Rare Diseases

Research, Therapies and Social Impact

ALL ANIMALS ARE EQUAL
BUT SOME ANIMALS ARE MORE EQUAL THAN OTHERS
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Introduction

- **Definition:** Health conditions affecting a small proportion of the population (often ≤1 in 2,000).
- **Scale:** >7,000 rare diseases, impacting over 300 million people globally.
- **Key challenge:** Individually rare, collectively common — yet often invisible in health systems.

Epidemiology and Classification

- **Prevalence:** Most are ultra-rare; many remain undiagnosed.
- **Onset:** Around 70% begin in childhood.
- **Etiology:** Majority are genetic; others are autoimmune, infectious, or idiopathic.
- **Resources:** Orphanet as a central database for diseases, genes, and orphan drugs

Diagnostic challenges

- **Diagnostic odyssey:** Years of consultations, misdiagnoses and unnecessary tests.
- **Barriers:** Limited awareness, overlapping symptoms, lack of standardized pathways.
- **Emerging solutions:** Genomic sequencing, AI-assisted pattern recognition, international registries

Research landscape

- **Underfunding:** Small patient populations → limited commercial incentives.
- **Orphan drug legislation:** Special regulatory frameworks to stimulate R&D (e.g., market exclusivity, fee reductions).
- **Collaborative models:** Global networks, biobanks, and patient registries to pool data and samples.

Current therapies

- **Orphan drugs:** Targeted treatments for a subset of rare diseases; many conditions still lack any specific therapy.

- **Therapeutic approaches:**
  - **Small molecules & biologics** (e.g., enzyme replacement).
  - **Gene therapy & gene editing** for monogenic diseases.
  - **Supportive care** (symptom control, rehabilitation, palliative care).

- **Access issues:** High costs, reimbursement hurdles, geographic inequities.

Future directions in therapy

- **Personalized medicine:** Genotype-based treatment selection and prognosis.
- **Platform technologies:** Viral vectors, RNA therapies, and genome editing platforms that can be adapted across diseases.
- **Real-world evidence:** Use of registries and electronic health records to evaluate long-term safety and effectiveness

Social and psychological implications

- **Isolation and stigma:** “Invisible” illnesses, lack of understanding from society and even clinicians.
- **Family burden:** Emotional stress, financial strain, caregiving responsibilities, impact on employment and education.
- **Mental health:** Higher rates of anxiety, depression, and burnout among patients and caregivers.
- **Advocacy role:** Patient organizations as key sources of information, support, and policy pressure.

Health systems and policy

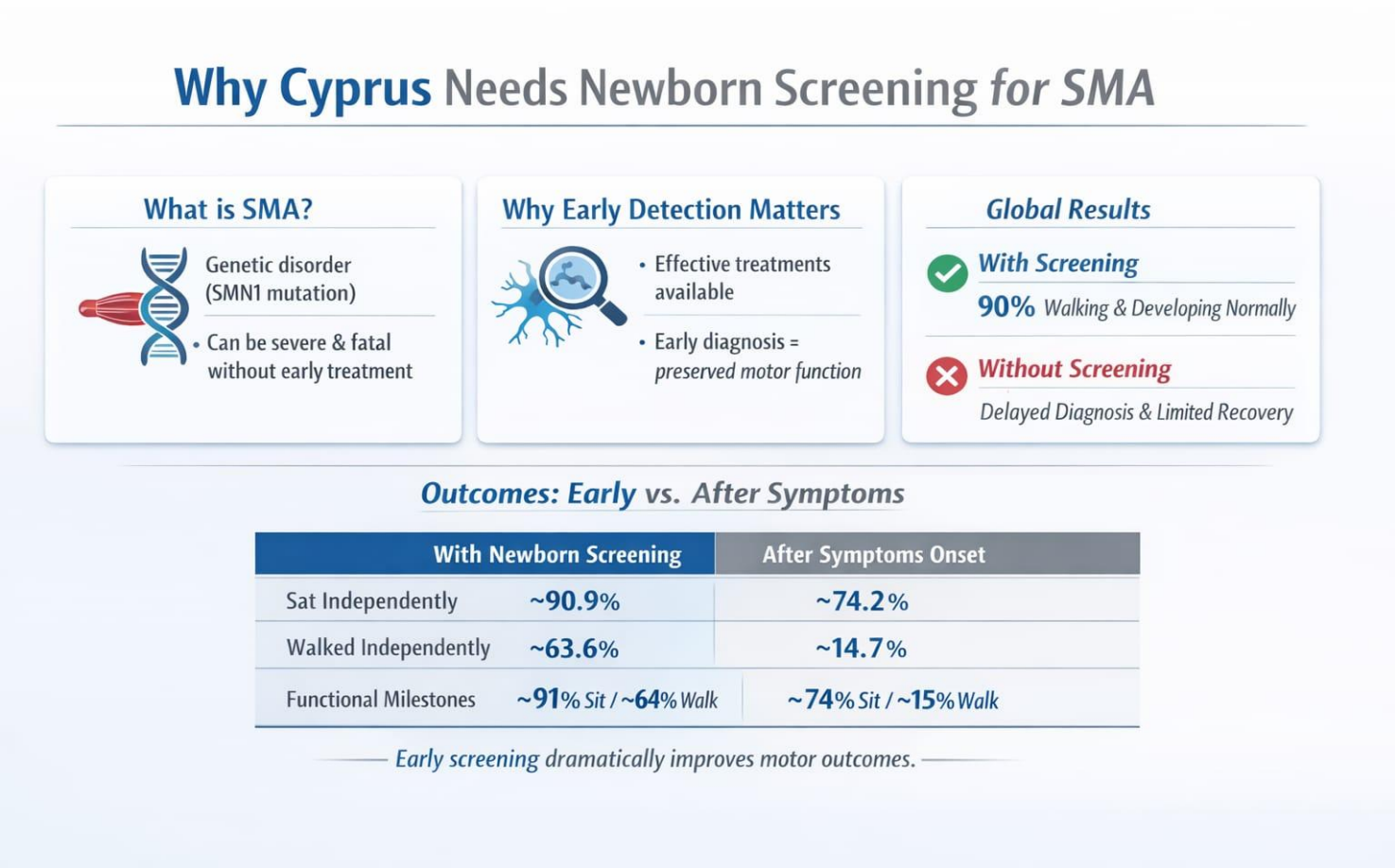
- **Equity issue:** Rare diseases framed as a global health priority for inclusion and universal health coverage.
- **Primary care role:** Early recognition, coordination of referrals, and long-term support.
- **Policy tools:** National rare disease plans, centers of expertise, cross-border care, and data-sharing frameworks.

Case vignette

- **Short story:** A child with a progressive neuromuscular disorder—years to diagnosis, limited local expertise, family relocates for care.

- **Teaching points:** Importance of early suspicion, genetic testing, multidisciplinary care, and psychosocial support

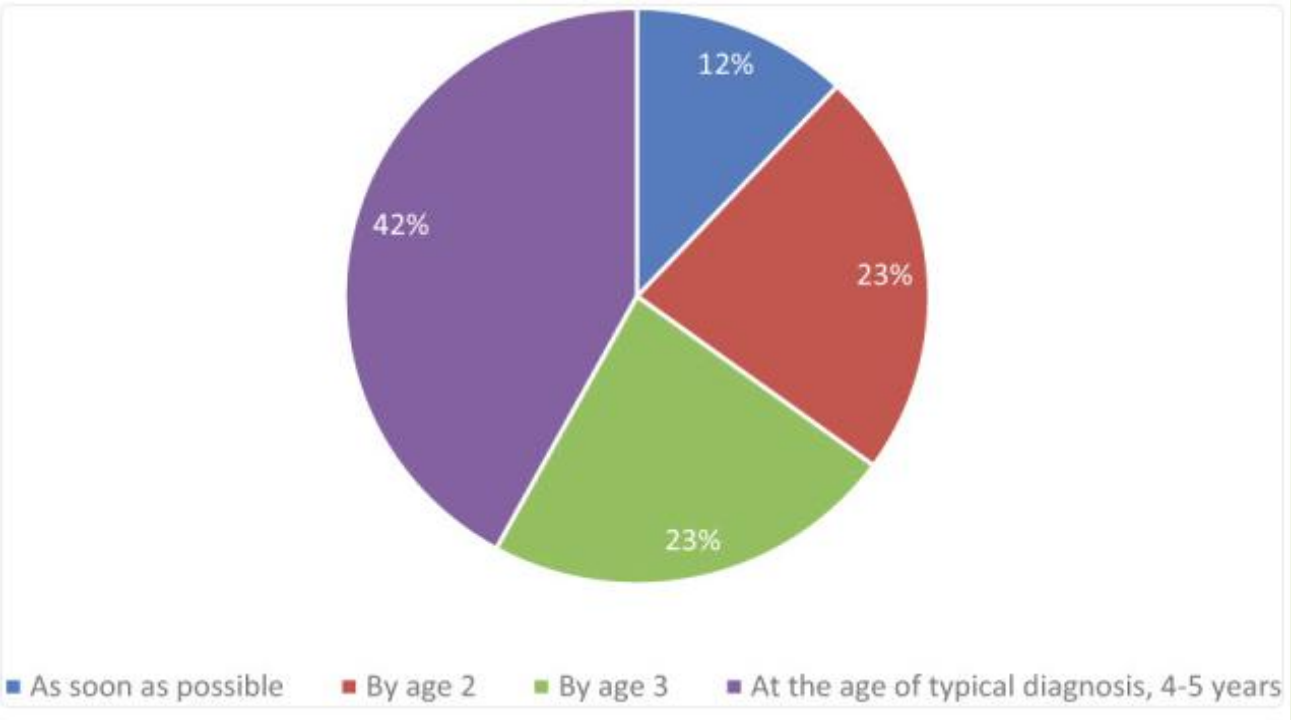
Being Realistic from Pervention to NBS Programs



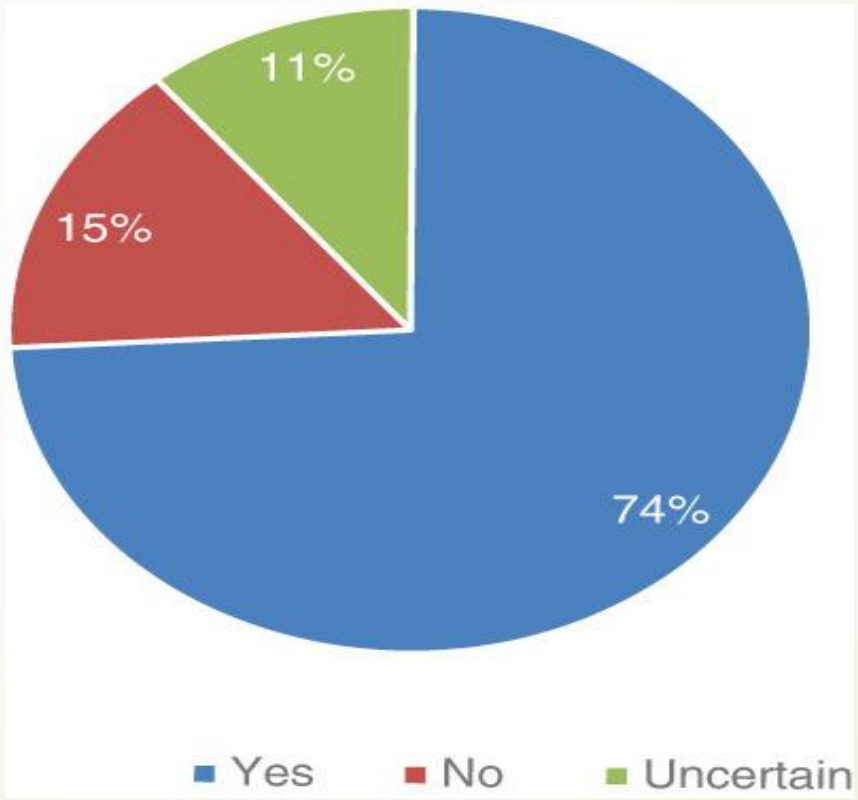
Duchenne expert physician perspectives on Duchenne newborn screening and early Duchenne care

- Duchenne Parent Project carried out a short survey that was developed and distributed to physicians who are responsible for providing care for patients with Duchenne at Certified Duchenne Care Centers across the USA.
- Despite massive advances in therapy, the average age of diagnosis for Duchenne has not changed in 30 years and is still around 4.5years.
- In a nutshell the vast majority agrees that the earliest the diagnosis the maximum results

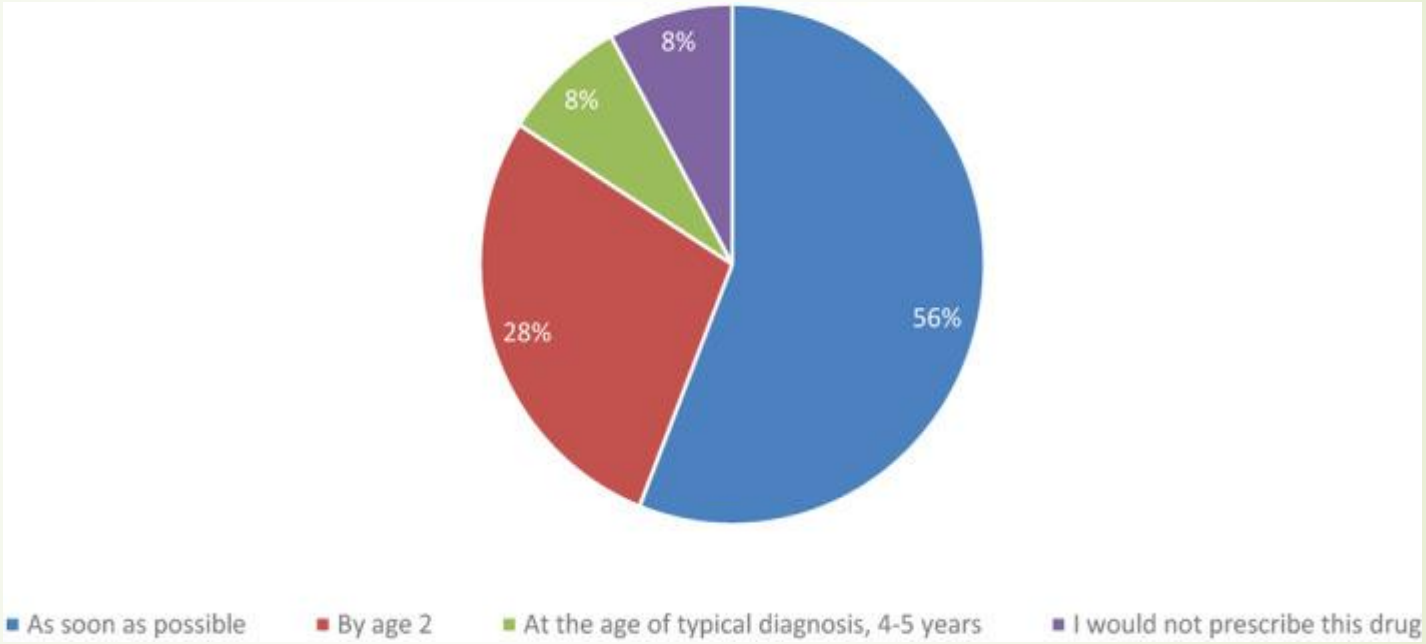
Recommended age to initiate corticosteroids



Benefit to newborn screening for dystrophinopathies



Optimal time to begin exon skipping therap



Orphan-Drug Access & Reimbursement

Country	Availability	Delay	Notes
Germany	90–100%	Weeks–months	Fastest access in EU
Denmark	85–95%	Months	High willingness to fund
Belgium	80–90%	Months	Strong early access
Slovenia	70–80%	6–18 months	Good alignment
Greece	60–70%	1–2 years	Improving
Malta	50–60%	1–3 years	Special access
Slovakia	40–50%	2–4 years	Strict HTA
Cyprus	40–55%	1–3 years	Many individual approvals

www.efpia.eu/media/olabqd20/cra-efpia-root-causes-of-unavailability-and-delay-in-smaller-markets-2025-report-final-8-may-2025-stc.pdf

Newborn Screening Comparison

Country	Conditions	SMA	SCID
Germany	25–35+	Yes	Yes
Denmark	20–30+	Yes	Yes
Belgium	20–30+	Yes	Yes
Slovenia	20+	Yes	Yes
Slovakia	20+	Yes	Yes
Greece	10–12	No	No
Malta	5–10	No	No
Cyprus	4–6	No	No

Genetic Testing Capacity

Country	WES/WGS Access	National Center	Notes
Germany	Excellent	Many	Routine genomic medicine
Denmark	Excellent	Multiple	National genomic strategy
Belgium	Excellent	Multiple	Strong academic labs
Slovenia	Very good	Yes	Pediatric genetics
Greece	Good	Several	Long waits
Slovakia	Good	Yes	Growing capacity
Malta	Limited	No	Sends samples abroad
Cyprus	Very good	Yes (CING)	Strong diagnostics

Specialized Centers & Expertise

Country	Centers	ERN Participation	Notes
Germany	Many	Very high	Dense network
Denmark	Many	High	Excellent coordination
Belgium	Many	High	Strong integration
Slovenia	Several	High	Pediatric focus
Greece	Several	Moderate	Uneven distribution
Slovakia	Several	Moderate	Developing
Malta	Very few	Low	Relies on UK/Italy
Cyprus	1–2 hubs	Moderate	CING + Makarios

Cross-Border Care Dependence

Country	Dependence	Destinations
Germany	Very low	Internal
Denmark	Very low	Internal
Belgium	Low	Internal
Slovenia	Low–moderate	Austria, Italy
Greece	Moderate	Germany, UK
Slovakia	Moderate	Czech Republic
Malta	High	UK, Italy
Cyprus	Very high	Greece, Israel, Germany, UK

WHO/Europe report
16 September 2025

Out-of-Pocket Burden

Country	Burden	Notes
Germany	Very low	Strong insurance
Denmark	Very low	Universal coverage
Belgium	Low	Good reimbursement
Slovenia	Low–moderate	Solid public system
Greece	Moderate–high	Austerity effects
Slovakia	Moderate	Co-payments
Malta	Moderate	Limited services
Cyprus	High	Travel, private tests

Out-of-Pocket Healthcare Spending in Europe
Source Eurostat 09/2025

Case Example: SMA

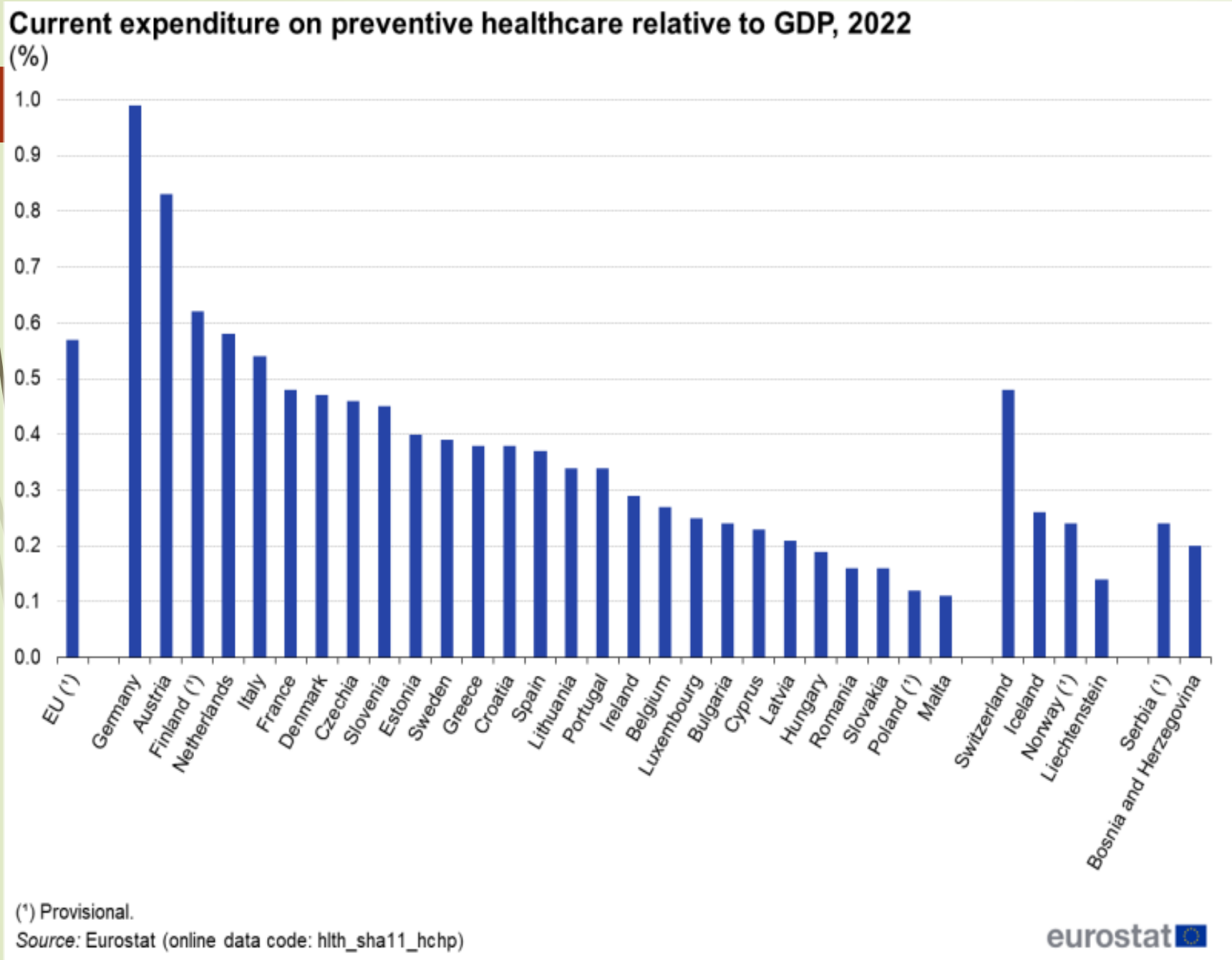
- Germany/Denmark: screened at birth → treated pre-symptomatically
- Slovenia/Belgium: early detection → strong outcomes
- Greece: diagnosis often delayed
- **Cyprus**/Malta: no screening → symptoms appear before diagnosis
- Families may need to travel or fundraise

Summary: Cyprus Position

- **Strengths:**
- Strong genetic diagnostics (CING)
- Active patient organizations
- Effective cross-border pathways

- **Weaknesses:**
- Very small newborn screening panel
- Limited orphan-drug reimbursement
- Few specialized centers
- High out-of-pocket burden

- **Overall:**
- Above Malta
- Similar to Greece and Slovakia
- Below Slovenia
- Far below Belgium, Denmark, Germany



Preventive healthcare expenditure in the EU reached roughly 5.5% of total health spending in 2022.

- Per Inhabitant Spending (2022): The EU average was €202 per inhabitant. Germany (€458), Austria (€411), and the Netherlands (€312) were the leaders, while Poland (€22), Romania (€24), and Bulgaria (€31) spent the least.
- Share of Total Health Spending: In 2022, 5.5% of total EU health expenditure went to prevention, down from 6.1% in 2021 but up from 2.9% in 2019.
- Lowest Spending Countries (2022): Malta (€19.6 million), **Cyprus (€62.5 million),** and Latvia (€82.0 million) recorded the lowest total amounts, each spending less than €100 million.

Social welfare

Care allowances from the Social Inclusion Department

The responsibility for financing the provision of Care to the People with Disabilities lies on the Department for Social Inclusion of People with Disabilities. The Persons apply to the Department, they are evaluated by the special committee / multidisciplinary team the basis of disability, and motor difficulties and get the approval for the benefit.

- Recipients of Severe motor disability allowance

Promoters should be under 65 years old, who cannot walk and permanently use a wheelchair, make no movement in both lower limbs. Amount allowance € 407

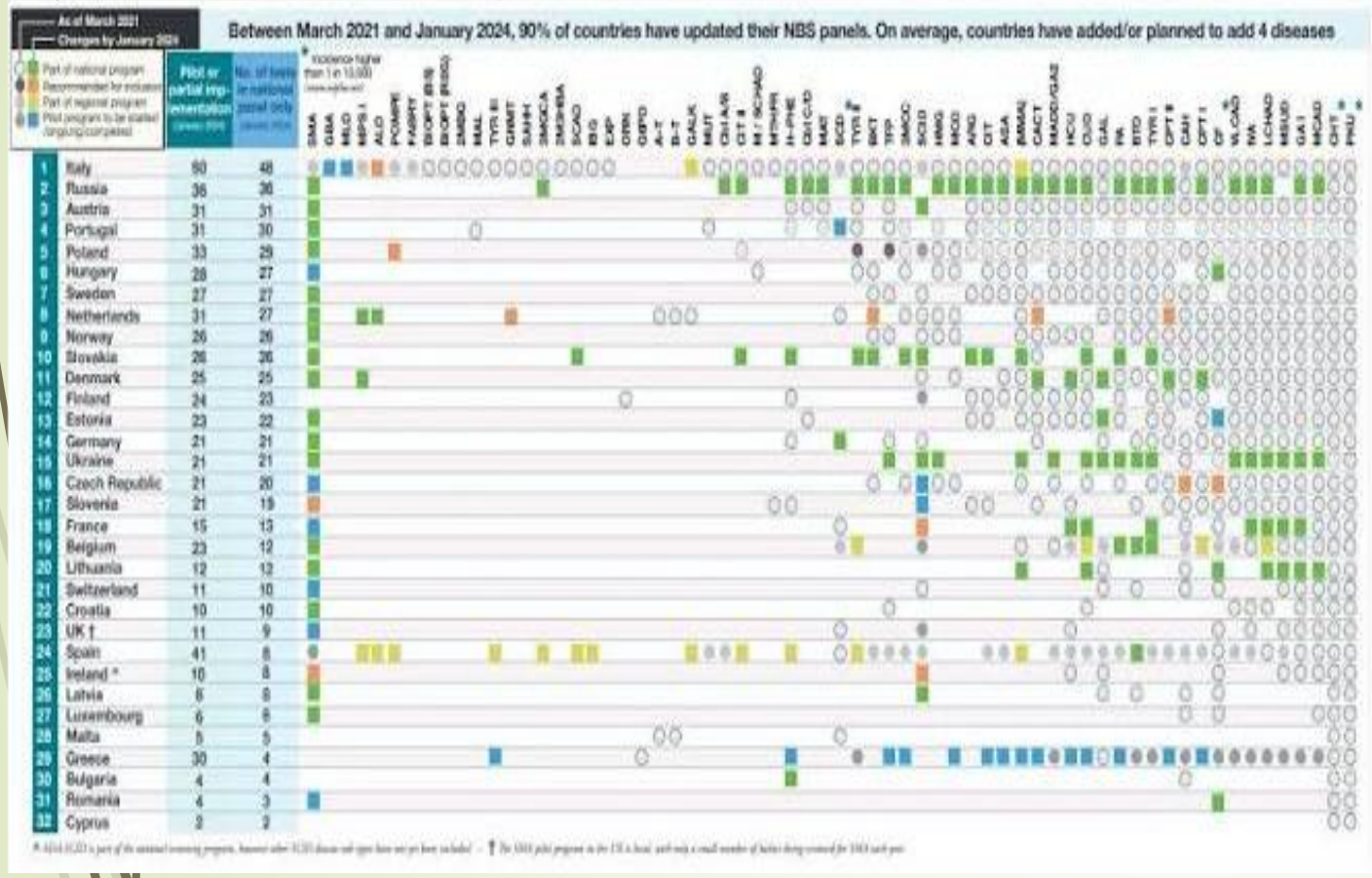
- Care Allowance Scheme for Paraplegic Persons

The beneficiaries are persons with minimal movement in both lower limbs and are wheelchair users. The allowance amount is €400 per month.

- Care allowance Scheme for Quadriplegic Persons

The beneficiaries are persons with minimal or no movement at all, in all four limbs. The allowance is €900 monthly.

Current European NBS landscape



- As illustrated in the “NBS matrix” (Figure 1), we found that there are large disparities between countries in the number and types of diseases that are included in national NBS programmes. For example, some countries such as Italy, Portugal and Austria, screen for over 30 diseases as part of their national panel20, with Italy leading the way in Europe by screening for more than 45 diseases. By contrast, many countries were found to screen for significantly fewer diseases, including the UK which tests for less than 10 diseases in its national panel, whilst ***Cyprus is only testing for two***.
- Figure 1 also highlighted trends in the frequency that each disease is included across NBS programmes, with phenylketonuria (PKU) and congenital hypothyroidism (CHT) being universally screened for across all 32 countries in-scope. It is noted that they have a relatively high incidence compared to other screened diseases (both have incidences of greater than 1 in 10,000, whilst other diseases included in programmes can have incidence rates as low as 1 in 250,000).21 However, there are other diseases which have similarly high incidence rates,such as sickle cell disease, that is nationally screened for in less than 30% of countries.

Key messages

- **Recognition:** Rare diseases are individually rare but collectively a major public health issue.
- **Innovation:** Advances in genomics and orphan drug development are transforming diagnosis and treatment, but gaps remain.
- **Justice:** Ensuring access to care, therapies, and social support is fundamentally an equity and human rights question.

Future Steps: Improving Access to New Medicines for Rare Diseases

1. Strengthen Research & Development Incentives

- • Expand and refine orphan drug policies (e.g., incentives similar to the Orphan Drug Act).
- • Increase public–private partnerships.
- • Support platform technologies (gene therapy, mRNA, precision medicine).
- • Encourage global data sharing for ultra-rare conditions.

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2. Improve Early Diagnosis & Data Infrastructure

- • Expand newborn screening programs.
- • Invest in rare disease registries and natural history studies.
- • Use AI and genomic sequencing for faster diagnosis.
- • Improve cross-border data interoperability.

3. Accelerate Regulatory Pathways

- • Expand adaptive and conditional approvals.
- • Strengthen collaboration between regulators (e.g., European Medicines Agency and U.S. Food and Drug Administration).
- • Use real-world evidence to support earlier access.
- • Implement rolling review processes for breakthrough therapies.

Future Steps: Improving Access to New Medicines for Rare Diseases

4. Reform Pricing & Reimbursement Models

- • Introduce outcome-based payment agreements.
- • Use risk-sharing models between payers and manufacturers.
- • Develop pooled procurement strategies for small patient populations.
- • Increase transparency in pricing frameworks.

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5. Strengthen Patient-Centered Approaches

- • Involve patient advocacy groups in decision-making.
- • Incorporate patient-reported outcomes in clinical trials.
- • Ensure equitable access across regions and socioeconomic groups

6. Enhance Global Collaboration

- • Promote international rare disease networks.
- • Support regulatory harmonization initiatives.
- • Facilitate cross-border clinical trials.
- • Improve access in low- and middle-income countries.

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7. Promote Sustainable Innovation

- • Balance incentives with affordability.
- • Encourage development beyond “profitable” rare diseases.
- • Monitor long-term safety and effectiveness of advanced therapies (e.g., gene and cell therapies).

To conclude, rare diseases may be uncommon, but collectively they constitute a significant global health challenge. Scientific research and innovative therapies are advancing at an unprecedented pace, offering real hope for earlier diagnosis and more effective treatments. Yet progress in medicine alone is not enough.

As a society, we have both a responsibility and an opportunity to raise awareness, to promote equitable access to care, to support research and innovation and above all, to stand beside every person living with a rare disease.