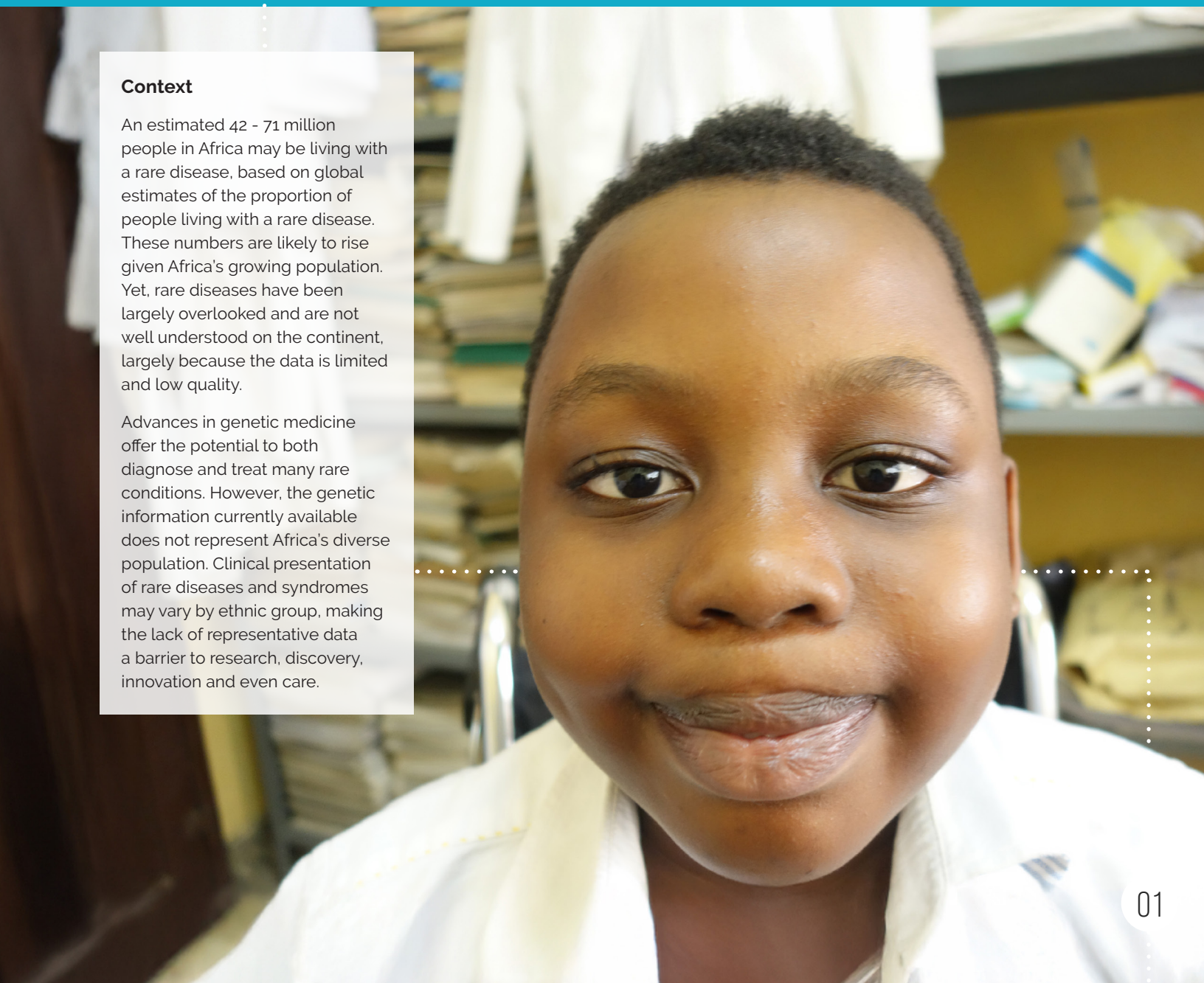
CASE STUDY: African Rare Diseases Initiative (Democratic Republic of the Congo)
PILLAR: 2 (Equipping Providers)

A network of researchers advancing and scaling genomic medicine in Africa



Context

An estimated 42 - 71 million people in Africa may be living with a rare disease, based on global estimates of the proportion of people living with a rare disease. These numbers are likely to rise given Africa's growing population. Yet, rare diseases have been largely overlooked and are not well understood on the continent, largely because the data is limited and low quality.

Advances in genetic medicine offer the potential to both diagnose and treat many rare conditions. However, the genetic information currently available does not represent Africa's diverse population. Clinical presentation of rare diseases and syndromes may vary by ethnic group, making the lack of representative data a barrier to research, discovery, innovation and even care.

African Rare Diseases Initiative (ARDI)

Overview of program

The **African Rare Diseases Initiative (ARDI)** is a new locally-led effort that seeks to build a network for genomic research and advance provider training to better diagnose and manage rare diseases in Africa. ARDI aims to fill a major global gap in rare disease research by including previously overlooked populations in genetic studies.

ARDI is funded by the U.S. National Human Genome Research Institute as part of the Advancing Genomic Medicine Research program, which aims to foster innovation and advance the field of genomics in clinical care. This program has supported projects across the U.S. and the ARDI — through the Universite de Kinshasa in the Democratic Republic of Congo (DRC) — is currently the only international project.

The initiative's objectives are to:

1. Build the first collaborative infrastructure for rare disease research in Africa, including establishing a multidisciplinary network of researchers
2. Strengthen the capacity of health personnel in Africa to identify and treat rare diseases through training and education
3. Identify families with a rare disease through a mobile app and website
4. Generate and disseminate clinical and genomic knowledge on rare diseases in Africa

ARDI officially began in the DRC in July 2023, with plans to scale across the continent. Health care workers in the DRC, including health care providers and laboratory technicians, have expertise in infectious diseases given their experience managing the response to outbreaks such as Ebola and mpox. However, they do not have the sufficient resources or training to diagnose rare diseases. As part of the project, the ARDI team established the Reference Center for Rare and Undiagnosed Diseases, within the Center for Human Genetics of the University of Kinshasa, which is equipped to analyze whole genome sequencing results.

ARDI was founded to build a network of hospitals to support families and children living with or suspected of having a rare disorder. A priority is encouraging parents throughout the country to go to one of these hospitals to get their child tested.

Raising families' awareness of rare diseases

Families in the DRC have limited awareness of developmental disorders and genetic testing. Like many countries in Africa, the DRC lacks the support system, infrastructure and expertise to offer patients and families the care they deserve. Until 2009, the country did not have a single local clinical geneticist.

The challenge of diagnosis is compounded because children with severe symptoms are often kept at home, away from schools and other community centers that are often able to detect signs of a possible disorder. While there has been some access to diagnostic testing for rare diseases through limited in-kind donations or small scale research projects, families often wait years for results.

Parents learn about ARDI through churches, hospitals or schools that host informational meetings where the ARDI team explains the project's objectives, the benefits of genetic testing, and the value of receiving a diagnosis. ARDI offers one on one meetings to parents who want to speak privately.

The Reference Center for Rare and Undiagnosed Diseases, in conjunction with ARDI, also uses social media to connect with individuals who have not attended a meeting. Because the target population often relies on WhatsApp, the Center uses this communication tool to show the location of the network hospital closest to them.

To further engage communities, ARDI is developing a mobile app and an online platform for families and others who suspect a rare disease. They can use the app to submit a direct request to join a research project that could hopefully lead to answers about their condition. Patients and their families are then connected to the closest clinical site for a clinical consultation with the local team as well as remote genetics specialists from the University Hospital of Kinshasa and other medical specialities when applicable.

Patients with a phenotype that is likely related to a genetic disorder and their parents provide samples for genetic testing. Partners such as Baylor College of Medicine in the U.S. perform whole genome sequencing. Raw sequencing data are returned to the local team in Kinshasa for bioinformatic analysis and clinical interpretation. The team communicates the diagnosis to the patient and their family and then connects them with appropriate treatment and support.

Background on ARDI

Prior to the launch of ARDI, the Center for Human Genetics of the University of Kinshasa received consent from 231 families between 2010 and 2015 to gather samples from their children which were sent to a lab in Belgium to be tested. Unfortunately, due to supply chain issues, more than half the samples were lost. The Center then became involved with the Deciphering Developmental Disorder (DDD-Africa) research project, led by the University of the Witwatersrand in South Africa, which offered exome sequencing to 150 Congolese families.

The Sanger Institute performed the sequencing using the same quality standards offered to patients in the UK enrolled in the DDD-UK study. Another 150 families received whole genome sequencing through an in-kind donation from Illumina's iHope program. The ARDI team created the Reference Center for Rare and Undiagnosed Diseases leveraging the lessons learned from participating in these efforts.

Results

While still in its early stages, ARDI is a promising African-led initiative and an example of how to advance locally-led genetic research and innovation with the potential to scale to other African countries.

ARDI has expanded to 11 of the 26 provinces and formed a National Rare and Undiagnosed Diseases Network across the DRC, including Bas-Uele, Equateur, Kasaï-Central, Kasaï-Oriental, Kinshasa, Kongo-Central, Maï-Ndombe, Maniema, Nord-Kivu and Sud-Kivu. The University of Kinshasa hosts the national Reference Center for Rare and Undiagnosed Diseases and the first provincial Reference Center is in Kindu. The other sites are expected to evolve into provincial reference centers as well.

Between July 2023 and December 2024, more than 200 families have contacted ARDI, and about 40% were deemed eligible for genomic sequencing based on their phenotype trajectory. To date, 10 of these individuals have been diagnosed.

Learnings

- **Build and leverage local infrastructure:** It was important to take advantage of the increasingly available smart phones when developing tools — including an electronic harmonized and digitalized health record and a mobile app — to improve multi-site and multidisciplinary medical collaborations and enhance interactions with the community.
- **Build local expertise:** Even though the DNA samples are sequenced in the U.S. as part of this global collaboration, it has been critical to ensure that local researchers in Kinshasa own the raw data and are responsible for analysis and reporting — given ARDI's goal of building local capacity.
- **Train local health providers — not just specialists:** ARDI has found that it is important to train general practitioners, pediatricians and other frontline providers in genetic and clinical information related to diagnosis given that there are only three medical geneticists in a country with over 100 million people.
- **Collaborate with communities:** To encourage families to participate in genetic testing, it has been important for ARDI to work with trusted institutions, such as churches and schools, which agreed to host meetings to introduce the initiative to community members.
- **Understand and respect the cultural context:** A deep appreciation of local cultural practices has enabled the team to be more effective when looking for genetic patterns among families and within communities and offering genetic counseling. The team has also been sensitive to language issues, including discussing the project in a patient's spoken language and using language that does not blame the mother when her child is diagnosed with a rare disease to avoid stigma
- **Maximize limited resources:** ARDI put a system in place to prioritize genomic sequencing for individuals who, based on a clinical consultation, were more likely to have a genetic disease that could lead to a new diagnostic discovery. These patients included those with a moderate to profound developmental/intellectual disability, multisystem congenital malformation, familial and/or syndromic epilepsy, or neuromuscular disease.

Goals & next steps

ARDI's goal over the next four years is to consult with 1,500 families and use whole genome sequencing to diagnose at least 300 families with rare diseases. To sustain and expand this initiative, ARDI is committed to building the capacity of health providers to diagnose and try to treat people living with a rare disease, starting with the DRC and expanding across the African continent. The team hopes that other African countries will be willing to share samples and data to continuously generate information about this understudied genetic pool — ultimately accelerating rare disease diagnosis. Likewise, ARDI would like to implement a newborn screening program — a major step in advancing diagnosis efforts.

ARDI is currently working with the Jackson Laboratory, a U.S. based laboratory dedicated to discovering precise genomic solutions for diseases, to identify potential treatments, including targeted gene therapies, for rare diseases diagnosed within the Reference Center for Rare and Undiagnosed Diseases.