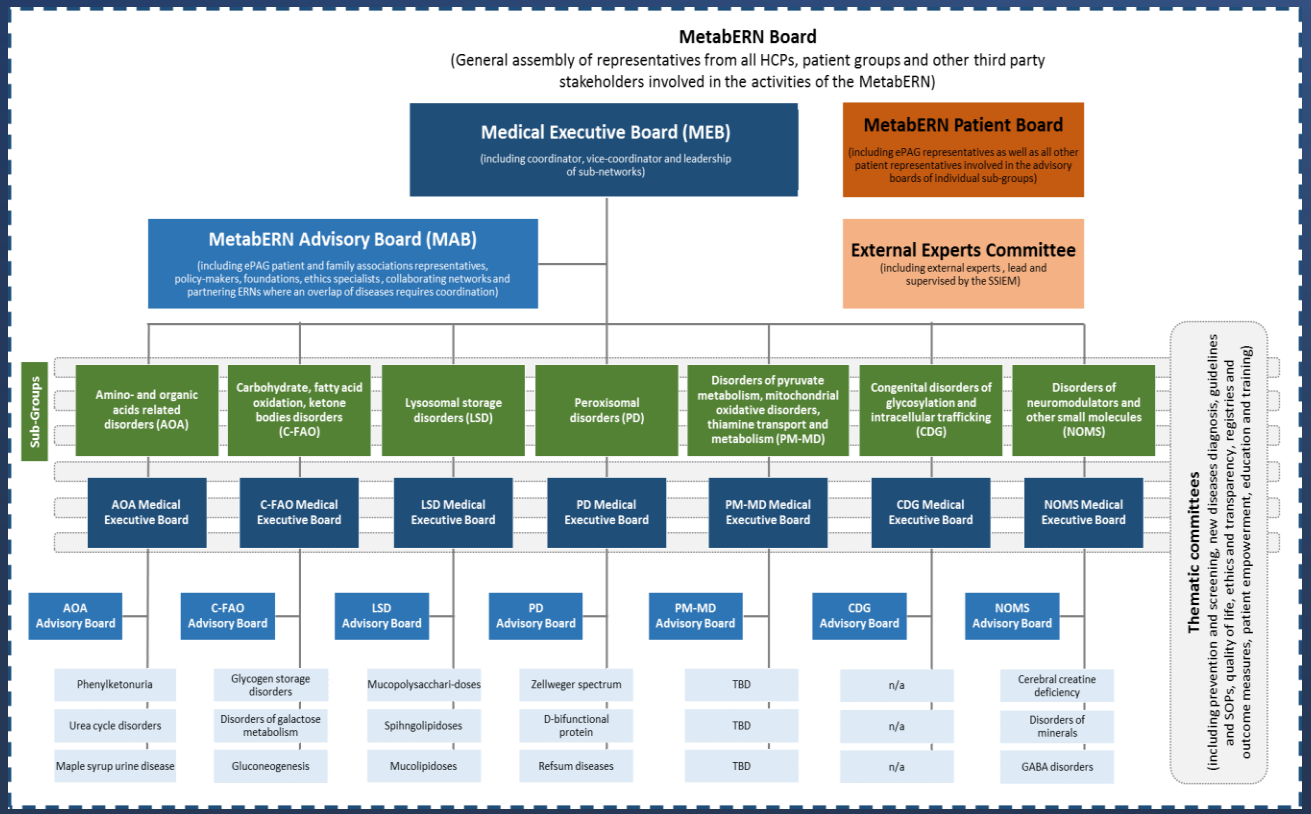
POSITIVE EFFECTS Fundamental for early diagnosis of some rare disorders, can be life-changing since it permits the early delivery of appropriate therapy, preventing long-term disability or even premature death

NEGATIVE EFFECTS Causes harm, e.g. by medicalising families who receive a false positive result or by over-treatment of children with an ambiguous or mild phenotype

MetabERN

78 HCPs from 23 countries

94 HCPs from 27 countries with the inclusion of the new full Members in January 2022)
44 Patient Organizations



MetabERN:
How we share, how we care

Prevention

- Increase **awareness** amongst general public and Health care professionals, health authorities and relevant stakeholders on inherited metabolic disease (IMDs)
- Dissemination of new and revision of existing health information, **scientific publications**

Screening

- Facilitate and harmonise the **newborn screening** in EU
- Use of the Unified-IMD registry to study the **natural history** of asymptomatic and symptomatic state of diseases

Diagnosis

- Enhance speedy **diagnosis** by promotion of diagnostic expert consultation (CPMS) and training sessions
- Improve access to the best diagnostics (biochemical/genetic) and to **genome-wide genetic investigations** through active collaboration with Orphanet and ERNDIM

Treatment & Facilitation of access to the best diagnostics

- Revise/develop of **Care pathways & Guidelines**
- Facilitate **Clinical Trials/Research** (defining research priorities and disseminating research-related information)
- **Create big databases with patients data**
- Improve the Regulatory process for medicines
- Participate in the production of White papers and Recommendations

Follow up

- Assess the effectiveness and efficiency of clinical processes
- Develop a common programme on **Transition from childhood to adulthood**

Education and Training needs

- Participate in and provide input and insights from patients and HCPs in **Education of patients**
- **Instruct general practicioners** on how to follow patients
- Promote the MetabERN Education website (https://metab.ern-net.eu/) dedicated to **capacity-building, education & training.**

Social framework

- Share the **'Quality of Life'** surveys and outcomes measurement
- Facilitate the provision of social care services

Inclusiveness

- Continue collaboration with **other ERNs** through the ERN-Coordinators Platform (on a strategic level) and through on-going consultations with overlapping networks (at a practical level)

Patient Empowerment

Recent achievements to start the journey:

- A dedicated group on **patient empowerment** has been established
- The **Patient Board governance structure** is up and running including the Patient Executive Committee (PEC). The PEC is the voice of all patient representatives involved in the subnetworks and Work Packages in order to improve their involvement and enable their feedback to be heard by HCPs.
- Patients have been involved in addressing their **specific needs, preferences and priorities** (Survey, feedback systems, etc.)

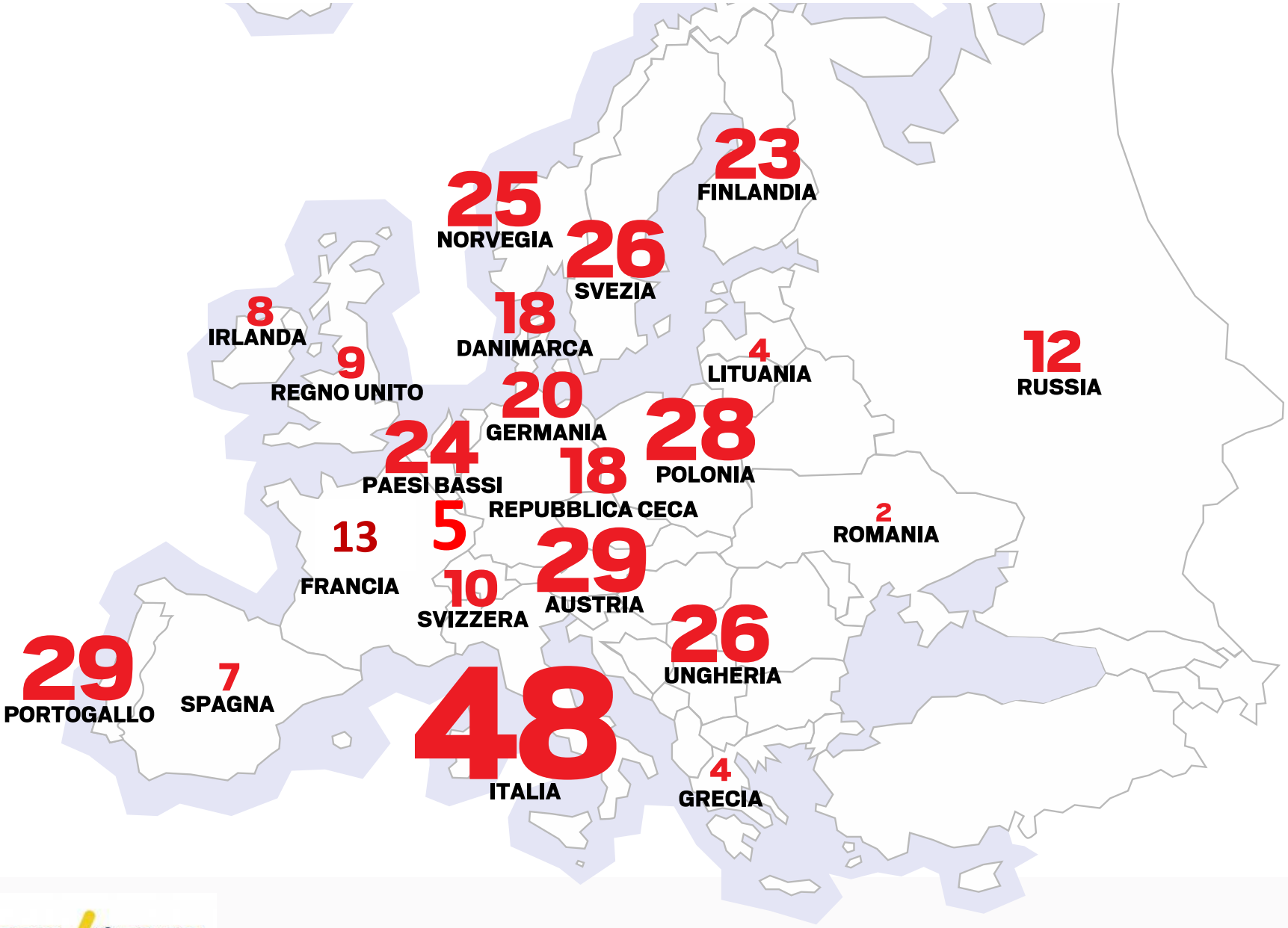
ALL WITH ONE GOAL IN MIND: OUR PATIENTS!

Go FAIR: UIMD Unified Registry for Inherited Metabolic Disorders as a model for collaborative research

F – findable
A – accessible
I – interoperable
R – reusable

Module 1 **Common data elements**	• **Common Data Elements** (JRC) • **IEMbase** nosology • **Orphanet** and **OMIM**
Module 2 **Clinical & cognitive phenotype**	• **Human Phenotype Ontology (HPO)** • **Standard IQ tests**
Module 3 **Patient perspective**	• **PedsQL** • **WHOQOL**
Module 4 **Treatment**	• **WHO ATC classification system**
Module 5 **Biochemical markers**	• **IEMbase:** selection of biomarkers • **Human Metabolome Database (HMDB)**
Module X **Newborn screening**	• Parameters for **diagnostic process quality**, **cost-benefit** and **cost-effectiveness** of NBS programs

European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)



The NBS of IMDs in Europe, an example to discuss

SSIEM ANNUAL SYMPOSIUM 2019
3-6 SEPTEMBER | ROTTERDAM, THE NETHERLANDS

ISNS
International Society for Neonatal Screening

European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

NBS collaborative meeting MetabERN & ISNS

Agenda:

11-12: Introduction

11:00-11.10: Maurizio Scarpa/Trine Tangeraas MetabERN:
Welcome and introduction (& points of discussion)

11.15-11.30: Gerard Loeber ISNS:

Screening practices in Europe 2018 –what has changed since 2009 and the 2010-2011 EHAC project

11.30-11.40: Jim Bonham ISNS

The points of agreement and potential barriers to achieving a European Screening Panel

11.45-12.00: Stefan Koelker MetabERN

U-IMD and its future role in NBS outcome studies

12:00-13:00: Discussion

EU2022.CZ

Czech Presidency of the Council of the European Union

European Reference Network
for rare or low prevalence complex diseases

Network Hereditary Metabolic Disorders (MetabERN)

PROGRAMME JULY 23, 2022

Time	Programme	Speaker
13:15 – 13:30	WELCOME	
	Prof. Vlastimil Válek, MD, PhD., MBA, EBIR (TBC) Minister of Health of the Czech Republic **Jakub Dvořáček MSc., LLM** Deputy Minister of Health of the Czech Republic **Lumír Kantor, M.D** (video presentation) Senate of the Parliament of the Czech Republic **Prof. Milan Macek Jr., MD., DSc.** National Coordination Center for Rare Disease **Prof. Viktor Kožich, M.D, CSc.** Coordination Center for Neonatal Screening **Ondřej Májek, RNDr. PhD** National Screening Centre, Institute of Health Information and Statistics of the Czech Republic	
13:30 – 15:30	**SESSION I. – NEWBORN SCREENING (NBS): A GATEWAY TO EARLY DIAGNOSIS** (CHAIRS: Dr. Gulcin Gulmus and Prof. Viktor Kožich)	
13:30-13:50	Overview of European NBS activities-synergies and overlaps	**Prof. Jim Bonham,** United Kingdom
13:50-14:05	Role of European Reference Networks for rare diseases in NBS	**Prof. Maurizio Scarpa,** Italy
14:05-14:20	Developing a blueprint of NBS in Europe: overview of workstreams	**Dr. Peter Schieler** The Netherlands
14:20-14:35	Key indicators for planning, monitoring and evaluation of newborn screening: international context and future perspectives for cooperation	**Dr. Ondřej Májek,** Czech Republic
14:35-14:50	The tower of Babel: why do we need case definitions?	**Dr. Rolf Zetterstroem,** Sweden
14:50-15:05	The key role of registries in assessing clinical outcome	**Prof. Stefan Koelker,** Germany
15:05-15:20	Experience with expanding NBS in Czechia	**Ms. Anna Arellanesová,** Czech Association for Rare Diseases, Czech Republic
15:20 – 15:45	**Coffee break**	
15:45 – 16:30	**SESSION II. – CURRENT EXPERIENCE AND FUTURE DEVELOPMENTS IN NBS** (CHAIRS: Ms. Anna Arellanesová and Prof. Maurizio Scarpa)	
15:45-16:05	Newborn screening: the perspective of people with RD and future potential	**Dr. Antoni Montserrat,** EURORDIS
16:05-16:20	The use of a patient management system to improve long-term outcome	**Dr. Rolf Zetterstroem,** Sweden
16:20-16:35	Screen4care EU IMI project	**Prof. Alessandra Ferlini,** Italy
16:35-17:10	Panel discussion (CHAIRS: Dr. Antoni Montserrat and Dr. Peter Schielen)	
	Ms. Martine Pergent IPOPI President/Screen4rare, France **Mr. Stelios Kympouropoulos** MEP (TBC) **Dr. Jose Valverde** European Commission, DG SANTE Unit B3 (TBC)	

July 23, 2022 Brno Technical meeting under CZ EU Presidency-
Early diagnosis of patients with rare disorders in the EU: crucial role of the newborn screening

screen4rare

European Reference Network | MetabERN
European Reference Network for Hereditary Metabolic Disorders

ISNS
International Society for Neonatal Screening

IPOPI
INTERNATIONAL PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES

European Reference Networks

RITA

European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

What have we achieved so far?

- Brought this together with the formation of Screen4Rare (comprising ESID, IPOPI, ISNS and the European Reference Networks) in 2020 with a dedicated website
- The formation of an EU Health Policy Platform
- The formation of an MEP Alliance including Roberta Metsola – the new President of the European Parliament – January 2022
- A series of high level meetings
  - The ERN Screening Group – 14th September 2021
  - This accompanying event of the Slovenian Presidency – 11th October 2021
  - 'Moving toward NBS as a System' – A special event at the ISNS European Symposium – 11th November 2021
  - Meetings in London, Turku and at the EU Parliament to celebrate 'International Neonatal Screening Day' – 28th June 2022
  - Appropriately as we consider Mendel's legacy, this event important supported by the Czech Presidency
- An impressive series of publications – such as the recent paper: Newborn Screening by Genomic sequencing: Opportunities and Challenges, Bick et al, Int J Neonatal Screen, 8, 40 part of a Special Issue in IJNS focusing on Newborn Screening in Europe.
- The aim is to form an Expert Screening Group in the EU with EC support

NOVEMBER 28-29 2022
MetabENR NBS MEETING
FRANKFURT

screen4rare

ISNS International Society for Neonatal Screening

European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

METABERN POSITION ON NBS

1. The NBS program should be regarded and implemented as an **integrated system**, not as a single, isolated test

2. The NBS system should **include the following key aspects**:

- Technical
- Ethical
- Logistical
- Educational
- Evaluation/quality improvement

3. The NBS system requires a **coordinated management**:

- Before birth
- After birth

→

- Testing and reporting
- Problem of false positives
- Follow-up and treatment of the affected child
- Family assistance & psychological support
- Long term follow-up and transition
- Maintaining records and using information exchange systems
- Integrating NBS modules in registries
- Overall integration of screening

International Journal of Neonatal Screening

MDPI

Review

Towards Achieving Equity and Innovation in Newborn Screening across Europe

Jaka Sikonja [1,2,†], Urh Groselj [1,2,*,†], Maurizio Scarpa [3], Giancarlo la Marca [4,5], David Cheillan [6], Stefan Kölker [7], Rolf H. Zetterström [8,9], Viktor Kožich [10,11], Yann Le Cam [12], Gulcin Gumus [12], Valentina Bottarelli [12], Mirjam van der Burg [13], Eugenie Dekkers [14], Tadej Battelino [1,2], Johan Prevot [15], Peter C. J. I. Schielen [16] and James R. Bonham [16,17,*]

Comment

The Lancet Regional Health - Europe 2022;13:

Newborn screening as a fully integrated system to stimulate equity in neonatal screening in Europe

Maurizio Scarpa,[a,] James R. Bonham,[b] Carlo Dionisi-Vici,[c] Johan Prevot,[d] Martine Pergent,[d] Isabelle Meyts,[e] Nizar Mahlaoui,[f] and Peter C.J.I. Schielen[g]*

European Reference Network for rare or low prevalence ... diseases

...k ...ary Metabolic ...rs (MetabERN)

1. Selection of (new) conditions in NBS panels should be based on published criteria, the proce- dures should be standardised, open to public scrutiny and the result of deliberations should be published.
2. Information (preferably communicated during pregnancy) describing the diseases to be tested and the implications of a positive result should be available to parents to permit an informed choice concerning participation.
3. Clear case definitions of the screened disorders should be determined when screening is being planned.
4. Screening should be undertaken in laboratories whose accreditation demonstrates compliance with international standards for laboratory perfor- mance (e.g., ISO15189).
5. Laboratories and programmes should be able to produce data on key performance indicators relat- ing to the entire NBS process, including blood sampling, transport conditions, blood spot quality, time to generate a laboratory result and refer screen positive cases.
6. Information should be available to parents at the time of clinical referral, the first contact should be with an experienced physician able to offer support, and, when appropriate, genetic counselling should be provided.
7. Confirmatory testing should be established and consistently applied with a short and defined turn- around time to allay parental anxiety and stress.
8. Plans to assess long term outcome data should be in place and reported.
9. Screen negative results should be reported to all parents and form part of the child health record.
10. Policies to store and access residual blood-spot samples should be defined and practice monitored. NBS programs should be coordinated, and perfor- mance managed on a national basis to encourage continuous improvement.

Moving towards NBS as a system: setting up the Roadmap

Secure European Funding

Involve national policymakers

- Mapping of and involving policymakers on the right level (national/federal, regional, medical associations)
- Find out what questions they have on NBS

Mapping of common diseases across Europe

- Identify common diseases in NBS-programmes across Europe

Share best practices

- Sharing of best practices by putting them in a repository in cooperation with Screen4Rare
- Using one or two existing models as examples of good practice for MS to learn from
- Identifying possible governance structures for NBS
- Lessons learnt from European research study on NBS

Define clear case definitions & unified terminology

- Confirmatory testing as a prerequisite for case definitions
- Encourage editors to scrutinize terminology in publications is one option.
- Accreditation of NBS labs through ISNS→ all labs report the same data
- Identifying relevant HPO terms and choose from predefined list of the clinical presentations for follow-up and case definition.

Develop a European model for confirmatory diagnostic testing

- Case definitions linked to national confirmatory tests → European model for confirmatory diagnostic testing → classify what was found--> translate into treatment modality.

Secure European Funding

Design and implement an NBS-module in the U-IMD

- Enter screen positives in a database and export these to clinical units using the registries
- Make sure existing registries are interoperable with the U-IMD NBS-module

Carry out long-term outcome studies

- Register all positive cases
- Look back at existing data
- In a multi-centred way to avoid discrepancies

Publish in peer-reviewed journals & learn from studies

- Develop publication scheme incorporating the information from previous steps on Roadmap

Set up a standing committee with topical subgroups

- Decide on participants (policymakers, representatives of national health institute)
- Joint Research Centre can play a role
- Establish subcommittees on clear case definitions, unified terminology , use of registries, patient perspectives, legal and ethical issues (GDPR, interoperability registries, etc.)

ALL WITH ONE GOAL IN MIND: OUR PATIENTS!

European Reference Network for rare or low prevalence complex diseases

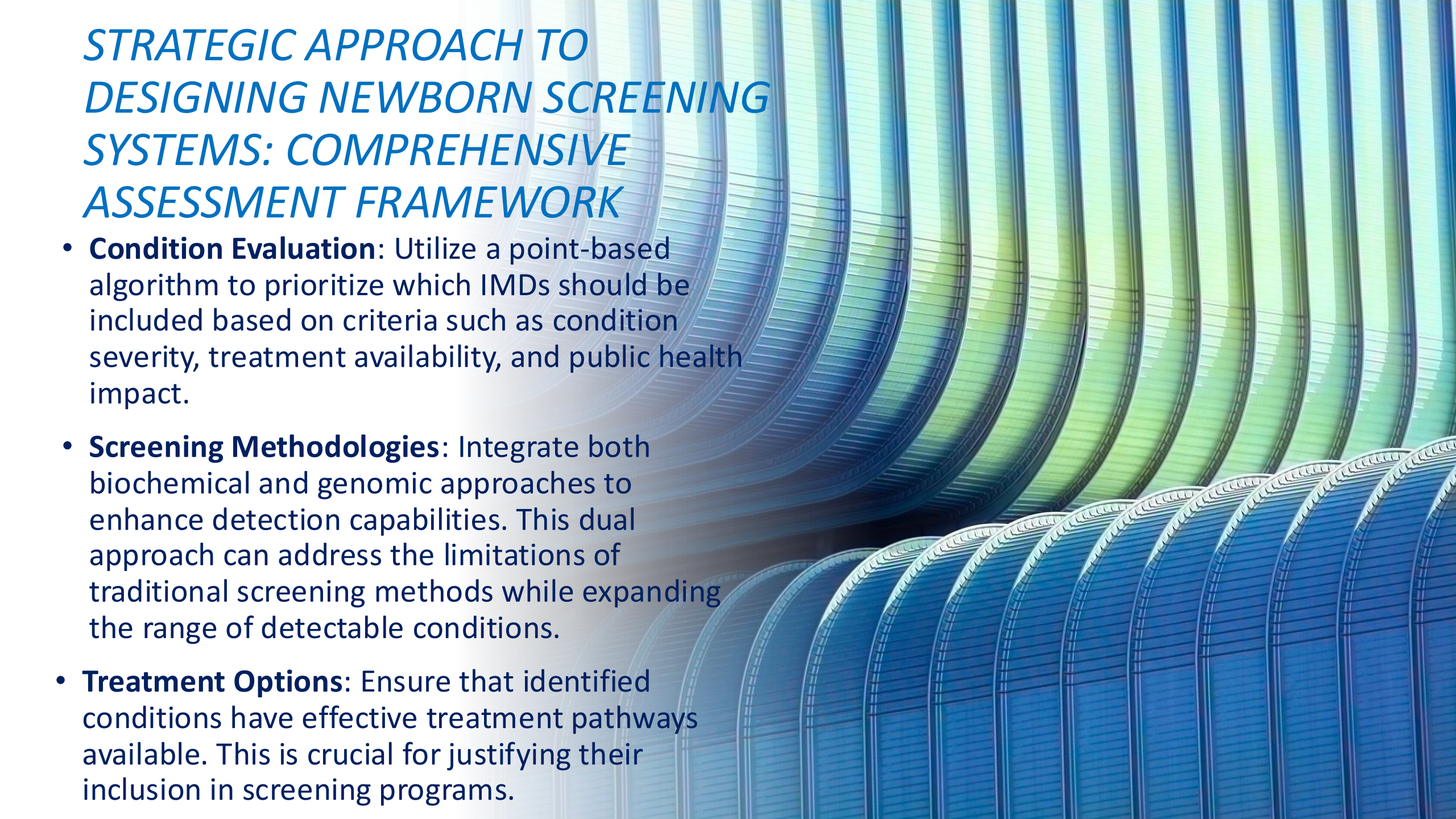
Network Hereditary Metabolic Disorders (MetabERN)

ISNS International Society for Neonatal Screening

screen4rare

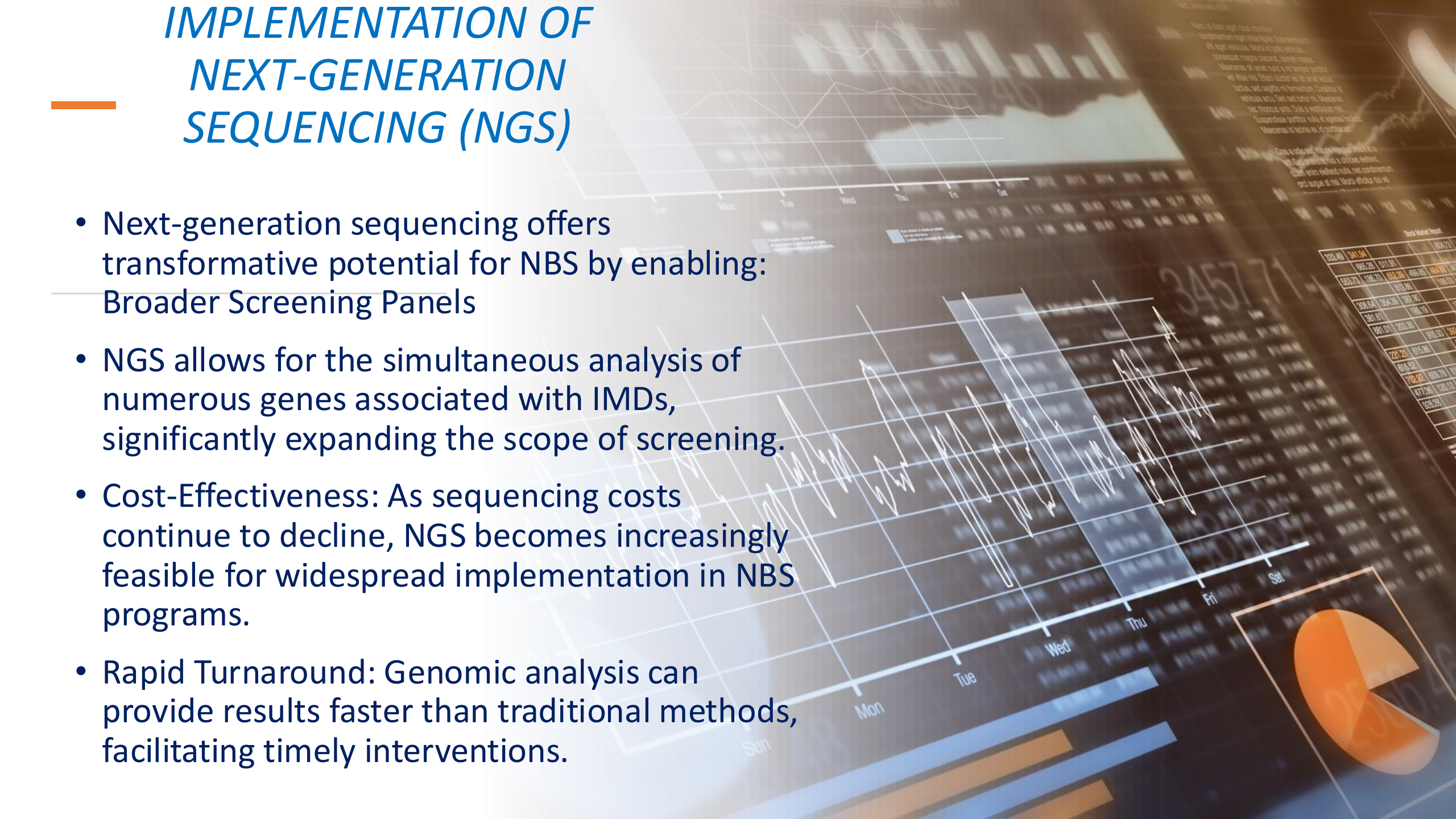
STRATEGIC APPROACH TO DESIGNING NEWBORN SCREENING SYSTEMS: COMPREHENSIVE ASSESSMENT FRAMEWORK

- **Condition Evaluation**: Utilize a point-based algorithm to prioritize which IMDs should be included based on criteria such as condition severity, treatment availability, and public health impact.
- **Screening Methodologies**: Integrate both biochemical and genomic approaches to enhance detection capabilities. This dual approach can address the limitations of traditional screening methods while expanding the range of detectable conditions.
- **Treatment Options**: Ensure that identified conditions have effective treatment pathways available. This is crucial for justifying their inclusion in screening programs.



IMPLEMENTATION OF NEXT-GENERATION SEQUENCING (NGS)

- Next-generation sequencing offers transformative potential for NBS by enabling: Broader Screening Panels
- NGS allows for the simultaneous analysis of numerous genes associated with IMDs, significantly expanding the scope of screening.
- Cost-Effectiveness: As sequencing costs continue to decline, NGS becomes increasingly feasible for widespread implementation in NBS programs.
- Rapid Turnaround: Genomic analysis can provide results faster than traditional methods, facilitating timely interventions.



CHALLENGES AND CONSIDERATIONS

- While integrating genomic technologies into NBS presents numerous advantages, several challenges must be addressed:
  - **Ethical Concerns**: Issues surrounding informed consent, data privacy, and potential psychological impacts on families must be carefully managed.
  - **Interpretation of Results**: The complexity of genomic data interpretation necessitates specialized training for healthcare providers to ensure accurate diagnosis and counseling.
  - **Infrastructure Requirements**: Implementing NGS requires significant investment in laboratory infrastructure and bioinformatics capabilities.

FUTURE DIRECTIONS IN NBS: THE PERSONALIZED MEDICINE APPROACHES

The future of NBS lies in personalized medicine, where screening results could inform tailored treatment plans based on an infant's genetic profile. This shift would require:

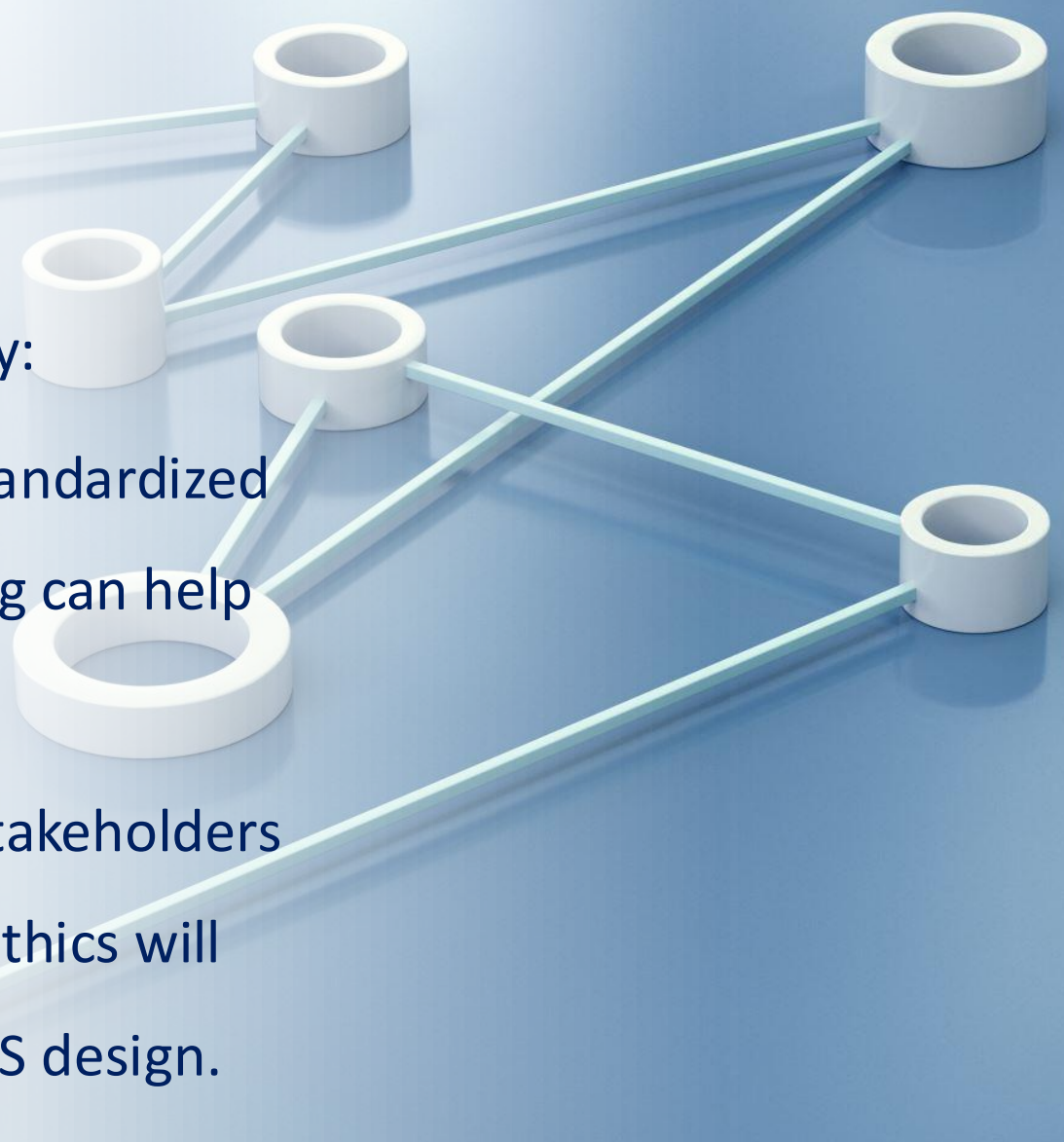
-**Integration with Health Information Systems**

-Integration of AI systems

-**A robust health information exchange system** is essential for tracking outcomes and coordinating care among various healthcare providers.

-**Longitudinal Follow-Up**: Establishing systems for long-term follow-up of screened infants to monitor health outcomes and treatment efficacy is critical.

GLOBAL COLLABORATION AND STANDARDIZATION



- To enhance the effectiveness of NBS globally:

-**International Guidelines**: Development of standardized protocols for implementing genomic screening can help reduce disparities between countries.

-**Collaboration Across Disciplines**: Engaging stakeholders from public health, genetics, pediatrics, and ethics will foster a more comprehensive approach to NBS design.

European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

Moving towards NBS as a system: the next steps

MONITORING, EVALUATION UPDATING OF NBS SYSTEM

- Defining guidelines & framework for the monitoring, evaluation and updating the NBS system
- observatory of new treatments and drugs that require NBS to ensure real access to newly authorized treatments/drugs

SETTING UP NBS EXPERT ADVISORY COMMITTEE (NBS-EAC)

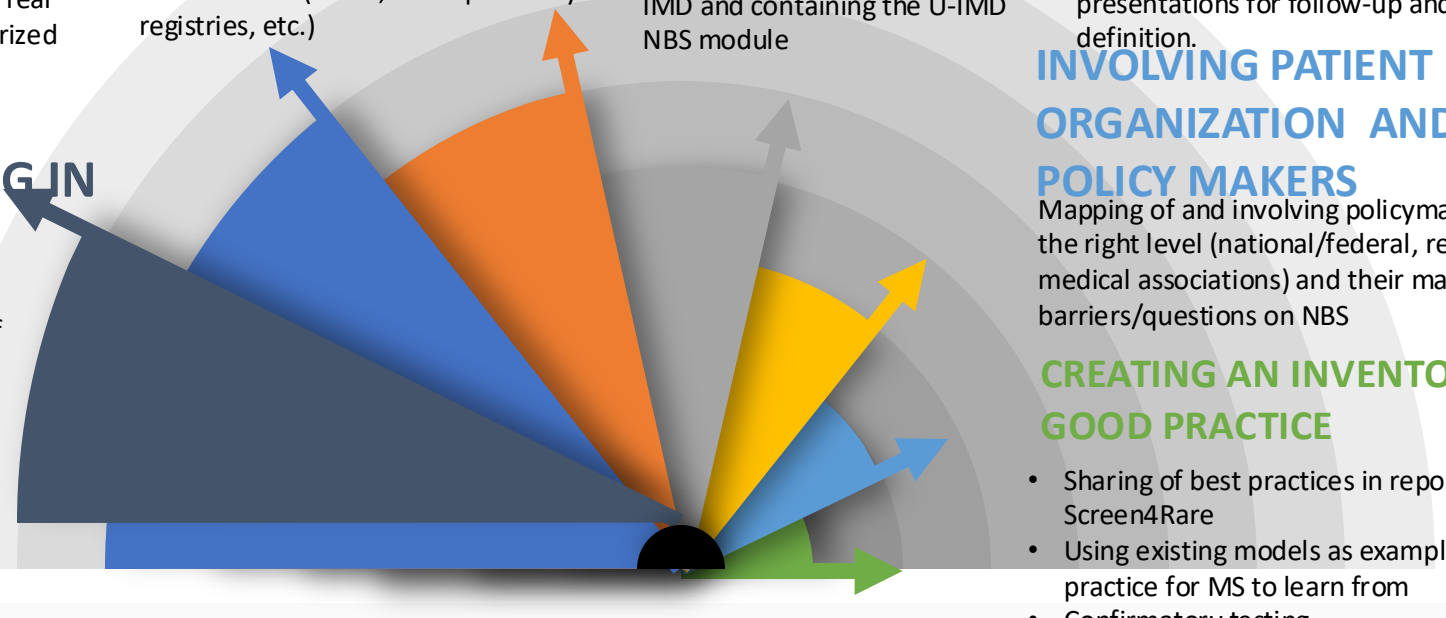
Decide on participants (policymakers, representatives of national health institute) Joint Research Centre can play a role
Establish subcommittees on clear case definitions, unified terminology , use of registries, patient perspectives, legal and ethical issues (GDPR, interoperability registries, etc.)

DEVELOPING A NBS MODULE IN U-IMD

Enter screen positives in the U-IMD registry or an existing registry interoperable with U-IMD and containing the U-IMD NBS module

DEFINING CLEAR CASE DEFINITIONS & UNIFIED TERMINOLOGY

- Develop a European model for confirmatory testing
- Encourage editors to scrutinize terminology in publications is one option.
- Accreditation of NBS labs through ISNS (all labs reporting the same data)
- Identifying relevant HPO terms and choose from predefined list of the clinical presentations for follow-up and case definition.



PUBLISHING IN JOURNALS

- Publish the results of the outcomes of the projects in medical journals
- Creating unified terminology by approaching journals about this topic

INVOLVING PATIENT ORGANIZATION AND NATIONAL POLICY MAKERS

Mapping of and involving policymakers on the right level (national/federal, regional, medical associations) and their main barriers/questions on NBS

CREATING AN INVENTORY OF GOOD PRACTICE

- Sharing of best practices in repository Screen4Rare
- Using existing models as examples of good practice for MS to learn from
- Confirmatory testing

European Reference Network
for rare or low prevalence complex diseases
Network Hereditary Metabolic Disorders (MetabERN)

STAKEHOLDERS TO BE INVOLVED IN NBS SYSTEM

1. Government Agencies
2. Healthcare Providers
3. Public Health Organizations
4. Laboratories
5. Professional Associations

6. Parents and Caregivers
7. Patients and Advocacy Groups
8. Insurance Providers
9. Education Institutions
10. Technology Developers
11. Quality Assurance Organizations
12. Community Organizations
13. Ethics Committees and Bioethicists
14. Media and Communications Firms
15. Research and Development Entities
16. Legislative Bodies

CONCLUSION

- Designing an effective newborn screening system for inherited metabolic diseases today and in the future requires a strategic integration of traditional biochemical methods with advanced genomic technologies.

- By addressing current challenges and leveraging innovative approaches like next-generation sequencing, we can enhance early detection capabilities, impact on the proper management of the patients, improve treatment outcomes, and ultimately safeguard the health of newborns worldwide.

- ERNs are instrumental to coordinate and create networks of all the stakeholders needed to optimize NBS as a system.











AIMPS
ASSOCIAZIONE ITALIANA
MUCOPOLISACCARIDOSI

BRAINS FOR BRAIN

European Reference Network
MetabERN
European Reference Network for Hereditary Metabolic Disorders

IMPSN
International MPS Network
Mucopolysaccharide and Related Diseases

18TH INTERNATIONAL MPS SYMPOSIUM
FLORENCE, ITALY
June 4-7, 2026

20 YEARS BACK FOR THE NEXT 20

INNOVATION,PROGRESS FUTURE