

Reckoning With the Rare Disease Landscape

Reframing Rare Diseases
as a Strategic Priority for Healthy Aging
and Health System Sustainability

**A 16 Country Policy Landscape Assessment
across the Life Course**

Argentina · Australia · Brazil · China · France · Germany ·
Italy · Japan · Mexico · Netherlands · Norway · Poland ·
Saudi Arabia · Spain · Türkiye · United Kingdom

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Rare Disease Policy & Treatment Landscape Assessment

Acronyms

AAC	Accès Compassionnel	CGT	Cell and Gene Therapy	EUCERD	European Union Committee of Experts on Rare Diseases
AAP	Accès Précoce	CISN	Consejo Interterritorial del Sistema Nacional de Salud	EURORDIS	European Rare Diseases Organisation
ACHSE	Allianz Chronischer Seltener Erkrankungen	CMAP	Charged Market Access Programme	FA	Friedreich's ataxia
AELMHU	Asociación Española de Laboratorios de Medicamentos Huérfanos	COFEPRIS	Comisión Federal para la Protección contra Riesgos Sanitarios	FADEPOF	Federación Argentina de Enfermedades Poco Frecuentes
AIFA	Agenzia Italiana del Farmaco	COMP	Committee for Orphan Medicinal Products	FDA	U.S. Food and Drug Administration
ALS	Amyotrophic lateral sclerosis	CONETEC	Comisión Nacional de Evaluación de Tecnologías de Salud (Argentina)	FEBRARARAS	Federação Brasileira de Associações de Doenças Raras
AMIIF	Asociación Mexicana de Industrias de Investigación Farmacéutica	CONITEC	Comissão Nacional de Incorporação de Tecnologias no SUS (Brazil)	FEDER	Federación Española de Enfermedades Raras
AMNOG	Arzneimittelmarktneuordnungsgesetz	CORD	Chinese Organization for Rare Disorders	FEMEXER	Federación Mexicana de Enfermedades Raras
ANMAT	Administración Nacional de Medicamentos, Alimentos y Tecnología Médica	CRMR	Centres de Référence Maladies Rares	G-BA	Gemeinsamer Bundesausschuss
ANR	Agence Nationale de la Recherche	CTIS	Clinical Trials Information System	GAPRD	Global Action Plan on Rare Diseases
ANVISA	Agência Nacional de Vigilância Sanitária	DGOS	Direction Générale de l'Offre de Soins	GCOA	Global Coalition on Aging
AOTMiT	Agencja Oceny Technologii Medycznych i Taryfikacji	DMD	Duchenne muscular dystrophy	GDP	Gross Domestic Product
APPG	All-Party Parliamentary Group	DNN	Dépistage Néonatal National	genomDE	German Genome Sequencing Program
ASMR	Amélioration du Service Médical Rendu	DS	Dravet syndrome	GKV	Gesetzliche Krankenversicherung
ATTR	Transthyretin amyloidosis	DSOA	Disability Support for Older Australians	GKV-SV	GKV-Spitzenverband
ATTRwt-CM	Wild-type transthyretin amyloid cardiomyopathy	EAMS	Early Access to Medicines Scheme	GP	General Practitioner
ATU	Autorisation Temporaire d'Utilisation	ECRIN	European Clinical Research Infrastructure Network	GRDPN	Global Rare Disease Policy Network
BI	Budget Impact	ECZA	Expertisecenter Zeldzame Aandoeningen	HST	Highly Specialised Technologies
BNDMR	French National Database for Rare Diseases	EFPIA	European Federation of Pharmaceutical Industries and Associations	HTA	Health Technology Assessment
BOE	Boletín Oficial del Estado	EJPRD	European Joint Programme on Rare Diseases	ICD-11	International Classification of Diseases, 11th Revision
BRL	Brazilian Real	EMA	European Medicines Agency	ICER	Incremental Cost-Effectiveness Ratio
CCAA	Comunidades Autónomas (Autonomous Communities)	ERDERA	European Rare Diseases Research Alliance	IMSS	Instituto Mexicano del Seguro Social
CEA	Cost-Effectiveness Analysis	ERN	European Reference Network	INSERM	Institut National de la Santé et de la Recherche Médicale
CENAGEM	Centro Nacional de Genética Médica			IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IRDiRC	International Rare Diseases Research Consortium
IRUD	Initiative on Rare and Undiagnosed Diseases
ISSSTE	Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado
JARDIN	Joint Action on Integration of ERNs into National Health Systems
JPMA	Japan Pharmaceutical Manufacturers Association
JPY	Japanese Yen
KFSH-RC	King Faisal Specialist Hospital & Research Center
LSDP	Life Saving Drugs Program
MBS	Medicare Benefits Schedule
MCDA	Multi-Criteria Decision Analysis
MHRA	Medicines and Healthcare products Regulatory Agency
MoH	Ministry of Health
MRCT	Multi-Regional Clinical Trial
MZEB	Medizinisches Zentrum für Erwachsene mit Behinderung
NAMSE	Nationales Aktionsbündnis für Menschen mit Seltenen Erkrankungen
NBS	Newborn Screening
NDIS	National Disability Insurance Scheme
NFZ	Narodowy Fundusz Zdrowia
NGS	Next-Generation Sequencing
NHS	National Health Service
NHSA	National Healthcare Security Administration
NICE	National Institute for Health and Care Excellence

NKSD	Nasjonal kompetansetjeneste for sjeldne diagnoser
NMPA	National Medical Products Administration
NRDL	National Reimbursement Drug List
NSAP	National Strategic Action Plan for Rare Diseases
ODA	Orphan Drug Act
ODD	Orphan Drug Designation
OECD	Ośrodek Ekspercki Chorób Rzadkich (Rare Disease Expert Center)
OMP	Orphan Medicinal Product
PACE	Patient and Clinician Engagement
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PFMG	French Genomics Medicine Initiative
PGD	Preimplantation genetic diagnosis
PhRMA	Pharmaceutical Research and Manufacturers of America
PKU	Phenylketonuria
PLN	Polish Złoty
PMDA	Pharmaceuticals and Medical Devices Agency (Japan)
PMO	Programa Médico Obligatorio
PNMR	Plan National Maladies Rares
PUMCH	Peking Union Medical College Hospital
QALY	Quality-Adjusted Life Year
RARE-NL	National hub for rare disease therapy development (Netherlands)
RD	Rare Disease
RDI	Rare Disease International
RDRS	Rare Disease Reference Services

RENEPOF	Registro Nacional de Personas con Enfermedades Poco Frecuentes
RVA	Rare Voices Australia
SAR	Saudi Riyal
SFDA	Saudi Food and Drug Authority
SGK	Sosyal Güvenlik Kurumu
SHGP	Saudi Human Genome Program
SMA	Spinal muscular atrophy
SMN	Survival motor neuron
SMR	Service Médical Rendu
SpainRDR	Spanish Rare Diseases Registries Research Network
SSN	Servizio Sanitario Nazionale
STA	Single Technology Appraisal
STF	Supremo Tribunal Federal (Federal Supreme Court, Brazil)
SUDEP	Sudden Unexpected Death in Epilepsy
SUS	Sistema Único de Saúde
TGA	Therapeutic Goods Administration
UN	United Nations
UNIAMO	Federazione Italiana Malattie Rare
URRBMI	Urban and Rural Resident Basic Medical Insurance
WES	Whole Exome Sequencing
WGS	Whole Genome Sequencing
WHA	World Health Assembly
WHO	World Health Organization
ZSE	Zentren für Seltene Erkrankungen

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Introduction

This paper examines how 16 countries are addressing rare diseases at the intersection of innovation, equity, and population aging – where policy is working, where it is falling short, and what the next decade demands. It is the product of a collaboration between the Global Coalition on Aging (GCOA) and the Global Rare Disease Policy Network (GRDPN), drawing on literature review, policy analysis,¹ and expert interviews² across each of the 16 countries studied.

Today, over 300 million people worldwide live with one of an estimated 7,000 rare diseases, and this number is rising.³ While any single rare disease affects a small share of the population – no more than 1 in 2,000 people in any World Health Organization's region⁴ – these conditions collectively represent a substantial and growing public health challenge, one increasingly intertwined with global population aging.

Why Now: Rare Disease at the Intersection of Aging

Two key forces are driving this growth. First, demographic change is expanding the at-risk population approximately 1.1 billion people worldwide are now aged 60 or older, a figure projected to reach 2.1 billion by 2050.⁵ As populations age, the number of people living with adult- and older-adult-onset rare diseases may rise substantially, even if underlying incidence rates remain stable.

Second, advances in diagnosis, standards of care, and disease-modifying therapies are altering the natural history of many rare diseases. Individuals who once died in infancy or childhood are increasingly surviving into adulthood and older age, while improved clinical awareness is also leading to greater recognition of rare diseases across the life course. More than a quarter of people with rare diseases live with adult-onset conditions or were not diagnosed until adulthood.⁶ As a result, rare diseases are no longer predominantly a pediatric or early-life concern. They are a life-course issue that intersects directly with population aging, health system sustainability, and the growing care needs of older adults.

The burden of rare disease extends far beyond prevalence. Within nine European sample countries (France, Germany, Italy, The Netherlands, Poland, Romania, Spain, Sweden, and The United Kingdom), the economic and social burden associated with rare diseases is estimated at \$1.46 trillion (USD) every year.⁷ Meanwhile, in Japan, the total economic burden of Nanbyo (rare diseases) reaches ¥9.9 trillion,⁸ or nearly \$66 billion (USD). These figures reflect not only direct medical costs but also substantial losses in productivity, caregiver strain, and reduced quality of life. As more people live and age with rare diseases, those impacts may accumulate over longer lifespans. Moreover, new rare disease therapies are not cures, meaning that individuals whose lives are extended will often continue to require regular and complex care. This compounds pressure on health systems already struggling to meet current demands, even before the full effects of population aging are felt.

Progress and Persistent Gaps

As evidenced in this report, over the past several decades, countries around the world have taken meaningful steps to address these negative impacts. Many have established national rare disease strategies, created specialized centers of expertise, and adopted positive discrimination mechanisms such as accelerated regulatory pathways, orphan drug incentives, and dedicated reimbursement channels. These steps have enabled improved access to diagnosis, treatment, and care, while also supporting scientific advances leading to new therapies.

Despite this progress, persistent gaps continue to limit the potential of innovation and prevent patients from receiving timely, equitable care. Early and accurate identification of rare diseases remains a significant challenge,⁹ as screening and genetic testing are still not widely or consistently accessible, leading to delays in diagnosis that can span five years.¹⁰ Further, while scientific tools and therapeutic platforms have expanded rapidly, reimbursement frameworks have not kept pace. Traditional cost-effectiveness analyses often disadvantage orphan drugs, restricting the introduction of breakthrough treatments and perpetuating inequities between health systems.¹¹

A Reframed Priority

All of these issues become even more consequential as populations age and develop comorbidities. As key innovations enable people with rare diseases to live longer, healthier lives, healthcare systems already facing workforce shortages, rising costs, and increasing demand will struggle to keep pace unless policy frameworks are adapted to better support sustainable access and treatment pathways. Even today, rare diseases impose substantial societal costs through diagnostic delays, lost productivity, and caregiver burden. The economic stakes are already significant: a 2023 study across Germany, France, and Italy found that the average burden for rare diseases is approximately €107,000 per patient per year – 15 times greater than the €7,000 average for common illnesses. Critically, indirect costs (including caregiver burden, home modifications, and travel) rise from 29% to 45% of total costs when no treatment is available.¹²

A reframed understanding of rare diseases is needed: one that recognizes them as a public health and economic priority shaped by demographic change, and positions rare disease innovation as a catalyst for stronger, more adaptive, and more equitable health systems that serve aging populations worldwide. In practical terms, effective rare disease policy is effective aging policy, and the countries that align these agendas now will be better prepared for the decades ahead.

The need for urgent action has never been greater. Funding gaps, policy limitations, and workforce shortages are converging with one of the most consequential demographic shifts in modern history: by 2050, the global population aged 65 and over is expected to nearly double to approximately 1.7 billion, and the population aged 80 and over is projected to more than triple by 2074.^{13,14} With this report, the Global Coalition on Aging (GCOA) partnered with the Global Rare Disease Policy Network (GRDPN) to examine how countries are responding to these intersecting pressures, where meaningful progress is being made, and what opportunities exist to meet the growing needs of populations with rare diseases across the life course, now and in the decades ahead.

Timeline: Milestones in the Rare Disease Space

» National Policy Frameworks » Global Action

1983	» US Orphan Drug Act (ODA) Signed	- The first legislation of its kind. - Sought to provide market incentives for pharmaceutical manufacturers to develop orphan drugs.
1997	» Orphanet Database Launched	French INSERM establishes Orphanet, the world's first comprehensive online database dedicated to information on rare disease and orphan drugs.
1999	» EU Orphan Drug Regulation	The European Union adopts Regulation (EC) No.141/2000, which went into force the following year, establishing the Committee for Orphan Medicinal Products (COMP) and creating the EU's orphan medicinal product (OMP) incentive framework – including 10 years of market exclusivity, protocol assistance, and reduced regulatory fees – to stimulate the development of therapies for rare diseases.
2005	» 2005: First National Plan for Rare Diseases launched in France	France becomes the first EU Member State to adopt a national rare disease plan, launching what would become a successive series of plans (PNMR1 in 2005, PNMR2 in 2011, PNMR3 in 2018, PNMR4 in 2025) that has shaped the European rare disease policy model.
2008	» First Rare Disease Day	EURORDIS launches global awareness campaign, with the goal of raising awareness for rare diseases as a public health issue among the public, policymakers, and researchers.
2009	» Spain's National Rare Disease Strategy	Spain's national strategy also serves as the basis for regional autonomous community plans. The strategy was updated in 2014 and experts interviewed for this report expect updates by the end of 2026.
2011	» EU Cross-Border Healthcare Directive	Directive 2011/24/EU establishes the right of EU citizens to seek health-care in other Member States and be reimbursed by their home system. For people living with rare diseases – who often struggle to obtain timely diagnosis, specialist expertise, or appropriate treatment – this Directive plays a particularly important role. Although implementation remains suboptimal. The Directive also provides the legal foundation for ERNs, the most important EU instrument for rare disease expertise.
2011	» IRDiRC Established	Launched at the joint initiative of the European Commission and the US National Institutes of Health, the International Rare Diseases Research Consortium was founded to promote international collaboration in rare disease research.

2011	»	Argentina's Legislation on Rare Diseases	
2013	»	Germany's National Action Plan for People with Rare Diseases	
2013	»	Netherlands' National Plan for Rare Diseases (expired)	
2013	»	UK Strategy Rare Diseases	
2014	»	Brazil's National Policy for Comprehensive Care for People with Rare Diseases	
2015	»	Rare Diseases International Launched	Rare Diseases International, a global alliance of patient organizations, was launched, aiming to strengthen advocacy efforts and raise awareness for rare diseases worldwide.
2015	»	Japan's Act on Medical Care for Patients with Intractable Diseases	
2016	»	NGO Committee for Rare Diseases	EURORDIS and Agrenska Foundation establish the NGO Committee for Rare Diseases under the UN umbrella, promoting multi-stakeholder collaboration and actions for rare diseases within the United Nations system.
2017	»	European Reference Networks Launch	The European Reference Networks (ERNs) was launched, serving as cross-border networks that bring together European hospital centers of expertise and reference to tackle rare diseases.
2017	»	APEC Action Plan on Rare Disease	
2018	»	China's First National Rare Disease List (Second List in 2023)	
2019	»	Adoption of Rare Diseases into the UN Political Declaration	Member States included rare diseases in a UN Political Declaration on Universal Health Coverage for the first time.
2019	»	European Joint Programme on Rare Diseases (EJP RD) Launched	The first EU-scale programme dedicated to building an integrated European rare disease research ecosystem. Coordinated by INSERM (France) with €150M in funding, EJP RD integrated funding mechanisms, FAIR data infrastructure, diagnostics, training, and translational research across Member States.
2019	»	Rare 2030 Foresight Study Launched	Initiated by the European Parliament and led by EURORDIS, this two-year project convened over 250 experts, patients, and stakeholders to develop policy recommendations for rare diseases through 2030. It concluded in 2021 with eight key recommendations that have shaped European rare disease policy direction.
2020	»	Australia's National Strategic Action Plan for Rare Diseases	
2021	»	First UN Resolution on Rare Diseases	The UN General Assembly unanimously adopted its first-ever resolution on rare diseases, titled "Addressing the Challenges of Persons Living with a Rare Disease and their Families."
2021	»	Norway's National Strategy for Rare Diagnoses	

2021	»	UK Rare Diseases Framework 2021–2027 (expiring in 2027)	
2023	»	EU Pharma Package Proposed	The European Commission proposed the EU Pharma Package, a major revision of the EU's pharmaceutical legislation, that will reshape orphan drug regulation by reducing baseline orphan market exclusivity from 10 years to 9 years and rewarding "breakthrough" medicines with up to 11 years.
2023	»	Italy's National Rare Disease Plan	
2023	»	Türkiye's Rare Diseases Health Strategy and Action Plan	
2024	»	Poland's Plan for Rare Diseases 2024–2025 (expiring)	
2024	»	The Aotearoa New Zealand Rare Disorders Strategy	
2024	»	2024: Official Launch of ERDERA	Building on EJP RD, the European Rare Diseases Research Alliance (ERDERA) is launched as the EU flagship strategic partnership for rare disease research, encompassing 180 organisations from 37 countries with more than €380M in funding – making it the largest rare disease research and innovation partnership globally.
2025	»	WHA Resolution on Rare Diseases Adopted	The World Health Assembly unanimously adopts the resolution "Rare Diseases: a Global Health Priority for Equity and Inclusion," officially recognizing rare diseases as a global health priority and mandating the WHO to develop a 10-year Global Action Plan (2025 – 2035).
2025	»	Political Agreement on the EU Pharma Package	A provisional political agreement between the European Council and Parliament on the final, revised rules of the EU Pharma Package was reached.
2025	»	RDI-Lancet Commission on Rare Diseases Launched	The Rare Diseases International (RDI)-Lancet Commission on Rare Diseases was launched to address the lack of data on rare diseases and generate evidence- and equity-informed recommendations, implementable and impactful across all countries to improve the lives of persons living with rare diseases.
2026	»	WHO Global Action Plan Development	The WHO begins drafting a 10-year Global Action Plan on Rare Diseases (GAPRD), in consultation with key stakeholders, to be submitted for adoption at the WHA 2028. Complementary regional action plans are being developed in parallel as part of this work.

A Global Inflection Point

The rare disease field stands at a critical juncture, marked by the unanimous adoption of the 2025 World Health Assembly Resolution that designates rare diseases as a global health priority and calls for the development of a ten-year WHO Global Action Plan.¹⁵ This development constitutes the most substantial multilateral commitment to rare diseases to date and creates a limited but significant opportunity to influence the agenda prior to the plan's anticipated adoption in 2028. This surge in political attention is occurring alongside rapid advances in biomedical science have redefined the prognosis for conditions like spinal muscular atrophy (SMA), Amyotrophic lateral sclerosis (ALS) and Friedreich's ataxia (FA), while the therapeutic pipeline continues to expand for a widening set of rare conditions, including Dravet Syndrome, Duchenne muscular dystrophy (DMD), sickle cell disease, transthyretin amyloidosis (ATTR), cystic fibrosis, hemophilia A and B, and Huntington's disease.

Despite these advances, the findings throughout this report shows a substantial gap persists between what is scientifically possible and what is equitably accessible. Many national rare disease strategies remain in early stages of development, are inconsistently implemented, lack funding or national coordination, or are constrained by limited timeframes, and the majority of the estimated 300 million individuals affected by rare diseases worldwide continue to face barriers to diagnosis, treatment, and coordinated care. The intersection of emerging political commitment, accelerating scientific progress, and incomplete policy infrastructure renders the current period not only a moment of opportunity but of heightened urgency. The choices made by policymakers, patient advocates, researchers, and industry stakeholders in the coming years will be decisive in determining whether the potential of this period is translated into meaningful and widespread improvements for rare disease communities.

Executive Summary Landscape Analysis:

Two intersecting dynamics of population aging raise the stakes of nearly every system-level challenge described in this report. First, advances in diagnosis and disease-modifying therapy mean that people with rare diseases, including those once considered exclusively pediatric, are more often surviving into adulthood and requiring care across longer lifespans. Second, the populations of nearly every country studied are aging rapidly, which will increase the absolute number of people living with certain adult-onset rare diseases even if underlying incidence rates hold steady. As populations age, the diagnostic delays, reimbursement mismatches, workforce shortages, and access inequities described below will affect more patients and carry heavier downstream costs. That reality makes the case for treating rare disease policy and healthy aging as intersecting priorities rather than parallel tracks.

National Strategy and Policy Frameworks

National rare disease strategies have proliferated across the countries studied, helping to elevate rare diseases within national health agendas and formalize commitments to screening, diagnosis, and coordinated care. However, the maturity and durability of these frameworks vary widely, and few are designed for the demographic pressures ahead. Several leading strategies, including the UK Rare Diseases Framework and the Netherlands' National Plan, are approaching the end of their planned horizons without publicly scoped successors, creating a near-term policy inflection point at which priorities can be reassessed and frameworks better aligned with evolving diagnostic technologies and therapeutic pipelines. Progress is further complicated by the fact that countries do not share a common definition of rare disease, a fragmentation that ripples through orphan drug policy, clinical research, and cross-border care. Taken together, national strategies have provided an important foundation, but most remain limited by gaps in implementation planning, funding consistency, and accountability mechanisms: gaps that will widen as rare disease populations age and grow.

Diagnostics and Screening

Countries have made measurable progress in strengthening diagnostic infrastructure, particularly through the expansion of newborn screening and broader availability of whole genome and exome sequencing. These advances have improved early detection for conditions like SMA and shortened diagnostic journeys for many hereditary conditions. Yet diagnostic systems remain built primarily around pediatric and neonatal presentations, leaving them poorly configured for the adult-onset and late-presenting rare diseases that will grow in prevalence as populations age. Across the countries studied, multi-year diagnostic delays between symptom onset and diagnosis remain the norm rather than the exception, reflecting limited access to genetic testing, specialist shortages, fragmented referral pathways, and low rare disease awareness in primary care. The consequences are particularly acute for older adults, whose symptoms are often misattributed to normal aging and whose diagnostic journeys extend longest in health systems with the fewest genetic specialists.

Treatment Access and Reimbursement

Despite rapid scientific progress, the vast majority of rare diseases still lack an approved treatment, and reimbursement frameworks across the countries studied have not kept pace with the pipeline that does exist. Standard QALY-based cost-effectiveness thresholds struggle to accommodate the fundamentals of orphan drug development, including small and geographically dispersed patient populations, limited natural history data, and high per-patient trial costs. These same thresholds doubly disadvantage therapies for older patients, valuing interventions less because of rarity and again because of shorter remaining life expectancy. Newer models, including outcomes-based pricing, managed access agreements, and coverage with evidence development, are beginning to offer alternatives, but their adoption remains uneven. Looming changes to EU orphan market exclusivity beginning in late 2028 or early 2029 have raised further concerns that commercial incentives for follow-on indications and pediatric rare disease research will weaken at precisely the moment they are most needed.

Access to approved therapies also varies sharply across geographies, both within and between countries. Rural communities face persistent barriers to specialized care, and workforce shortages in geneticists, neurologists, and metabolic specialists are documented across Saudi Arabia, the UK, Spain, Italy, the Netherlands, and much of Latin America. Japan's ongoing "drug lag and drug loss" challenge, in which globally available therapies reach Japanese patients years after approval elsewhere, illustrates how national regulatory timelines can compound these barriers even in otherwise well-resourced health systems.

Funding imbalances compound these challenges. Compared to disease areas like oncology, rare diseases receive fewer research dollars and commercial incentives.¹⁶ Even when promising therapies emerge, the inherent difficulty of conducting clinical trials for rare diseases – including small and geographically dispersed patient populations, limited natural

history data, and the high per-patient cost of trial recruitment and retention – creates additional barriers to bringing treatments from bench to bedside. The high cost and complexity of conducting clinical trials for rare diseases – driven by small and geographically dispersed patient populations, limited natural history data, and the high per-patient cost of recruitment and retention – further constrains the pipeline of available treatments. This disparity not only creates a gap in policy attention but also impacts the development and deployment of new therapies and emerging diagnostic tools.

Cross-Country Heterogeneity as a Structural Barrier.

Cutting across these gaps is the significant heterogeneity in how countries approach rare disease policy. Priorities, evidentiary standards, willingness to pay, and availability of early-access tools differ widely, producing what amounts to a geographic lottery in which a patient's access to diagnosis, treatment, and coordinated care depends as much on where they live as on what therapies exist. These inequities show up within countries as well, with specialists and centers of expertise clustering in major urban areas across Italy, Spain, Brazil, France, Mexico, and Türkiye. Heterogeneity also raises the cost and complexity of

bringing orphan drugs to market and constrains the international networks, including European Reference Networks, shared registries, and multi-regional trials, that increasingly underpin progress no single country can achieve alone.

A Critical Moment for Rare Disease Policy

As of 2025, the WHO Resolution on Rare Diseases and forthcoming Global Rare Disease Action Plan signal meaningful momentum, but that momentum coincides with a demographic shift that will test whether these systems can scale.¹⁷ Countries that treat rare disease policy and healthy aging as intersecting priorities will be better positioned to meet both challenges. In practical terms, that means addressing the systemic weaknesses described throughout this report, from diagnostic delays and reimbursement mismatches to workforce shortages and fragmented governance, before population aging and longer survival with rare diseases place further stress on already-strained health systems.

Methodology

This report is based on an extensive review and analysis of the rare disease policy and implementation landscape across 16 countries: Argentina, Australia, Brazil, China, France, Germany, Italy, Japan, Mexico, the Netherlands, Norway, Poland, Saudi Arabia, Spain, Türkiye, and the United Kingdom. Incidence and prevalence data across these countries has been standardized to a per 100,000 basis for ease of comprehension and comparability. All epidemiological figures are approximate estimates drawn from the best available published sources. Where country-specific peer-reviewed estimates were unavailable, reputable non-academic sources or global estimates were used and are labeled as such.

These countries were selected to capture a broad range of geographies, health-system structures, and economic contexts, providing a comprehensive picture of how rare diseases are prioritized and addressed worldwide.

This report assesses the rare disease landscape using a two-pronged methodological approach:

ASSESSMENT APPROACH	1. Literature Review:
	Drawing on academic publications, national policy documents, regulatory guidance, government reports, and analyses from patient organizations and international health institutions.
	2. Expert Interviews:
	Highlighting key insights from policymakers, patient advocates, academic researchers, clinicians, and healthcare system leaders across the 16 countries.

The analysis focuses on three facets of the rare disease policy and treatment landscape. The following facets were selected because, together, they capture the full continuum of care for people living with rare diseases and reflect the policy levers most strongly associated with long-term system performance, equity, and sustainability.

RARE DISEASE FACETS	1. Diagnostics and screening:
	Assessing country-level approaches to early identification, genetic testing availability, and screening.
	2. Treatment access and reimbursement:
	Understanding how health systems evaluate, fund, and deliver therapies for rare conditions, including the role of orphan drug policies and cost-effectiveness frameworks.
	3. National policy and governance:
	Evaluating the presence and maturity of national rare disease strategies, centers of expertise, care coordination mechanisms, and long-term sustainability plans.

Importantly, these three facets are also increasingly relevant in the context of population aging. While many rare diseases present in childhood, advances in diagnostics and treatment have significantly increased survival into adulthood and older age. At the same time, rare diseases also include late-onset manifestations or age-related disease progression, creating new demands on health systems that were not originally designed to manage rare conditions across the life course.

Across these areas, this policy paper seeks to identify gaps, areas of progress, and opportunities for strengthening rare disease systems. The goal is to provide a practical, comparative perspective that can inform policymakers, advocates, and health-system leaders as they work to improve outcomes for people living with rare diseases.

Limitations

Several limitations and assumptions shape this analysis. First, rare disease definitions, epidemiological estimates, and reimbursement statistics are not always directly comparable across countries due to differences in national classification criteria, data infrastructure, and reporting conventions; where possible, figures have been standardized or contextualized, but residual variation remains. Second, the analysis reflects the policy landscape as of late 2025 and early 2026, and several countries in the dataset – including the United Kingdom, Spain, the Netherlands, and Poland – are at or near inflection points in their national strategies, meaning conditions on the ground

may continue to evolve. Third, expert interviews capture informed perspectives from a targeted set of stakeholders and are not intended to be statistically representative of each country’s broader rare disease community. Fourth, quantitative indicators such as diagnostic delay, reimbursement rates, and screening coverage are drawn from the most recent publicly available sources, and in a limited number of cases reliable national-level data could not be identified. In particular, existing evidence on the intersection of population aging and rare disease remains thin: few countries systematically collect or publish data on adult-onset and late-onset rare diseases, survival into older age with rare conditions, or the downstream implications for geriatric and long-term care, and much of the analysis in this report on aging-related dimensions therefore draws on inference from adjacent data sources rather than from dedicated national evidence bases. Fifth, published epidemiological data on the specific rare diseases profiled in the country snapshots (spinal muscular atrophy, Dravet syndrome, amyotrophic lateral sclerosis, and Friedreich ataxia) are uneven across the 16 countries. Peer-reviewed, population-based prevalence or incidence studies exist for only some countries and conditions, and where they do exist, they are often regional rather than national, several years old, or based on differing case definitions and methods. Where no reliable published estimate could be identified, the snapshot reports the figure as data unavailable rather than substituting an estimate. The figures shown are therefore approximate, are not always directly comparable across countries, and should be read as indicative of the scale of each condition rather than as precise counts.

Rare Disease Policy Landscape: Country Ratings

Across the 16 countries assessed, priorities, evidentiary standards, and willingness to pay for rare disease therapies vary widely. What qualifies as sufficient evidence of effectiveness in one country's reimbursement process may fall short in another. Early and flexible access tools, such as managed entry agreements or compassionate use pathways, are well-developed in some systems and largely absent in others. Reimbursement frameworks range from models that presume added benefit for orphan drugs to rigid cost-effectiveness thresholds that structurally disadvantage them. Even clinical expertise on specific rare diseases varies considerably, both across and within countries. The result is a fragmented global landscape in which a patient's access to diagnosis, treatment, and coordinated care depends heavily on where they live, not solely on what therapies exist or what the evidence supports.

This section translates the country-level analysis conducted for this report into a comparative view of how the 16 countries assessed perform across three core domains of rare disease policy: treatment access and reimbursement, diagnostics and screening infrastructure, and national governance. The relative strength of these domains will increasingly determine how well health systems can meet the joint challenges of rare disease and population aging, as longer lifespans and a growing share of adult-onset diagnoses place additional stress on infrastructure that, in many countries, is still maturing. The ratings that follow therefore capture not only current state, but the distance between current capacity and the pressures ahead.

Ratings are based on a structured assessment of publicly available policy documents, regulatory frameworks, clinical guidelines, epidemiological data, and patient advocacy materials, calibrated across countries with particular attention to orphan drug access, newborn screening scope, diagnostic delay, and the presence and maturity of a national rare disease policy framework. They reflect rare disease-specific system performance rather than general health system quality. The detailed country snapshots that informed these ratings, covering policy frameworks, clinical infrastructure, epidemiology, and stakeholder perspectives for each country, can be found in the appendix.

MATURITY STAGES

RELATIVELY ADVANCED	Comprehensive systems in place with minimal systemic barriers
PROGRESSING	Functional structures exist but persistent gaps constrain outcomes. Arrows used to indicate the direction of recent momentum: ⬆️ upward movement and progress, ➡️ little or no change, ⬇️ or declining momentum
EARLY-STAGE	Foundational frameworks are emerging, but significant structural and capacity gaps remain

1. National Governance Framework

INDICATORS (1) National plan status + targets/integration,
(2) Formal rare disease definition,
(3) Dedicated governance/coordinating body

COUNTRY	PLAN STATUS	DEFINITION	GOVERNANCE BODY	MATURITY
Argentina	Law 26.689 (2011); underfunded, uneven implementation across provinces	Yes (aligned with EMA/WHO)	RENEPOF registry + Honorary Advisory Board (formal patient seat; implementation uneven across provinces)	PROGRESSING ↔
Australia	NSAP (2020); no dedicated Commonwealth funding or measurable milestones	Yes (fewer than 5 per 10,000)	No permanent institutional home; delivery uneven across jurisdictions	PROGRESSING ↔
Brazil	National Policy (2014); funding frozen since 2014; regional variation	Yes (fewer than 65 per 100,000)	No guaranteed patient representation in governance bodies	PROGRESSING ↓
China	No national plan; First and Second Rare Disease Lists (2018, 2023) only	Not codified in law (expert-defined benchmark)	National Network (400+ hospitals) but no formal governance body	PROGRESSING ↑
France	PNMR4 (2025-2030); funded; 26 measurable objectives	Yes (EU definition)	PNMR steering committee; patients formally embedded in governance	RELATIVELY ADVANCED
Germany	National Action Plan for Rare Diseases (2013); 52 measures, 7 policy areas; operationalized through NAMSE + ZSE network	Yes (EMA adherent)	NAMSE coordination body links government, providers, and advocates	RELATIVELY ADVANCED
Italy	National Rare Disease Plan 2023-2026 under Law 175 (2021); €25M/yr funding	Yes (EMA adherent)	National Rare Disease Committee under Ministry of Health; ERN participation	PROGRESSING ↑
Japan	Nanbyo Law; active, well-funded, with designated disease subsidies	Yes (Shitei-Nangyo: fewer than 0.1% of population + other criteria; ODD system uses <50,000 patients)	Formal governance through intractable disease system	RELATIVELY ADVANCED
Mexico	No coordinated national rare disease strategy	Article 224 of health law: <5 per 10,000; recognizes all WHO ICD-11 rare diseases (EMA/WHO-aligned)	No dedicated governance body or coordinating mechanism	EARLY-STAGE
Netherlands	Expired (2013); successor under discussion	Yes (EMA adherent)	Multi-stakeholder coordination body advises Ministry of Health	PROGRESSING ↔
Norway	National Strategy (2021); 5 core objectives; relatively new	Yes (WHO/EMA aligned)	Norwegian Center for Rare Diseases (consolidated from 9 centres into single center with 8-9 units)	PROGRESSING ↔
Poland	Plan for Rare Diseases 2024-2025; expiring	Yes (fewer than 1 per 2,000)	Centers of Expertise developing; ERN participation expanding	PROGRESSING ↑
Saudi Arabia	No published plan; National Policy for Genetic Diseases Project completed, pending Minister of Health approval (aligned with Vision 2030)	Yes (1 per 2,000)	No coordinated policy oversight structure	EARLY-STAGE
Spain	2014-2023 plan expired; revised strategy under development (expected 2026); fragmented across 17 Autonomous Communities	Yes (EMA adherent)	17 autonomous communities govern independently; limited national coordination	PROGRESSING ↔
Türkiye	First national strategy (early stage, limited implementation)	Yes (fewer than 1 per 2,000)	Responsibility spread across multiple ministries; no dedicated body	EARLY-STAGE
United Kingdom	UK Rare Diseases Framework 2021-2027 (expiring); devolved governance	Yes (fewer than 1 per 2,000)	Fragmented across 4 nations (England, Wales, Scotland, Northern Ireland)	PROGRESSING ↔

2. Diagnostics and Screening Infrastructure

INDICATORS (1) Newborn screening panel scope + SMA inclusion,
(2) Genetic testing reimbursement and accessibility,
(3) Designated reference centers or centers of expertise

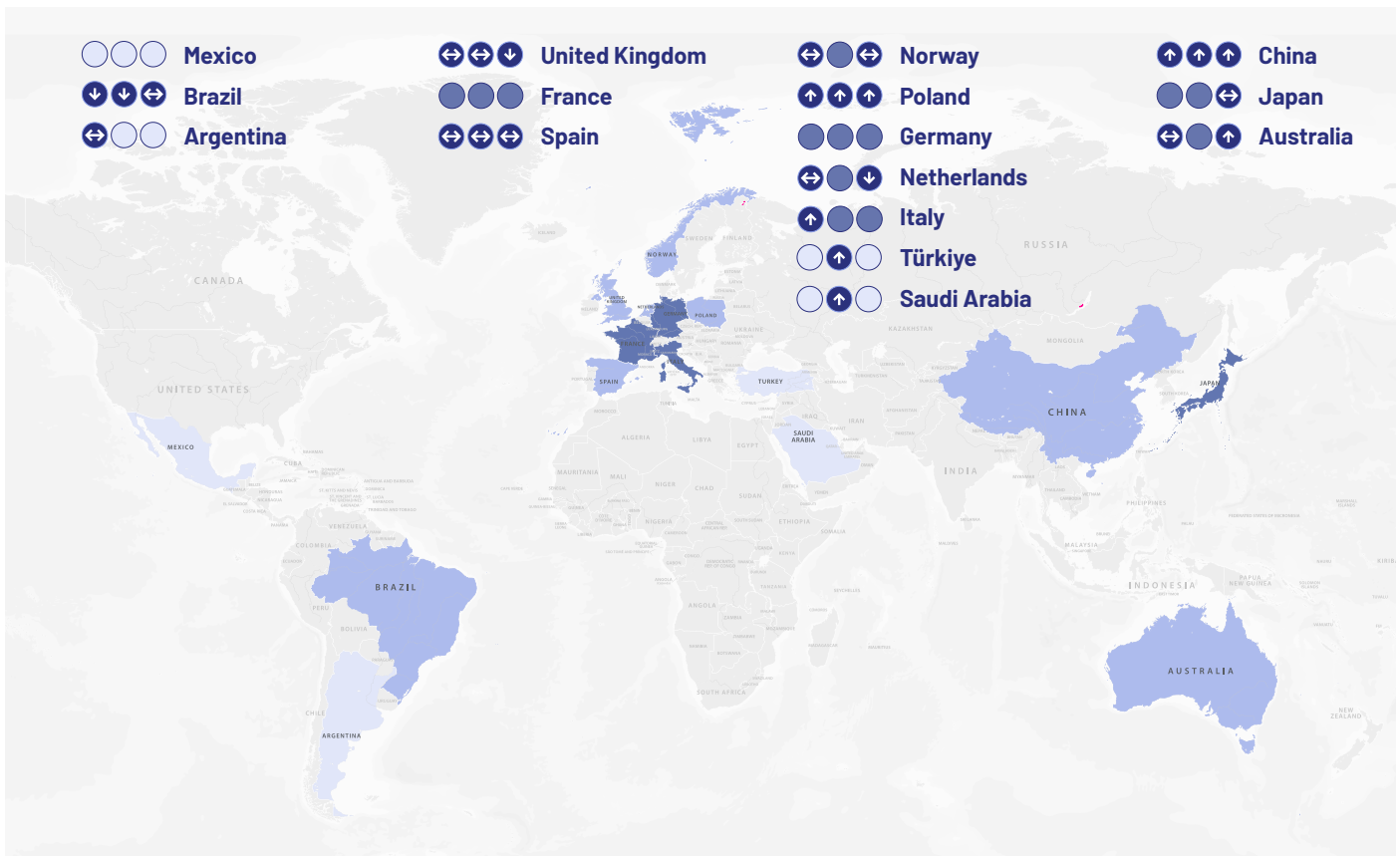
COUNTRY	NBS PANEL SCOPE	GENETIC TESTING ACCESS	REFERENCE CENTERS / CENTERS OF EXPERTISE	MATURITY
Argentina	6 conditions nationally (Buenos Aires screens 20+); no SMA	CENAGEM available; advanced sequencing often uncovered; judicial appeals needed	Specialists concentrated in 4 provinces; 3 geneticists trained per year	EARLY-STAGE
Australia	32 conditions including SMA	Available but referral-dependent; wait times for public; private costs	\$500M Genomics Health Futures Mission; no formal reference center network	RELATIVELY ADVANCED
Brazil	Limited (exact number unclear); basic panel	300–400 geneticists for 213M; 80% concentrated in South/Southeast	27 RDRS + 9 specialized services; major geographic gaps	PROGRESSING ↓
China	Variable (PKU + CH nationally; SMA pilot programs only)	Not covered by insurance; only 5.3% of physicians feel adequately informed	400+ hospital network anchored by PUMCH; capacity uneven across regions	PROGRESSING ↑
France	16 conditions	Available through CRMR reference center network	Extensive CRMR reference center network across the country	RELATIVELY ADVANCED
Germany	19 conditions	Broad access via university hospitals and ZSE network	Three-tier ZSE model (Type A/B/C); awareness gaps limit utilization	RELATIVELY ADVANCED
Italy	40+ conditions (mandatory, nationwide)	Available; ERN-integrated across most regions	ERN participation in all but 7 regions	RELATIVELY ADVANCED
Japan	20 conditions	Advanced diagnostic technologies available	Well-developed specialist referral system	RELATIVELY ADVANCED
Mexico	1–6 conditions; no SMA; no uniform national program	Minimal infrastructure for genetic testing	No formal reference center network	EARLY-STAGE
Netherlands	27 conditions	Widely covered by health insurance when clinically indicated	~350 recognized Centers of Expertise (ECZAs)	RELATIVELY ADVANCED
Norway	30 conditions including SMA (expanding to 39)	Free with referral through university hospitals	Norwegian Center for Rare Diseases (recently restructured into single center with 8–9 units, ~200 staff)	RELATIVELY ADVANCED
Poland	30 conditions	Available but slow; often ordered late in diagnostic process	44 designated Rare Disease Expert Centers (OECRs); ~140 clinical geneticists; ERN participation expanding	PROGRESSING ↑
Saudi Arabia	21 conditions	Strong carrier screening program; limited RD-specific diagnostics	Limited specialized rare disease infrastructure	PROGRESSING ↑
Spain	22 conditions in common national portfolio (expanding to 25); SMA approved by CISCN but awaiting BOE legal mandate (expected end 2026)	Available but significant regional variation	358 centers (110 in ERNs); fragmented across 17 autonomous communities	PROGRESSING ↔
Türkiye	6 conditions	Government-funded PGD/IVF + mandatory premarital SMA carrier screening; WES/NGS available in major centers (up to 80% yield in consanguineous families); not systematically reimbursed	National reference centers designated for neuromuscular/rare conditions (none EUCERD-certified); urban-concentrated	PROGRESSING ↑
United Kingdom	10 conditions (well below international peers)	WGS available via NHS Genomic Medicine Service	NHS Genomic Medicine Service exists; limited NBS constrains early detection	PROGRESSING ↔

3. Treatment Access and Reimbursement

INDICATORS

- (1) Countries reimbursement framework and its flexibility for rare diseases
 (2) Orphan drug incentive strength,
 (3) Early/flexible access pathways

COUNTRY	REIMBURSEMENT FRAMEWORK FLEXIBILITY	ORPHAN DRUG INCENTIVES	EARLY/FLEXIBLE ACCESS PATHWAYS	MATURITY
Argentina	CONETEC non-binding; courts override HTA decisions	None (no market exclusivity, tax credits, or fee waivers)	Judicial amparo as primary route; ANMAT expedited approval for drugs authorized in reference countries	EARLY-STAGE
Australia	Unofficial QALY ~AUD \$45-60K; LSDP for ultra-rare conditions	Some (Orphan Drug Program fee waivers; 13% first-pass approval rate)	LSDP; managed access emerging via 2024 HTA Review	PROGRESSING 
Brazil	QALY threshold BRL 120K (3x standard but still low for orphan drugs)	No market exclusivity/tax credits; ANVISA Resolution 205/2017 expedited approval pathway (up to 365 days)	ANVISA Resolution 205/2017 expedited pathway; judicialization restricted by 2024 STF ruling	PROGRESSING 
China	No formal CEA; NRDL annual price negotiation model	Emerging (priority review and market exclusivity introduced)	Priority review pathway (70-130 days); hospital uptake 25-41%	PROGRESSING 
France	Benefit-based assessment (SMR/ASMR); no QALY threshold	Yes (EU framework)	AAP + AAC (among Europe's strongest early access systems)	RELATIVELY ADVANCED
Germany	AMNOG presumed added benefit for orphan drugs	Yes (EU framework)	Early access mechanisms available	RELATIVELY ADVANCED
Italy	QALY used; 82% of EMA orphan drugs available	Yes (EU framework)	82% of EMA-approved orphan drugs reimbursed through SSN; Law 207/2024 restricts advocacy involvement (10-year rule)	RELATIVELY ADVANCED
Japan	CEA limited to large-market-size drugs (most orphan drugs outside scope); ultra-expensive drugs assessed regardless of market size	Some (priority review, reduced fees, market exclusivity)	Regulatory incentives for early access	PROGRESSING 
Mexico	No formal HTA flexibility for rare diseases	None	No structured access pathways	EARLY-STAGE
Netherlands	Strict CEA threshold; no ultra-rare exception	Yes (EU framework)	Limited managed entry agreements	PROGRESSING 
Norway	Severity-weighted HTA (higher WTP for severe conditions)	Some (EU/EEA framework)	Very limited; individual exception pathway since April 2025 only	PROGRESSING 
Poland	Low QALY threshold	Yes (EU framework)	Medical Fund (2020 Act) fast-track pathway for innovative/orphan drugs; ~33% of EMA-approved non-oncology orphan drugs available; ~5% without indication restrictions	PROGRESSING 
Saudi Arabia	Emerging HTA body (not yet operational)	Some	No structured orphan drug accommodations	EARLY-STAGE
Spain	No rare disease-specific HTA flexibility	Yes (EU framework)	~67% of EMA-approved orphan drugs reimbursed (104/156 as of 2025); informal ~€22-25K/QALY threshold in practice	PROGRESSING 
Türkiye	No HTA flexibility for rare diseases	None	Foreign Drug List + Named Patient Programs; individual applications and legal cases for many therapies; limited early access	EARLY-STAGE
United Kingdom	HST pathway with higher threshold for ultra-rare	Some (MHRA orphan designation with 10-year market exclusivity; CGT Catapult innovation support)	50% of non-oncology orphan drugs unreimbursed; declining access	PROGRESSING 



4. Summary: Cross-Domain Maturity Assessment

COUNTRY	NATIONAL GOVERNANCE FRAMEWORK	SCREENING AND DIAGNOSIS	ACCESS AND REIMBURSEMENT
Argentina	PROGRESSING	EARLY-STAGE	EARLY-STAGE
Australia	PROGRESSING	RELATIVELY ADVANCED	PROGRESSING
Brazil	PROGRESSING	PROGRESSING	PROGRESSING
China	PROGRESSING	PROGRESSING	PROGRESSING
France	RELATIVELY ADVANCED	RELATIVELY ADVANCED	RELATIVELY ADVANCED
Germany	RELATIVELY ADVANCED	RELATIVELY ADVANCED	RELATIVELY ADVANCED
Italy	PROGRESSING	RELATIVELY ADVANCED	RELATIVELY ADVANCED
Japan	RELATIVELY ADVANCED	RELATIVELY ADVANCED	PROGRESSING
Mexico	EARLY-STAGE	EARLY-STAGE	EARLY-STAGE
Netherlands	PROGRESSING	RELATIVELY ADVANCED	PROGRESSING
Norway	PROGRESSING	RELATIVELY ADVANCED	PROGRESSING
Poland	PROGRESSING	PROGRESSING	PROGRESSING
Saudi Arabia	EARLY-STAGE	PROGRESSING	EARLY-STAGE
Spain	PROGRESSING	PROGRESSING	PROGRESSING
Türkiye	EARLY-STAGE	PROGRESSING	EARLY-STAGE
United Kingdom	PROGRESSING	PROGRESSING	PROGRESSING

Country-by-Country Comparative Analysis

Across the 16 countries examined, this analysis surfaces both meaningful progress and persistent structural gaps. The section begins by examining why rare diseases are increasingly relevant to healthy aging, and why this shift raises the stakes for health systems that are already under strain. It then organizes the country-level findings into a structured cross-country comparison across four dimensions: (1) diagnostics and screening infrastructure, (2) workforce capacity, (3) treatment access and reimbursement models, and (4) national governance frameworks. The detailed country profiles that inform this analysis are provided in Appendix D.

Workforce capacity is broken out here because it is a cross-cutting constraint that shapes outcomes across diagnostics, access, and governance alike. Although it did not lend itself to a ratable column in the country ratings, a standalone discussion allows for direct comparison of where specialist shortages are most acute and how they shape each country's results. The comparison identifies leading practices, common challenges, and systemic patterns that distinguish countries making durable progress from those where policy intent has yet to translate into equitable outcomes. Two themes cut across all four dimensions: cross-country heterogeneity remains a significant barrier to consistent progress, and population aging will place growing pressure on rare disease systems that are already strained.

Rare Diseases in an Era of Longer Lives

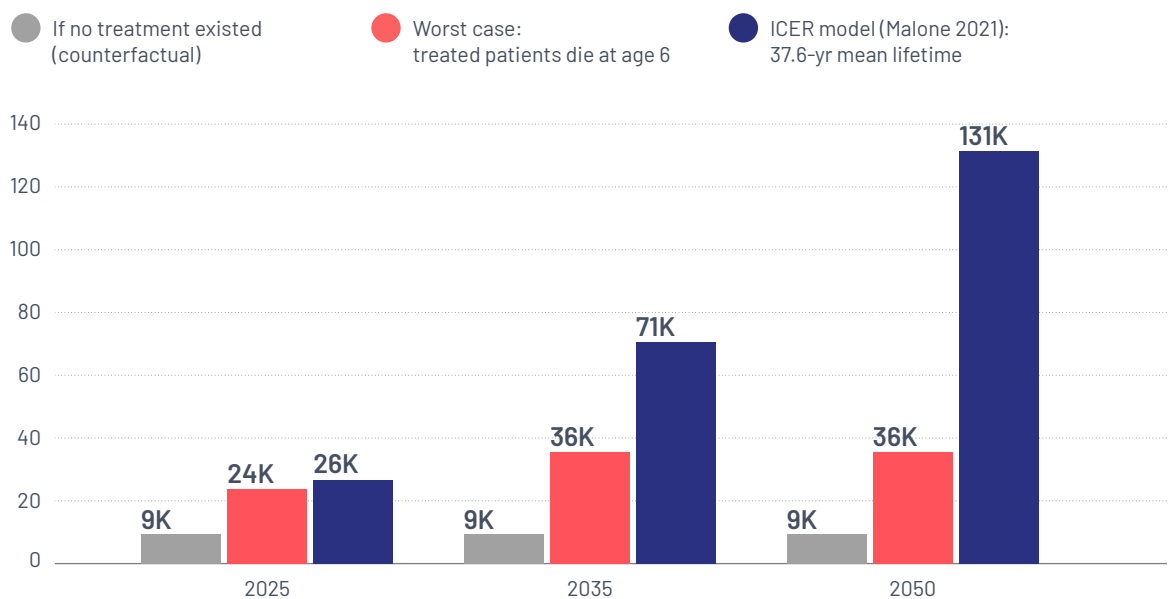
Rare diseases are no longer only a pediatric or early-life policy issue. Across our conversations with medical providers, researchers, and policymakers around the world, two key intersections between rare diseases and healthy aging consistently came into focus. Each creates distinct pressures on health systems; together, they raise the prospect of rare disease populations growing larger, older, and more clinically complex in health systems already struggling to meet today's demands.

The first intersection is rare-disease-specific. Disease-modifying therapies, improved standards of care, and earlier diagnosis are altering the natural history of conditions once considered uniformly fatal in childhood. Because new therapies are not cures, treated patients who survive into adulthood will

continue to require ongoing – and often complex – care for years or decades, expanding the population living with affected conditions even if underlying incidence rates hold steady.

Spinal muscular atrophy (SMA) Type 1 offers one illustration. Historically, infants with SMA Type 1 rarely survived past age two,¹⁸ and global prevalence sat near 9,000* cases.¹⁹ Following the introduction of disease-modifying therapies over the past decade, treated infants now reach school age and beyond. We constructed an illustrative model that holds incidence steady and varies only the assumed lifetime of treated patients to show how this could play out at scale: under a conservative assumption that treated patients survive only to age 6, global cases roughly quadruple by 2035; applying the 37.6-year mean lifetime used in the ICER cost-effectiveness analysis published by Malone et al. (2021),²⁰ the model produces approximately 131,000 cases by 2050 – more than fourteen times the no-treatment scenario. These figures are illustrative, not predictions.

Prevalent SMA Type 1 cases, global (thousands)



Illustrative scenario for global prevalent SMA Type 1 cases. The counterfactual (gray) reflects prevalence in the absence of disease-modifying therapy; the "worst case" (green) assumes treated patients survive only to age 6; the ICER-aligned scenario (blue) applies the 37.6-year mean lifetime assumption from Malone et al. (2021).²¹ Figures are model outputs, not predictions, and are sensitive to the underlying lifetime assumption.

*Estimate derived from incidence data, not reported directly. SMA Type 1 birth incidence is approximately 6 per 100,000 live births (Verhaart et al. 2017). Applied to the roughly 140 million live births worldwide each year, this yields on the order of 8,000 to 9,000 new Type 1 cases annually; 9,000 is used here as the baseline. Because untreated SMA Type 1 historically rarely survived past age two, annual incidence and point prevalence effectively converged, so this figure also approximates the historical global living prevalence that serves as the model's starting point.

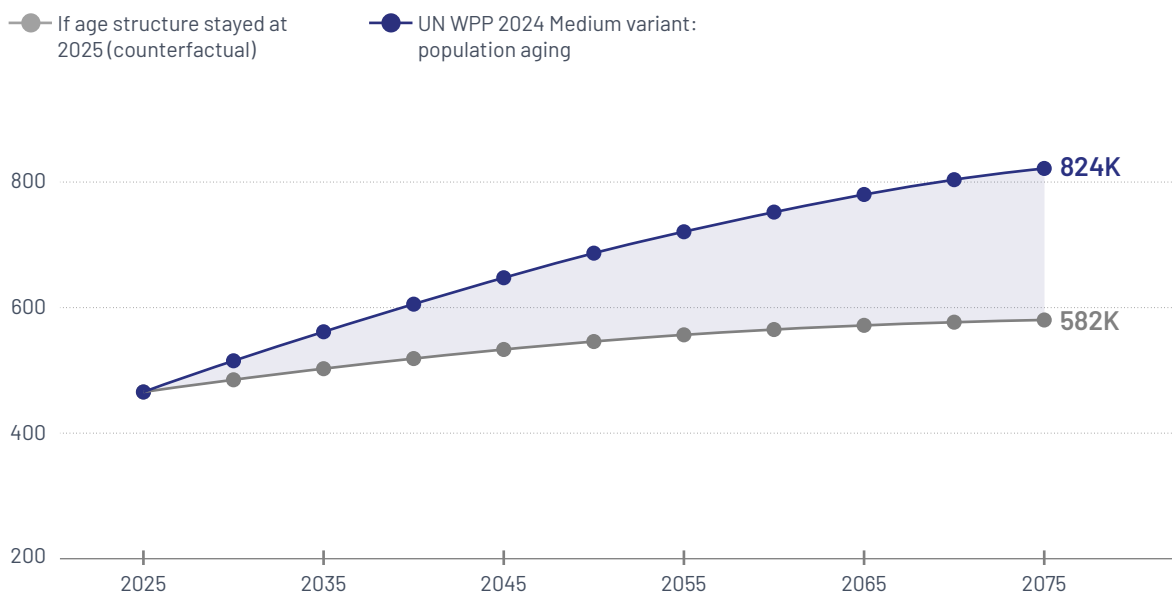
Similar dynamics could emerge across Friedreich's ataxia, Duchenne muscular dystrophy, sickle cell disease, and other conditions where new therapies are reshaping prognoses for what were historically lethal childhood diagnoses.

A related dynamic sits alongside therapeutic progress. As one expert interviewee observed during the development of this report, rare diseases themselves are "aging." Scientific understanding and clinical awareness have advanced considerably over the past two decades, and with that advancement has come — and continues to come — broader recognition of rare diseases across the life course. Conditions once assumed to manifest only in childhood are increasingly diagnosed in adults, and adult-onset and late-onset presentations are receiving closer attention. Together with treatment-driven survival, this points toward a future in which more people live with rare disease diagnoses, across more years of life, than at any prior point.

The second key intersection is demographic and applies independently of any change in treatment or diagnosis. Roughly 1.1 billion people worldwide are now aged 60 or older, and the United Nations projects this figure will reach 2.1 billion by 2050.²² As age structures shift, the number of people living with later-onset rare diseases could grow substantially.

Amyotrophic lateral sclerosis (ALS) offers a useful example. Peak ALS incidence occurs between ages 65 and 75,²³ making the condition particularly sensitive to demographic aging. Applying the same illustrative modeling approach — holding incidence steady and varying only the global age structure — yields approximately 582,000 prevalent cases by 2075 if age structure is held at 2025 levels, versus approximately 824,000 under the United Nations' 2024 World Population Prospects medium-variant projection.²⁴ The 242,000-case gap reflects the contribution of demographic aging alone within the model. As above, these are illustrative, not predictions.

Prevalent ALS cases, global (thousands)



The counterfactual (gray dashed) holds global age structure constant at 2025 levels; the medium-variant scenario (blue) applies the United Nations' 2024 World Population Prospects projection.²⁵

Similar logic could apply to a range of other adult- and older-adult-onset rare diseases for which the at-risk population is concentrated in older age groups.

If these two intersections unfold as the dynamics above suggest, they would raise the stakes of nearly every system-level finding in this report. Diagnostic infrastructure built around pediatric presentations may need to evolve to accommodate adult and late-onset cases. QALY-based reimbursement may struggle with therapies for older patients, where fewer remaining life-years yield a higher cost per QALY — a structural challenge compounded for rare disease therapies, whose cost-effectiveness analyses already carry high uncertainty. Adult subspecialty workforces may face new pressures as historically pediatric patient populations move into adult care. And patients may face strain at every transition between pediatric, adult, and geriatric care. The country-level findings that follow assess where systems may be well placed to absorb these pressures — and where they may not.

Diagnostics and Screening Infrastructure

Across the countries examined, newborn screening programs represent the most widely adopted diagnostic tool, though the scope and consistency of these programs vary dramatically. Italy screens for the most conditions (40+),²⁶ followed by Australia (32+),²⁷ Norway (30, with expansion planned to 39),^{28,29} and Poland (30).^{30,31} At the other end of the spectrum, Mexico (1–6),³² Argentina (6),^{33,34} and Türkiye (6)^{35,36} maintain far narrower programs, limiting early detection to a small subset of treatable conditions. Most other countries fall in a middle range of 10–27 conditions. Across the board, these programs are designed to detect pediatric-onset conditions at birth, leaving no comparable screening pathway for the substantial share of rare diseases that present in adulthood or progress with age.

SMA inclusion in newborn screening has emerged as a meaningful benchmark of screening ambition. As of 2025, the majority of countries in this dataset have incorporated SMA into their national or regional screening panels, including France, Germany, Norway,

Poland, Türkiye, and more. Notably, Türkiye has achieved 97% screening coverage since adding SMA in 2022, identifying ~300 cases among ~1.8 million infants.³⁷ By contrast, China and Mexico have not yet moved beyond pilot-stage screening for SMA, and the UK's Generation Study remains in a research phase rather than routine implementation.

Despite these investments, diagnostic delay remains a persistent challenge across nearly all countries. Only France achieves an average delay of 2–3 years, enabled by its strong network of reference centers and structured referral pathways.³⁸ Most countries cluster between 5 and 7 years, including Australia, Germany, the Netherlands, Norway, Poland, Saudi Arabia, and the UK. The most extreme delays appear in Mexico (8 years on average),³⁹ Argentina (5–10 years),⁴⁰ and Poland (5–10 years),⁴¹ where workforce shortages and geographic fragmentation compound structural barriers to timely diagnosis. For older patients, these delays are likely longer still, as symptoms of adult-onset rare diseases are frequently misattributed to normal aging or common chronic conditions.

Access to advanced genomic technologies, including whole genome sequencing and whole exome sequencing, is expanding but remains unevenly distributed. Countries such as Australia, France, Germany, the Netherlands, Norway, and the UK offer broad access to these tools, though availability is often concentrated in university hospitals and urban centers. In China, Brazil, Argentina, and Saudi Arabia, advanced sequencing remains limited by reimbursement constraints, institutional capacity, or geographic concentration. These disparities mean that the diagnostic potential of genomic medicine is not yet translating into equitable access across or within countries.

Workforce Capacity

Workforce shortages in clinical genetics, neurology, and related specialties represent a binding constraint on rare disease systems that directly affect diagnostic timelines, screening effectiveness, and the capacity of health systems to deliver coordinated care.

The UK reports just 1.1 neurologists per 100,000 people, well below the EU average of 5–7.⁴² Spain (3.5 per 100,000)⁴³ and Argentina (2.9)⁴⁴ also fall below European benchmarks. Italy has a relatively high overall ratio (9 per 100,000), but only about half of its neurologists practice in the public system, and geographic concentration in the north leaves southern regions underserved.^{45,46}

Clinical genetics capacity is similarly constrained. Mexico has just one geneticist per 100,000 people in Mexico City and as few as one per 500,000 residents in many states, with no formal genetic counseling profession.⁴⁷ Saudi Arabia reports approximately 40 clinical geneticists and 14–41 genetic counselors nationwide for a population of 36.8 million.^{48,49,50} Poland's 140 clinical geneticists serve approximately 38 million people, with wait times of 2.5–3 years for specialist appointments.⁵¹ Argentina's national genetic center trains only three clinical geneticists per year, a pace insufficient to meet growing demand.⁵²

China illustrates a distinctive pattern: while the neurology workforce has expanded three- to five-fold over the past 30 years, clinical genetics is not recognized as a formal medical specialty, and only ~5% of physicians report feeling adequately informed about rare diseases.^{53,54,55} In Germany, despite strong infrastructure, only ~45% of primary care physicians are aware of the ZSEs network, limiting appropriate referrals.⁵⁶

Across the board, these workforce gaps are amplified by geographic concentration. Specialists tend to cluster in capital cities and academic medical centers, leaving rural and regional populations with limited access to timely diagnosis and expert care.

This pattern holds in high-income and middle-income countries alike, and it directly contributes to the diagnostic delays and access inequities documented throughout this report. As populations age, demand for geriatric care and chronic disease management will compete for the same limited pool of neurologists, geneticists, and metabolic specialists, placing additional pressure on rare disease systems unless workforce capacity expands in parallel.

Treatment Access and Reimbursement

Reimbursement frameworks represent perhaps the most consequential source of cross-country variation in rare disease outcomes. Across the countries examined, the gap between the highest- and lowest-access systems is substantial, shaped by fundamental differences in how countries evaluate, price, and fund therapies for rare disease patient populations. In practice, this means that patients with the same condition, living in countries with comparable income levels, can face fundamentally different prospects for treatment access depending on how their system is designed.

Countries that have built explicit accommodations for rare diseases into their evaluation frameworks, whether through presumed benefit, clinical benefit assessments, flexible thresholds, or dedicated ultra-rare pathways, consistently demonstrate stronger access than those applying standard evaluation frameworks without adaptation. Germany's AMNOG framework illustrates this principle most clearly. Orphan drugs are presumed to offer added benefit upon market authorization, bypassing the need for comparative evidence or formal cost-effectiveness thresholds at the point of entry. New medicines can be reimbursed immediately following EMA approval, positioning Germany as one of the most accessible markets in Europe for rare disease therapies. France takes a distinct but similarly supportive approach, evaluating drugs on clinical benefit (SMR/ASMR) rather than cost-per-QALY, with approximately 78% of EMA-approved orphan drugs ultimately receiving reimbursement.⁵⁷ Italy achieves comparable access, with approximately 82% of EMA-approved orphan drugs (50 of 61 approved between 2018 and 2021) reimbursed through its National Health Service, supported by flexible QALY application and a fast-track mechanism for innovative medicines.⁵⁸

At the other end of the spectrum, countries that rely on rigid QALY-based thresholds without dedicated orphan drug accommodations consistently demonstrate lower access. Poland's threshold, set at approximately three times GDP per capita, continues to drive high rejection rates for orphan drugs. According to the IQVIA Patients W.A.I.T. Indicator 2024 Survey, Poland made only 38% of centrally-approved orphan drugs (2020–2023 cohort) available to patients as of January 2025, below the EU average of 41% and with an average time from EU marketing authorization to availability of 768 days.⁵⁹ Importantly, a negative HTA recommendation does not always preclude reimbursement – selected products such as omaveloxon and tofersen obtained reimbursement in 2025 despite unfavorable HTA outcomes – but such decisions remain the exception rather than the rule. The Netherlands applies severity-weighted thresholds of €20,000–€80,000 per QALY but provides no distinct pathway for ultra-rare conditions.⁶⁰

Even well-resourced systems can fall short when frameworks do not adequately accommodate rare disease characteristics. Norway's severity-weighted HTA framework allows higher willingness-to-pay for the most severe conditions, but therapies delivering disease stabilization or incremental functional benefit – particularly for slower-progressing or adult-onset conditions – often struggle to demonstrate sufficient cost-effectiveness. Similarly, the UK's NICE framework, despite its Highly Specialized Technologies pathway allowing thresholds up to £300,000 per QALY, has seen its European ranking decline from 2nd in 2013 to 11th in 2024, as narrow eligibility criteria and routing limitations restrict the pathway's practical reach. As a result, nearly one quarter of MHRA-approved orphan drugs are never submitted to NICE for appraisal.⁶¹

Where structured reimbursement pathways are absent altogether, patients are often forced into judicial or ad hoc mechanisms. In Argentina and Brazil, access to high-cost therapies frequently depends on court proceedings, reflecting gaps between legal entitlements and routine coverage decisions. Mexico's fragmented formulary system produces significant within-country variability, with coverage decisions made independently by each public institution. China has made rapid progress through NRDL expansion,

which now includes more than 100 rare disease drugs, but limited hospital uptake (estimated at only 25–41% of hospitals stocking approved therapies) constrains real-world access even for reimbursed products.⁶²

These patterns reinforce a central finding of this analysis: the design of a country's HTA process appears to be a strong predictor of orphan drug accessibility. Where systems accommodate the unique characteristics of rare diseases (small evidence bases, high per-patient costs, and limited patient populations) access outcomes are meaningfully stronger. Where standard frameworks are applied without adaptation, the result is delayed or denied access for patients who have few or no therapeutic alternatives. This dynamic carries particular implications for aging populations: QALY-based models that weight remaining life-years inherently assign lower value to treatments for conditions diagnosed later in life, regardless of clinical benefit.

National Governance and Policy Frameworks

Thirteen of the 16 countries in this assessment have established some form of national rare disease strategy or policy framework. China, Mexico, and Saudi Arabia are the notable exceptions, each operating with partial or informal policy structures rather than comprehensive national plans. Among countries with formal strategies, maturity and durability vary considerably.

France, Germany, and Japan represent the most mature governance models. France launched its fourth national rare disease plan (PNMR4) in 2025, operationalizing 26 objectives across care, research, and industry. Germany's 2013 National Action Plan has been independently evaluated and found to have "improved markedly" rare disease care, supported by the multi-stakeholder NAMSE coordination body and a formal ZSE certification process. Japan's Nanbyo Law provides statutory authority for the designation, financing, and delivery of care for intractable diseases through a structured three-tier hospital network spanning all 47 prefectures.

Several countries face near-term governance inflection points. The UK Rare Diseases Framework (2021–2026), the Netherlands’ 2013 National Plan, Spain’s 2014–2023 strategy, and Poland’s 2024–2025 plan are all at or near expiration, and successor strategies are not yet clearly articulated in all cases. Spain’s revised strategy is expected in 2026, and the Netherlands is working toward a new plan supported by the RARE-NL initiative launched in 2024. These transitions present both risk and opportunity: without timely renewal, hard-won infrastructure may erode, but the revision process also creates space to address implementation shortfalls and align with emerging diagnostic and therapeutic capabilities.

Among countries without formal strategies, progress is still occurring but through fragmented mechanisms. China’s First and Second National Rare Disease Lists (2018 and 2023) formally recognize 207 conditions and anchor care coordination through a 400+ hospital network, but the absence of a unified strategy leaves incentive structures and access pathways variable. Mexico’s Article 224 provides a legal definition but no implementation framework. Saudi Arabia’s 2023 multi-stakeholder workshop endorsed the creation of a national definition and coordination mechanisms, but these have not yet materialized into policy.

A related gap across governance structures is the uneven availability of data on the societal cost of rare diseases. Some countries, such as the UK, have produced comprehensive estimates of the economic burden rare diseases impose on their health systems, economies, and communities. In most countries in this dataset, however, comparable data either does not exist or is limited to narrow disease-specific studies. This absence matters. Without a clear picture of the full economic and social impact of rare diseases, policymakers lack the evidence base needed to justify sustained investment, set priorities, and make the case for dedicated funding. Countries that have quantified the societal cost of rare diseases are better positioned to anchor their strategies in concrete fiscal arguments; those that have not risk treating rare diseases as a secondary concern relative to conditions where the economic case is more readily available. As

populations age, the societal cost of rare diseases will grow alongside the number of affected individuals, making this data gap increasingly consequential for fiscal planning.

Further, a recurring theme across governance structures is the gap between policy intent and implementation. Even in countries with mature strategies, translation to consistent practice remains uneven, often constrained by insufficient implementation planning, unclear accountability mechanisms, variable governance structures, and, critically, the absence of dedicated and sustained funding.

Cross-Country Policy Heterogeneity

The preceding four dimensions reveal not only shared challenges but a striking degree of divergence in how countries define, prioritize, and operationalize rare disease policy. This heterogeneity is itself a significant structural barrier, distinct from the specific gaps within any single dimension. As aging populations expand the number of people living with rare diseases, the consequences of this fragmentation will affect a growing share of patients in every country examined.

Country-level differences span everything from rare disease definitions and evidentiary standards to willingness to pay for orphan therapies, availability of early access tools, and the depth of clinical expertise available for specific conditions. Significant differences exist not only between high-income and middle-income countries but among countries with comparable economic resources and regulatory maturity. Germany reimburses orphan drugs immediately upon EMA approval with presumed added benefit, making 76% of centrally-approved orphan drugs available to patients;⁶³ Poland, operating under the same EU regulatory framework, reaches only 38% availability for the same cohort.⁶⁴ France achieves average diagnostic delays of 2–3 years;⁶⁵ the UK, with a similarly well-resourced health system, averages 4–6.⁶⁶

This fragmentation has consequences at every level. For patients, it creates a geographic lottery in which access to diagnosis and treatment depends heavily on where someone lives. Patients who seek or require care across borders face additional barriers, as treatments available and reimbursed in one country may not be covered by the patient's home system. For drug developers, navigating a patchwork of regulatory requirements, HTA processes, and pricing frameworks raises the cost and complexity of bringing orphan drugs to market, particularly for ultra-rare conditions where the commercial case is already marginal. For international collaborative infrastructure, including European Reference Networks, shared registries, and multi-regional clinical trials, divergent national definitions and evidence thresholds limit the reach of tools that depend on a degree of cross-border consistency to function effectively.

The difficulty of addressing this fragmentation is compounded by the fact that most levers for change sit at the national or even regional level. Unlike issues that can be resolved through a single EU-wide policy action, many of the gaps documented in this report require parallel reform efforts across dozens of separate jurisdictions, each with its own political dynamics, fiscal constraints, and institutional structures. Greater alignment, whether through shared definitional frameworks, mutual recognition of evidence packages, or coordinated approaches to HTA and reimbursement, would amplify the impact of reforms that individual countries pursue on their own. Without such alignment, the pattern documented throughout this analysis, in which a patient's prospects are determined as much by geography as by the state of the science, is likely to persist.

Synthesis: Cross-Cutting Patterns Across 16 Countries

Taken together, the cross-country comparison reveals several overarching patterns that cut across individual dimensions and country contexts. These patterns inform the recommendations that follow in the conclusion of this report, where we outline an action framework for modernizing diagnostics, accelerating access, and strengthening governance to meet the evolving needs of rare disease populations worldwide.

Diagnostic delay is near-universal, but not inevitable:	France's achievement of a 2–3 year average delay demonstrates that structured referral networks, strong reference centers, and sustained investment can meaningfully compress timelines. Most other countries remain in the 5–7 year range, suggesting that infrastructure alone is insufficient without deliberate attention to GP education, referral coordination, and specialist distribution.
Workforce shortages are a universal bottleneck:	Every country in the report faces shortages in clinical genetics, neurology, or both. These shortages directly limit diagnostic capacity, slow referral pathways, and undermine the effectiveness of even well-designed screening programs. Addressing workforce gaps is not a secondary priority; it is foundational to the functioning of every other element of rare disease infrastructure.
HTA design is a strong lever for treatment access:	The countries with the highest orphan drug reimbursement rates do not rely on strict QALY-based thresholds and often build explicit accommodations for rare diseases into their evaluation frameworks. Countries relying on standard cost-effectiveness thresholds without adaptation consistently underperform on access, often by wide margins.
Policy maturity does not guarantee equitable access:	Countries with well-established national strategies, including the UK, Norway, and the Netherlands, still exhibit significant gaps in orphan drug availability, diagnostic delay, or workforce capacity.
Aging populations will intensify existing pressures:	In countries with rapidly aging populations, including Japan, Italy, Germany, China, and the UK, the burden of adult-onset and late-presenting rare diseases is expected to grow. HTA frameworks that assign lower value to interventions in populations with shorter remaining life expectancy, screening systems oriented primarily toward pediatric conditions, and specialist networks concentrated in urban academic centers are all poorly configured for this demographic shift. Countries that proactively integrate rare disease policy into healthy aging agendas will be better positioned to serve their populations equitably over the coming decades.
Cross-country heterogeneity is a structural barrier in its own right:	The variation documented across this analysis is not merely descriptive. Divergent definitions, evidentiary standards, reimbursement frameworks, and access tools create a fragmented landscape that limits cross-border collaboration, raises barriers to orphan drug development, and ensures that patient outcomes remain shaped significantly by geography. Because most levers for change sit at the national or even regional level, progress requires parallel reform efforts across dozens of separate jurisdictions rather than a single coordinated intervention. Greater alignment, whether through shared frameworks, mutual recognition, or coordinated policy learning, would amplify the impact of reforms that individual countries pursue on their own.

CONCLUSION: Moving Rare Disease Policy into the Future

Rare disease policy has advanced substantially in the past decade, yet progress remains uneven across countries and persistent gaps continue to limit improvements in diagnosis, treatment access, and care coordination. These gaps demand attention on their own terms, but they take on added urgency in the context of global demographic change. By 2050, the population aged 60 and older will reach 2.1 billion worldwide, and the number of people living with or newly diagnosed with rare diseases will grow as well.⁶⁷ While many countries now have national rare disease frameworks, expanded newborn screening programs, or orphan drug pathways, patients frequently still experience diagnostic delays of five years or longer and face inconsistent access to therapies across health systems.

The analysis presented in this report highlights both meaningful progress and clear opportunities for improvement. Across the 16 countries examined, rare disease systems are evolving but often lack the governance structures, diagnostic capacity, and reimbursement models needed to fully support patients and caregivers over the life course. Systems built primarily around pediatric-onset conditions and younger patient populations are not configured for the demographic reality that lies ahead.

Moving rare disease policy forward will require coordinated action across several core areas: strengthening national governance structures, modernizing diagnostic systems, expanding clinical capacity, supporting innovation, adapting reimbursement frameworks, and strengthening international collaboration. Together, these policy priorities can help countries build rare disease systems that support both current patients and future generations as populations age and new therapeutic technologies emerge.

Strengthen National Rare Disease Governance

Many countries included in this analysis have adopted national rare disease strategies or policy frameworks. However, these strategies often lack sustained funding, clear accountability structures, or centralized coordination mechanisms. Strengthening governance structures can help ensure that rare disease initiatives are implemented effectively and that policy commitments translate into measurable improvements in diagnosis, treatment access, and patient outcomes.

RECOMMENDATIONS

1. Establish dedicated rare disease offices within national health ministries.

Governments should create specialized rare disease units within Ministries of Health responsible for coordinating policy development, overseeing implementation of national strategies, and integrating rare disease considerations across regulatory agencies, reimbursement systems, research programs, and public health initiatives.

2. Adopt and fund comprehensive national rare disease strategies.

Countries should develop national rare disease plans with clearly defined goals, implementation timelines, and dedicated funding streams to support diagnostics, treatment access, research, and care coordination.

3. Adopt formal national definitions of rare disease.

Countries that have not codified a legal definition should adopt one through legislation or regulation to ensure clarity in regulatory pathways, research prioritization, and reimbursement eligibility.

4. Establish dedicated and ring-fenced funding for rare disease policy implementation.

National rare disease strategies should be supported by protected funding streams that cannot be diverted to other health priorities.

5. Integrate aging as a core dimension of national rare disease strategies.

Countries developing or renewing national rare disease plans should account for the full intersection of rare disease and aging. This includes diagnostic pathways for conditions that present later in life, but also sustained care infrastructure for the growing number of patients diagnosed in childhood who will survive into adulthood and – as treatments continue to advance – old age. Training requirements should extend to geriatricians and general internists, who increasingly encounter rare disease patients but are rarely equipped to manage their conditions. Reimbursement frameworks should be evaluated for structural biases that disadvantage patients with fewer remaining life-years, regardless of when their disease was first diagnosed.

Expand Early Detection and Diagnostic Capacity

Delayed diagnosis remains one of the most consistent challenges across countries. Despite advances in genomic medicine and expanded screening programs, many patients continue to experience diagnostic journeys lasting five years or longer. For patients with adult-onset rare diseases, these delays are often compounded by misattribution of symptoms to normal aging. Improving early detection, for conditions that present across the lifespan and not only in childhood, is therefore one of the most effective ways to reduce disease burden and enable timely treatment.

RECOMMENDATIONS

1. Expand newborn screening programs to include all treatable rare diseases.

Governments should update national newborn screening panels to include rare conditions with reliable screening methods and effective treatments while ensuring consistent implementation across regions. Countries should also explore systematic approaches to identifying adult-onset rare diseases, including integration of rare disease screening criteria into routine primary care assessments for older adults. Countries considering expansion of screening programs can use pilot initiatives to evaluate the feasibility of screening for additional rare diseases and generate real-world evidence on clinical impact.

2. Invest in national genomic testing infrastructure.

Countries should expand access to whole genome and whole exome sequencing through public funding, reimbursement coverage, and expanded laboratory capacity.

3. Reduce diagnostic delays by strengthening rare disease capacity in primary care.

Governments should expand rare disease education in medical training and continuing education for primary care providers, geriatricians, and general internists while deploying clinical decision-support tools and standardized referral pathways. Training should include recognition of rare disease presentations in older adults, where symptoms are most likely to be misattributed to age-related conditions.

Strengthen the Rare Disease Workforce and Care Infrastructure

Workforce shortages remain a major constraint across rare disease systems. Even where diagnostic technologies and treatments are available, limited numbers of trained specialists can delay diagnosis, restrict access to care, and create geographic disparities in treatment availability. As populations age, growing demand for geriatric and chronic disease care will compete for the same specialist workforce, making investment in clinical capacity a matter of increasing urgency.

RECOMMENDATIONS

1. Expand the rare disease clinical workforce.

Governments should increase training capacity for geneticists, neurologists, metabolic specialists, and other relevant clinicians through expanded residency positions and fellowship programs.

2. Expand the role of non-physician rare disease specialists.

Health systems should invest in training programs for genetic counselors, rare disease nurses, and other allied health professionals who can support diagnosis, care coordination, and patient management.

3. Create rare disease patient navigator programs.

Governments or health systems should fund navigator roles to guide patients through diagnostic pathways, treatment access, reimbursement systems, and long-term care coordination.

4. Improve public awareness and early recognition of rare diseases.

Governments should support national awareness initiatives that educate the public about rare disease symptoms and promote earlier engagement with healthcare systems.

Strengthen Incentives for Rare Disease Innovation

Scientific progress in rare diseases has accelerated rapidly in recent years, with advances in gene therapies, molecular diagnostics, and precision medicine creating new opportunities for treatment. Sustaining this progress requires policy environments that support research, encourage drug development, and reduce barriers to innovation.

RECOMMENDATIONS

1. Establish strong orphan drug incentive frameworks.

Governments should adopt or strengthen policies supporting rare disease drug development, including market exclusivity provisions, regulatory fee waivers, expedited review pathways, tax credits for clinical trial costs, and public research grants.

2. Recognize rare disease research as a driver of broader medical innovation and high knowledge-based economy.

Many scientific discoveries originating in rare disease research later benefit broader patient populations, meaning that investments in rare disease research strengthen the wider biomedical innovation ecosystem. Rare disease research activities generate substantial spillover benefits, driving advances in diagnostic technologies, therapeutic platforms, and understanding of fundamental biological mechanisms that enhance healthcare innovation broadly. These research investments yield positive economic returns through job creation in specialized sectors, attraction of biomedical talent and enterprises, and acceleration of broader scientific progress.

Modernize Reimbursement and Access Pathways

Innovation in rare diseases has, in many cases, advanced faster than reimbursement systems have adapted. Traditional health technology assessment frameworks often struggle to accommodate small patient populations, limited clinical evidence, and high treatment costs. These frameworks carry an additional limitation for aging populations: QALY-based models that weight remaining life-years assign systematically lower value to treatments for conditions diagnosed later in life, creating a structural barrier to access for older rare disease patients.

RECOMMENDATIONS

1. Adopt flexible reimbursement models for rare disease therapies.

Health systems should expand the use of policy tools such as coverage with evidence development, managed access agreements, conditional reimbursement programs, and outcomes-based pricing arrangements.

2. Create early access pathways for serious rare diseases.

Governments should establish regulatory mechanisms allowing patients with life-threatening rare diseases to access promising therapies before full reimbursement decisions are finalized.

3. Reduce HTA and reimbursement delays for rare disease therapies.

Countries should streamline regulatory and reimbursement review processes by establishing accelerated HTA pathways, parallel regulatory-reimbursement reviews, or dedicated review tracks.

4. Strengthen stakeholder engagement in access decision-making.

Governments and health systems should encourage structured dialogue between payers, regulators, manufacturers, clinicians, and patient organizations to improve evidence generation and facilitate timely access to therapies.

Support Patients and Caregivers

Rare diseases often impose significant financial, social, and emotional burdens on patients and families. Even where medical treatments are reimbursed, individuals frequently face substantial indirect costs related to care coordination, travel for specialized services, and lost income for caregivers.

RECOMMENDATIONS

1. Provide financial and social support for rare disease patients and caregivers.

Governments should expand policies that offset the costs of living with rare diseases, including caregiver support programs, disability benefits, and coverage for non-medical services required for long-term care.

Strengthen International Collaboration

Because rare diseases affect relatively small patient populations, international collaboration is essential for advancing research, improving diagnosis, and expanding treatment access. Collaborative research networks, shared registries, enabling cross-border access to care, and coordinated regulatory frameworks can help accelerate scientific discovery and improve patient outcomes.

RECOMMENDATIONS

1. Strengthen international coordination on rare disease policy and regulation.

Governments should collaborate through regional and international institutions to align regulatory pathways, clinical trial requirements, and evidence standards.

2. Enable cross-border access to specialized rare disease care.

Countries should establish reimbursement agreements and regulatory frameworks allowing patients to receive treatment in other countries when appropriate expertise or therapies are unavailable domestically.

3. Promote greater policy alignment across rare disease systems.

Governments and international institutions should work toward greater consistency in regulatory standards, reimbursement models, and access pathways across comparable markets.

The next phase of rare disease policy will require continued investment, clear prioritization, robust implementation mechanisms, and alignment across diagnostic, regulatory, and access pathways. The demographic window is narrow: countries that act now to strengthen these systems will be better prepared for the aging-driven growth in rare disease populations that lies ahead.

The rare disease policy agenda and the healthy aging agenda are converging. Funding gaps, workforce shortages, and approval and access barriers that limit rare disease care today will affect a growing number of patients as populations age. Countries that address these gaps now will build systems capable of supporting their populations across the full life course; those that delay risk compounding both challenges simultaneously.

An approach focused on innovation, system resilience, and optimization will equip countries and health systems with the capacity to manage both demographic change and emerging therapies. This means accelerating fit-for-purpose reimbursement models, strengthening national action plans to ensure coordinated care across sectors, and designing diagnostic and access pathways that serve patients at every stage of life. At its heart, effective rare disease policy is effective aging policy.

Appendix

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Appendix A: Priority Conditions – Clinical Overview and Rationale

This appendix provides brief context and rationale for inclusion of four rare conditions examined in the report. The selected conditions represent a cross-section of rare neurological and genetic diseases with varying onset patterns, treatment landscapes, and levels of policy visibility. Together, they offer a structured lens through which to examine how rare disease prevalence and policy attention evolve across diverse national contexts. The rare conditions are: Spinal muscular atrophy (SMA), Friedreich ataxia (FA), Amyotrophic lateral sclerosis (ALS), and Dravet syndrome (DS).

Spinal muscular atrophy (SMA)

SMA is a rare genetic neuromuscular disorder caused by mutations in the SMN1 gene, leading to progressive loss of motor neurons and muscle weakness. SMA affects approximately 1 in 10,000 live births globally and is the leading genetic cause of infant mortality.^{68,69} The disease spectrum ranges from severe infantile onset (Type 1) to milder adult-onset forms (Type 4). SMA was selected as a priority condition because it represents one of the most significant success stories in rare disease treatment, with three disease-modifying therapies now available. Its inclusion in newborn screening programs across multiple countries provides a benchmark for evaluating diagnostic infrastructure and early intervention capacity. The dramatic improvement in outcomes when treatment is initiated early has fundamentally altered the natural history of SMA – patients who would previously have faced severe disability or early mortality are now surviving into later life, creating new imperatives not only for newborn screening policy but also for long-term care infrastructure, transition services, and ongoing monitoring frameworks.

Amyotrophic lateral sclerosis (ALS)

ALS is a progressive neurodegenerative disease characterized by the degeneration of upper and lower motor neurons, leading to muscle weakness, paralysis, and ultimately respiratory failure. With a prevalence of approximately 5–8 per 100,000 people in most countries,⁷⁰ ALS is one of the more common rare neurological conditions. Median survival from symptom onset is typically 2–5 years. ALS was selected because of its direct relevance to aging populations: the peak incidence occurs between ages 55 and 75, making it a condition whose burden will grow as populations age.⁷¹ ALS also illustrates the challenges of reimbursing treatments with modest clinical benefit in the context of a rapidly progressive disease, and highlights the need for palliative and supportive care frameworks alongside pharmacological treatment.

Friedreich ataxia (FA)

Friedreich's Ataxia is a rare inherited neurodegenerative disorder caused by a mutation in the FXN gene, resulting in progressive damage to the nervous system and the heart. It is the most common hereditary ataxia, with an estimated prevalence of 2–4 per 100,000 people in most populations.⁷² Onset typically occurs in childhood or adolescence, and the condition progressively impacts mobility, coordination, speech, and cardiac function. FA was included as a priority condition because it exemplifies the lifelong burden of rare diseases on patients and health systems. As individuals with FA survive into adulthood and older age, their care needs become increasingly complex, requiring coordination across neurology, cardiology, rehabilitation, and social support. FA thus provides a clear case for why rare disease policy must be integrated into broader healthy aging frameworks.

Dravet syndrome (DS)

Dravet syndrome is a severe, treatment-resistant form of epilepsy that typically manifests in the first year of life, most commonly due to mutations in the SCN1A gene. Incidence is estimated at approximately 1 per 33,000 to 1 per 15,500 live births.^{73,74} Beyond seizures, DS is associated with developmental delays, cognitive impairment, motor difficulties, and an elevated risk of sudden unexpected death in epilepsy (SUDEP). DS was selected because it highlights the diagnostic challenges inherent in rare epilepsies, where misdiagnosis is common and genetic testing is often not performed early enough. It also illustrates the limitations of current reimbursement frameworks in accommodating treatments for pediatric rare diseases with complex, lifelong care needs. Additionally, as survival rates improve, the growing population of adults living with DS underscores the importance of transition care and long-term support systems.

Appendix B: Country Definitions of Rare Disease

REGION / AUTHORITY	DEFINITION OF RARE DISEASE
World Health Organization (WHO)	≤ 1 in 2,000 people ⁷⁵
Australia	< 5 per 10,000 people ⁷⁶
Argentina	Aligned with EMA / WHO (≤ 1 in 2,000 or EU equivalent) ⁷⁷
Brazil	< 65 per 100,000 people ⁷⁸
China	Definition not codified, instead described by expert consensus to meet at least one of the following: • Incidence in newborns < 1 per 10,000, or • Prevalence < 1 per 10,000, or • Total affected population < 140,000⁷⁹
European Union / EMA	< 5 in 10,000 people ⁸⁰
Japan (Orphan Drug / Nanbyo)	Orphan drug: < 50,000 patients Intractable disease: prevalence < 0.1% of population
Mexico	Aligned with EMA & WHO (orphan drug eligibility) ⁸¹
Poland	< 1 per 2,000 people ⁸²
Saudi Arabia	< 1 per 2,000 people ⁸³
Türkiye (Turkey)	< 1 per 2,000 people ^{84,85}
United Kingdom	< 1 per 2,000 people ⁸⁶
United States (Orphan Drug Act)	< 200,000 affected persons nationally ⁸⁷

*Please see country specific reports for more information.

Appendix C: Country Snapshots | Interpreting the Current-State of Each Country’s Rare Disease Approach

For each of the 16 countries included in the rare disease policy landscape assessment, we have compiled a comprehensive snapshot of their current state and how they compare across the data set.

Each snapshot will feature benchmarks for both population and policy. Prevalence and incidence figures are labeled by measure. All are approximate estimates from the best available published sources; where country-specific data were unavailable, global estimates are shown and labeled as such.

Population Benchmarks	Policy Benchmarks
Total Population	Status of Policy Framework (yes, no, yes—expiring)
Total Population Living With a Rare Disease	Number of Conditions Included in Newborn Screening
Estimated Birth Prevalence of SMA*	Access to Genetic Testing
Estimated Prevalence of ALS	Average Diagnostic Delay
Estimated Prevalence of FA	HTA Status
Estimated Birth Incidence of DS	Influencers: Leveraging effectively to support rare disease approval and reimbursement
Population Aged 65+ (2024)	Followers: Not leveraging or leveraging ineffectively
Projected Population Aged 65+ (2050)	Orphan Drug Incentives (no incentives, some incentives, strong incentives)**
	Cost-effectiveness Analysis (none, QALY low threshold, QALY high threshold)
	Societal Cost of Rare Disease
	National Rare Disease Definition

*Sometimes referred to Estimated Birth Incidence.

***“No incentives” = No formal orphan drug designation or incentive mechanisms exist at the national level. Access to orphan drugs, where it occurs, relies entirely on informal or ad hoc pathways (e.g., individual patient applications, case-by-case import authorizations); “Some incentives” = A formal orphan drug designation exists, accompanied by at least one structured incentive (e.g., tax credits, reduced regulatory fees, or protocol assistance), but the framework is partial – lacking either market exclusivity provisions or a comprehensive early access infrastructure; “Strong incentives” = A comprehensive orphan drug incentive framework is in place, combining market exclusivity, fee reductions, and priority review, alongside at least one structured early access pathway (e.g., named patient programs or compassionate use). The framework is actively enforced and applies consistently across rare disease categories.

This report tracks prevalence and policy attention across all 16 countries, through an analytical framework placing particular focus on four rare conditions:

- Spinal muscular atrophy (SMA),
- Friedreich's ataxia (FA),
- Amyotrophic lateral sclerosis (ALS),
- and Dravet syndrome (DS).

These conditions were selected, in large part, because they represent a cross-section of rare neurological and genetic diseases with varying onset patterns, treatment landscapes, and levels of policy visibility. Please see the appendix for brief clinical overviews of each condition and our reasoning for its inclusion as a priority condition in this assessment.



Argentina



Rare Disease Prevalence or Incidence Estimates*

+3.6M⁸⁸

SMA Birth Incidence



10 per 100K live births^{89,90}
(global estimate; country-specific data unavailable)

FA Prevalence

Data Unavailable

ALS Prevalence



8.86 per 100K⁹¹

DS Birth Incidence



3.0–6.5 per 100K live births (global estimate)^{92,93}

Population (2025)

45.9M⁹⁴

Population Aged 65+ (2024)

(12% of the total population)

5,673,637⁹⁵

Population Aged 65+
Projected (2050)

(~20% of the total population)

9,636,000⁹⁶

Rare Disease Benchmarking

Rare Disease Policy Framework

Yes

Orphan Drug Incentives

None

Newborn Screening

Screens for 6 conditions

Cost-Effectiveness Analysis

None

Average Diagnostic Delay

5–10 years

Societal Cost of Rare Disease

No information found

National Rare Disease Definition

Aligned with EMA/WHO⁹⁷

Gaps

Limited newborn screening process creates disparities in diagnostic access across regions

Fragmented care across the national health system leads to inconsistent access pathways

No orphan drug incentives lead to slower approvals, implementation, and access

Reimbursement processes requiring legal action slow and discourage testing and treatment pathways

Opportunities

Buenos Aires City's broader screening panel offers a tested model for extending early detection nationwide

Argentina's dependence on judicial routes to treatment access points to an opportunity to strengthen the clarity and authority of the CONETEC process

The absence of a dedicated orphan drug framework leaves room to strengthen registration conditions and research investment

CENAGEM provides an existing base from which to address Argentina's limited clinical genetics capacity

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Diagnostic and Screening Landscape

Argentina maintains a national newborn screening program, but deployment of the program is inconsistent across the country. For example, Buenos Aires City screens for more than 20 conditions, while the mandatory minimum nationally is 6. These inconsistencies result in geographic inequities in early detection.^{98,99}

Genetic testing is available through Argentina's national genetic center (CENAGEM) via their public network and private laboratories¹⁰⁰. However, advanced sequencing for patients that would cover a broader spectrum of rare diseases is frequently not covered under the Mandatory Medical Program (PMO).^{101,102} As a result, some patients still rely on judicial appeals to secure reimbursement for testing.¹⁰³ This model contributes to lengthy diagnostic delays and access gaps.

Argentina also experiences constrained specialist capacity, with approximately 2.9 neurologists per 100,000 people nationwide and limited growth in the genetics workforce.¹⁰⁴ Currently, CENAGEM trains only around three clinical geneticists per year, leading to a workforce unable to match need and demand to rare disease screening and treatment.¹⁰⁵

As Argentina's population ages – with projections indicating that roughly 25% of residents will be over age 60 by 2050¹⁰⁶ – the intersection between rare disease and aging will become increasingly significant. Adult-onset conditions such as ALS, which peaks in incidence between ages 65 and 75,¹⁰⁷ are likely to place growing demands on a diagnostic system already strained by regional inequities. At the same time, the country's heavy reliance on judicial amparo actions to secure treatment access may disproportionately disadvantage older patients, who could face greater barriers in navigating complex legal processes while managing disease progression.

Treatment Access and Reimbursement Landscape

Coverage for rare diseases is legally mandated under Argentina's rare disease policy framework, Law 26.689, which establishes a right to diagnosis and treatment for rare conditions. In practice, however, access to high-cost therapies frequently depends on judicial amparo, reflecting gaps between legal entitlements and routine coverage decisions.

SMA represents a relative success story within this context: all three available therapies are accessible in the country, and Argentina negotiated the lowest published price for onasemnogene abeparvovec globally.^{108,109} This success, however, was driven in large part by the advocacy of patient groups, whose organized voice helped secure access – an advantage that many other rare disease communities do not share.

Argentina's HTA is conducted by CONETEC, but its recommendations are not binding to the Ministry of Health, and negative assessments are often overturned by the courts.¹¹⁰ This model contributes to high levels of judicialization and uncertainty in reimbursement pathways.

Argentina does not currently offer dedicated orphan drug incentives (i.e., market exclusivity, tax credits, or fee waivers). The lack of these incentives contributes to delays in treatment availability and high relative prices for some drugs – though, the national regulator (ANMAT) offers expedited approval pathways for medicines authorized in reference countries.¹¹¹

National Policy Frameworks

Law 26.689 was established in 2011 to provide mandatory coverage for rare diseases and created the National Registry of Patients with Rare Diseases (RENEPOF).¹¹² While the law provides a clear legal foundation, implementation has been uneven, limiting its impact on access and care coordination.

Workforce development remains a persistent constraint within the policy framework. Specialist expertise is concentrated in four provinces, and limited training capacity continues to restrict the availability of clinicians with rare disease and genetics expertise.⁹ These shortages undermine effective implementation of national policy commitments.



Patient Advocacy and Impact

Argentina's rare disease advocacy ecosystem is nationally coordinated through FADEPOF, which represents 60+ patient organizations and advocates for an estimated 3–4 million people living with rare diseases. FADEPOF serves as the primary interface between patient groups and federal health authorities.

Patient representatives hold a formal seat on the National Rare Diseases Program's Honorary Advisory Board, enabling structured engagement with the Ministry of Health. Advocacy influence is strongest at the national policy level, though implementation and access outcomes remain inconsistent across provinces.

Country-Specific Recommendations

1. Expand national newborn screening beyond the current 6 conditions to include SMA and other high-impact treatable diseases, using Buenos Aires City's expanded program as a scalable model.
2. Strengthen HTA processes by making CONETEC assessments more transparent and enforceable, reducing reliance on judicial amparo for treatment access.
3. Invest in clinical genetics workforce development by expanding CENAGEM's training capacity from three geneticists per year to at least ten, with targeted placements in underserved provinces.
4. Develop dedicated orphan drug incentives, including market exclusivity provisions and fee waivers, to encourage drug registration and reduce pricing uncertainty.



Australia



Rare Disease Prevalence or Incidence Estimates*

2M¹¹³

SMA Birth Incidence

8.3 per 100K live births¹¹⁴

FA Prevalence

Data Unavailable

ALS Prevalence

6.4 per 100K¹¹⁵

DS Birth Incidence

3.0–6.5 per 100K live births (global estimate)^{116,117}

Population (2025)

27.5M¹¹⁸

Population Aged 65+ (2024)

(18% of the total population)**4.82M**¹¹⁹Population Aged 65+
Projected (2050)**(22.5% of the total population)****7.5M**¹²⁰

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes	Orphan Drug Incentives	Some
Newborn Screening	Screening number unknown	Cost-Effectiveness Analysis	QALY, low threshold
Average Diagnostic Delay	5-7 years	Societal Cost of Rare Disease	No validated national estimate; Western Australian cohort data suggest rare disease patients represent ~2% of the population but account for 9.9% of hospital discharges and 10.5% of inpatient days. ¹²¹
National Rare Disease Definition	Fewer than 5 per 10,000 people ¹²²		

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Gaps

Fragmented care across the national health system leads to inconsistent access pathways

Limited access to orphan drugs with slow approval times for drugs and wait times for patients

Geographic disparities concentrate access to specialists in urban areas

Integration gaps between the NDIS and aged care systems produce inconsistent eligibility and support levels across the two systems

No validated national cost-of-illness estimate for rare diseases, limiting economic case-making for reform

Parallel HTA pathways (PBAC and LSDP) create complexity and delays for ultra-rare therapies¹²³

Lack of national coordination and sustainable funding for implementation of the National Strategic Action Plan, leaving delivery uneven across jurisdictions

Shortage of genetic counsellors constrains diagnostic capacity and limits timely access to genomic services, particularly for older adults and patients outside metropolitan centres

Limited formal recognition of rare disease as a priority population in national health planning frameworks, constraining cross-sector investment and system-level accountability.

Opportunities

The gap between LSDP eligibility and standard HTA assessment creates room for evidence standards better suited to rare disease therapies

Low participation suggests that the Orphan Drug Program's potential is not yet fully realized

The 2024 HTA Review provides a ready policy roadmap for a more coherent approach to ultra-rare therapy assessment

The boundary between the NDIS and aged care presents a clear opportunity to improve continuity of support across the life course

The NSAP provides an established national framework that could support more consistent implementation and accountability

Western Australian burden data provide a strong starting point for a national evidence base on the costs of rare disease

Diagnostic and Screening Landscape

Australia operates a universal Newborn Bloodspot Screening program, providing nationwide coverage for early detection of at least 32 conditions, including congenital hypothyroidism, cystic fibrosis, SMA, and severe combined immunodeficiency.¹²⁴ Beyond newborn screening, the country also leverages a range of advanced diagnostic technologies, including WES, WGS, targeted gene panels, proteomic testing, and reproductive carrier screening.^{125,126,127} Together, these technologies support diagnosis across the life course.

While genetic services are available, access to these services typically requires a referral from a GP. This requirement can lead to diagnostic delays, as accepted referrals move directly to a waitlist for a patient's local public hospital. Private genetic services generally offer shorter wait times, but these services involve additional out-of-pocket costs that limit access for some populations.¹²⁸ Access is further constrained by a national shortage of genetic counsel-

lors, which lengthens wait times, limits the capacity of services to interpret results and support families, and disproportionately affects older adults and patients outside metropolitan centres.

Australia's aging population – with approximately 22.5% of Australians projected to be aged 65 and over by 2050¹²⁹ – is likely to expose persistent gaps in rare disease care for older adults. Referral-dependent access to genetic services can create particular challenges for elderly patients, whose rare conditions may be misattributed to age-related decline or more common disorders. For example, wild-type transthyretin amyloid cardiomyopathy (ATTRwt-CM), an age-associated rare cardiomyopathy, remains underdiagnosed across many care settings in Australia. The Genomics Health Futures Mission discussed below represents a forward-looking investment that could help close these gaps, particularly if genomic testing is more routinely integrated into diagnostic workups for older patients with atypical clinical presentations.



Treatment Access and Reimbursement Landscape

Australia operates a universal health benefits system, providing free or subsidized access to healthcare services nationwide.¹³⁰ Coverage for rare disease care is supported through the Medicare Benefits Schedule (MBS), which reimburses clinical services, diagnostics, and specialist consultations for eligible patients.¹³¹

Access to rare disease therapies is facilitated through the Pharmaceutical Benefits Scheme (PBS), which subsidizes a range of orphan drugs.¹³² For patients with ultra-rare and life-threatening conditions, the Life Saving Drugs Program (LSDP) provides fully subsidized access to essential medicines, covering approximately 12 conditions and more than 17 medicines.

Australia's HTA pathway involves a two-step process: 1.) market authorization for regulation through the Therapeutic Goods Administration (TGA) – which includes an Orphan Drug Program that waives application and evaluation fees for new medications^{133,134} – and 2.) government subsidy decisions that direct funds to preferred health technologies.^{135,136} While the Orphan Drug Program does provide some support and structure for drug access, in practice its benefits are limited. Between 2018 and 2023, only 13% of drugs submitted to the program received a positive recommendation upon first submission, while an additional 50% were approved after resubmission. Those rates resulted in 87% of applications failing to meet the qualifications for the program's fee waiver.¹³⁷

While Australia does not apply a formal Incremental Cost-Effectiveness Ratio (ICER) threshold, an unofficial range of approximately AUD \$45,000–\$60,000 per QALY is often referenced in reimbursement deliberations.¹³⁸ This benchmark, even if unofficial, can limit access and approvals for rare disease therapies that don't meet the PBS or LSDP criteria.

The 2024 Health Technology Assessment Policy and Methods Review, commissioned by the Department of Health, Disability and Ageing, set out 50 recommendations to modernize Australia's HTA system. Its rare-disease package proposes that PBAC become the sole HTA advisory body for ultra-rare disease therapies – effectively consolidating the separate LSDP pathway – and recommends more flexible evidentiary standards, managed access arrangements, and a dedicated ultra-rare disease evaluation framework.¹³⁹ Medicines Australia and Rare Voices Australia have welcomed these directions while cautioning that implementation, funding, and timelines remain uncertain.^{140,141}

National Policy Frameworks

Australia's rare disease policy is guided by the National Strategic Action Plan for Rare Diseases (NSAP), established in 2020 and developed by Rare Voices Australia at the request of the Commonwealth Government. This framework sets national priorities across three pillars: increasing awareness and education, strengthening care and support, and advancing research and data. The plan provides a national roadmap for improving coordination across health systems and elevating rare diseases within broader health policy agendas.¹⁴²

Australia is further investing in rare disease access and support via the Genomics Health Futures Mission, a \$500.1 million national investment aimed at expanding genomic research, improving access to genetic testing and diagnosis, and supporting more personalized treatment approaches.¹⁴³

Together, these initiatives establish a strong policy foundation, though translation into consistent practice remains dependent on jurisdictional capacity, health system integration, and – most critically dedicated national coordination and sustained Commonwealth funding to operationalize the NSAP and related strategies across the life course.

A potential structural gap sits at the interface of Australia's disability and aged care systems. Australians already enrolled in the National Disability Insurance Scheme (NDIS) can choose to remain as part of the scheme after turning 65 and are required to transition into the aged care system only if they enter residential aged care or permanent in-home aged care. However, Australians first diagnosed with a rare disease after age 65 cannot access the NDIS at all, leaving them dependent on an aged care system that is not designed around the complexity and nature of rare disease. The Commonwealth Disability Support for Older Australians (DSOA) program preserves continuity of disability supports for a legacy cohort who transitioned under earlier arrangements, but it is not available to Australians diagnosed with rare diseases later in life, producing inconsistent entitlements based on age at diagnosis rather than clinical need.¹⁴⁴ Aged care does provide certain supports – such as respite – that can exceed what NDIS offers, reinforcing that the priority is better integration across both systems rather than extending one to substitute for the other. Full implementation of the NSAP, with dedicated Commonwealth investment to operationalize its priorities, remains essential to closing these gaps across the life course.¹⁴⁵



Patient Advocacy and Impact

Australia has one of the most integrated rare disease advocacy models globally, representing approximately 2 million people living with rare diseases. Rare Voices Australia (RVA) serves as the national peak body, representing 100+ patient organizations.

Led by RVA, patient organizations played a central role in developing and implementing the National Strategic Action Plan for Rare Diseases and hold formal positions within HTA and reimbursement structures, including the Life Saving Drugs Program and PBAC advisory processes. Advocacy influence is sustained across policy, access, and implementation.

Country-Specific Recommendations

1. Strengthen integration between the NDIS and aged care systems so that Australians living with rare diseases receive consistent, needs-based supports across both systems, including extending Disability Support for Older Australians (DSOA), so there is equivalent eligibility to people diagnosed after age 65 who cannot currently access NDIS, while preserving aged care provisions (such as respite) that exceed what NDIS offers.
2. Operationalize the National Strategic Action Plan for Rare Diseases with dedicated Commonwealth funding, explicit aging-related objectives, and measurable implementation milestones – positioning Australia as an exemplar of integrating aging into national rare disease policy.
3. Establish a National Office for Rare Diseases within the Department of Health, Disability and Ageing to provide a permanent institutional home for NSAP delivery, cross-jurisdictional coordination, and stewardship of rare disease policy across the life course, including the specific needs of older Australians.
4. Commit ring-fenced, multi-year Commonwealth funding for NSAP implementation – including a national rare disease workforce strategy that expands the genetic counsellor pipeline – so that the plan's priorities translate into sustained action rather than aspirational policy.
5. Commission a national rare disease cost-of-illness study to quantify direct and indirect costs, filling the current evidence gap (Western Australian cohort data suggest rare disease patients represent ~2% of the population but account for 9.9% of hospital discharges) and strengthening the economic case for reform.
6. Develop a nationally consistent approach to genomic testing and genetic counsellor reimbursement to ensure equitable access to advanced diagnostics and expert interpretation regardless of jurisdiction.
7. Expand telehealth-enabled genetic and rare disease specialist consultations for rural and remote populations to reduce geographic disparities in access to expertise.
8. Implement the 2024 HTA Review's rare disease package – consolidating ultra-rare disease assessment under PBAC, adopting flexible evidentiary standards (including real-world evidence and managed access arrangements), and establishing a dedicated ultra-rare disease evaluation framework – so that therapies previously routed through the Life Saving Drugs Program receive faster, more predictable decisions.



Brazil



Rare Disease Prevalence or Incidence Estimates*

13M¹⁴⁶

SMA Birth Incidence		7–9 per 100K live births ^{147,148}
FA Prevalence		0.8 per 100K ^{149,150,151}
ALS Prevalence		5 per 100K ¹⁵²
DS Birth Incidence		3.0–6.5 per 100K live births (global estimate) ^{153,154}

Population (2025)

213M¹⁵⁵

Population Aged 65+ (2024)	(11% of the total population)	23.42M ¹⁵⁶
Population Aged 65+ Projected (2050)	(29.3% of the total population)	66.5M ^{157,158}

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes	Orphan Drug Incentives:	None
Newborn Screening	Screening number unknown	Cost-Effectiveness Analysis	QALY, low threshold
Average Diagnostic Delay	5–8 years	Societal Cost of Rare Disease	No information found
National Rare Disease Definition	Fewer than 65 per 100,000 people ¹⁵⁹		

Gaps

Low GP awareness impacts preliminary screenings and timely, accurate diagnoses

Geographic disparities concentrate access to specialists in certain regions

Shortage of reference centers limits ability to meet the needs and demands of the Brazilian population

Reimbursement not optimized for orphan drugs, limiting access and creating lengthy reimbursement timelines

Opportunities

Brazil's existing screening and reference-service infrastructure provides a platform for identifying more treatable conditions earlier

The concentration of specialist services in the south and southeast leaves substantial room to improve geographic equity in the north and northeast

Existing university hospitals and state facilities provide a foundation for more connected diagnostic pathways

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Diagnostic and Screening Landscape

Brazil operates a universal National Neonatal Screening Program, providing nationwide access to early screening for selected conditions.¹⁶⁰ Diagnosis and care for rare diseases are supported through a network of 27 Rare Disease Reference Services (RDRS) and nine specialized care services.¹⁶¹

In an effort to improve coordination across the health system, Brazil established a Care Pathway for People with Rare Conditions. This pathway is designed to organize care flows, integrate services across levels of care, and define appropriate interventions at each stage of the patient journey.¹⁶² While this framework provides a structured approach on paper, access to diagnostic expertise remains uneven – particularly across geographic regions.

Brazil's rare disease workforce is severely constrained, with only an estimated 300–400 clinical geneticists serving a population of 215 million. Approximately 80% of registered geneticists are located in Brazil's South and Southeast regions,¹⁶³ creating substantial regional disparities in access to genetic diagnosis and specialized care across the country.

Treatment Access and Reimbursement Landscape

Brazil operates a universal public healthcare system (SUS), which funds a significant share of rare disease diagnosis and treatment, alongside a parallel private health insurance market. Within SUS, orphan drugs are primarily provided through the Specialized Component of Pharmaceutical Services, offering eligible treatments free of charge once incorporated into the system.¹⁶⁴ These incorporation decisions into SUS are informed by CONITEC, whose assessments are largely driven by pharmacoeconomic parameters rather than efficacy and safety considerations alone, and are heavily dependent on available budget at the Ministry of Health.¹⁶⁵

Currently, access to treatments not incorporated into the SUS can be obtained through judicial proceedings. However, this practice has shown to pose a substantial economic burden, with approximately \$274M of this expenditure going towards 11 drugs for the treatment of 1,334 patients.¹⁶⁶ As of 2025, Brazil is in the process of changing this approach to limit judicialization as an access point for treatment.¹⁶⁷ In September 2024, the Federal Supreme Court (STF) issued a landmark ruling establishing stricter criteria for court-ordered

access to medicines not incorporated into SUS. Under the new framework, patients must demonstrate administrative denial, the absence of a therapeutic alternative in SUS, and either unlawfulness or undue delay in CONITEC's incorporation decision. The ruling represents an attempt to balance the constitutional right to health with the sustainability of SUS, though its implementation and impact on rare disease access remain to be seen.

These access and financing reforms are unfolding alongside a major demographic shift that will further test system capacity. By 2050, the share of Brazil's population aged 65 and over is projected to nearly triple. In a health system where genetic specialists are heavily concentrated in South and Southeast Brazil, aging populations in the North and Northeast are likely to face compounding barriers to rare disease diagnosis. Together, these demographic and geographic disparities reinforce the urgency of strengthening sustainable, system-based access pathways as reliance on judicialization is reduced.

Brazil includes a cost-effectiveness analysis in their assessment process for rare diseases. The QALY threshold for rare diseases is currently set at BRL 120,000 per capita.¹⁶⁸ While this threshold is three times higher than the standard threshold of BRL 40,000 used for non-orphan drugs, it is still on the lower end compared to orphan drug costs and other QALY-based models. At this threshold, access to many high-cost therapies would be limited for patients.¹⁶⁹

Approval is managed by the Brazilian Health Regulatory Agency (ANVISA), which has approved approximately 143 treatments for rare diseases.¹⁷⁰ Of these, 96 medicines have been incorporated into SUS, covering 54 specific rare diseases.¹⁷¹ This disparity creates key access gaps for patients seeking specialized treatment.

National Policy Frameworks

Brazil's National Policy for Comprehensive Care for People with Rare Diseases was established in 2014. This framework provides national guidelines for diagnosis, treatment, and long-term care within SUS and provides financial incentives to support implementation. However, the policy is significantly underfunded: reimbursement rates provided to reference centers have been frozen since 2014, and there is no adequate budget to increase the number of reference services, which remain particularly scarce in the Northeast, North, and Midwest regions. Execution varies considerably by region and service capacity.¹⁷²



At the regulatory level, ANVISA Resolution 205/2017 introduced an expedited approval pathway for orphan drugs, accelerating review timelines and allowing qualifying medicines to be commercialized within up to 365 days.¹⁷³ Together, these measures provide a formal policy and regulatory foundation for rare disease care, while broader challenges remain around access consistency and system sustainability.

Patient Advocacy and Impact

Brazil's rare disease advocacy landscape is active but institutionally fragmented. FEBRARARAS represents approximately 50 patient associations nationwide, complemented by disease-specific groups such as Instituto Vidas Raras that engage directly with poli-

cymakers. Notable initiatives include Casa Hunter's Casa dos Raros (House of the Rare), a fully integrated hospital offering multidisciplinary care for rare disease patients.

Despite strong grassroots mobilization, patient organizations lack guaranteed representation in key rare disease decision-making bodies. Advocacy groups participate in advisory forums linked to health insurance regulation and disability rights, but limited formal inclusion in rare disease governance continues to constrain impact on access and reimbursement.

Country-Specific Recommendations

1. Expand the National Neonatal Screening Program to include SMA and other treatable conditions, building on the existing RDRS network.
2. Prioritize the establishment of new Rare Disease Reference Services in underserved northern and northeastern regions, where 80% of the population currently lacks proximate access to genetic specialists.
3. Raise or adapt the QALY threshold for orphan drugs beyond BRL 120,000 to better accommodate the cost profiles of rare disease therapies and reduce reliance on judicial proceedings for access.
4. Strengthen coordinated care partnerships between university hospitals and state health facilities to reduce fragmentation and accelerate diagnostic timelines.



China



Rare Disease Prevalence or Incidence Estimates*

20M¹⁷⁴

SMA Birth Incidence



10 per 100K live births^{175,176,177}

FA Prevalence

Data Unavailable

ALS Prevalence



2.91 per 100K¹⁷⁸

DS Birth Incidence



3.0–6.5 per 100K live births (global estimate)^{179,180}

Population (2025)

1.416B¹⁸¹

Population Aged 65+ (2024)

(15% of the total population)

206,629,972¹⁸²

Population Aged 65+ Projected (2050)

(26% of the total population)

366,000,000¹⁸³

Rare Disease Benchmarking

Rare Disease Policy Framework	No	Orphan Drug Incentives:	Some ¹⁸⁴
Newborn Screening	Variable ¹⁸⁵	Cost-Effectiveness Analysis	None
Average Diagnostic Delay	~4 years ¹⁸⁶	Societal Cost of Rare Disease	No information found
National Rare Disease Definition	"The latest definition of rare disease in China was released on September 11, 2021 at the third multidisciplinary expert seminar on the definition of rare diseases/orphan drugs in China. A rare disease is defined as a condition satisfying at least one of the following three criteria: an incidence among newborns of less than 1/10,000, a prevalence of less than 1/10,000, and an affected population of less than 140,000." This definition is not codified into law but is considered a guiding national benchmark used by official bodies. ¹⁸⁷		

Gaps

Low clinician awareness impacts preliminary screenings and timely, accurate diagnoses

Geographic disparities concentrate access to specialists in urban regions

Treatment disparities exist between disease and drug lists, with 75 diseases currently having no approved treatment

Reimbursement not optimized for orphan drugs, limiting access and creating lengthy reimbursement timelines

Workforce shortages persist in part due to lack of clinical genetics specialty

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Opportunities

The National Rare Disease Lists provide a ready framework for identifying additional conditions suitable for national screening

China's large market remains underused as a destination for orphan drug development and registration without a formal designation framework

The lack of formal recognition for clinical genetics leaves room to strengthen the specialty and its contribution to diagnostic capacity

The gap between NRDL listing and hospital availability represents a major opportunity to convert formal coverage into real-world access

Trial requirements for imported therapies create an opening to make greater use of real-world evidence and avoid unnecessary duplication

China's market scale and manufacturing base give it substantial leverage to reduce rare disease drug costs

The gap between NRDL reimbursement and patients' remaining costs creates a potential role for commercial insurance

Diagnostic and Screening Landscape

China operates a near-universal national newborn screening program for conditions like phenylketonuria (PKU) and congenital hypothyroidism.¹⁸⁸ However, expanded newborn screening varies significantly by province. Additionally, screening for other rare conditions, like SMA, currently only takes place within pilot programs.¹⁸⁹

Genetic testing is also currently not covered by universal insurance in China, though large-scale initiatives seek to demonstrate the potential of genomic approaches. For example, the UPWARDS project tested approximately 94,000 individuals across 32 provinces and achieved a diagnostic yield of around 30%.¹⁹⁰

While China has substantially expanded its neurology workforce by an estimated three- to five-fold over the past 30 years, clinical genetics is not recognized as a formal medical specialty.¹⁹¹ Genetic services are largely concentrated in tertiary hospitals, and overall clinician awareness remains low, with only 5.3% of physicians reporting that they feel adequately informed about rare diseases.¹⁹²

Beyond workforce constraints, several structural and social barriers compound diagnostic delays. Medical records in China remain siloed within individual hospital systems,¹⁹³ meaning rare disease

patients – who typically visit multiple hospitals and departments over the course of their diagnostic odyssey – are often unable to consolidate their records, leading to repeated testing and loss of critical diagnostic evidence.¹⁹⁴ In remote and socioeconomically disadvantaged regions, limited awareness of rare diseases,¹⁹⁵ financial barriers to seeking specialist care, and in some areas historically higher rates of consanguineous marriage further increase disease burden and delay diagnosis.¹⁹⁶ It is worth note that consanguineous marriages have been prohibited by Chinese law since 1981,¹⁹⁷ so past practices are likely not reflective of current reality, even if there are lingering effects. Stigma and social stereotyping also remain a persistent challenge for patients and families navigating the diagnostic pathway.^{198,199,200}

These structural and workforce gaps will become more consequential as China's population ages. China is undergoing one of the most rapid aging transitions globally, with the population aged 65 and over projected to reach approximately 366 million by 2050.²⁰¹ This demographic shift is expected to increase the burden of adult-onset and age-associated rare diseases, such as ALS and cardiac amyloidosis. Without broader integration of genomic testing and rare disease expertise into routine clinical care, particularly beyond tertiary centers, the risk of delayed or missed diagnosis among older patients is likely to grow.



Treatment Access and Reimbursement Landscape

China's National Reimbursement Drug List (NRDL) now includes more than 100 rare disease drugs, reflecting growing policy attention to treatment access – a significant shift from just a few years ago, when rare disease drugs first began entering the list in 2019.²⁰² In practice, however, real-world availability is constrained by limited hospital uptake. As of 2022, China's national hospitals are estimated to have 25–41% of available rare disease drugs.²⁰³ This limited uptake significantly restricts patient access even for reimbursed therapies.

SMA illustrates both the progress and persistent limitations of this evolving system. Nusinersen's inclusion in the 2021 NRDL – following a landmark 95% price reduction – marked the first time a high-cost rare disease therapy achieved national reimbursement coverage. Today, both nusinersen and risdiplam are approved by the National Medical Products Association (NMPA) and included on the NRDL, though onasemnogene abeparvovec remains unapproved. Despite NRDL inclusion, outpatient reimbursement under the Urban and Rural Resident Basic Medical Insurance (URRBMI) is typically capped at ≤1,000 RMB in most provinces.²⁰⁴ That reimbursement cap leaves many rare disease therapies financially out of reach for patients. More broadly, reimbursement rates vary considerably across diseases, drugs, and provinces, and for drugs not yet included on the NRDL, patients must bear the full cost themselves – a burden the vast majority cannot sustain.

While many newer orphan drugs are not yet registered or commercially available within China, contributing to persistent gaps between global innovation and domestic access, the regulatory environment is improving. In 2024, the NMPA approved 48 first-in-class innovative drugs – the highest in the past five years – and completed 110 drug applications through its priority review pathway, a 29% year-on-year increase.²⁰⁵ Rare diseases are a particular focus of these reforms: the priority review program shortens standard review timelines from 200 to 130 working days, with further acceleration to 70 days for urgently needed medicines already approved overseas.²⁰⁶ Orphan drugs are also now eligible for market exclusivity and prioritized access to NRDL negotiations, signaling China's intent to close the gap between domestic availability and global innovation.²⁰⁷

Two experimental mechanisms have been introduced to broaden access to drugs not yet formally approved by the NMPA. The Hainan Free Trade Port permits foreign companies to import and sell drugs in the special trade port without NMPA market authorization, while the Greater Bay Area (GBA) initiative allows innovative drugs and devices approved in Hong Kong and Macao to be made available in designated health organizations within the GBA. However, both mechanisms require patients to travel to these specific locations to access treatment, and all costs are borne entirely out of pocket, as neither pathway qualifies for social insurance reimbursement. In practice, this means access remains limited to patients with the financial means and physical ability to travel, leaving the majority of rare disease patients unable to benefit.²⁰⁸

National Policy Frameworks

China's rare disease policy is anchored in the First and Second National Rare Disease Lists, launched in 2018 and 2023, respectively. These lists formally recognize 207 rare conditions in total – 121 in the First List and 86 in the Second – and function as a national catalog that prioritizes them within China's health system.²⁰⁹ These lists play a central role in shaping diagnosis, treatment access, and reimbursement discussions at the national level.

Care delivery is supported through the National Network for Rare Disease Diagnosis and Treatment.²¹⁰ This network links more than 400 hospitals nationwide, anchored by Peking Union Medical College Hospital (PUMCH).²¹¹ While the network has expanded geographic reach, capacity and expertise remain uneven across regions, limiting consistent implementation.

Currently, reimbursement decisions rely on annual NRDL negotiations, with price reduction serving as the main mechanism for access rather than QALY-based thresholds. Complementary measures like tax incentives, accelerated review pathways, and the “Urgently Needed Overseas Drugs” list have improved availability for certain therapies. However, China does not operate an optimised orphan drug designation system, leaving incentives fragmented and access pathways variable.²¹² Significant progress has been made in defining rare diseases nationally, encouraging innovation, establishing favorable policy on generics, and expanding the NRDL to include rare disease therapies. National initiatives and government mandates in these areas are well-intentioned; however, in the absence of reinforcement mechanisms to ensure consistent implementation across provinces and institutions, their real-world effectiveness remains uncertain.



Patient Advocacy and Impact

China's rare disease advocacy sector has expanded rapidly over the past decade, led by CORD, which represents 100+ patient organizations across 60+ rare diseases. Advocacy efforts focus on awareness, diagnostic access, clinical trial recruitment, and reimbursement inclusion.

Patient groups increasingly engage with regulators such as the NMPA and NHSA, contributing to successful inclusion of therapies in the National Reimbursement Drug List. However, patient involvement in early development and formal decision-making is not currently consistent or robust.

Country-Specific Recommendations

1. Expand national newborn screening programs beyond PKU and congenital hypothyroidism to include SMA and other conditions identified on the National Rare Disease Lists.
2. Formalize an orphan drug designation system to provide structured incentives for drug registration and availability within China's market.
3. Recognize clinical genetics as a formal medical specialty to address the critical workforce gap in diagnostic capacity and clinician awareness.
4. Strengthen hospital-level access pathways to improve uptake of NRDL-listed rare disease drugs, addressing the current gap where only 41% of hospitals stock approved therapies.
5. Develop targeted GP education programs to raise clinician awareness of rare diseases beyond the current 5.3% adequacy rate.
6. Pursue meaningful reductions in drug costs through a combination of domestic innovation incentives, expanded generic drug pathways, and large-scale government purchasing agreements that leverage China's market size to negotiate lower prices.
7. Develop a policy framework enabling commercial insurance to supplement social medical coverage for rare disease therapies, reducing out-of-pocket burden and broadening sustainable access beyond the NRDL reimbursement cap.



France

Rare Disease Prevalence or Incidence Estimates*

~3M²¹³

SMA Birth Prevalence



8.3 per 100K live births²¹⁴

FA Prevalence



2.3 per 100K²¹⁵

ALS Prevalence

~8,000 people living with ALS²¹⁶

DS Birth Incidence



3.0–6.5 per 100K live births (global estimate)^{217,218}

Population (2025)

68.5M²¹⁹

Population Aged 65+ (2024)

(22% of the total population)

15,181,834²²⁰

Population Aged 65+ Projected (2050)

(27.5% of the total population)

19,189,075^{221,222}

Rare Disease Benchmarking

Rare Disease Policy Framework

Yes²²³

Orphan Drug Incentives:

Yes, through EU incentives

Newborn Screening

Screens for 16 conditions^{224,225}

Cost-Effectiveness Analysis

None^{226,227}

Average Diagnostic Delay

2–3 years²²⁸

Societal Cost of Rare Disease

No Information Found

National Rare Disease Definition

as per EU definition (< 5 cases per 10,000 people)

Gaps

Workforce shortages persist in part due to lack of neurologists and geneticists

Geographic disparities concentrate access to specialists in urban regions

Despite France's low average diagnostic delay, certain disease areas continue to experience long wait times and limited treatment options

Opportunities

France's mature CRMR network provides a strong foundation for deeper links between specialist centers and community-based care

Strong regulatory and reimbursement infrastructure creates room to shorten the remaining delay between approval and patient access

Regional disparities are concentrated enough to make targeted workforce and service investment especially high impact

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.

Diagnostic and Screening Landscape

France operates a national neonatal screening program (Dépistage Néonatal National, DNN) covering all newborns,²²⁹ aimed at detecting rare, severe, and predominantly genetic diseases. As of 2025, the program screens for 16 conditions, following its recent expansion to include SMA,²³⁰ reflecting continued investment in early detection.

France's specialist capacity is slightly below EU averages, with 4.4 neurologists per 100,000 people.²³¹ Additionally, those specialists tend to be concentrated in the south and in certain urban departments (such as Île-de-France) and dramatically lower in rural northern areas and in overseas departments, creating regional variation that affects access to timely specialist assessment.²³²

France currently outperforms the average EU diagnostic delay of 4.7 years with an average delay of 2–3 years for rare diseases,²³³ enabled by strong specialized centers and referral networks. However, an estimated 25% of patients remain undiagnosed for five to fifteen years, underscoring ongoing challenges in recognizing and routing rare disease cases through the health system.²³⁴

Looking ahead, sustaining France's diagnostic performance will require continued adaptation as demographic pressures increase. With more than 26% of the population projected to be aged 65 and over by 2050, diagnostic pathways will need to better account for adult-onset and late-presenting rare diseases. Complementing public infrastructure, the AFM-Téléthon model, which raises approximately €80–95 million annually for rare disease research, illustrates how sustained philanthropic investment can accelerate innovation and reinforce national rare disease capacity.

Treatment Access and Reimbursement Landscape

In France, rare disease care and treatments are primarily financed through the public national health insurance system – this includes high-cost therapies for ultra-rare conditions.²³⁵

France's HTA determines drug pricing and reimbursement based on clinical benefit assessments (SMR and ASMR), rather than a formal QALY-based cost-effectiveness threshold.²³⁶ This approach classifies each

drug based on level of clinical benefit (i.e., significant, moderate, minor, and nonexistent), then prices accordingly.²³⁷

While this approach facilitates coverage for many orphan drugs, access is often delayed by the length of the assessment and negotiation process. Median timelines from evaluation to reimbursement are approximately 360 days, and around 78% of EMA-approved orphan drugs ultimately receive reimbursement.²³⁸

To partially mitigate these delays, France operates one of Europe's most established early access frameworks. Originally launched in 1992 as the Autorisation Temporaire d'Utilisation (ATU), the program was reformed in July 2021 and replaced by two streamlined pathways: the Early Access Authorization (Accès Précoce, AAP) and the Compassionate Access Authorization (Accès Compassionnel, AAC). The AAP enables patients with serious, rare, or disabling conditions to access innovative therapies either before marketing authorization or during the gap between authorization and formal reimbursement, with eligible treatments receiving full public reimbursement. Since the reform, over 100,000 patients have been treated through these pathways, and the framework has enabled therapies to reach French patients an average of 200 days before their first regulatory approval from the FDA or EMA.²³⁹

National Policy Frameworks

France launched its 4th National Plan for Rare Diseases (PNMR4) in 2025, covering the period through 2030 and structuring national rare disease policy around three strategic pillars: care, research, and innovation/industry.²⁴⁰ Building on the legacy of PNMR1–3, PNMR4 is operationalized through 26 objectives designed to strengthen early and equitable diagnosis, improve care pathways, accelerate therapeutic development, expand access to innovation, and reinforce national infrastructures including data, genomics, and coordination capacities.²⁴¹ France continues to invest heavily in its national network of Rare Disease Reference Centres (CRMRS), diagnostic programmes, and strategic infrastructures such as BNDMR (French National Database for Rare Diseases), PFMG2025 (French Genomics Medicine Initiative), and Health Data Hub, thereby reinforcing its position as one of Europe's most integrated rare disease ecosystems. France is coordinating 5 out of the 24 ERNs and its Ministry of Health and Prevention (DGOS) is leading work package on data in the JARDIN Joint Action further supporting integration of ERNs in national healthcare systems.

France's research and innovation leadership is further amplified through its long-standing strategic role in shaping European rare disease policy and funding. Through INSERM and ANR, France played a foundational role in launching and coordinating successive programmes: E-Rare, E-Rare-2, E-Rare-3, then the European Joint Programme on Rare Diseases (EJP RD; €150M), and now ERDERA (European Rare Diseases Research Alliance; >€380M), the largest rare disease research and innovation partnership globally, fully aligned with PNMR4 priorities. EJP RD enabled integration of funding, FAIR data, diagnostics, training, and translational research while directly strengthening French initiatives such as PNMR3, PFMG2025, BNDMR, CAD, and links to ERNs. ERDERA now extends this by positioning France as a leader of a federated European rare disease ecosystem model, integrating public-private partnerships, clinical trial readiness, advanced therapies, and pan-European diagnostic pipelines. Beyond EU frameworks, France's strategy is reinforced through active participation in the International Rare Diseases Research Consortium (IRDiRC) and ECRIN, ensuring that French national priorities are both supported by and instrumental in broader European and international rare disease research, innovation, and therapeutic development agendas.²⁴²

Patient Advocacy and Impact

France has one of Europe's most institutionalized rare disease advocacy environments, with an estimated 3 million people affected across ~7,000 rare diseases.²⁴³ Patient organizations are formally embedded in health system governance through national rare disease plans and clinical networks. At a national level, Alliance Maladies Rares brings together 230+ patient associations and coordinates policy engagement, awareness, and representation across France's 23 Rare Disease Health Networks, which later informed the EU's European Reference Network model.

France maintains a strong advocacy foundation through organizations like AFM-Téléthon, which was a founding member of EURODIS and raises €80-95 million annually to fund rare disease research, clinical trials, and care infrastructure. French patient organizations hold formal roles in HTA and health system governance through participation in assessments led by Haute Autorité de Santé and representation via France Assos Santé.

Country-Specific Recommendations

1. Accelerate reimbursement timelines for orphan drugs, targeting a reduction from the current median of 360 days to under 200 days through streamlined negotiation processes.
2. Expand workforce training in neurology and genetics to address regional shortages, particularly in rural northern areas and overseas departments.
3. Strengthen the hub-and-spoke model connecting rare disease reference centers (CRMR) with community-based GPs to improve early recognition and timely referrals.
4. Maintain and build upon France's leadership through the new PNMR4 plan (2025-2030) by ensuring measurable KPIs and dedicated funding for each of the 26 objectives.



Germany

Rare Disease Prevalence or Incidence Estimates*

~4M²⁴⁴

SMA Birth Incidence		11.7 per 100K live births ²⁴⁵
FA Prevalence		1.56 per 100K ²⁴⁶
ALS Prevalence		8 per 100K ²⁴⁷
DS Birth Incidence		4.7 per 100K ²⁴⁸

Population (2025)

83.5M²⁴⁹

Population Aged 65+ (2024)	(23% of the total population)	19,372,164 ²⁵⁰
Population Aged 65+ Projected (2050)	(~33% of the total population)	24,000,000 ²⁵¹

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes ²⁵²	Orphan Drug Incentives:	Yes, through the EU system ²⁵³
Newborn Screening	Screens for 19 conditions ²⁵⁴	Cost-Effectiveness Analysis	None ²⁵⁵
Average Diagnostic Delay	5-6 years ²⁵⁶	Societal Cost of Rare Disease	No information found
National Rare Disease Definition	EMA Definition Adherent		

Gaps

Low clinician awareness impacts preliminary screenings and timely, accurate diagnoses

Low cross-sector coordination between three ZSE tiers, primary care, and community services.

Lack of fiscally sustainable ZSE funding structures

Opportunities

An established 19-condition national panel provides a strong base for the continued evolution of newborn screening

The three-tier ZSE model creates a pathway for extending coordinated care beyond university-based centers

Low GP awareness of the ZSE network leaves existing specialist capacity underused

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Diagnostic and Screening Landscape

Germany offers broad access to genetic testing through university hospitals and its national network of Centers for Rare Diseases (ZSEs). These ZSEs are supported by a three-tier care model spanning comprehensive reference centers (Type A), disease-specific centers (Type B), and local care (Type C).^{257,258}

Germany has experience integrating advanced genomic techniques into clinical practice through pilot projects like TRANSLATE-NAMSE, which demonstrated that genomic testing combined with interdisciplinary case review can significantly shorten diagnostic timelines, reducing time to diagnosis to approximately six months. Building on these lessons, Germany has now launched the German Genome Sequencing Program (genomDE) under the BfArM Modellvorhaben Genomsequenzierung framework, designed to systematize whole-genome sequencing within routine care and shorten the diagnostic odyssey at national scale — directly addressing the limitation of earlier pilots that did not prove scalable beyond their initial settings.²⁵⁹

While Germany benefits from a strong clinical trial infrastructure, coordination across hospitals, specialists, and community-based care remains uneven, with adult patients particularly affected — the 2023 federal evaluation found that adults are more often stuck in uncoordinated care pathways and struggle to access high-quality care close to home. Additionally, only 46% of primary care physicians have adequate awareness of ZSE centers, limiting their usage and effectiveness.²⁶⁰ This adult-coordination gap is especially consequential given that, although roughly 70% of rare diseases have a childhood onset, the proportion of adults living with rare disease is growing and will likely continue to grow as therapeutic advances enable more pediatric patients to reach adulthood.²⁶¹

Taken together, these coordination and awareness gaps will become more consequential as demographic pressures increase. As Germany confronts one of Europe's most rapidly aging populations — with nearly 30% projected to be aged 65 and over by 2050 — broader diffusion of genomics-enabled and interdisciplinary diagnostic models will become increasingly important.²⁶² Adult-onset rare conditions, including some hereditary neuropathies and cardiac amyloidosis, are likely to present more frequently in primary care settings, where awareness of rare diseases and referral pathways remains uneven.

Treatment Access and Reimbursement Landscape

Germany provides universal coverage through statutory health insurance, covering roughly 90% of the population, with the remaining 10% covered by private health insurance. Regardless of insurance type, once a medicine receives EMA approval and enters the AMNOG process, it is reimbursed for all insured patients immediately, with a free pricing period of 6 months before negotiated prices take effect — without an upfront cost-effectiveness hurdle.²⁶³

Under Germany's 2011 AMNOG law, orphan drugs are presumed to offer added benefit and face no initial comparative evidence requirements. This enables Germany to set prices through post-approval negotiations rather than QALY thresholds. However, recent GKV Financial Stabilization Act reforms have tightened this model by reducing the orphan revenue threshold from €50M to €30M and shortening the free pricing period from 12 to 6 months.²⁶⁴

National Policy Frameworks

Germany's National Action Plan for People with Rare Diseases (2013) established 52 measures across seven policy areas.²⁶⁵ In 2023, an evaluation by the Federal Ministry of Health assessing the efficacy of the framework concluded that rare disease care has “improved markedly” — particularly through the build-out of Centres for Rare Diseases — yet the same review made clear that Germany's central rare disease challenge is no longer the absence of strategy on paper but incomplete implementation. Many patients still do not benefit from the documented gains, coordinated care pathways are still missing, and the review identified especially poor access ratings for psychological care, social-law support, and access to Medizinische Zentren für Erwachsene mit Behinderung (MZEb), alongside long waits including at specialist centres.²⁶⁶

A second persistent gap identified in the federal evaluation lies in the “non-core” pathways that are essential to daily life: psychosocial care, social counselling, rehabilitation, care services, MZEB access, and assistance with aids and appliances. These supports remain inconsistently available, and their absence falls hardest on adult patients and on families managing complex, lifelong conditions, undermining the system-level gains documented in the official review.



Implementation of the framework is coordinated through Germany's National Action League for People with Rare Diseases (NAMSE) – an organization comprising the Federal Ministries of Health and of Education and Research, along with leaders from +25 stakeholder organizations.²⁶⁷

In 2021, Germany introduced a formal certification process for Type A ZSEs to strengthen quality and coordination of care, with the national recognition process for Type B centres launched in February 2026 to extend that certification framework to disease-specific centres. Together with the launch of the German Genome Sequencing Program (genomDE), these steps reflect ongoing optimization of Germany's rare disease infrastructure: the legal and organizational scaffolding (G-BA rare disease centre rules, A-centre certification, Type B recognition, genomDE) is now in place, putting Germany in a position to scale beyond the academic centres that have led implementation to date.²⁶⁸

Patient Advocacy and Impact

ACHSE (Allianz Chronischer Seltener Erkrankungen) serves as Germany's national umbrella for rare disease advocacy, comprising 130+ patient organizations that represent approximately 4 million people. As a collective, ACHSE serves as the primary conduit for patient engagement in federal health policy across the country.

Patient advocacy is formally integrated through NAMSE, a tripartite initiative involving the Federal Ministries of Health and Research alongside ACHSE. Patient representatives hold advisory rights across Gemeinsamer Bundesausschuss (G-BA) processes and contribute to HTA evaluations via IQWiG, though without voting power. This limitation directly impacts how much patient advocates can influence benefit assessment outcomes despite consistent participation.

Country-Specific Recommendations

1. Complete and accelerate the certification rollout for Type B and Type C Centers for Rare Diseases – building on the February 2026 Type B recognition launch – to extend the ZSE network beyond academic settings.
2. Secure and standardize long-term financing for rare disease centres through dedicated federal funding mechanisms that reduce dependence on project-based grants and place core ZSE operations on stable budgetary footing.
3. Scale interdisciplinary case management and patient navigation models within and around the ZSE network, with particular focus on adult patients, to close the coordinated-care gap identified in the 2023 federal evaluation.
4. Systematize the use of the German Genome Sequencing Program (genomDE) as a standard component of the diagnostic pathway, building on lessons from TRANSLATE-NAMSE to shorten the diagnostic odyssey at national scale.
5. Strengthen “non-core” support pathways – including psychosocial care, social-law counselling, rehabilitation services, MZEB access, and aids and appliances – that the 2023 evaluation identified as having especially poor access ratings.
6. Launch a national GP education initiative on rare diseases and ZSE referral pathways, targeting the 54% of primary care physicians who lack adequate awareness of the system.
7. Expand newborn screening to include additional treatable conditions, building on the current 19-condition program.



Italy

Rare Disease Prevalence or Incidence Estimates*

2M²⁶⁹

SMA Birth Prevalence		9–14 per 100K live births ^{270,271}
FA Prevalence		2–4 per 100K ^{272,273}
ALS Prevalence		5.27–12.26 per 100K ^{274,275,276,277}
DS Birth Incidence		3.0–6.5 per 100K live births (global estimate) ^{278,279}

Population (2025)

58.93M²⁸⁰

Population Aged 65+ (2024)		14,516,972 ²⁸¹
Population Aged 65+ Projected (2050)		18,926,200 ²⁸²

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes	Orphan Drug Incentives:	Yes, through EU system
Newborn Screening	Screens for 40+ conditions ²⁸³	Cost-Effectiveness Analysis	QALY
Average Diagnostic Delay	5.4 years, 8–10 for adolescents	Societal Cost of Rare Disease	No information found
National Rare Disease Definition	EMA Definition Adherent		

Gaps

Geographic disparities concentrate access to specialists in certain regions, with older adults facing additional barriers due to comorbidities and mobility challenges.

Workforce shortages persist in part due to lack of neurologists and geneticists – particularly in underserved regions

Fragmented data and registries impede appropriate calibration across disease areas

Limited patient advocacy opportunities during drug development

Opportunities

The Undiagnosed Rare Diseases Network provides a platform for connecting research, industry, regional care, and healthy-aging priorities

Italy generates substantial clinical and research data, but fragmented sharing limits its value across regions and disease areas

The uneven distribution of referral centers makes geographically targeted investment especially high impact

The 10-year eligibility rule leaves Italy's established patient advocacy community underused in drug development

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.

Diagnostic and Screening Landscape

Italy provides obligatory and free nationwide newborn screening for approximately 40 inherited metabolic diseases. In addition to the mandatory screening, several regions have implemented extended programs that allow for early diagnosis of more than 50 rare metabolic, genetic, and endocrine conditions – including SMA in 14 of the regional panels.²⁸⁴

Across the country, 132 accredited hospital facilities are authorized to conduct next-generation sequencing (NGS) testing,²⁸⁵ enabling access to advanced genomic diagnostics. Despite this infrastructure, diagnostic delays remain substantial. As of 2024, the average time to diagnosis is 5.4 years, with longer delays of 8–10 years for adolescents.^{286,287}

While specialist availability in Italy is relatively high overall, with approximately 9 neurologists per 100,000 people, only about half practice within the public health system.^{288,289} Additionally, Italy sees wide variability between regions, with neurologists appearing to be focused on the north.^{290,291}

Disparities between regions and urban and rural areas are exacerbated by unclear diagnostic pathways. These pathways represent a gap in effective data sharing and coordinated care, limiting communication between providers and extending diagnostic timelines.

Treatment Access and Reimbursement Landscape

Italy's public National Health Service (SSN) finances a substantial share of orphan drug access. As of 2023, approximately 82% of EMA-approved orphan drugs (50 of 61 approved between 2018 and 2021) are reimbursed through the SSN.²⁹²

Italy's HTA process for drug reimbursement is managed by the Italian Medicines Agency (AIFA).²⁹³ Through this process AIFA assesses the innovative status of medicines and implementing appropriate reimbursement measures. AIFA incorporates some QALY analyses as one input among several during the HTA rather than as a strict threshold.²⁹⁴ This approach results in greater reimbursement flexibility for rare disease therapies.

Targeted care for rare diseases is delivered by approximately 260 regional referral centers, formally recognized within the national health system, covering all 20 Italian administrative regions. Over 70 of these centers support specialized care across the EU via European Reference Networks (ERNs) across all but 7 regions. This relationship builds cross-border clinical collaboration into Italy's model.²⁹⁵

National Policy Frameworks

Italy's National Rare Disease Plan 2023–2026 prioritizes faster access to diagnosis and treatment, improved care coordination, and the development of standardized care pathways. Enacted pursuant to Law 175 of 10 November 2021 and supported by EUR 25 million in annual funding from the national health fund, the plan sets out defined objectives, actions, tools, and indicators, with an explicit focus on reducing geographic inequalities and promoting innovation across the health system.²⁹⁶ However, today recent laws (law 207/2024) limit the involvement and impact of patient advocacy due to policy requirements that advocacy groups be active for 10 years prior to any involvement in drug development.²⁹⁷

For its rare disease policy implementation, Italy uses the EMA orphan drug designation framework.²⁹⁸ This framework provides fast-track options for orphan drugs during reimbursement review to improve speed to access for rare disease therapies. Research and innovation are further supported through national clinical trial networks and participation in European collaborations, including ERN-RND.²⁹⁹

The effectiveness of these policy and access frameworks will be increasingly shaped by Italy's demographic and regional realities. Italy has one of the oldest populations in Europe, with more than 24% already aged 65 and above, making alignment between rare disease and aging policy especially urgent. While the country benefits from a strong specialist infrastructure, access remains uneven: seven regions have no referral centers, and neurologists are disproportionately concentrated in the north. For older adults with rare diseases, these disparities are further compounded by mobility limitations and comorbidities that make long-distance travel to specialist centers particularly burdensome.



Patient Advocacy and Impact

Italy's rare disease advocacy ecosystem is nationally coordinated through UNIAMO, which represents 200+ patient associations and an estimated 2 million people living with rare diseases. UNIAMO holds legal recognition as an organization of public utility, strengthening its standing within national health governance.

Patient representatives hold formal seats on multiple national bodies, including the Ministry of Health's National Rare Disease Committee and boards overseeing ethics and newborn screening. While regional variability persists in implementation, national-level advocacy ensures consistent patient visibility in priority-setting and policy design.

Country-Specific Recommendations

1. Expand the Italian Undiagnosed Rare Diseases Network to strengthen collaboration across university centers, industry partners, and regional health systems, ensuring that healthy aging and rare disease care are integrated.
2. Address the geographic concentration of specialists and referral centers by investing in telemedicine infrastructure and targeted workforce development in southern regions and the seven regions with no referral centers.
3. Reform Law 207/2024 to remove the 10-year activity requirement for patient advocacy organizations seeking involvement in drug development, enabling earlier and broader patient engagement.
4. Improve cross-regional data sharing and registry harmonization to support more accurate calibration of care across disease areas and reduce diagnostic delays.



Japan



Rare Disease Prevalence or Incidence Estimates*

N/A

SMA Birth Incidence		5.1 per 100K live births ³⁰⁰
FA Prevalence		Data Unavailable
ALS Prevalence		9.9 per 100K ³⁰¹
DS Birth Incidence		3K nationwide or 2.4 per 100K ³⁰²

Population (2025)		123M ³⁰³
Population Aged 65+ (2024)	(30% of the total population)	36.92M ³⁰⁴
Population Aged 65+ Projected (2050)	(37% of the total population)	35.86M ^{305,306}

Rare Disease Benchmarking			
Rare Disease Policy Framework	Yes	Orphan Drug Incentives:	Some
Newborn Screening	Screens for 20 diseases	Cost-Effectiveness Analysis	Most orphan drugs effectively exempt; CEA applies primarily to drugs with large market sizes, and to ultra-expensive drugs regardless of market size.
Average Diagnostic Delay	No information Found	Societal Cost of Rare Disease	No information found
National Rare Disease Definition	National Designated Rare Disease Definition (Shitei-Nangyo): Fewer than 0.1% of the population and other 4 conditions ^{307,308}		

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Gaps

Drug lag and drug loss: 43% of orphan drugs approved in the U.S. remain unapproved in Japan, with approval lags of 1–5 years and some therapies never reaching Japan at all due to commercial viability concerns.³⁰⁹

Declining pharma investment signals: the grant rate for priority-review designations under the Orphan Drug Designation system has been declining, which industry stakeholders attribute to resource constraints at PMDA.³¹⁰

Economic viability of innovative therapies is deteriorating: regenerative medicinal products manufactured outside Japan often become unprofitable because yen-denominated purchase prices rise sharply with overseas cost increases and a weak yen, while medical fees (provider reimbursement) are kept low to contain healthcare spending.³¹¹

Pricing and CEA methodology are misaligned: a drug's contribution to dimensions such as patient convenience is recognized under drug pricing rules but often ignored in cost-effectiveness assessment, reducing predictability for developers and dampening R&D motivation.

Nanbyo coverage has gaps: while robust for designated intractable diseases, the system provides limited information and support pathways for patients with rare conditions outside current designated categories, a growing concern as Japan's aged population expands and more adult-onset rare diseases emerge.

Opportunities

Japan's scientific capacity and market size give it the potential to regain priority status for global rare disease launches

Inconsistency between pricing and cost-effectiveness assessment creates uncertainty about how clinical value will be rewarded

The existing ODD pathway and Japan's global research links provide a platform for faster rare disease development and review

Japan's advanced manufacturing base is an asset for building a more resilient supply of cutting-edge therapies

Economic volatility has exposed the need for pricing and fee policies that better preserve the viability of innovative therapies

Population aging makes the limits of the Nanbyo system increasingly consequential for adult-onset and late-presenting conditions

Diagnostic and Screening Landscape

Japan has a distinctive, nationally organized approach to the diagnosis and management of rare diseases – referred to predominantly as “intractable diseases” in Japan's policies and disease categorizations.^{312,313} This approach leverages a three-tier hospital network across all 47 prefectures: 1.) Intractable Disease Treatment Core Hospitals; 2.) Field-Specific Core Hospitals; 3.) Intractable Disease Medical Cooperation Hospitals.³¹⁴ Diagnostic efforts are further supported by the

Initiative on Rare and Undiagnosed Diseases (IRUD), which focuses on multidisciplinary evaluation for patients with complex or unresolved conditions.^{315,316}

Japan operates a universal Newborn Mass Screening program covering approximately 20 conditions nationwide.³¹⁷ Beyond newborn screening, genetic services are broadly available within the intractable disease hospital network, supporting diagnosis across a range of conditions included within existing frameworks.³¹⁸

Treatment Access and Reimbursement Landscape

Japan operates a universal healthcare system with a co-payment model.³¹⁹ Under this model, patients with designated intractable diseases have capped out-of-pocket payments; however, this copay support is available only to patients who meet a certain threshold of disease severity. The country's Intractable Diseases Act also provides subsidies for medical and nursing care for eligible patients. Typically, treatments for intractable diseases are delivered through prefecture- or city-designated institutions, in accordance with Japan's designated hospital network.^{320,321}

Japan takes a post-launch reassessment HTA approach, with specialized processes for orphan drugs. Japan's CEA framework is primarily limited to drugs with large market sizes, so it effectively has no impact on most orphan drugs; however, for ultra-expensive drugs, a cost-effectiveness assessment is performed regardless of market size.^{322,323,324} The framework is designed to prioritize early access while reserving cost scrutiny for high-budget-impact treatments, and once a therapy is approved, the time required for patients to gain access – from approval through insurance coverage – is relatively short by international standards.

Regulatory incentives for orphan drugs include priority review, reduced fees, and 10 years of market exclusivity.^{325,326} Japan also leverages a premium-based pricing system intended to reflect clinical value and innovation, with pricing premiums applied during initial drug price calculation to stimulate R&D incentives.³²⁷ While these mechanisms support availability within the intractable disease framework, access remains closely tied to disease classification and institutional designation.

The more pressing challenge for Japan is attracting and sustaining pharmaceutical investment in innovative rare disease therapies. Drug lag and drug loss remain the top policy priority flagged by JPMA, PhRMA, and EFPIA: over 50% of orphan drugs approved in the U.S. remain unapproved in Japan, approval lags of 2–5 years persist, and some therapies never reach the Japanese market due to commercial viability concerns.^{328,329} Industry stakeholders have raised concerns about a decline in priority-review designations under the Orphan Drug Designation (ODD) system, which appears linked to resource constraints at PMDA. At the same time, regenerative medicinal products manufactured outside Japan are increasingly unprofitable: their yen-denominated purchase prices rise

sharply as overseas production costs and the weak yen pull prices up, while medical fees (reimbursement for providers) are kept low to contain healthcare spending, making these treatments even less financially sustainable.

A further challenge is the lack of alignment between drug pricing rules and CEA methodology. A drug's contribution to dimensions such as patient convenience is recognized under pricing rules but is often ignored in the CEA process. These inconsistencies reduce predictability for developers and dampen R&D incentives, compounding the structural pressures on Japan's rare disease innovation ecosystem.

National Policy Frameworks

Japan's rare and intractable disease policy framework is anchored in the Act on Medical Care for Patients with Intractable Diseases (Nanbyo Law), which outlines medical, social, and financial support for patients with designated intractable diseases. The law underpins access to subsidized care, coordinated service delivery, and eligibility criteria tied to formally recognized disease categories.³³⁰

Regulatory support for innovation is governed through Japan's Orphan Drug Designation (ODD) system. This designation provides priority review in most cases for orphan drugs and devices targeting conditions affecting fewer than 50,000 patients nationwide. Designated products benefit from preferential regulatory treatment including reduced fees and 10 years of market exclusivity. The decline in priority-review designations granted under ODD, which pharmaceutical stakeholders link to PMDA resource constraints, poses a direct risk to the timely availability of innovative rare disease therapies in Japan.³³¹

To support alignment with international rare disease frameworks, Japan has developed the Nanbyo Disease Ontology, which maps designated intractable diseases to conditions recognized in Orphanet and other global databases. This initiative facilitates international data sharing and research collaboration, while maintaining its national classification systems.³³²

Against this policy backdrop, Japan's demographic profile will play an increasingly central role in shaping rare disease care needs. Japan is the world's most aged society, with more than 29% of its population already aged 65 and over, making rare disease policy closely intertwined with aging policy. The Nanbyo

system provides a highly structured framework for designated intractable diseases, but conditions outside these categories may receive more limited recognition and support. As the older population continues to grow, adult-onset and late-presenting rare conditions will require closer integration with geriatric and primary care pathways, and broader coverage under Nanbyo to enable access to innovative therapies.

Patient Advocacy and Impact

Japan's rare disease advocacy ecosystem is broad and increasingly coordinated, with an estimated 300,000 members represented through Japan Patients Association and allied organizations. Advocacy focuses on Nanbyo, a category embedded in national legislation.

Patient organizations contributed directly to the Nanbyo Act and participate in disease designation, policy review, and professional training oversight. New platforms such as the J-PEP Patient Expert Platform are expanding opportunities for structured patient engagement, though influence remains primarily consultative.

Country-Specific Recommendations

1. Strengthen incentives for pharmaceutical investment in Japan by introducing more timely adjustments to drug prices and medical fees in response to economic shifts (FX, inflation, input costs), preventing innovative therapies – including regenerative medicines manufactured abroad – from becoming commercially unviable.
2. Harmonize drug pricing rules and cost-effectiveness assessment methodology so that dimensions of clinical value recognized in pricing (e.g., patient convenience) are treated consistently in CEA, reducing unpredictability and strengthening R&D incentives.
3. Close the drug lag and drug loss gap by expanding Japan's participation in global multi-regional clinical trials (MRCTs) for rare disease therapies, and by strengthening PMDA capacity for the Orphan Drug Designation priority-review pathway to reverse the declining grant rate.
4. Support domestic manufacturing of cutting-edge rare disease therapies, including regenerative medicines, to insulate supply from FX volatility and overseas input-cost pressures, and to position Japan as a priority launch market for innovative therapies.
5. Broaden the Nanbyo system to enhance access to innovative drugs and expand financial support for patients with rare conditions outside current designated categories – a priority that grows in importance as adult-onset and late-presenting rare diseases emerge across Japan's aging population
6. Invest in GP and specialist education and clinical decision-support tools to reduce diagnostic delays for rare conditions not captured by newborn screening, with particular attention to age-associated rare diseases.



Mexico



Rare Disease Prevalence or Incidence Estimates*

~8M³³³

SMA Birth Incidence



10 per 100K live births³³⁴
(global estimate; country-specific data unavailable)

FA Prevalence

Data Unavailable

ALS Prevalence



3.06 per 100K (regional estimate for South America)³³⁵

DS Birth Incidence



3.0–6.5 per 100K live births (global estimate)^{336,337}

Population (2025)

132M³³⁸

Population Aged 65+ (2024)

(8% of the total population)

10,794,162³³⁹

Population Aged 65+
Projected (2050)

(20.2% of the total population)

28,700,000³⁴⁰

Rare Disease Benchmarking³⁴¹

Rare Disease Policy Framework

No

Orphan Drug Incentives:

None

Newborn Screening

Screens for 1-6 conditions

Cost-Effectiveness Analysis

None

Average Diagnostic Delay

8 years

Societal Cost of Rare Disease

No information found

National Rare Disease Definition

Defined in relation to orphan drug eligibility. Aligned with EMA & WHO.³⁴²

Gaps

Workforce shortages persist in most states, with specialists concentrated in major cities

Fragmented payer and approval systems that lead to unequal treatment access and legal appeals

Slow reimbursement pathways due to no HTA or orphan drug program

Opportunities

AMIIF's registry initiative offers an initial building block for a more coordinated national rare disease framework

Fragmented formulary processes across public institutions create a clear opportunity to improve consistency and predictability in coverage

Wide variation in state screening practices leaves substantial room to improve equity in early detection

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Diagnostic and Screening Landscape

Mexico does not operate a uniform national newborn screening program. Current mandates cover 1-6 conditions, depending on the institution. This results in substantial variability in early detection across states and regions. While some institutions screen for more than 60 conditions, others test for fewer than 6.³⁴³ A 2022 proposal to expand newborn screening nationally to 67 conditions was ultimately rejected due to resource constraints, reinforcing existing inequities across the system.³⁴⁴

Diagnostic capacity is further constrained by a severe shortage of genetic specialists. Only Mexico City meets the benchmark of at least one geneticist per 100,000 people.³⁴⁵ Many, more rural, states have approximately one geneticist per 500,000 residents or none at all.³⁴⁶ Mexico also lacks a distinct genetic counseling profession, placing additional pressure on limited specialist resources.³⁴⁷

These constraints contribute to prolonged diagnostic journeys. The average time to diagnosis is approximately 8 years, with patients consulting 6-8 specialists before receiving a diagnosis.³⁴⁸

Taken together, these screening and workforce limitations create sustained structural barriers to timely diagnosis and care. Long diagnostic journeys place a significant burden on patients and families and increase the risk of missed or late identification of rare conditions. As Mexico's population ages, these pressures are likely to intensify, particularly for older patients presenting with late-onset or atypical rare diseases. The absence of a formal genetic counseling profession further constrains system capacity to guide patients through complex diagnostic and care pathways.

Treatment Access and Reimbursement Landscape

Mexico's healthcare system is highly fragmented, with multiple public institutions – including IMSS, ISSSTE, and IMSS-Bienestar – each maintaining its own formularies and coverage rules.³⁴⁹ This fragmentation results in significant variability in access to rare disease treatments.

While Mexico's regulatory agency, COFEPRIS, approves orphan drugs, Mexico lacks a unified reimbursement or HTA pathway for rare disease therapies.³⁵⁰ Instead, coverage decisions are made independently by institutional formularies, leading to inconsistent inclusion of approved medicines. Between 2010 and 2021, COFEPRIS approved 95 treatments for rare diseases, yet only a limited subset has been incorporated into public formularies.³⁵¹

Access to high-cost therapies frequently depends on legal action (amparo) or manufacturer-led patient access programs, particularly for conditions requiring expensive, long-term treatment.³⁵² Mexico does not operate a national cost-effectiveness framework specific to orphan drugs, and while patient access programs can provide interim relief, they do not function as a systemic or sustainable solution for equitable access.³⁵³

National Policy Frameworks

Mexico does not have a comprehensive National Rare Disease Plan. Instead, the policy framework is defined through Article 224 of Mexican health law, which establishes the national definition of rare diseases (affecting fewer than 5 in 10,000 people) and formally recognizes all rare diseases included in the WHO ICD-11 classification.^{354,355} While this framework provides a legal basis for recognition, it does not translate into a coordinated national strategy for diagnosis, care, or access.

Mexico is in the process of developing a national rare disease registry to support epidemiological tracking and inform future policy planning, though the registry is not yet fully operational.³⁵⁶ At the regulatory level, Mexico does not offer dedicated orphan drug incentives, but does recognize approvals from reference agencies like the FDA and EMA to for domestic regulatory filings.³⁵⁷

Mexico experiences significant workforce constraint – with limited rare disease education and training for GPs. Specialist training is largely centralized within national institutes, restricting broader system capacity and contributing to persistent gaps in implementation and access.³⁵⁸



Patient Advocacy and Impact

Mexico's rare disease advocacy community is active and internationally connected but faces declining formal access to policymaking. FEMEXER serves as the primary national federation and has played a central role in education, awareness, and government engagement.

However, the dissolution of the CAERSER advisory body in 2024 significantly weakened institutionalized patient input into rare disease policy. Patient engagement currently relies on informal dialogue with health authorities rather than structured participation in regulatory or HTA processes.

Country-Specific Recommendations

1. Develop and adopt a comprehensive National Rare Disease Plan with clear priorities, a defined budget, measurable outcomes, and an implementation timeline. Industry efforts through AMIIF (the Mexican Association of Pharmaceutical Industry) to establish a rare disease registry represent a positive first step toward formalizing the national approach and could serve as a foundation for broader plan development.
2. Streamline and harmonize the formulary listing processes across IMSS, ISSSTE, and IMSS-Bienestar to reduce fragmentation in rare disease therapy coverage. While the reimbursement pathway itself is government-defined, aligning formulary inclusion criteria and timelines across institutions could meaningfully reduce access delays and lessen patients' reliance on legal amparo to obtain treatment. Progress on a National Rare Disease Plan (Recommendation 1) could further support improved reimbursement timelines.
3. Expand and standardize the national newborn screening program beyond the current 1–6 conditions, with a phased plan targeting high-impact treatable conditions. The pharmaceutical industry already offers patient testing for specific diseases as value-added services, and coordination between industry stakeholders and public affairs teams could help build the case for expanded government investment in screening programs.
4. Invest in expanding the genetics workforce beyond Mexico City, including establishing regional training programs and a formal genetic counseling profession.



Netherlands

Rare Disease Prevalence or Incidence Estimates*

1.2M³⁵⁹

SMA Birth Incidence		~9.6 per 100K live births ³⁶⁰
FA Prevalence		1.67 per 100K ³⁶¹
ALS Prevalence		8.51 per 100K ³⁶²
DS Birth Incidence		3.0–6.5 per 100K live births ^{363,364}

Population (2025)

18.4M³⁶⁵

Population Aged 65+ (2024)	(20% of the total population)	3,687,959 ³⁶⁶
Population Aged 65+ Projected (2050)	(28% of the total population)	4,800,000 ³⁶⁷

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes, Expired ³⁶⁸	Orphan Drug Incentives:	Yes, through EU system
Newborn Screening	Screens for 27 conditions ³⁶⁹	Cost-Effectiveness Analysis	Yes, low threshold ³⁷⁰
Average Diagnostic Delay	5–6 years ³⁷¹	Societal Cost of Rare Disease	No information found
National Rare Disease Definition	EMA Definition Adherent		

Gaps

Workforce shortages persist for clinical geneticists, genetic counselors, and metabolic specialists

Geographic disparities concentrate access to specialists and targeted treatment centers to urban areas

Strict cost-effectiveness thresholds and slow reimbursement pathways delay access to orphan drugs for many rare diseases

Opportunities

The expiration of the 2013 plan, alongside RARE-NL's research mission, creates a timely opening to renew national rare disease governance

The gap between conventional cost-effectiveness standards and the realities of orphan drugs creates room for more flexible access arrangements

The established 27-condition panel provides a strong base for the next phase of newborn screening

Long waits in genetics, neurology, and metabolic care reveal a significant specialist-capacity gap

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Diagnostic and Screening Landscape

The Netherlands operates a relatively robust national newborn bloodspot screening program that, as of 2025, covers 27 rare congenital disorders.³⁷² Beyond newborn screening, genetic testing is widely available in the Netherlands, with targeted gene panels and exome sequencing generally being covered by health insurance when clinically indicated. While these tests are generally accessible via university medical centers, that access is still largely concentrated in urban areas – creating geographical disparities to care.

Similarly, diagnostic care in the Netherlands is concentrated within a network of approximately 350 recognized Centers of Expertise (ECZAs), most of which are based at eight academic hospitals.³⁷³ Most ECZAs are specific to individual diseases, which supports highly specialized care but also limits access for individuals who live far from their specialized center.

Nationally, the Netherlands has an estimated 204 clinical geneticists.³⁷⁴ However, access is constrained by demand, with typical wait times of 4–6 months for specialist consultations.^{375,376}

Despite strong infrastructure, diagnostic delays persist. The average time to diagnosis remains 5–6 years, driven in part by limited GP familiarity with rare diseases and lengthy referral cycles before patients reach appropriate specialist services.³⁷⁷

Treatment Access and Reimbursement Landscape

The Netherlands operates a system of universal health insurance with a regulated basic benefits package. However, this system does not automatically reimburse for new medicines. High-cost therapies in particular are placed in a temporary lock prior to full reimbursement assessment – excluding them from coverage during the price negotiation period.³⁷⁸

Reimbursement decisions are informed by cost-effectiveness thresholds linked to disease severity, ranging from approximately €20,000 per QALY for mild conditions to €80,000 per QALY for severe diseases.³⁷⁹ There is no distinct threshold for ultra-rare conditions, meaning orphan drugs are assessed within the same severity-based framework.³⁸⁰ Consequently, this threshold excludes many higher-cost orphan drug treatments – limiting access for many individuals with rare diseases.

Currently, the timeline from EMA approval to reimbursement is approximately one year, with locked drugs experiencing an average additional delay of around 10 months during assessment and negotiation.³⁸¹ These timelines contribute to delayed patient access despite regulatory approval.

Beyond reimbursement timelines, delivery capacity and care navigation also shape real-world access in the Netherlands. The country's network of roughly 350 recognized Centers of Expertise provides deep specialization, but this highly concentrated model can be difficult for some older patients to navigate, particularly those with mobility limitations or multiple comorbidities. With typical wait times of 4–6 months for specialist genetics consultations, adult-onset rare conditions in older populations may face additional diagnostic delay relative to more urgent pediatric presentations.³⁸² The 2024 launch of RARE-NL, focused on therapy development and drug repurposing, signals a forward-looking strategy that could help expand innovation and treatment options, including for aging rare disease cohorts.³⁸³



National Policy Frameworks

The latest Netherlands National Plan for Rare Diseases launched in 2013 and recently reached its expiry period.³⁸⁴ Implementation for the plan was supported by a multi-stakeholder coordination body that advises the Ministry of Health. While the plan established a foundational approach to coordination and care, it is now dated, and discussions are underway regarding a successor strategy expected in 2026.³⁸⁵

In 2024, the Netherlands launched RARE-NL, a national hub focused on rare disease therapy development and drug repurposing – emphasizing innovation and translational research.³⁸⁶

The Netherlands operates under the EU orphan drug designation framework, reinforcing centralized oversight of access and funding for rare disease treatments. At the end of 2025, the EU passed a policy update for this framework to shift orphan drug exclusivity from 10 years to 9 years, with extensions available for breakthrough therapies and additional innovation criteria. This change allows exclusivity to reach up to 11 years (up to 12 in limited cases) and will take effect in 2028.³⁸⁷

Patient Advocacy and Impact

The Netherlands has one of Europe's longest-standing rare disease advocacy networks, coordinated nationally by the Vereniging Samenwerkende Ouder- en Patiëntenorganisaties (VSOP), the national patient alliance for rare and genetic diseases. Founded in 1979, VSOP represents approximately 90 patient and parent organizations³⁸⁸ and is recognized by EURORDIS as the Dutch national alliance for rare diseases.³⁸⁹

VSOP's advocacy focuses on care organization, research, and access to treatment. The organization led the development of the 2021 vision document for a National Strategy for Rare Diseases 2030,³⁹⁰ operates the Zicht op Zeldzaam platform to connect users with patient organizations and centers of expertise,³⁹¹ and coordinates patient organizations' assessments of candidate centers of expertise as part of the Ministry of Health's designation process.³⁹²

Patient influence is strongest in shaping care quality and the designation of centers of expertise, while involvement in reimbursement decisions remains consultative.³⁹³ Zorginstituut Nederland invites input from patient organizations during lock assessments,³⁹⁴ and VSOP participates in its Round Table on Orphan Drugs,³⁹⁵ but strict cost-effectiveness thresholds and lock-related delays limit advocates' influence over access decisions. A 2024 patient manifesto also helped prompt a parliamentary motion calling for a successor national plan, which is expected in 2026.³⁹⁶

Country-Specific Recommendations

1. Develop a successor to the expired 2013 National Plan for Rare Diseases, incorporating updated goals, measurable KPIs, and dedicated funding aligned with RARE-NL's research mission.
2. Expand reimbursement pathways through managed entry and outcomes-based agreements to provide earlier access for orphan drugs that do not meet standard cost-effectiveness thresholds.
3. Broaden newborn screening beyond the current 27 conditions, with prioritized inclusion of SMA and other treatable neuromuscular conditions.
4. Increase training pipeline capacity for clinical geneticists, genetic counselors, and metabolic specialists to reduce the current 4–6 month wait times for specialist consultations.



Norway

Rare Disease Prevalence or Incidence Estimates*

300K³⁹⁷

SMA Birth Incidence		10 per 100K live births ³⁹⁸ (global estimate; country-specific data unavailable)
FA Prevalence		0.55 per 100K ^{399,400,401}
ALS Prevalence		7.63 per 100K ⁴⁰²
DS Birth Incidence		~1 per 100K ⁴⁰³

Population (2025)

5.6M⁴⁰⁴

Population Aged 65+ (2024)	(19% of the total population)	1,046,766 ⁴⁰⁵
Population Aged 65+ Projected (2050)	(23.4% of the total population)	1,439,600 ⁴⁰⁶

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes	Orphan Drug Incentives:	Some
Newborn Screening	Screens for 30 conditions^{407,408} (with planned expansion to 39)	Cost-Effectiveness Analysis	Yes, high threshold
Average Diagnostic Delay	5-6 years	Societal Cost of Rare Disease	No information found
National Rare Disease Definition	National rare disease strategy definition in line with WHO, EMA⁴⁰⁹		

Gaps

Lengthy delays from market authorization to patient access create key treatment gaps

Underperformance in orphan drug availability compared to Nordic peers– with only 34% of EMA-approved drugs available compared to 69% and 41% from Sweden and Denmark, respectively

Fragmented care coordination across health, education, and social sectors to inconsistent access pathways

Opportunities

Norway's university-based centers provide natural anchors for extending specialist expertise across a geographically dispersed population

Nordic collaboration offers Norway a practical route to strengthen its comparatively limited access to orphan drugs

The Nordic Roadmap offers a shared benchmark for addressing delays in reviews of high-unmet-need therapies

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Diagnostic and Screening Landscape

Norway operates one of Europe's most comprehensive national newborn screening programs, covering 30 conditions (with plans to expand to 39), including SMA.^{410,411} This program benefits from near-universal participation across the country, with only 15-20 families opting out each year.⁴¹²

Beyond newborn screening, genetic testing is widely available through university hospitals and is generally free for patients with a doctor's referral, with no insurance requirement. However, these facilities tend to be concentrated in Oslo and other urban areas. The Norwegian Center for Rare Diseases – recently restructured into a single center comprising 8-9 units and approximately 200 employees, including the Frambu Resource Center – serves as the country's primary knowledge hub for rare diseases. Its role focuses on building, coordinating, and disseminating expertise across the health system rather than providing direct clinical treatment.⁴¹³

Despite this strong infrastructure, diagnostic delays persist for conditions not included in newborn screening. Average time to diagnosis for these conditions remains 5-6 years,⁴¹⁴ underscoring ongoing challenges in early recognition and referral beyond the neonatal period.

Norway's rural geography means patients in remote areas have less access to specialized care, with those who have complex needs often relocating closer to cities. Additionally, children generally receive better coordinated care than adults, and transitions between pediatric and adult care systems are problematic – a gap that stakeholders identify as a key area for improvement. There is also a recognized need for a national rare disease registry to better understand prevalence and population needs; while a registry is currently under development, it has not yet been fully operationalized.⁴¹⁵ Stakeholders further note the importance of earmarked state funding to ensure rare diseases are not crowded out by larger disease groups competing for the same resources.

Treatment Access and Reimbursement Landscape

Norway operates a universal, tax-funded healthcare system, with comprehensive coverage provided through the National Insurance Scheme and minimal patient copayments for participants over age 16.⁴¹⁶ Decisions on whether new medicines are publicly

funded are made through the national Nye Metoder process, and once a treatment is approved, it is made available nationally to all patients who meet the approved indication, ensuring uniform access across the country regardless of geography or provider.⁴¹⁷

Norway's approach is intentionally designed to secure nationwide equity in access rather than allowing regional variation, phased uptake, or early local adoption. As a result, assessments of clinical benefit, cost effectiveness, and pricing must be completed at a national level before any patients gain access. While this centralized model is a core strength of the system, it also helps explain why reimbursement decisions in Norway can take longer than in countries that permit earlier or more fragmented forms of access.

Access and pricing decisions for new medicines are informed by a severity-weighted HTA framework, which allows higher willingness-to-pay per QALY for more severe conditions. This framework supports increased flexibility for rare, high-cost conditions by using an "absolute shortfall" measure rather than a fixed threshold.⁴¹⁸

However, while Norway's severity-weighted HTA framework allows higher willingness-to-pay for the most severe conditions, it does not consistently accommodate the evidence and value profiles typical of rare diseases. Therapies that primarily deliver disease stabilization, incremental functional benefit, or address conditions with slower progression or adult onset often struggle to demonstrate sufficient cost-effectiveness, particularly given conservative treatment of uncertainty and limited trial data.⁴¹⁹

Norway's firm pricing and negotiation stance, combined with limited use of managed access or early access mechanisms, further constrains availability. Although an individual exception pathway was introduced in April 2025, it remains case-specific and non-scalable, offering limited relief from broader access delays.^{420,421} As a result, opportunities remain to introduce greater flexibility in evidence acceptance and access pathways while preserving Norway's strong commitment to equity, national consistency, and fiscal sustainability.

As Norway's population continues to age, these access and evidence assessment constraints are likely to become more consequential for rare disease care. Adult-onset and late-presenting rare conditions, including neurological and genetic disorders with slower progression, will represent a growing share of diagnostic and treatment demand. In this context, HTA



approaches that rely heavily on short-term measurable gains and conservative assumptions around uncertainty may be less well aligned with therapies that primarily stabilize function or delay decline in older patients. Strengthening flexible evidence frameworks and scalable access pathways will therefore be increasingly important to ensure that rare disease policy remains responsive under demographic change while maintaining Norway's core principles of equity and sustainability.⁴²²

National Policy Frameworks

Norway's National Strategy for Rare Diagnoses launched in 2021 with a focus on five core objectives: faster diagnosis, equitable access to treatment, improved care pathways, better support for daily living, and strengthened knowledge development.⁴²³ The strategy provides a national structure for coordination across health services while emphasizing system-wide improvement.

As a member of the European Economic Area (EEA), Norway follows the EU orphan drug designation framework, with marketing authorization through the EMA and national oversight by the Norwegian Medicines Agency. At the end of 2025, the EU passed a policy update for this framework to shift orphan drug exclusivity from 10 years to 9 years, with extensions available for breakthrough therapies and additional

innovation criteria. This change allows exclusivity to reach up to 11 years (up to 12 in limited cases) and will take effect in 2028.^{424,425}

Norway is also actively engaged in European and international collaboration through participation in ERNs, the JARDIN Joint Action, IRDiRC, and the European Joint Programme on Rare Diseases, reinforcing its integration into cross-border research, data sharing, and policy initiatives.

Patient Advocacy and Impact

Norway lacks a dedicated rare disease-specific patient umbrella, with advocacy instead led by Funksjonshemmedes Fellesorganisasjon, which represents 92 member organizations across the broader disability community.⁴²⁶ Rare disease interests are therefore embedded within a wider disability advocacy framework.

Patient organizations contributed to development of the National Strategy for Rare Diagnoses and engage regularly with parliament and the NKSD network of Centres of Expertise. However, advocacy influence is strongest in awareness-raising and agenda-setting rather than reimbursement outcomes, reflecting Norway's centralized and technocratic access framework.

Country-Specific Recommendations

1. Introduce hub-and-spoke care models that connect regional hospitals to university-based rare disease centers, reducing geographic barriers for patients in rural areas.
2. Expand the use of managed access and outcomes-based agreements to accelerate access for orphan drugs, addressing the current gap where only 34% of EMA-approved drugs are available compared to 69% in Denmark.
3. Streamline HTA timelines by implementing expedited review pathways for therapies addressing high unmet need, in alignment with the Nordic Roadmap for Rare Diseases.
4. Strengthen cross-sector care coordination between health, education, and social services to ensure consistent access pathways for patients with complex rare conditions.



Poland



2.5–3M⁴²⁷

Rare Disease Prevalence or Incidence Estimates*

SMA Birth Incidence		13.5 per 100K live births ⁴²⁸
FA Prevalence		0.4 per 100K ⁴²⁹
ALS Prevalence		4.8–9.6 per 100K ⁴³⁰ (European regional estimate; no country-specific data)
DS Birth Incidence		3.0–6.5 per 100K live births (global estimate) ^{431,432}

Population (2025)		38.1M⁴³³
Population Aged 65+ (2024)	(20% of the total population)	7.36M ⁴³⁴
Population Aged 65+ Projected (2050)	(30% of the total population)	10M ⁴³⁵

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes, expiring	Orphan Drug Incentives:	Yes, through EU system
Newborn Screening	Screens for 30 conditions ^{436,437}		
Average Diagnostic Delay	4 years ^{438,439}		
Societal Cost of Rare Disease	Rare diseases affect 2–3 million people in Poland and generate substantial indirect costs, including loss of productivity among caregivers, high costs of informal care, and system inefficiencies from diagnostic delays. ⁴⁴⁰ NFZ data indicates rare disease drug programme expenditure grew from approximately PLN 1.7–2.0 billion (2021) to around PLN 3 billion annually (2025), representing 20–30% of total drug programme budgets.		
National Rare Disease Definition	Fewer than 1 per 2,000 people ⁴⁴¹		

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Gaps

Reimbursement indications are narrowly scoped: while EU member states on average make 58% of reimbursed technologies available without indication restrictions, in Poland this share is only approximately 5%,⁴⁴² meaning many orphan drugs that achieve formal reimbursement remain accessible only to narrowly defined patient subgroups

HTA methodology is not adapted to rare diseases: reliance on a single cost-effectiveness threshold and limited systematic acceptance of real-world evidence and patient-reported outcomes create barriers for ultra-rare conditions with small evidence packages

Geographic and regional disparities persist: specialist access is concentrated in urban academic centers, and availability of reimbursed therapies varies across voivodeships, with a median 137-day lag between reimbursement listing and first dispensing under new drug programs⁴⁴³

Severe caregiver burden for families supporting individuals with rare diseases, with over 80% reporting a serious impact on daily functioning, employment, and mental health⁴⁴⁴

Opportunities

The expiration of the 2024–2025 plan creates a near-term opportunity to secure continuity and clarify the legal basis for rare disease policy

The Medical Fund has the potential to become a more consistent bridge between innovation and routine reimbursement

Poland's current HTA framework leaves important clinical and societal dimensions of rare disease value insufficiently captured

Established European models provide a ready precedent for giving patient perspectives a more formal place in Poland's HTA deliberations

Poland's recent EU leadership and expanding ERN participation create momentum for a stronger role in European rare disease policy

Diagnostic and Screening Landscape

Poland operates a comprehensive national newborn screening program covering 30 conditions, including SMA as of March 2022.⁴⁴⁵ However, while this program was expanded overall genetic testing remains slow across the country.

That testing is available through university hospitals and specialized centers – which currently concentrate access in urban areas. In total, Poland has designated 44 Rare Disease Expert Centers (OECRs), equating to approximately one center per 860,000 residents.⁴⁴⁶ ~140 clinical geneticists operate across these centers, creating limited availability relative to population needs.⁴⁴⁷ These workforce constraints create lengthy wait times of 2.5–3 years for specialist appointments.⁴⁴⁸

As a result, diagnostic delays remain substantial. The average time to diagnosis ranges from 5–10 years, exceeding European averages and underscoring persistent challenges in specialist access, referral pathways, and system coordination.^{449,450}

Patients with rare diseases in Poland continue to experience a prolonged diagnostic odyssey, with average time to diagnosis extending over several years, reflecting persistent barriers in specialist access, referral pathways, and system coordination.⁴⁵¹ A contributing factor to these delays is the time required to access and complete genetic testing, which is often ordered late in the diagnostic pathway and associated with long waiting periods for both referral and test results.

ALS exemplifies this shift, as recent Polish clinical guidelines recommend genetic testing for all patients diagnosed with ALS,⁴⁵² with test results directly determining eligibility for targeted treatment.

Treatment Access and Reimbursement Landscape

Poland provides universal health coverage through the National Health Fund (NFZ). Orphan drugs require a positive reimbursement decision from the Ministry of Health, informed by assessment from the Agency for Health Technology Assessment and Tariff System (AOTMiT).⁴⁵³ AOTMiT applies a cost-effectiveness threshold of approximately PLN 215,000 per QALY, roughly three times GDP per capita, without a separate threshold for rare or ultra-rare conditions.⁴⁵⁴

In an expert interview conducted for this report, Marcin Czech, a former Polish Vice Minister of Health, noted that cost-effectiveness is only one of several inputs into the final reimbursement decision: decision-makers retain discretion to reimburse therapies even when cost-effectiveness assessments are negative, as has been the case for the SMA therapies. Among mitigating factors, unmet medical need, meaning whether the patient population has alternative therapeutic options, carries the most weight; scarcity, rarity, and disease severity on their own are weighted less heavily, though severity can serve as a mediating factor when paired with substantial unmet need. Rare-disease features that complicate these appraisals include small target populations, reliance on single-arm studies, shorter observation periods, and in some cases limited demonstrated benefit within the targeted population.

Rare disease reimbursement has improved meaningfully in recent years. Time from application to decision for rare disease drugs fell from approximately 714 days in 2018 to 209 days in 2023, and the number of new rare disease reimbursements rose from fewer than ten per year on average between 2012 and 2020 to 43 in 2023.⁴⁵⁵ As of early 2025, approximately 33% of EMA-approved non-oncology orphan drugs are available in Poland, with a median time to availability of 704 days, reflecting gradual alignment with broader European performance even as Poland continues to trail the largest Western European markets.^{456,457}

The larger access challenge is the scope of what is reimbursed rather than whether a drug appears on the reimbursement list. While EU member states on average make 58% of reimbursed technologies available without indication restrictions, in Poland this share is only approximately 5%, meaning many orphan drugs that formally achieve reimbursement are accessible only to narrowly defined patient subgroups. Additional real-world friction comes from a median 137-day delay between reimbursement decision and first drug sale under new drug programs, and persistent regional variation in specialist infrastructure.⁴⁵⁸

The Medical Fund, established under the 2020 Act on the Medical Fund, introduced a faster dedicated pathway for highly innovative medicines covering both oncology and rare disease indications, and for the first time codified orphan drug criteria in Polish law. In practice it operates as an early-access-style mechanism, funding selected therapies with the expectation that real-world evidence will be gathered during use, and it can expedite subsequent reimbursement review. Several high-profile rare disease therapies – including several for SMA – have since achieved reimbursement.⁴⁵⁹

Poland's reimbursement framework does not yet formally include rare-disease-specific assessment criteria such as MCDA, systematic use of real-world evidence, or structured inclusion of patient-reported outcomes. The most recent major legislative update, a 2023 amendment to the Reimbursement Act governing drug reimbursement decisions, shortened procedural timelines but stopped short of introducing them.⁴⁶⁰ Poland's 2021–2023 Rare Disease Plan did, however, commit to introducing MCDA for rare disease HTA, and that direction appears to be advancing: expert interviews for this report indicate that a multi-stakeholder group is reviewing the HTA process for rare diseases and Poland's MCDA guidelines, with reported aims including broadening what counts as a benefit of a rare disease therapy and giving decision-makers greater flexibility in reimbursement decisions.⁴⁶¹

As Poland's population ages, these structural features are likely to become more visible. Adult-onset and late-presenting rare conditions, often supported by smaller evidence packages and higher per-patient costs, will test a framework still built around a single cost-effectiveness threshold and narrowly scoped reimbursed indications. Building on the Medical Fund as a more predictable and scalable pathway, and adapting HTA methodology for small-population therapies, will be central to preserving equity in rare disease treatment under demographic change.

National Policy Frameworks

Poland's Plan for Rare Diseases 2024–2025, adopted by the Council of Ministers on 13 August 2024 as successor to the 2021–2023 plan, is a comprehensive framework spanning screening and diagnosis (including newborn screening), education, treatment, Expert Centers for Rare Diseases, a national rare disease registry, a Rare Disease Patient Card, and a patient information platform.⁴⁶² The plan is funded, with approximately PLN 100 million allocated to implementation, and the Ministry of Health serves as the central coordinating body. Plan development drew on broad stakeholder participation, including



Ministry officials, clinicians and geneticists, scientists, health economists, patient organizations and umbrella groups, industry, and payer and HTA representatives. Even so, the plan's short time horizon underscores the need for longer-term strategic continuity, and no successor has yet been announced to carry implementation forward.⁴⁶³

To support information sharing and system coordination, Poland launched a Rare Diseases Information Platform in October 2023, however, the Polish register remains under development.⁴⁶⁴ At the European level, Poland operates under the EU orphan drug designation framework and participates in ERNs and the JARDIN Joint Action, reinforcing alignment with broader EU initiatives.

In 2025, Poland elevated rare diseases as a policy priority during its EU Council Presidency, including hosting a major conference focused on advancing an EU-level Action Plan for Rare Diseases, signaling increased political attention to the issue.^{465,466}

Patient Advocacy and Impact

Rare diseases affect an estimated 2.5–3 million people in Poland, with national advocacy coordinated through the National Forum for Rare Disease Therapies ORPHAN. The Forum represents 95+ patient organizations and serves as the primary voice for rare disease policy engagement.⁴⁶⁷

Advocacy groups maintain active dialogue with the Ministry of Health, parliamentary committees, and the National Health Fund, contributing to legislative development and orphan drug financing discussions. The Ministry during our expert interview for Poland was characterized as operating an “open door” policy under which patient organizations can request meetings with the Minister and senior officials, and indicated that the Ministry has established a patient advisory body and that patients have standing to speak at hearings. Despite these access points, patient organization participation in AOTMiT review itself remains primarily consultative rather than structured, with opportunities to formalize engagement in line with practices in France, Germany, Sweden, and Scotland.⁴⁶⁸

Country-Specific Recommendations

1. Develop a permanent successor to the 2024–2025 Plan for Rare Diseases and codify a national definition of rare and ultra-rare disease in the Reimbursement Act to anchor long-term policy continuity. The new framework should formalize transition-of-care pathways from pediatric to adult services, which remain a major systemic gap in Poland.
2. Adapt HTA methodology for small-population therapies by introducing multi-criteria decision analysis (MCDA) alongside the standard cost-effectiveness threshold, expanding systematic acceptance of real-world evidence and patient-reported outcomes, and narrowing the gap between reimbursement approval and broad indication access.
3. Expand the Medical Fund as the primary predictable, scalable pathway for highly innovative rare disease therapies, with clearer publication schedules, transparent MCDA deliberation, and integration into the broader reimbursement architecture so that fast-track access does not depend on a single annual listing cycle.
4. Formalize patient organization participation throughout AOTMiT reimbursement review, including standing representation on the Patient Organization Council, structured consultation on draft HTA reports, and publication of deliberative outputs, to align Poland with established models in France, Germany, Sweden, and Scotland.
5. Systematically address caregiver burden as a core policy priority. Given that more than 80% of families affected by rare diseases report a severe impact on daily functioning, employment, and mental health, Poland should develop dedicated caregiver support programmes, including respite care, psychosocial support, and formal recognition of informal care within health and social policy frameworks.



Saudi Arabia

Rare Disease Prevalence or Incidence Estimates*

SMA Birth Prevalence

Data Unavailable

FA Prevalence

Data Unavailable

ALS Prevalence

Data Unavailable

DS Birth Incidence

Data Unavailable

1.2–2.1M⁴⁶⁹

Population (2025)

34.6M⁴⁷⁰

Population Aged 65+ (2024)

(3% of the total population)

1.04M⁴⁷¹

Population Aged 65+ Projected (2050)

(25% of the total population)

10,000,000⁴⁷²

Rare Disease Benchmarking

Rare Disease Policy Framework	No	Orphan Drug Incentives:	Some
Newborn Screening	Screens for 21 conditions ^{473,474}	Cost-Effectiveness Analysis	Emerging (new HTA body announced but not yet fully operational)
Average Diagnostic Delay	5–7 years ^{475,476}	Societal Cost of Rare Disease	No information found
National Rare Disease Definition	1 per 2,000 people ⁴⁷⁷		

Gaps

Lack of policy and care coordination due to absence of national plan and rare disease registry

Geographic disparities concentrate access to specialists and targeted treatment centers to urban areas

Low orphan drug availability limits treatment access across the country

No rare-disease-specific evaluation for reimbursement

Opportunities

The 2025 consensus definition and Saudi genomic infrastructure provide the building blocks for a coordinated national rare disease framework

The ongoing development of HTA creates an unusually early opportunity to account for orphan drugs within the system's core design

Saudi Arabia's investment in genomic medicine provides a strong foundation for expanding clinical genetics and counseling capacity beyond major cities

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.

Diagnostic and Screening Landscape

Saudi Arabia faces a particularly high burden of rare genetic diseases, driven in part by consanguinity rates exceeding 50% – among the highest globally. The country has the highest autosomal recessive birth rate in the world, with founder mutations accounting for approximately 40% of the total mutation pool.⁴⁷⁸ In response, Saudi Arabia has established a national newborn screening program covering 16 diseases, though implementation remains inconsistent, limiting uniform early detection.^{479,480} The Saudi Human Genome Program represents a more substantial investment in national genomic capacity, sequencing approximately 56,000–65,000 samples,⁴⁸¹ identifying 3,000 novel mutations, and developing 13 gene panels.^{482,483,484} This project signals significant progress for genetic testing and carrier screening, but capacity remains concentrated in urban areas.

Across the country, Saudi Arabia experiences a substantial workforce shortage – with only around 40 clinical geneticists and ~14 – 41 certified genetic counselors nationwide.^{485,486,487} As a result, patients outside major referral centers face longer and more complex diagnostic pathways.

These constraints contribute to persistent diagnostic delays of 5–7 years.^{488,489} Faster diagnosis is possible for individuals who receive care at highly specialized institutions such as King Faisal Specialist Hospital & Research Center (KFSH-RC). However, this disparity exposes a gap between national investment in genomic innovation and equitable, system-wide diagnostic access.

Treatment Access and Reimbursement Landscape

All Saudi nationals benefit from basic healthcare coverage, including free access to government facilities.⁴⁹⁰ Beyond this, private health insurance covers over 13 million beneficiaries – including more than 8 million non-Saudi residents⁴⁹¹ – though private insurance does not guarantee coverage for rare disease treatments. As of 2024, 41.3% of Saudis also held private insurance.⁴⁹² This dual structure contributes to uneven access and creates variability in treatment availability across patient groups.

These dynamics are evident in SMA care. Saudi Arabia has approved three disease-modifying therapies for SMA, and while all nationals are entitled to healthcare coverage, real-world access to these treatments

remains inconsistent in practice. This is largely due to the fragmented nature of institutional formularies – each system, including MoH, National Guard, MODA and KFSH, must independently approve the inclusion of new treatments, creating variability in availability across sites. As a result, approximately 64% of hospitals report supportive care as the only available option, reflecting persistent implementation barriers for high-cost therapies beyond a small number of specialized centers.⁴⁹³

Saudi Arabia's HTA processes are still evolving. Decision-making considers budget impact and clinical value, but there is no formal QALY threshold specific to rare diseases. While the country does leverage an informal of approximately SAR 50,000–75,000 per QALY, this range does not accommodate the higher cost of orphan drugs for ultra-rare conditions. Per SFDA guidelines, manufacturers must provide at least one economic evaluation study (Budget Impact Analysis, Cost Effectiveness Analysis, or Cost Utility Analysis) for new products.^{494,495} Due to a lack of structured orphan drug accommodations, many internationally approved therapies remain unavailable in Saudi Arabia.⁴⁹⁶

National Policy Frameworks

Saudi Arabia does not have a published national rare disease policy framework. However, the National Policy for Genetic Diseases Project (completed by the national committee for Genetic Diseases) is pending approval by the Minister of Health, and represents a significant step toward a more structured national approach.^{497,498} The Policy is explicitly aligned with the three objectives of the National Health Sector Transformation Program under Vision 2030 (easing access to healthcare services, improving the value of healthcare services, and strengthening prevention against health threats), and is organized around four pillars: comprehensive prevention, efficient diagnosis, effective treatment, and integrated care.⁴⁹⁹ The country also lacks a standardized rare disease definition, or active national patient registry, resulting in fragmented policy oversight and limited system-wide coordination.⁵⁰⁰

In 2023, a multi-stakeholder workshop endorsed establishing a national definition, diagnostic criteria, and coordination mechanisms, signaling growing recognition of the need for a more structured policy approach. However, this endorsement has yet to produce a comprehensive strategy.^{501,502}



Building on this momentum, a 2024–2025 Delphi consensus led by Dr. Ahmed Al-Jedai recommends a differential cost-effectiveness threshold for rare diseases, proposing a multiplier of up to 3x the standard SAR 50,000–75,000 per QALY – equivalent to a target threshold of roughly SAR 150,000–225,000 per QALY. This recommendation is supported by a Multi-Criteria Decision Analysis (MCDA) framework that prioritizes disease severity and lack of available alternatives, and represents the most concrete policy proposal to date for improving rare disease treatment access in Saudi Arabia.⁵⁰³

Currently, Saudi Arabia's regulatory program does not currently include formal market exclusivity provisions, limiting its strength as a long-term incentive framework.⁵⁰⁴ Additionally, workforce development initiatives to expand training programs, telemedicine capacity, and genomic specialization are slow moving, with no promise of near-term impact.

Patient Advocacy and Impact

Saudi Arabia's rare disease advocacy landscape remains nascent, with no established national patient umbrella organization. Initial patient-focused initiatives emerged in late 2024, but these remain limited in scope and institutional reach.^{505,506}

Patient participation in policymaking is currently ad hoc, with limited formal mechanisms for engagement in HTA or access decisions. While awareness is increasing, sustained advocacy impact is constrained by structural and developmental gaps.

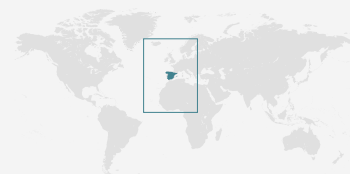
These recommendations become increasingly urgent given Saudi Arabia's rapidly aging population. With 10.3 million residents aged 65 and older, the prevalence of late-onset rare diseases is expected to rise significantly. Adult-onset conditions requiring diagnostic precision and timely therapeutic access will strain an infrastructure currently optimized for pediatric and early-onset presentations. Strengthening the diagnostic capacity, treatment access mechanisms, and governance framework outlined below will be essential to address the growing burden of rare disease in an aging society.

Country-Specific Recommendations

1. In 2025, a multisectoral consensus established a formal rare disease definition for Saudi Arabia – life-threatening or chronic conditions with a prevalence under 5 per 10,000 – tailored to prioritize genetic conditions within the Saudi healthcare ecosystem. Building on this milestone, Saudi Arabia should now develop and adopt a formal National Rare Disease Plan and active national patient registry to translate this definitional foundation into coordinated policy oversight and system-wide implementation.
2. Leverage the newly established rare disease definition to accelerate structured reimbursement pathways within the evolving HTA framework, including explicit orphan drug accommodations through the SFDA and Ministry of Health that exceed the informal SAR 50,000–75,000 per QALY threshold, in line with the Delphi consensus recommendation of SAR 150,000–225,000 per QALY.
3. Invest in expanding the genetics workforce by scaling training programs for clinical geneticists and genetic counselors beyond the current approximately 40 and 14–41 respectively.
4. Leverage the Saudi Human Genome Program's infrastructure to build a nationally integrated diagnostic network that extends advanced genomic capacity beyond major urban referral centers.



Spain



Rare Disease Prevalence or Incidence Estimates*

3M⁵⁰⁷

SMA Birth Incidence		~12.7 per 100K live births ⁵⁰⁸
FA Prevalence		1.97 per 100K ^{509, 510, 511}
ALS Prevalence		5.4–8.38 per 100K ^{512, 513}
DS Birth Incidence		348–540 total or 0.71–1.10 per 100K ⁵¹⁴

Population (2025)

49.2M⁵¹⁵

Population Aged 65+ (2024)	(21% of the total population)	10,329,304 ⁵¹⁶
Population Aged 65+ Projected (2050)	(25.4% of the total population)	13,700,000 ^{517, 518}

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes ⁵¹⁹	Orphan Drug Incentives:	Through EU system
Newborn Screening	Screens for 22 pathologies in the common portfolio, with plans to expand further ⁵²⁰	Cost-Effectiveness Analysis	No
Average Diagnostic Delay	6.18 years ⁵²¹	Societal Cost of Rare Disease	No information found
National Rare Disease Definition	EMA Definition Adherent		

Gaps

Geographic disparities concentrate access to specialists in key regions and urban areas

Lagging rare disease screening policies lengthen diagnostic timelines, particularly for conditions like SMA

Improved orphan drug approval rates limit treatment access across the country

Decentralized healthcare governance creates disparities in implementation of care across regions

Opportunities

The expected 2026 strategy creates a timely opening to reduce variation across the autonomous communities

Spain's strong rare disease trial base and ERDERA participation position it to play a larger role in translational and gene-therapy research

The gap between Spain's specialist capacity and the European average highlights a high-impact workforce opportunity

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.

Diagnostic and Screening Landscape

Spain's mandatory national newborn screening program covers 22 conditions in the common national portfolio (with plans for further expansion to 25), reaching nearly 350,000 newborns annually.^{522,523} However, some Autonomous Communities (CCAA) have expanded screening beyond the national baseline, with some testing for up to 37 conditions, creating wide regional variation in early detection for rare diseases.⁵²⁴

SMA screening has now been formally incorporated into Spain's common national newborn screening portfolio. Following approval by the Consejo Interterritorial del Sistema Nacional de Salud (CISN), Ministerial Order SND/356/2026 was officially published in the Boletín Oficial del Estado (BOE) in April 2026, making SMA newborn screening legally mandatory nationwide. Under the Order, Spain's 17 Autonomous Communities have a maximum of one year from the regulation's entry into force to adapt their newborn screening programmes and integrate SMA into the heel-prick test, supporting a progressive and harmonised rollout across the country. As of publication, several CCAAs had already implemented SMA screening ahead of the mandate and others were nearing completion.⁵²⁵

Diagnostic delays remain common across the country. More than half of patients experience a median delay of ~6 years.⁵²⁶ These delays are exacerbated by decentralized referral pathways and specialist shortages. Currently, Spain has approximately 3.4 neurologists per 100,000 people, well below the EU average of 5–7.⁵²⁷

Demographic change will further test Spain's decentralized rare disease diagnostic model. As the proportion of older adults increases over the coming decades, a larger share of rare disease presentations is likely to emerge through adult and geriatric care pathways rather than pediatric channels. In a system where screening scope, referral practices, and specialist availability vary across Autonomous Communities, this shift may widen existing regional differences in time to diagnosis. Strengthening interregional coordination and standardized referral protocols will be increasingly important to ensure consistent recognition of late-presenting rare diseases.

Treatment Access and Reimbursement Landscape

Spain sees improved reimbursement rates for orphan drugs – reimbursing approximately 67% of EMA-approved products, with 104 of 156 authorized therapies funded as of 2025.⁵²⁸ While Spain does not apply a formally stated or publicly codified cost-effectiveness threshold for orphan drugs, independent analyses suggest that reimbursement decisions in practice often align with an informal QALY threshold of €22,000–€25,000.⁵²⁹

Treatment delivery for rare diseases is typically organized through a network of 358 nationwide reference centers for low-prevalence pathologies, 110 of which are part of ERNs.^{530,531} However, these centers are unevenly distributed geographically, and disease-specific expertise is not consistently available across regions. This uneven distribution contributes to variability in access and places additional burden on patients who must travel to access specialized care, especially those in rural areas.

National Policy Frameworks

Spain's latest national rare disease strategy plan spanned 2014–2023, with regional autonomous plans emanating from the national framework across Spain's 17 Autonomous Communities. A revised national strategy is currently under development.⁵³² The updated framework, expected in 2026, aims to introduce refreshed goals, clearer implementation mechanisms, and defined KPIs to strengthen coordination, access, and system accountability.^{533,534} Signaling growing federal attention to patient-level evidence, in March 2026 the Ministry of Health commissioned a study by KPMG to analyze the physical, emotional, and social dimensions of rare disease patient experience.⁵³⁵

Spain operates under the EMA orphan drug designation and regulatory pathways, aligning national policy with European standards. At the end of 2025, the EU passed a policy update for this framework to shift orphan drug exclusivity from 10 years to 9 years, with extensions available for breakthrough therapies and additional innovation criteria.^{536,537} This change allows exclusivity to reach up to 11 years (up to 12 in limited cases) and will take effect in 2028.^{538,539}

Approval times for medicines in Spain have improved in recent years, according to the Market Access Report 2025 on orphan medicinal products published by AELMHU (Asociación Española de Laboratorios



de Medicamentos Huérfanos), Spain's association of orphan drug manufacturers. The report documents accelerated market entry timelines and enhanced transparency in reimbursement decision-making.⁵⁴⁰

The country is also actively engaged in European research and clinical trial networks, including SpainRDR, which is approved within the IRDiRC framework.⁵⁴¹ Spain also has a strong research foundation, 845 of the 1,944 clinical trials authorized through the EU's new Clinical Trials Information System (CTIS) operating in Spanish sites.⁵⁴² Additionally, 1 in 4 of all clinical trials in Spain are currently focused on rare diseases.⁵⁴³

Patient Advocacy and Impact

Spain's rare disease advocacy landscape is anchored by FEDER, which brings together 400+ associations representing more than 3 million people across 1,500+ rare conditions. FEDER plays a central role in national awareness-raising and strategic policy engagement.

Patient organizations have contributed directly to Spain's National Rare Disease Strategy and provide expert input on screening and health planning through national and interterritorial mechanisms. However, advocacy influence on reimbursement and access decisions remains uneven due to Spain's decentralized health system.

Country-Specific Recommendations

- | | |
|----|---|
| 1. | Finalize and implement the revised National Rare Disease Strategy (expected 2026) with clear KPIs, dedicated funding, and consistent deployment mechanisms across all Autonomous Communities. |
| 2. | Standardize newborn screening nationally to include additional treatable conditions beyond the current 22 in the common national portfolio (which now includes SMA), working to reduce regional variation where some CCAA screen for up to 37 conditions. |
| 3. | Leverage Spain's strong clinical trial infrastructure and ERDERA participation to accelerate patient access to innovative therapies, building on the fact that 1 in 4 clinical trials in Spain already focus on rare diseases. |
| 4. | Invest in specialist training to address the current shortfall of 3.5 neurologists per 100,000 people, well below the EU average of 5–7. |



Türkiye

Türkiye's rare disease landscape is shaped by the prevalence of consanguineous marriages, which significantly increases the incidence of autosomal recessive genetic conditions, and by migration flows driven by its geopolitical position, which introduce genetic diversity and a wide spectrum of rare disease presentations.⁵⁴⁴

5–7M^{545,546}

Rare Disease Prevalence or Incidence Estimates*

SMA Birth Incidence		13.6 per 100K live births ⁵⁴⁷
FA Prevalence		Data Unavailable
ALS Prevalence		5.4–7.3 per 100K ^{548,549}
DS Birth Incidence		3.0–6.5 per 100K live births (global estimate) ^{550,551}

Population (2025)

85.7M⁵⁵²

Population Aged 65+ (2024)	(10.6% of the total population)	9.11M ⁵⁵³
Population Aged 65+ Projected (2050)	(21% of the total population)	20M ⁵⁵⁴

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes	Orphan Drug Incentives:	None
Newborn Screening	Screens for 6 conditions ^{555,556}	Cost-Effectiveness Analysis	No
Average Diagnostic Delay	N/A	Societal Cost of Rare Disease	High out-of-pocket burden reported among rare disease households (non-medical and supportive costs) ⁵⁵⁷
National Rare Disease Definition	Conditions affecting fewer than 1 per 2,000 – 1 per 10,000 individuals ^{558,559}		

Gaps

Geographic disparities concentrate access to specialists in major cities	Fragmented disease coding across the national registry constrains research and planning
Limited treatment access beyond SMA – requiring patients to resort to import mechanisms or legal action for access	Lack of data sharing and across hospitals including limited willingness to share information between institutions, undermines coordinated care, research, and system-level planning
No orphan drug incentives and low approval rates limit market entry	Limited public awareness of rare diseases, particularly among the general population, contributes to delayed diagnosis and low visibility of patient needs

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.

Opportunities

Türkiye's successful SMA program provides proof of concept for broader newborn screening

The lack of dedicated orphan drug legislation leaves a major policy gap in an otherwise developing rare disease framework

Orphanet identifiers offer a ready international standard for strengthening Türkiye's rare disease data infrastructure

The concentration of specialist expertise leaves substantial room to improve regional diagnostic access

Patient organizations already hold trusted relationships and information that could strengthen policy design and data quality

The trust and data held across government and patient organizations provide a strong foundation for a credible national registry

Diagnostic and Screening Landscape

Türkiye's newborn screening program covering 6 conditions – including SMA as of 2022.^{560,561,562} Since SMA's inclusion, approximately 97% of newborns have been screened for, with more than 1.76 million infants tested and 286 cases identified.⁵⁶³ This progress signals a strong national focus on SMA.

Türkiye continued this focus via mandatory premarital SMA carrier screening, with couples identified as dual carriers eligible for government-funded preimplantation genetic diagnosis (PGD) and IVF.⁵⁶⁴ Advanced genomic diagnostics, including Whole Exome Sequencing (WES) and Next-Generation Sequencing (NGS), are available in major centers and demonstrate high diagnostic yield of up to 80% in consanguineous families.^{565,566}

Despite these strengths, diagnostic access remains uneven. Türkiye's specialist workforce is insufficient to meet population needs, particularly outside of major urban areas. As a result, patients may travel long distances to access care, contributing to persistent regional disparities.

Insights from rare disease stakeholders in Türkiye underscore the depth of these diagnostic challenges. Primary care physicians and pediatricians often lack systematic training in recognizing rare conditions,

resulting in diagnostic odysseys that last years – and in some cases never reach resolution. Access to advanced genetic technologies such as next-generation sequencing remains unsystematic and is generally not covered by reimbursement systems. Although a national rare disease registry has recently been established, hospitals remain reluctant to share data due to trust and security concerns, limiting its effectiveness for diagnosis pathway planning. Consanguineous marriages remain relatively common (around 24% nationally), sustaining a steady incidence of rare genetic conditions, while expansion of the newborn screening program beyond its current six diseases has yet to materialize.^{567,568}

Alongside its strong focus on inherited pediatric conditions, Türkiye is also entering a period of demographic aging that will broaden the rare disease case mix. As the older adult population grows over the coming decades, a greater share of rare disease presentations is likely to involve adult-onset neurological and metabolic disorders that fall outside established newborn and carrier screening pathways. A system oriented toward early-life genetic detection but reliant on urban specialist centers may be less well configured for later-onset diagnostic pathways, highlighting the need to expand adult diagnostic capacity and regional specialist access.

Treatment Access and Reimbursement Landscape

Türkiye provides universal health coverage through the Social Security Institution (SGK), which has enabled full reimbursement of SMA treatments nusinersen and risdiplam – further demonstrating the country’s emphasis on SMA as a priority rare disease, though onasemnogene abeparvovec is not routinely reimbursed for SMA.^{569,570} Looking ahead, Türkiye plans to initiate domestic production of nusinersen by 2026, which could improve long-term affordability and supply stability.⁵⁷¹

Türkiye does not have a formal orphan drug incentive framework, and many rare disease therapies enter the system through the Foreign Drug List or Named Patient Programs before reimbursement. While these mechanisms provide a pathway for access, they often result in delays across the country.^{572,573}

Additionally, under Türkiye’s current reimbursement policy, families frequently incur significant out-of-pocket costs, particularly for special nutrition, medical devices, and travel to specialized centers.^{574,575}

Rare disease stakeholders in Türkiye emphasize that even after treatments receive European approval, inclusion in the national reimbursement system can take considerable time, during which patients must rely on individual applications, legal cases, or exceptional import mechanisms. Regional inequality in care access is acute, with specialist rare disease management concentrated in major urban reference centers. Early access programs and innovative reimbursement models remain limited due to budget constraints, rendering many high-cost rare disease treatments practically inaccessible. Stakeholders also note that patient organizations are rarely included in decision-making processes, meaning real-life patient needs are insufficiently reflected in health policy.⁵⁷⁶

National Policy Frameworks

Türkiye’s Rare Diseases Health Strategy and Action Plan launched in 2023 as the country’s first national strategy addressing rare diseases. The plan outlines priorities across awareness, early diagnosis, care delivery, and research, marking an important step toward a more coordinated national approach.

However, according to rare disease stakeholders, the five-year action plan is nearing its end and only a small portion of its objectives have been implemented. The gap between strategy and implementation remains a major challenge, with many goals not yet producing tangible results. Stakeholders underscore that addressing rare diseases requires stronger multi-stakeholder collaboration and increased budgetary commitment, noting that rare diseases are not solely the responsibility of the Ministry of Health but represent a broader societal issue that concerns multiple government bodies.^{577,578,579,580}

Despite this progress, Türkiye does not have a dedicated orphan drug designation or incentive system. And recent pricing reforms have introduced uncertainty for innovative reimbursement agreements.⁵⁸¹ While national reference centers have been designated for neuromuscular and rare conditions, none are currently EUCERD-certified, and services remain heavily concentrated in urban areas.^{582,583}

Türkiye currently reports only five rare disease registries, well below levels seen in many European countries. This limited data infrastructure constrains policy planning and long-term system coordination.^{584,585}

National Policy Frameworks

Türkiye has made recent progress in formalizing rare disease advocacy through the establishment of the Rare Diseases Federation in 2024, representing the country’s first national umbrella organization. Rare diseases are estimated to affect 5–7 million people nationwide.

Patient organizations contributed to development of the 2023–2027 Rare Diseases Health Strategy and Action Plan and participate in parliamentary inquiries and awareness initiatives. However, formal patient involvement in HTA and reimbursement decisions is very limited, with advocacy influence concentrated upstream in policy development instead of access outcomes.⁵⁸⁶



Country-Specific Recommendations

1. Enact dedicated orphan drug legislation to create structured policy incentives for drug registration, reimbursement, and market entry for rare disease therapies.
2. Expand the national newborn screening program beyond 6 conditions, building on the success of SMA screening (97% coverage, 286 cases identified) to include additional treatable rare diseases.
3. Integrate Orphanet identification codes into the national disease coding and registry systems to support standardized data collection, research, and cross-border collaboration.
4. Address geographic disparities in specialist access by establishing EUCERD-certified reference centers in underserved regions and expanding telemedicine infrastructure.
5. Strengthen early diagnosis pathways by improving rare disease awareness and referral guidance among primary care providers, including Türkiye's approximately 30,000 family physicians, to ensure timely referral to appropriate specialists and reduce diagnostic delay.



United Kingdom

Rare Disease Prevalence or Incidence Estimates*

+3.5M⁵⁸⁷

SMA Birth Prevalence		10 per 100K live births ^{588,589,590} (global estimate; country-specific data unavailable)
FA Prevalence		2 per 100K ⁵⁹¹
ALS Prevalence		11.9 per 100K ⁵⁹²
DS Birth Incidence		1.5 per 100K ⁵⁹³

Population (2025)		69.3M ⁵⁹⁴
Population Aged 65+ (2024)	(19% of the total population)	13.50M ⁵⁹⁵
Population Aged 65+ Projected (2050)	(25% of the total population)	18M ^{596,597}

Rare Disease Benchmarking

Rare Disease Policy Framework	Yes, UK's National Rare Diseases Plan extended to January 2027 ⁵⁹⁸	Orphan Drug Incentives:	Some ⁵⁹⁹
Newborn Screening	Screens for 10 conditions ^{600,601} (Scotland screens newborns for SMA; England begins adding SMA to the newborn blood spot test from October 2026 through a phased national in-service evaluation) ^{602,603}	Cost-Effectiveness Analysis	QALY, high threshold (ultra-rare only) ⁶⁰⁴
Average Diagnostic Delay	4-6 years ⁶⁰⁵	Societal Cost of Rare Disease	£200B per year ⁶⁰⁶
National Rare Disease Definition	Fewer than 1 per 2,000 people ⁶⁰⁷		

Gaps

Low clinician awareness impacts preliminary screenings and timely, accurate diagnoses

Severe shortages of clinical geneticists, genetic counsellors, and neurologists limit testing and referral capacity

Geographic disparities concentrate access to specialists in urban areas

Reimbursement gap for rare disease therapies as current pathways leave many orphan treatments without a clear or viable route to funded access, contributing to delays and uneven availability

*All prevalence and incidence figures shown are approximate estimates drawn from the best available published sources. Where country-specific data were unavailable, global estimates are shown and labeled as such.



Opportunities

The UK's experience with managed access provides a foundation for addressing evidence uncertainty in rare disease reimbursement

The gap between HST and STA creates space for a more fit-for-purpose evaluation route for rare disease medicines

NICE's existing modifier framework provides a mechanism for recognizing dimensions of value that standard appraisal may miss

The UK's genomic and specialist infrastructure is constrained by workforce shortages that limit diagnosis and treatment capacity

Diagnostic and Screening Landscape

The UK has made notable investments in genomic medicine, including the Generation Study, which is piloting whole genome sequencing for more than 200 conditions in 100,000 newborns. However, the UK's routine newborn screening panel remains limited to just 10 conditions, well behind countries such as Italy (40+) and Australia (32+), and stakeholders argue that a more ambitious expansion is overdue to improve early detection of treatable rare diseases.⁶⁰⁸ A significant step is now underway: from October 2026, England will begin screening newborns for SMA through a phased national in-service evaluation, with all screening laboratories expected to participate by October 2027.^{609, 610} Through the National Genomic Medicine Service, seven regional laboratory hubs provide access to genetic testing ranging from single-gene analysis to whole genome sequencing for eligible patients.^{611, 612}

Despite this advanced infrastructure, the UK faces significant workforce constraints, with approximately 1.1 neurologists per 100,000 people – well below the EU average. The UK is also experiencing a limited number of clinical geneticists nationwide, impacting timely diagnosis and access.^{613, 614}

Diagnostic delays in the UK are driven by a combination of factors beyond workforce shortages. With the national newborn screening panel covering only 10 conditions – comparatively few by international standards – many rare diseases escape detection at birth.⁶¹⁵ Where symptoms are not immediately apparent, diagnosis often depends on parental awareness and the engagement of primary care clinicians in making timely specialist referrals. Even once patients reach hospital, initial testing may not target the relevant condition, and progression from a general to a precise diagnosis can require access to hard-to-reach specialists. At a system level, limited interoperability and inconsistent data availability across NHS trusts restrict clinicians' access to complete patient records and constrain the use of anonymized patient data for cross-organiza-

tional analysis. This fragmentation reduces opportunities to identify patterns across cases, delays diagnosis and care, and limits systemwide learning, particularly for rare and complex conditions.⁶¹⁶

These compounding delays carry real consequences: for degenerative conditions, even when treatments or palliative options are known and available, delayed intervention causes avoidable suffering and generates higher long-term costs that earlier action could prevent.

Treatment Access and Reimbursement Landscape

The UK's National Institute for Health and Care Excellence (NICE) Standard Technology Appraisal (STA) applies strict cost-effectiveness thresholds to drug reimbursement, typically in the range of £25,000–£35,000 per QALY (following a threshold increase effective April 2026).⁶¹⁷ NICE's STA fails to appropriately consider rare disease medicines as it struggles to capture their full clinical and societal value. The STA requires rare disease medicines to meet same cost effectiveness thresholds as common condition treatments. While some flexibility exists for rare diseases, most rare disease therapies struggle to reach the willingness to pay threshold with enough certainty to be recommended for reimbursement by NICE.

For ultra-rare conditions, NICE does leverage a separate Highly Specialized Technologies (HST) pathway allowing higher thresholds of up to approximately £300,000 per QALY, but there are limitations to this pathway in practice.⁶¹⁸ Few therapies qualify for HST due to narrow eligibility criteria and routing of multi-indication products through standard appraisal processes. As a result, these reforms do not fully address the structural gap faced by many rare disease therapies that exceed standard thresholds yet do not qualify for the HST pathway.

Together, these strict criteria result in nearly one quarter of MHRA-approved orphan drugs never being submitted to NICE for appraisal. As a result, the UK's performance on orphan drug access has declined from ranking 2nd overall in Europe in 2013 to 11th in 2024.⁶¹⁹ Between 2020 and 2023, only 50% of EMA-approved non-oncology orphan drugs were reimbursed in England, compared to 85% in Germany, 74% in Italy, and 67% in France.⁶²⁰

In April 2026, NICE increased its cost-effectiveness thresholds, though it remains to be seen whether these adjustments will meaningfully improve access for rare disease therapies.⁶²¹ Industry stakeholders have called for a dedicated evaluation methodology for rare disease medicines to address the gap between NICE's HST programme and the standard STA programme, where many rare disease treatments currently fall. As a result, a substantial number of therapies that exceed standard cost effectiveness thresholds yet do not qualify for HST continue to lack a viable evaluation route. These structural limitations are further compounded by broader workforce constraints across key specialties, including neurology, which continue to restrict timely and equitable access to treatment.⁶²²

Population aging is likely to increase pressure on the UK's HTA framework for rare diseases, particularly for therapies targeting adult-onset and slowly progressive conditions. As more rare disease treatments focus on stabilizing function, delaying decline, or preserving quality of life in older patients, measured QALY gains may appear more incremental despite meaningful clinical and patient value. When combined with tightly bounded cost-effectiveness thresholds and restrictive routing into the HST pathway, such therapies may struggle to secure positive appraisals.

Economic analysis of ALS treatments shows that under current NICE evaluation methods including the Highly Specialized Technologies pathway, demonstrating cost effectiveness is difficult even for therapies priced at relatively low levels.⁶²³ This is largely due to the substantial and ongoing non-drug care costs associated with the condition, which continue to accrue regardless of treatment and heavily influence overall cost effectiveness outcomes.⁶²⁴ As a result, disease-modifying therapies priced at comparatively low levels may still fail to meet conventional thresholds once broader system costs are taken into account.

This dynamic strengthens the case for continued refinement of severity modifiers, uncertainty accommodations, and exploration of alternative assessment approaches such as low budget impact thresholds for rare disease medicines to ensure that value assessment remains aligned with an aging rare disease population and does not disadvantage therapies that deliver meaningful patient benefit at relatively modest population-level cost.

Care pathways for rare disease patients are inherently complex and expensive to construct, and to be effective must be tailored to the individual patient's needs. In practice, access to these pathways is uneven: well-resourced and determined families are often able to secure better outcomes from the system than those who are less advantaged, creating an equity gap that stakeholders describe as a structural barrier to fair treatment. Increased investment in specialist-trained social services staff could help ensure that existing resources reach a wider population of patients and carers. More broadly, the NHS has not yet fully reconciled the principle that people with life-changing rare conditions have the same right to the best available treatment as any other patient, notwithstanding the additional cost – cost that, when viewed across the whole of society, may well represent net savings through reduced long-term care burden, improved productivity, and avoided emergency interventions.

National Policy Frameworks

The UK Rare Diseases Framework (2021–2027, following a one-year extension agreed by ministers from all four nations) sets national priorities focused on faster diagnosis, improved clinician awareness, better care coordination, and access to treatment. The implementation of this framework is supported through action plans across England and the devolved administrations. Wales, Scotland, and Northern Ireland each maintain their own Rare Disease Action Plans, reflecting differences in governance and health system organization.⁶²⁵

In early 2026, the UK government confirmed through Parliamentary written answers the publication of England's action plans in February and acknowledged that, despite progress to date, significant unmet need remains for people living with rare conditions.⁶²⁶



Alongside this policy framework, the UK's regulatory and innovation environment continues to support rare disease research and development. Orphan designation through the MHRA provides a ten-year period of market exclusivity for qualifying conditions.⁶²⁷ In November 2025, the MHRA published a position paper on rare therapies, outlining a forward-looking regulatory framework focused on evidence generation, system sustainability, and international convergence.⁶²⁸

The UK's innovation ecosystem is further supported by the Cell and Gene Therapy (CGT) Catapult, which accelerates the development and commercialization of advanced therapies with direct relevance to rare disease treatment.^{629,630}

Regional disparities in specialist capacity remain significant. London, home to several major teaching hospitals, is considerably better served than most other cities or regions, and the NHS could do more to make information about national specialisms and centers of excellence easily accessible to referring clinicians.^{631,632} Stakeholders have also highlighted the need for improved sharing of suitably anonymized case-level data across the NHS to support faster pattern recognition and diagnosis. Closer and more systematic collaboration between researchers and clinicians represents a further opportunity: the NHS has historically been slow to adopt therapies and technologies developed in the UK that are taken up more rapidly elsewhere, and strengthening translational pathways could accelerate patient access to domestically developed innovations.

Patient Advocacy and Impact

The UK has one of Europe's most comprehensive models for patient involvement in rare disease policy, covering approximately 3.5 million people living with rare, genetic, or undiagnosed conditions. Genetic Alliance UK coordinates a network of 200+ patient organizations and serves as the secretariat for the All-Party Parliamentary Group on Rare, Genetic and Undiagnosed Conditions.^{633,634}

Patient input is structurally embedded across policy and access pathways, including the UK Rare Diseases Framework, NICE HTA processes, and NHS England advisory groups. Specialized mechanisms such as the Highly Specialized Technologies program and Scotland's PACE process provide enhanced consideration for orphan drugs, positioning patient advocacy as a meaningful contributor to access decisions under uncertainty.^{635,636}



Country-Specific Recommendations

1. Create a separate, dedicated evaluation pathway for rare disease medicines, led by the Department of Health and Social Care in partnership with NICE and the MHRA, to address the structural gap between NICE's HST program and the standard STA program. This pathway should target low-budget-impact, high-unmet-need rare disease therapies that do not qualify for HST but cannot demonstrate cost-effectiveness through the STA process, reversing the decline from 2nd to 11th in European orphan drug access rankings.⁶³⁷
2. Establish a National Clinical Director for Rare Diseases within NHS England to provide strategic clinical leadership.
3. Reform the Early Access to Medicines Scheme (EAMS) to create a reimbursed early-access pathway for rare disease medicines, introducing reimbursement during early access ("EAMS+") to bridge the gap between regulatory approval and NICE appraisal.⁶³⁸
4. Invest in workforce development for clinical genetics, genetic counselling, and neurology to address current shortfalls and progress toward the Association of British Neurologists' recommended minimum of 1.6 neurologists per 100,000 population.
5. Develop a successor to the UK Rare Diseases Framework (2021–2027) that strengthens cross-devolved coordination and includes defined funding commitments. Genetic Alliance UK is currently leading an independent process to develop a successor framework to present to the government; however, the government's own engagement process and approach to next steps has not yet been announced, and a clear government-led strategy is needed to ensure continuity.
6. Mandate interoperable, anonymized rare disease data sharing across NHS trusts to support faster diagnosis and enable clinicians to identify patterns across cases. Strengthen translational pathways between UK-based researchers and NHS clinicians to accelerate adoption of domestically developed therapies and technologies.
7. Expand the national newborn screening panel beyond the current 10 conditions, building on the SMA screening evaluation beginning in October 2026 and the existing Generation Study infrastructure and genomic medicine investments to add other high-impact treatable rare diseases.

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