



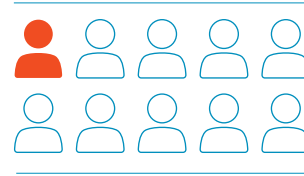
IN PURSUIT OF HEALTH EQUITY FOR THE RARE DISEASE COMMUNITY

INSIGHTS AND RECOMMENDATIONS TO IMPROVE THE DIAGNOSTIC JOURNEY



EXECUTIVE SUMMARY

An estimated 30 million, or 1 in 10, individuals of all races, ethnicities and backgrounds in the United States are affected by rare diseases.¹



While scientific advancements have improved clinical care for people living with rare diseases, more can be done to improve diagnosis, treatment and quality of life. These care gaps are clear illustrations of inequities disproportionately impacting individuals of diverse backgrounds and identities in the rare disease population.

Unfortunately, many with rare diseases experience a prolonged diagnostic journey, with an average time between six and nine years from symptom onset to diagnosis.^{1,2} Too many individuals must navigate a maze of specialist visits, tests, procedures and hospitalizations before receiving a correct diagnosis. People often feel alone, unsupported and lost during this process, leaving much room for improvement.³ The diagnostic journey is further complicated for individuals impacted by health inequities driven by systemic issues and factors, such as structural bias, institutional racism and the social determinants of health (SDOH).³ Obtaining a timely and accurate diagnosis is crucial to improving the care of and quality of life for all individuals living with rare diseases.^{2,3}

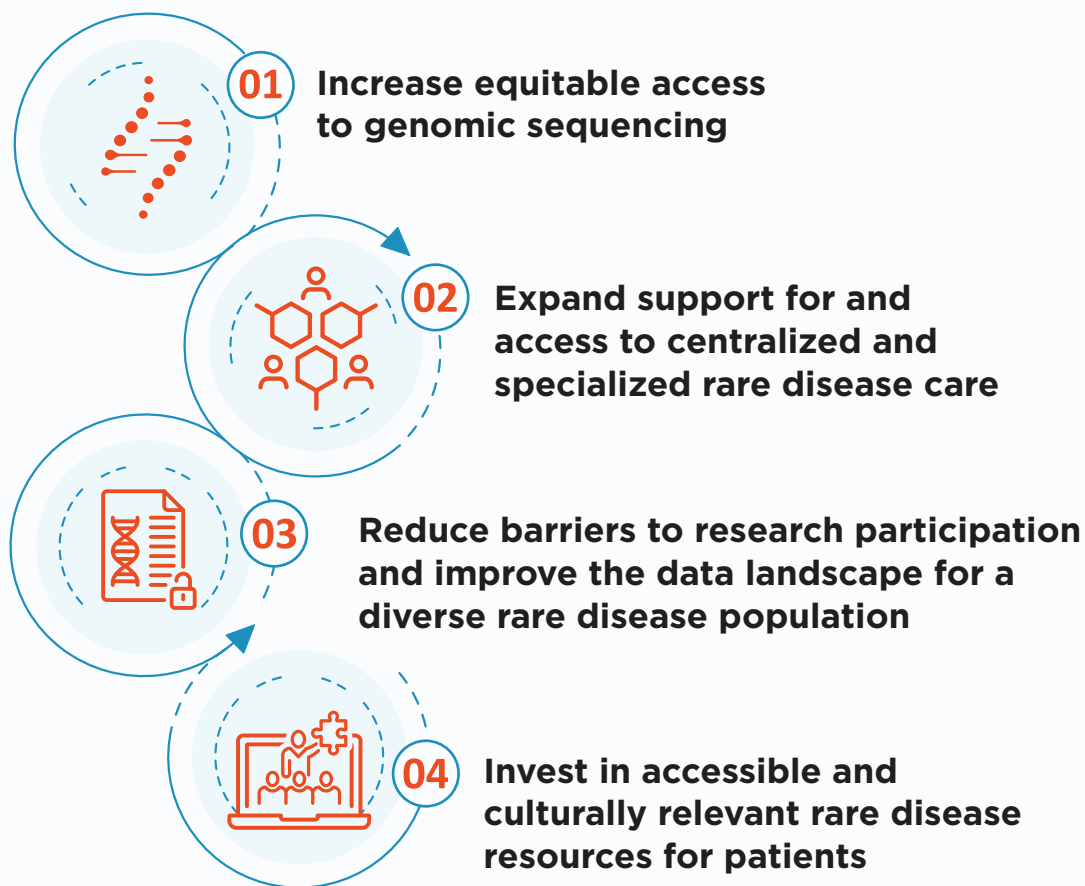
Takeda and the National Organization for Rare Disorders (NORD) share a commitment to uplifting and empowering those individuals, their families, and their support networks. In November 2021, Takeda published a white paper, *Reducing Time to Diagnosis for People Living with Rare Diseases: A Conversation on U.S. Policy Opportunities*, that proposed several policy solutions to shorten the diagnostic journey for people living with rare diseases.⁶ To continue the conversation, in this paper Takeda and NORD delve into policy opportunities and make recommendations for how leveraging such opportunities may reduce diagnostic barriers and advance health equity for the diverse group of individuals living with rare diseases.



HEALTH EQUITY MEANS THAT “EVERYONE HAS A FAIR AND JUST OPPORTUNITY TO BE AS HEALTHY AS POSSIBLE.”⁴

The social determinants of health are often referred to as the conditions in which people are born, grow, live, work and age.⁵

This paper explores four high-impact opportunities to shorten the time to diagnosis and improve health equity for all people living with rare diseases:



Takeda and NORD are committed to change. Together, we urge all stakeholders, including policymakers, regulators, payers, providers, community-based organizations and private industry to join us as we strive to shorten the diagnostic journey for the diverse population of individuals living with rare diseases.

Takeda and NORD share a commitment to uplifting and empowering individuals living with rare diseases, their families and their support networks.

While scientific advancements have improved clinical care for people living with rare diseases, more can be done to improve diagnosis, treatment, and quality of life. These gaps are particularly evident for individuals whose backgrounds contribute to the often-overlooked diversity of the rare disease population; further, they may be part of historically marginalized and/or underserved populations that have not fully benefitted from the progress made to-date. For the purposes of this paper, the term “diversity” broadly refers to the variable characteristics of race, ethnicity, primary spoken language, gender, sexual orientation, geographic location and socioeconomic status that are represented within the rare disease population.

In November 2021, Takeda published a white paper, *Reducing Time to Diagnosis for People Living with Rare Diseases: A Conversation on U.S. Policy Opportunities*, that proposed several policy solutions to shorten the diagnostic journey for people living with rare diseases.⁶ To continue the conversation, in this paper Takeda and NORD delve into policy opportunities, and make recommendations for how leveraging those opportunities may reduce diagnostic barriers and advance health equity for all individuals living with rare diseases.

This white paper was informed by conversations with patient advocates, rare disease and health equity experts, review of relevant literature and a health care roundtable. The roundtable was hosted by Takeda Pharmaceuticals and NORD in February 2023, and included a dozen leaders from across the health care landscape, including patient advocates, medical providers, rare disease researchers, pharmaceutical industry representatives and policy experts. The roundtable identified several key barriers in the diagnostic journey that impede health equity and may disproportionately impact individuals with rare diseases who are part of historically marginalized or underserved communities:

- Difficulty accessing care, such as genetic testing
- Lack of provider education about rare diseases and the diagnostic journey
- Inadequate care coordination to address SDOH
- Insufficient data on diverse populations with rare diseases
- Low levels of trust in the medical community
- Lack of accessible patient resources and educational materials

Roundtable participants also discussed opportunities for improving the patient experience and their recommendations informed the policy opportunities identified in this paper.

Takeda and NORD's shared focus on uplifting and empowering people living with rare diseases is evidenced by their respective missions of "better health, brighter future" (Takeda) and "improving the health and well-being of people with rare diseases by driving advances in care, research, and policy" (NORD). Both organizations strive to make important contributions to science, clinical care, policy and patient support, and they endeavor to improve the diagnostic journey for all individuals living with a rare disease, including those of diverse backgrounds.

More than 7,000 rare diseases have been identified, and new conditions and diseases are discovered every year.⁷ Although each specific rare disease affects a small percentage of the population, rare diseases are a significant public health challenge, impacting more than 30 million—or 1 in 10—Americans.^{1,8}

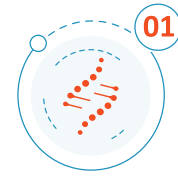
Obtaining a timely and accurate diagnosis is crucial to improving the care of and quality of life for all people living with rare diseases.² However, too many individuals must navigate a dizzying maze of specialist visits, tests, procedures and hospitalizations before receiving an accurate diagnosis, and some never do because of multiple factors.³ People often feel alone, unsupported and lost during this process, leaving much room to improve the patient experience.³

A prolonged diagnostic journey takes a profound toll on individuals, their families and their caregivers. The average time from symptom onset to a rare disease diagnosis is between six and nine years and could be even longer for individuals impacted by health inequities because of systemic barriers to health care.^{1,2,6} The medical and psychological toll, as well as the financial costs of the diagnostic journey are also substantial.^{3,9} Diagnostic delays have medical consequences, such as unnecessary tests, delayed treatment, disease progression and pain and suffering.³ A patient's feeling of uncertainty while they experience symptoms and search for a diagnosis is likely to cause stress, which can result in a significant emotional toll.⁹ Finally, the financial impact of a prolonged diagnostic journey includes direct costs, such as copays for specialist visits, diagnostic tests and hospitalizations, and indirect costs, such as lost wages and productivity for individuals with rare diseases and their caregivers.³

This paper builds on the three recommendations presented previously in *Reducing Time to Diagnosis for People Living with Rare Diseases: A Conversation on U.S. Policy Opportunities* for improving health outcomes for diverse populations with rare diseases: enhancing access to genetic tests; providing equitable access to care through centers of excellence and improved care coordination; and improving the data landscape. In addition, this paper explores a fourth opportunity: making rare disease patient materials more accessible and culturally relevant.⁶

OPPORTUNITY 1

Increase equitable access to genomic sequencing



As identified in the previous white paper, reducing barriers and providing widespread access to genomic sequencing, specifically whole genome and exome sequencing, has high potential to reduce the time to diagnosis, and is an important step toward achieving equity.⁶ Equitable access to genomic sequencing can transform the diagnostic journey for the diverse population of individuals with rare diseases.⁶

Often, rare diseases are multisystem and complex in nature. Some individuals may experience unusual combinations of signs and symptoms, while others may only display characteristics associated with more commonly seen conditions and may be incorrectly diagnosed with a condition such as autism spectrum disorder, epilepsy or dementia when the true cause is a rare disease.¹⁰

Approximately 80% of rare diseases stem from genetic origins, and whole genome and exome sequencing increases the likelihood of a person receiving a definitive diagnosis.¹¹

Genome sequencing is a comprehensive diagnostic test used to detect DNA variations in a genome. Sequencing can be used to diagnose many of the 6,000, or more, conditions for which the genetic basis is currently understood.^{10,12}



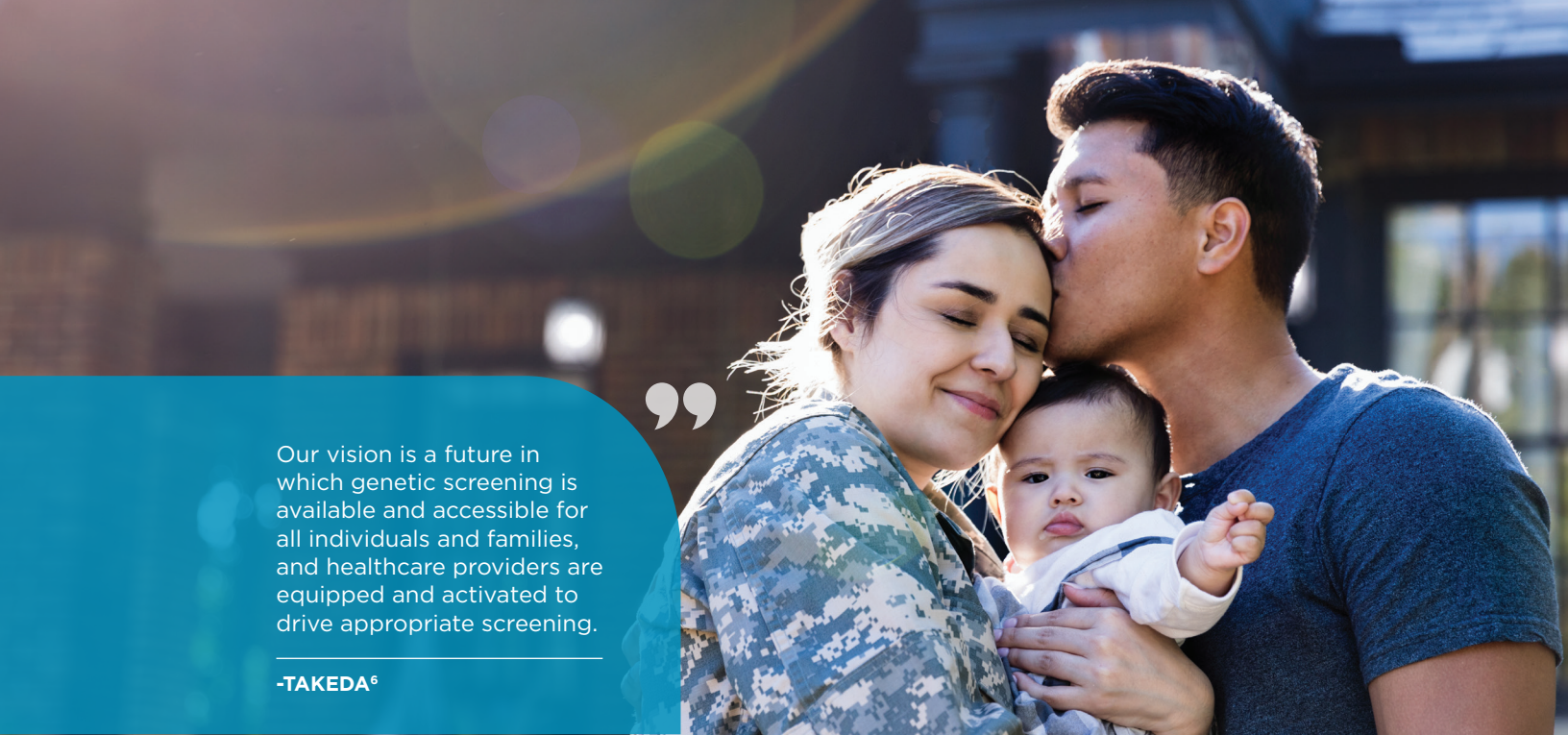
1 A medical geneticist, or other health care professional, collects the essential data on phenotype (observed physical, biochemical, and behavioral traits) and family history.^{10,12}



2 The genome data is generated and reviewed by a clinical laboratory geneticist.¹⁰



3 A physician correlates the genetic findings with the clinical phenotype information. Physicians may find genetic variants that may explain all or a component of the clinical presentation.¹⁰



Our vision is a future in which genetic screening is available and accessible for all individuals and families, and healthcare providers are equipped and activated to drive appropriate screening.

-TAKEDA⁶

The opportunity to confirm a rare disease diagnosis through genomic sequencing is particularly important for individuals who are part of populations often excluded from research data sets and rare disease clinical training materials. For example, although the majority of the 80,000 people worldwide with cystic fibrosis (CF) are White, an increasing proportion of people with CF are of other racial and ethnic backgrounds. Being aware of the increasingly diverse CF population is important for timely diagnosis and to improve outcomes. The Latino CF population, for instance, experiences increased morbidity and mortality compared to their White counterparts. The Latino CF population also has different genetic variants associated with the disease, and newborn screening panels have lower sensitivity to these variants. This scenario highlights the importance of improving genomic sequencing and newborn screening panels to capture a wider spectrum of variants observed in an increasingly diverse population.¹³ It can be concluded that when improved screening is combined with greater accessibility, more individuals with rare diseases will be properly diagnosed and treated.

Advances in technology have made genomic sequencing more accurate and less expensive.¹⁰ The cost of whole genome sequencing has decreased dramatically, and has led to an increase in coverage of whole genome and exome sequencing by payers.¹⁵⁻¹⁷ In fact, the cost of testing can be substantially less than that of a hospital stay. While the cost of a hospital stay varies by geographic location and other factors, the average cost is \$13,262 for a 4.6-day stay.²⁰ In addition to reducing unnecessary hospitalizations, an accurate diagnosis can reduce other unneeded procedures and tests, including the long-standing but misguided practice of performing multiple, sequential genetic tests for specific variants during the diagnostic journey.^{3,9} One study demonstrated that childhood genetic testing can result in significant cost savings for payers.²¹ Despite the opportunity for overall cost savings, providers and their staff must often navigate a series of insurance hurdles to receive reimbursement for genetic testing.



In 2020, 61% of Medicaid beneficiaries identified as Black, Hispanic, Asian American, or another non-White race or ethnicity.

also identified 27 state Medicaid programs, as well as the District of Columbia's, that do not provide any whole genome/exome sequencing coverage.²² This raises substantial concerns because Medicaid, an income-based program, disproportionately serves racial and ethnic minorities. In 2020, 61% of Medicaid beneficiaries identified as Black, Hispanic, Asian American, or another non-White race or ethnicity.²³

Difficulty obtaining insurance coverage for genetic testing is particularly challenging for individuals whose source of coverage is Medicaid. A 2021 report found that among individuals with private insurance, 71% had coverage for whole genome and exome sequencing, while only 39% of those with Medicaid insurance had coverage.²² The review

Rady Children's Hospital takes a unique approach to whole genome sequencing by offering it earlier and to a much broader range of patients than most health systems.³ For example, children admitted to the neonatal intensive care unit (NICU) at the hospital are automatically offered genome sequencing to diagnose any potential genetic conditions. The hospital also has 81 partner children's hospitals across North America that send medical records and DNA samples to the hospital for children who may benefit from genomic sequencing.¹⁸ According to one study, genomic sequencing yields more accurate results than targeted neonatal gene-sequencing for disease identification.¹⁹ According to Dr. Stephen Kingsmore, president, and CEO of Rady Children's Institute for Genomic Medicine, "Genomics is becoming increasingly recognized and democratized, but the need still vastly outweighs the provision—or the reimbursement."¹⁸



STANDARDIZE EQUITABLE COVERAGE OF GENOMIC SEQUENCING

As the benefits of whole genome sequencing become evident, standardizing equitable coverage is of paramount importance. Fortunately, progress is being made. Medicaid programs in California, Maryland, Michigan, Minnesota, and Oregon now cover whole genome sequencing more comprehensively, and private insurers recently updated their policies to include coverage.²⁴

INCREASE THE WORKFORCE DIVERSITY OF GENETIC COUNSELORS

The Government Accountability Office reported that in 2019, there were about 4,700 genetic counselors and 1,240 medical geneticists in 2020 certified to provide care in the U.S.²⁵ Although these numbers have increased in recent years, there is consensus that the workforce is insufficient to meet the current and future needs of the population seeking services.^{26,27} Genetic counselors work with patients to educate them on testing options, explain results, and help them understand how hereditary diseases might impact them and their families. The Bureau of Labor Statistics projected a 29% growth in genetic counselors between 2016 and 2026, which is significant given the estimated 7% average growth across all occupations.¹⁴ However, even as the field has grown, diverse representation of individuals entering the profession has lagged. As a result, the genetics workforce is not nearly as diverse as the population it serves. Of the genetic counselors who responded to the 2023 National Society of Genetic Counselors professional status survey, only 2% identified as Black and < 1% identified as Native American.²⁸ It is important that these professionals mirror the communities they serve to build engagement and trust.²⁹ A diverse workforce that has established trust within a community may be well positioned to also advance awareness and education about the importance of new diagnostic approaches, such as genetic counseling. One way to establish a more diverse workforce may be to make genetic counselors and medical geneticists eligible for the Health Resources & Services Administration's National Health Service Corps Title VII scholarships and loan reimbursement programs.³⁰



**IT IS WELL DOCUMENTED
THAT PEOPLE WANT
MEDICAL SERVICES FROM
PEOPLE WHO LOOK LIKE
THEM, AND GENETIC
COUNSELING IS NOT
AN EXCEPTION.**

BARBARA HARRISON
Assistant Professor and Genetic
Counselor Howard University¹⁴

EDUCATE PROVIDERS AND PATIENTS ABOUT GENOMIC SEQUENCING

With a shortage in the genetics workforce, education is needed for providers who are not specifically trained in ordering and interpreting genetic tests, as they play an increasingly important role in the diagnostic process. Many providers have limited knowledge and confidence in taking on such a role, but effective training programs may help overcome this barrier and could result in more equitable and accessible information for patients. This, in turn, may allay possible misperceptions and mistrust about genetic testing. In a recent study of a live interactive training program for providers in a neonatal intensive care unit setting, participation in the four-hour training led to an increase in providers' confidence in their ability to review, understand and use genome sequencing results to guide patient care.³¹ In addition to providers, it is essential for patients to be educated about the value and benefits of genomic testing, and as discussed in later recommendations, this information should be presented in clear, digestible and patient-friendly formats.³

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NORD is committed to breaking down silos and building bridges so that people living with a rare disease can achieve their best health and well-being. Our belief is that the Centers of Excellence program is the next big stride forward for rare disease patients and care to improve health equity and create critical new connections to resources and specialists across our nation.

-ED NEILAN
Chief Scientific and Medical Officer
NORD³⁵



OPPORTUNITY 2

Expand support for and access to centralized and specialized rare disease care



Takeda and NORD are committed to supporting the development of rare disease centers of excellence (CoEs). CoEs enhance efficiencies within the health care system and relieve individuals and their families of the burden of coordinating care across multiple medical specialists and care facilities. By helping patients and their families more easily navigate complex diagnostic and treatment pathways, CoEs can be effective facilitators of care continuity and improve access to health care services for people, including those in underserved communities.³² Research shows that care for people living with rare diseases is often not well coordinated.³³ These individuals must juggle multiple medical professionals practicing in different locations, and appointments on different days.^{33,34} This results in people with rare diseases and their caregivers often taking on the responsibility of booking appointments, following up on test results, and sharing medical information between various providers.³⁴ This is challenging for any family to manage, and could be even more so for individuals in rural areas, those who are low-income and non-English speaking or those who lack reliable transportation. Care coordination is a hallmark of the model of care provided at rare disease CoEs, and improving care coordination is an important strategy for achieving earlier diagnosis and improved outcomes.³²

Recognizing the critical importance of CoEs to the health and wellbeing of those living with rare diseases, NORD established the first national network of hospitals dedicated to the diagnosis, treatment and research of all rare diseases and addressing equitable access to each for people living with rare diseases in the US. The NORD Rare Disease Centers of Excellence network consists of 40 member organizations at the cutting edge of medical and scientific breakthroughs, who are committed to solving the greatest medical challenges and unmet needs of the rare disease community. Together, the NORD Rare Disease CoE members are collaborating to address four key areas: shortening the time to diagnosis, improving access to quality care, accelerating research and new therapy development, and training the next generation of rare disease clinicians and scientists.³²

Takeda partnered with the Children’s National Hospital Rare Disease Institute in Washington D.C., which was the first NORD-designated CoE, to support the hospital’s Rare Disease Clinical Activity Protocols (Rare-CAP) program.^{36,37} This program establishes a network for the development, dissemination and curation of protocols aimed to standardize diagnosis and care for people with rare diseases. Rare-CAP leverages many unique features to provide a protocol platform that reduces barriers for researchers, clinicians and patients in the determination of appropriate diagnoses and clinical care for individuals with rare diseases. These features include ongoing input from individuals with rare diseases and their families and an open “wiki” format for vetted contributors to provide near real-time updates for the latest, real-world data.^{36,37}

OPPORTUNITIES FOR ACTION

STRENGTHEN PARTNERSHIPS WITH PRIMARY CARE PROVIDERS (PCPS)

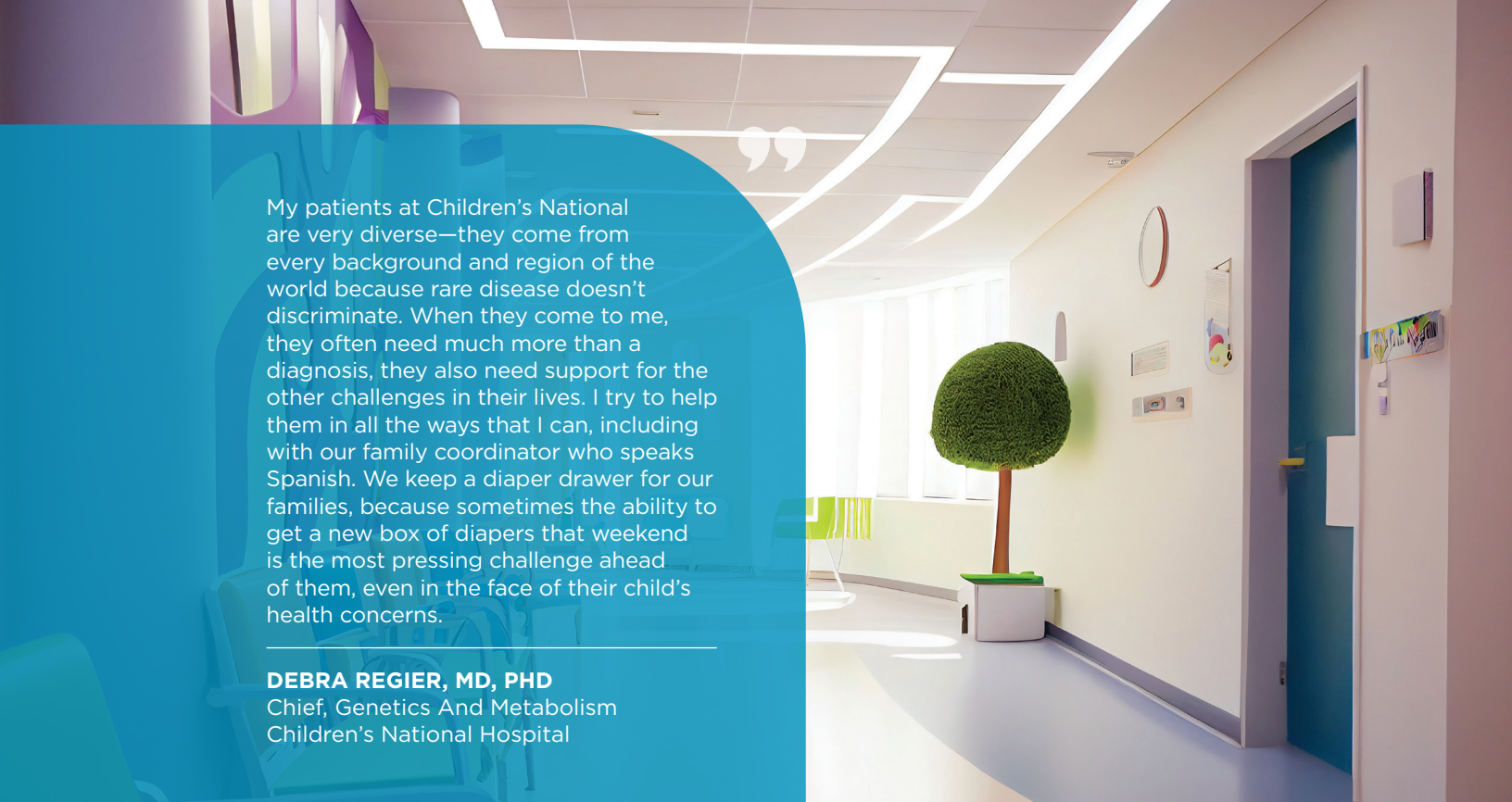
Many people seeking a diagnosis start with a visit to their PCP.³⁸ While the diagnosis may be made by a specialist, the PCP plays an important role in referring patients to specialists and in the ongoing coordination of care.³⁹ Stronger partnerships between rare disease specialists and PCPs in Federally Qualified Health Centers (FQHCs) and similar primary care settings may be valuable because these clinics provide care for medically underserved and low-income communities.⁴⁰ Creating a network of trusted health care providers who are culturally competent and representative of the population they care for may not only help advance care but may also help overcome the historical mistrust in the health care system by some communities.⁴¹

IMPROVE ACCESS AND EQUITY THROUGH TELEHEALTH

Recognizing that geographic distance and challenges with transportation, child care and time off work pose problems for people trying to access care, efforts should be made to provide telehealth services for both primary and specialty care.³ During the COVID-19 public health emergency, FQHCs and other providers provide care using telehealth services, which improved access and should continue post-pandemic.⁴⁴⁻⁴⁶ Additionally, telehealth consultations can enhance access to rare disease CoEs.³ Telehealth may be an effective tool for addressing equity issues and helping patients access providers who would otherwise be difficult to visit, as long as telehealth programs are accompanied by policies and support to ensure equitable access to technology, reliable internet connection and telehealth proficiency.⁴⁵

The Alliance to Cure Cavernous Malformation’s (CCM) Breaking Barriers program was born out of the need to connect Black patients with CCM research opportunities.⁴² The Breaking Barriers program model provides care coordination and also supports building partnerships, connecting patients to create community, and developing relevant patient materials.⁴³ The Alliance also trained CHWs in New Mexico to help act as care coordinators for the Hispanic CCM population in the state.³





My patients at Children’s National are very diverse—they come from every background and region of the world because rare disease doesn’t discriminate. When they come to me, they often need much more than a diagnosis, they also need support for the other challenges in their lives. I try to help them in all the ways that I can, including with our family coordinator who speaks Spanish. We keep a diaper drawer for our families, because sometimes the ability to get a new box of diapers that weekend is the most pressing challenge ahead of them, even in the face of their child’s health concerns.

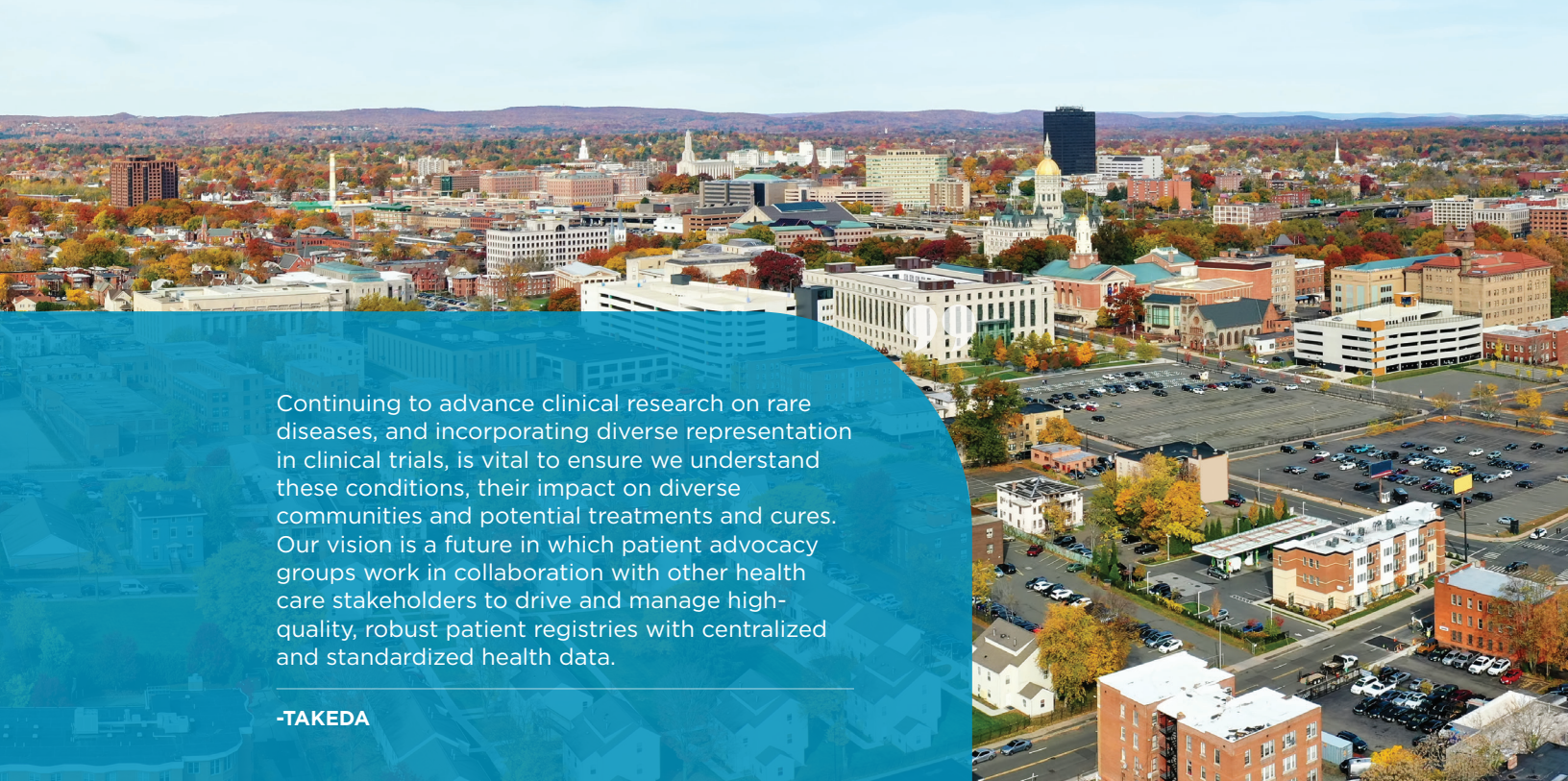
DEBRA REGIER, MD, PHD
Chief, Genetics And Metabolism
Children’s National Hospital

ENGAGE COMMUNITY HEALTH WORKERS (CHWS) IN CARE COORDINATION

CHWs are members of the community who provide support services such as:

- Culturally appropriate health promotion and education,
- Assistance accessing health services as well as nonmedical services,
- Translation,
- Social support, and
- Care coordination.⁴⁷

CHWs usually share a common ethnicity, language, socioeconomic background and life experience with the community members they serve.⁴⁷ CHWs also build trusting relationships with those they assist, making CHWs valuable team members to include in a care coordination plan and along the diagnostic journey.^{48,49} Research supports the effectiveness of CHWs in promoting health equity and reducing disparities.⁵⁰ In fact, CHWs can serve as a bridge between the health care system and patients from diverse backgrounds; however, as of April 2021, only 21 states allowed Medicaid reimbursement for services provided by CHWs.⁴⁹ Fortunately, progress is being made, and a growing number of states are implementing Medicaid coverage for CHW services.⁵⁰ However, the full scope of CHW activities are not always eligible for reimbursement, so until widespread reimbursement is available, health care providers who want to include CHWs on their care teams may face challenges.⁵⁰



Continuing to advance clinical research on rare diseases, and incorporating diverse representation in clinical trials, is vital to ensure we understand these conditions, their impact on diverse communities and potential treatments and cures. Our vision is a future in which patient advocacy groups work in collaboration with other health care stakeholders to drive and manage high-quality, robust patient registries with centralized and standardized health data.

-TAKEDA

OPPORTUNITY 3


Reduce barriers to research participation and improve the data landscape for a diverse rare disease population



Health care decisions are data driven, but because of the small number of individuals impacted by any given rare disease, providers often have few data to work with to guide diagnosis.

For example, in 2022, researchers from Johns Hopkins University published a systematic review of studies on a rare disease called hereditary hemorrhagic telangiectasia.⁵¹ Their findings showed a substantial lack of racial and ethnic data, which could negatively impact treatment and diagnosis in diverse patients.⁵¹ Unfortunately, similar findings apply to many rare diseases for which the diversity of the population is underrepresented or not represented in existing data sets.³

It is important that individuals of diverse backgrounds have access to genetic testing and that their genome sequences are incorporated into data sets to create a more representative profile of the human genome. The pangenome effort is making strides in this area and recently released a more diverse human reference genome that incorporates genetic information from racially and ethnically diverse individuals.⁵² Rare disease data sets should follow suit, and efforts should be made for them to better represent the diversity within each rare disease population.⁵²



Addressing disparities within clinical trials is a crucial step in addressing disparities in clinical care. Drugs and treatments may affect patients from different demographic groups in different ways. Diseases may present and progress differently in some populations as well. It is essential to have research data from a subject population that truly represents the clinical population if we are to provide equitable care to all.

NICOLE KRESSIN, RN, MSN
Clinical Research Specialist
University of Iowa⁵³

The lack of diversity in clinical trial participation has been noted by many organizations. A National Academy of Medicine (NAM) report in 2022 stated, “While progress has been made on some fronts, particularly with representation of White women in clinical trials and clinical research, progress has largely stalled on participation of racial and ethnic minority population groups. Additionally, older adults, pregnant and lactating individuals, LGBTQIA+ populations, and persons with disabilities remain underrepresented and even excluded from clinical trials and clinical research. An equitable clinical research enterprise would include trials and studies that match the demographics of the disease burden under study. However, we remain far from achieving this goal.”⁵⁴ The report described the consequences of this lack of diversity: “Lack of representation compounds health disparities in the populations currently underrepresented and excluded in clinical trials and clinical research. While achieving health equity and reducing health disparities requires far more than just equitable representation in clinical research, failure to achieve equity on this dimension leaves health disparities unaddressed and reinforces inequities.”⁵⁴

Numerous efforts are underway that aim to improve the diversity of data sets so that individuals from every background are sufficiently represented, and the data can be used to better inform the diagnostic journey.³ For example, patient organizations play a crucial role in data collection, and organizations such as Friedrich’s Ataxia Research Alliance and Parent Project Muscular Dystrophy have curated high-quality patient registries that support academic and industry research.⁵ The research community is also focused on recruiting more diverse populations into studies. One example is the National Institutes of Health-funded Rare Disease Clinical Research Network, which consists of 20 research consortia representing research sites all over the world and a wide range of rare diseases. This program launched a Diversity, Equity & Inclusion (DE&I) committee that seeks to drive change across the network.³

Decentralized trials are increasingly embraced as a tool to strengthen participation and diversity in clinical trials. Traditionally, trial participation involved traveling to a limited number of study sites and sometimes frequent specimen collection, multiple visits to the study site and collection of an individual's data. These requirements can create barriers to participation, especially among those who live in rural areas, have transportation challenges or family obligations. A decentralized trial is a more person-centric approach and utilizes new technologies, and data collection and analytics capabilities. For example, decentralized trials use innovative methods to communicate with participants in their own homes or at sites closer to where they live.⁵⁵ Although some trial requirements, such as imaging tests or physical examinations, must be done at a clinical trial site, a hybrid approach that allows some aspects of the trial to occur at home can reduce the burden of participation on patients and their families.⁵⁵

Improving clinical trial diversity is also supported by the U.S. Food and Drug Administration (FDA). In May 2023, the FDA released industry guidance for conducting decentralized clinical trials, noting that these trial designs can help facilitate rare disease research.⁵⁶ The Food and Drug Omnibus Reform Act of 2022 is a catalyst for increasing diversity in clinical research, requiring that most drug and device trials have diversity plans.⁵⁷ Creating more person-centric trials may lead to growing representation in data sets and ultimately help advance care—including a shorter diagnostic journey—for the diverse population of individuals living with rare diseases.

The American Thrombosis and Hemostasis Network (ATHN) focuses on collecting data about bleeding disorders. The ATHN data set consists of information provided by tens of thousands of patients from across the country. This data set is unique because it is representative of the general population and includes data representative of the racial and ethnic diversity of the U.S. It is also made up of individuals from different educational and economic backgrounds and with different insurance coverage.^{3,60}





APPROACH TRIAL DESIGN THROUGH AN EQUITY LENS

Approaching trial design through an equity lens is one way to ensure that the design does not make it more difficult for a diverse group of patients to participate. Adjustments to some trials may be needed, such as setting clear policies for when and how reimbursement is handled, inclusion of multilingual recruitment and consent documents, thoughtful consideration of the timing, location, and format of study visits (e.g., on-site versus virtual), and flexibility regarding other participation requirements.³ Such adjustments can reduce the burden for all individuals, but most importantly for those with the greatest barriers to participation.³ The Apoyo con Cariño trial conducted in Colorado is one example of these concepts in action.⁵⁸

FAIRLY COMPENSATE CLINICAL TRIAL PARTICIPANTS

Even when clinical trials are designed to be patient-centric, participating often necessitates taking time off work. This can pose a hardship for hourly workers or those without paid leave. In its report on clinical trial diversity, NAM recommended that in recognition of the greater burden that research participation may pose on historically underrepresented groups, federal regulatory agencies should allow for differential compensation to research participants and their caregivers according to the time and financial burdens of their participation. This could include compensation for expenses such as lost wages for those of lower socioeconomic status, transportation costs, dependent care and housing or lodging, where applicable.⁵⁴

FORM AUTHENTIC RELATIONSHIPS WITH COMMUNITY AND PATIENT ORGANIZATIONS TO BUILD TRUST IN THE RESEARCH PROCESS

It is important to establish trust early in the research process with community groups with whom researchers wish to partner. As an example, the NAM report includes a case study on the success of the regional Milwaukee office of the Wisconsin Alzheimer's Institute (WAI), which worked in partnership with African American community leaders since 2008. Over time, the WAI has observed a 400% increase in African American participants in its research projects.⁵⁴ This case study highlights the need to build trusting, long term relationships with community groups to improve diversity in clinical research.

The Apoyo con Cariño (Support with Caring) is an example of a clinical trial that used innovative strategies to increase diversity and improve retention within the trial. The trial was designed to be decentralized, with visits conducted remotely in individuals' homes. Study appointments were conducted outside of normal working hours and utilized bilingual health workers. The trial also engaged community health centers and safety-net health care providers. All of these efforts increased retention and participation of a diverse study population.^{58,59}





OPPORTUNITY 4

Invest in accessible and culturally relevant rare disease resources for patients



Because patients spend limited time in the clinic with providers, it is critical to equip them with relatable materials that help them better understand the diagnostic journey and learn more about their potential disease or condition, and learn about the important role they can play in research.³ Patient education materials serve several purposes: reinforcing information given by the health care provider following a visit; empowering individuals with knowledge, understanding, and skills to take an active role in their care; and providing information to family members and other caregivers so that they can support individuals with rare diseases throughout their journey.⁶¹

Educational materials can and should take many forms to resonate with different audiences.³ The Patient Empowerment Network, which advocates for all patients, notes that ideally, materials will serve as a signpost to other more detailed resources and even support groups.⁶¹

Organizations, such as NORD, produce patient education materials in paper form, videos and online forums.^{62,63} However, more materials are needed that appeal to individuals of varying backgrounds, are culturally relevant, and reflect the realities of different circumstances.³ To achieve any of these goals, patients and their communities should be involved in the development of materials.^{64,65} Resources that center on lived experiences, such as videos in which people living with rare diseases share their story, may better resonate with some individuals.⁶⁵



DIGITAL MATERIALS


While patient materials have traditionally taken the form of a pamphlet distributed in a health care provider's office, many people now access and consume materials differently. Some individuals may prefer a physical pamphlet, but resources should also be easily viewed on cell phones or tablets, be able to be shared by providers via text or email, and contain concise content.³ A recent study found that the ideal length of an informational video is 2 to 5 minutes, which increases the likelihood that it will be viewed.⁶⁶

CULTURALLY AND LINGUISTICALLY RELEVANT MATERIALS

Digital and print resources need to be available in multiple languages, accessible to individuals using assistive devices and easy to comprehend.⁶⁵ Educators need resources that resonate with the communities they hope to reach and contain content from trusted sources.

MATERIALS THAT EXPLAIN THE DIAGNOSTIC PROCESS

Many patient-focused materials are oriented toward individuals who have already been diagnosed with a disease.³ For individuals with an unknown diagnosis who are looking for answers, materials must offer hope and guidance on navigating and coping with uncertainty and setbacks during the diagnostic process.³



In order to move towards equity, we need to think intentionally towards how we can change the underlying systemic structures. Structural changes can start to happen on a hyper-local level and then be implemented on a national level.

MELISSA CREARY, PHD, MPH
Senior Advisor, Public Health, Policy
and Equity American Thrombosis
& Hemostasis Network, Inc.

CALL TO ACTION

What motivates Takeda and NORD is knowing that we can each play a part in achieving health equity and bettering the lives of individuals living with rare diseases.

We all have a role to play, whether it is reducing the time to diagnosis, taking steps to dismantle systemic and structural barriers to advance equity or working alongside our partners to improve the health care experience and outcomes for the diverse population of individuals with rare diseases. We believe these goals are also a priority for other stakeholders who work with the rare disease community, which provides opportunities to create cross-stakeholder collaborations that enable us to work toward our shared goals.

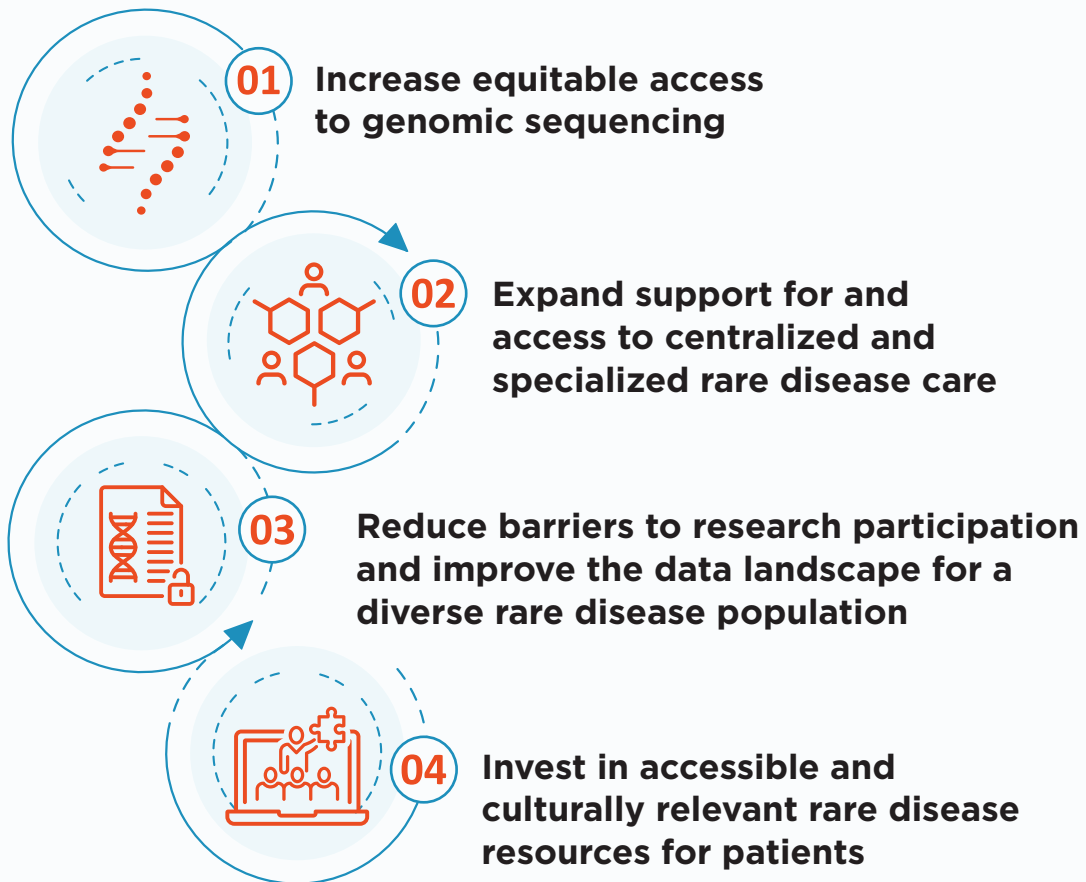
As this paper describes, there are many challenges that must be overcome to achieve these outcomes, but we believe the investments made to do so are both worthwhile and necessary.

At the conclusion of our prior white paper, we noted “Collaboration among health care stakeholders to effect fast and meaningful change is possible,” and we still believe that to be the case.⁶

All stakeholders, including policymakers, regulators, payers, providers, academics, advocacy groups, patients, community-based organizations private industry, and caregivers must be part of the solution because for the more than 30 million Americans living with one of the more than 7,000 identified rare diseases, there is an urgency to act.¹⁷

Some needed changes are systemic and institutional, while others involve actions that individuals and individual organizations can take. The power of each of these opportunities to bring about change should not be underestimated. A better experience for individuals with rare diseases is possible. We commit our organizations to being part of the solution and call on other stakeholders to join us in this effort.

This paper explores four high-impact opportunities to shorten the time to diagnosis and improve health equity for all people living with rare diseases:



Committing to change and acting on these opportunities will benefit all people with rare diseases. The opportunity before us is even more consequential for marginalized and underserved communities that experience additional barriers to care. This paper aims to inspire ongoing dialogue and collaboration among all the stakeholders who play a role in the lives of individuals with rare diseases. The time is now, and together we can improve the lives of millions.

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