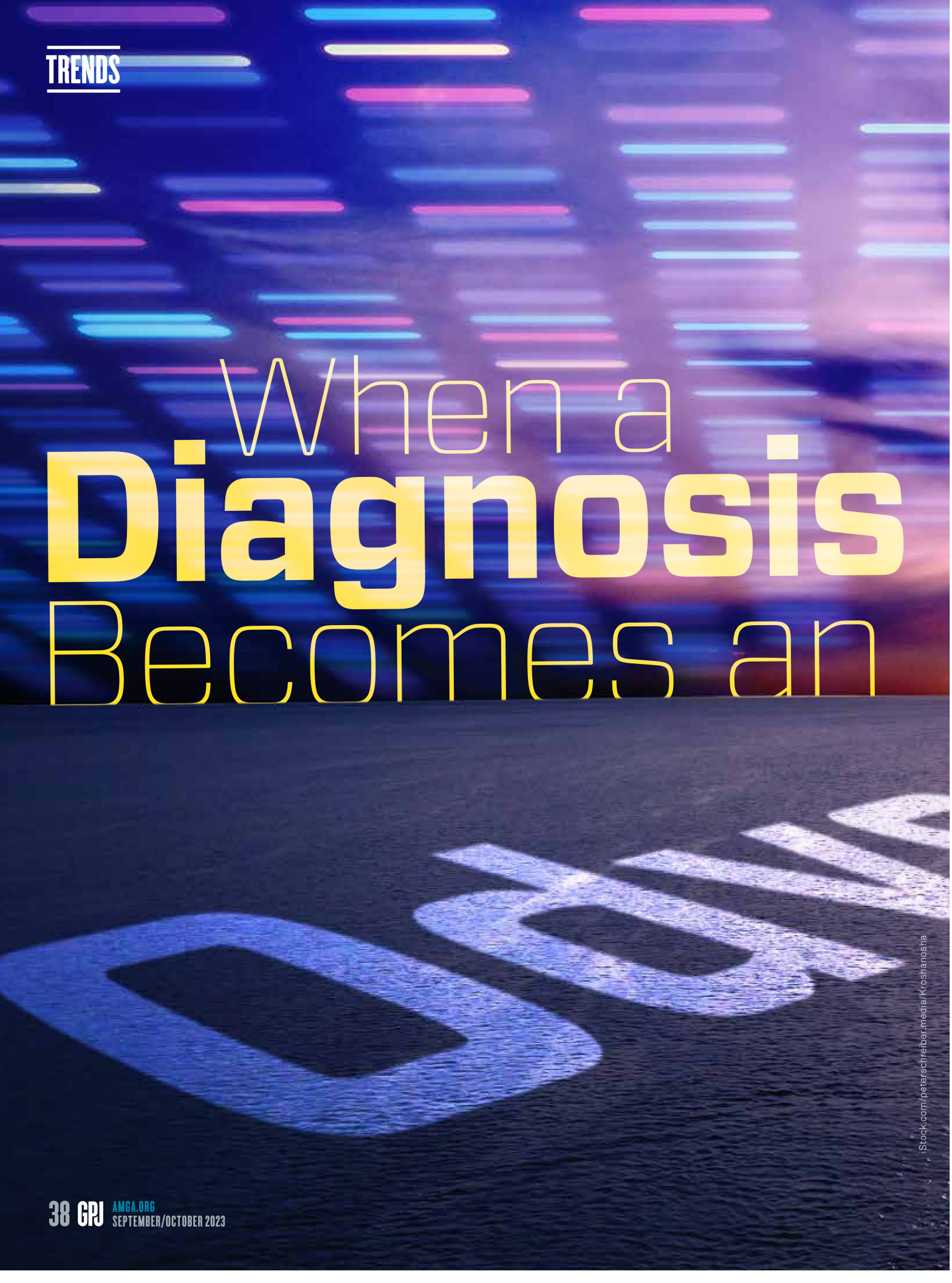
When a Diagnosis Becomes an



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Improving access to new gene therapies and therapeutic options for potential cures

By Andy Szczotka, PharmD

While there is currently no single physician who treats only rare diseases, there is growing familiarity in the medical community about new specialty drugs as well as novel gene and cell therapies to potentially "cure" some of an estimated 7,000 known rare diseases that affect 1 in every 10 Americans.

Physicians may already be aware of the rare disease diagnostic odyssey, a phrase coined by families and medical professionals affected by rare diseases to describe the long, complicated road for families fighting a rare disease. Global Genes, a rare disease advocacy nonprofit, reports that "patients living with rare disease visit an average of 7.3 physicians before receiving an accurate diagnosis," a process that takes an average of 4.8 years.[1]

Because so many rare diseases are progressive in nature, delayed diagnosis becomes one of the impediments to treatment. Patients see multiple providers, often outside of the patient's insurance network and geographic region, and diagnosis is likely hampered by limited diagnostic tools, misdiagnoses, and related hurdles.[2]

When prescribed and available, treatments for rare diseases have been shown to provide larger health gains on average than drugs for common conditions.[3] Regrettably, more than 95% of rare disease patients lack a Food and Drug Administration (FDA)-approved treatment for their condition,[4] and the unmet need for patients and families across many rare disease areas remains extremely high.

Specialty Pharmaceuticals

Undoubtedly, physicians are most familiar with "specialty" drugs, typically defined using elements of the following criteria, identifying an agent as a specialty medication:

- Used to treat rare or orphan diseases or complex chronic conditions
- High-touch disease state that involves one or more of the following for the medication:
  - + Requires special handling
  - + Requires special administration
  - + Requires special distribution or storage requirements
  - + Requires special monitoring
  - + Involves high-touch or frequent patient care management or clinical monitoring
  - + Distributed through a limited distribution network
  - + High costs, which are often prohibitive and add a barrier to patient access

The National Organization for Rare Disorders (NORD) produces a series of rare disease reports and boasts a searchable database of more than 1,200 rare disorders.

Significant Progress

According to the National Organization for Rare Disorders (NORD)—a 501(c)(3) patient advocacy organization dedicated to individuals with rare diseases and the organizations that serve them—advances in the body of knowledge related to rare disease and growing recognition that these diseases collectively affect millions of Americans are driving significant progress in the development of diagnostic tools and treatments.[15]

NORD's Online Physician Guides provide a free resource for clinicians about specific rare disorders to facilitate the timely diagnosis and treatment of their patients.[16] Family physicians, pediatricians, and other primary care providers play an important role in early identification and long-term management of patients with rare diseases. It is important for specialist and generalist alike to remain as current as possible in awareness of rare medical conditions.

Explore NORD's online physician resources at **rarediseases.org/clinicians-researchers.**

The "Orphan Drug" designation, which must be granted by FDA Form 4035, simply determines a company's qualification to receive the incentives provided under the Orphan Drug Act. An Orphan Drug treats a rare disease or condition and is designated as an orphan due to a limited market that makes it unlikely to be adopted by a pharmaceutical company.

However, FDA created incentives to help accelerate Orphan Drug development, encouraging a stream of new therapies for patients with currently untreatable conditions. These treatments are no longer a niche area of focus for developers, and orphan products have become one of the fastest growing areas of drug development—outpacing growth of the broad pharmaceuticals landscape and accounting for an increasingly large proportion of novel drugs hitting the market.[5] By 2026, orphans will make up a fifth of all prescription drug sales and almost a third of the global drug pipeline's value. High-profile orphan drugs include Keytruda®, Opdivo®, Revlimid®, Trikafta®, Soliris®, and others.

Gene and Cell Therapies

In contrast, physicians may not be as familiar with gene therapies largely because their practices may not include patients with rare diseases who would benefit and because of the low number of therapies approved. They are not simply another new class of specialty drugs to treat symptoms of a given disease. Specifically, gene therapy is a technique that modifies a person's genes to treat or cure disease. It is the process of replacing defective genes with healthy ones—adding new genes to help the body fight or treat disease or turn off genes that are causing

problems. Gene therapies use a target gene that expresses protein products at a sufficient level to cure—or at least ameliorate—a disease caused by a genetic defect.

Gene therapies involve the transfer of genetic material, usually in a carrier or vector, and the uptake of the gene into the appropriate cells of the body. They aim to cure by correcting the underlying genetic abnormalities causing the disease.[6] Cellular therapy (CT) involves the transfer of cells with the relevant function into the patient.

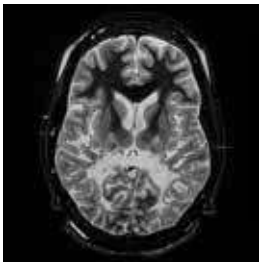
With more than 900 Investigational New Drug (IND) applications for ongoing clinical studies of gene therapy products underway—and FDA predicting they will be approving from 10 to 20 gene therapies per year—the availability of these groundbreaking drugs is becoming an emerging driver of change in specialty pharmacy benefit management.[6]

The current dilemma is that gene therapies provide hope for a potential cure but come with high upfront costs with no cost-minimization or elimination guarantees and impact on quality of life. Longevity of response to product is also in question. It may be too early to tell how long the effects of the treatments—restored vision, disease remission, etc.—will last. Perhaps it is a lifetime versus a specific time period. There are currently minimal patient follow-up data to know whether or not these products will be cures or if the disease may return. However, they could not only prevent much suffering but may also lead to long-term savings from a reduction in the attendant costs of care.

There are 24 Approved Products by the Office of Tissues and Advanced Therapies (OTAT).[7] Below is a sampling of the products and uses:

- Abecma–multiple myeloma
- Breyanzi–B-cell lymphoma
- Imlygic–melanoma
- Kymriah–acute lymphoblastic leukemia and B-cell lymphoma
- Luxturna–retinal dystrophy
- Provenge–prostate cancer
- Tecartus–acute lymphoblastic leukemia and mantle cell lymphoma
- Yescarta–follicular lymphoma and B-cell lymphoma
- Zolgensma–spinal muscular atrophy

New record-setting costs are gaining attention: recent FDA approval of Zynteglo®, a gene therapy for beta-thalassemia, a rare disorder requiring regular blood transfusions, carries a $2.8 million price tag.[8] For a short time period, it was the most expensive drug on a single-use basis in the United States and among the highest globally until FDA gave accelerated approval for Skysona®, or elicel, for the rare neurological disorder cerebral adrenoleukodystrophy (CALD). At $3 million per treatment with Skysona, it is now the priciest therapy in the world.[9]



Cerebral adrenoleukodystrophy (CALD), a neurological condition that manifests during childhood, occurs in about 1 in 21,000 boys between ages 4 and 10. It can now be treated with an FDA-approved gene therapy—Skysona—that costs $3 million per treatment, making it the most expensive gene therapy on Earth at present.

The Right Partner

In response, there is notable and growing reliance on strategic specialty pharmacy (SP) solution partners that provide a coordinated approach among stakeholders to address costs and provide monitoring programs to assess effectiveness, compliance, and adherence to treatment. The right SP partner excels at providing personalized, compassionate care and emotional support to patients and families and provides programs and services to streamline communications among pharmacies, patients, and healthcare providers. This level of coordinated care contributes to the best possible clinical outcomes.

This points to the importance of a patient-first approach that offers a human touch for people facing chronic illness and uncertainty while exceeding the limitations of the retail pharmacy business model. The ideal SP partner takes a multilevel approach to ensuring access.

SP Networks

A handful of dedicated solutions companies offer national networks of specialty pharmacies acting as Centers of Excellence across major specialty disease states. Typically, each pharmacy within the network is selected for its ability to provide exemplary and high-touch patient support. In networks that are optimally managed, home infusion service providers all meet the standards of excellence that serve patient needs for quality and accessibility that contribute to a positive experience and enhance response to treatment. In these select networks, patients can benefit from the utmost convenience and stay compliant to therapy.

Care coordinators. These specialized programs include expert care coordinators to work with providers as an extension of the care team, providing regular communication/updates to providers if a patient is noncompliant, cannot be reached, has side effects issues, or if medication cannot

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be filled for a reason. They develop personalized relationships with prescriber offices on behalf of patients and help ease office administrative burdens through prior authorization and appeal support services as explained below.

Financial solutions. High on the list of premier SP programs is the use of unique financial solutions to manage high-cost/gene cell therapies. One first-in-class program enables manufacturers to ensure that allotted copay funds are applied toward patient out-of-pocket costs and enables transparency into all copay transactions. This is a major step toward improved access to often life-saving treatment for all patients with rare and orphan diseases.

A loan-based assistance program now uses a pay-over-time approach to offset the high cost of exorbitant cell and gene therapies. These programs are truly revolutionary in how they address the unmet financial pharmaceutical needs in the SP industry, helping to eliminate financial barriers to treatment.

Prior Authorization

Prior authorization (PA) programs are now in place, offering tools to simplify the entire process and automate decision-making. This approach uses artificial intelligence (AI) decision-tree technology as well as appeals letters, which can be auto generated to support the appeals process and streamline patient access to therapy.

Alternative site of care. One initiative that is becoming standard is to identify alternative site-of-care programs that utilize low-cost sites that provide substantial savings to the patient and payer. These programs offer convenience for patient and caregivers/support team members and enhance opportunities for patient engagement and care.

Specialty carve-outs. Specialty drugs may be covered through either medical or prescription drug insurance, and coverage is usually tied to where the patient receives the drug.[10] If the patient takes a pill or self-injects the drug at home, it is most likely to be covered through a prescription drug benefit. If the patient receives the drug at a doctor's office, inpatient facility, or an outpatient clinic, it is most likely to be covered through the medical benefits portion of existing health insurance coverage. A significant trend is the adoption of specialty carve-outs that move specialty drugs away from traditional prescription drug management to a pharmacy benefit administrator (PBA) or SP

administrator. These arrangements provide cost savings, remove incentives to dispense product, and present opportunities for management and control of utilization management programs that align with payer expectations.

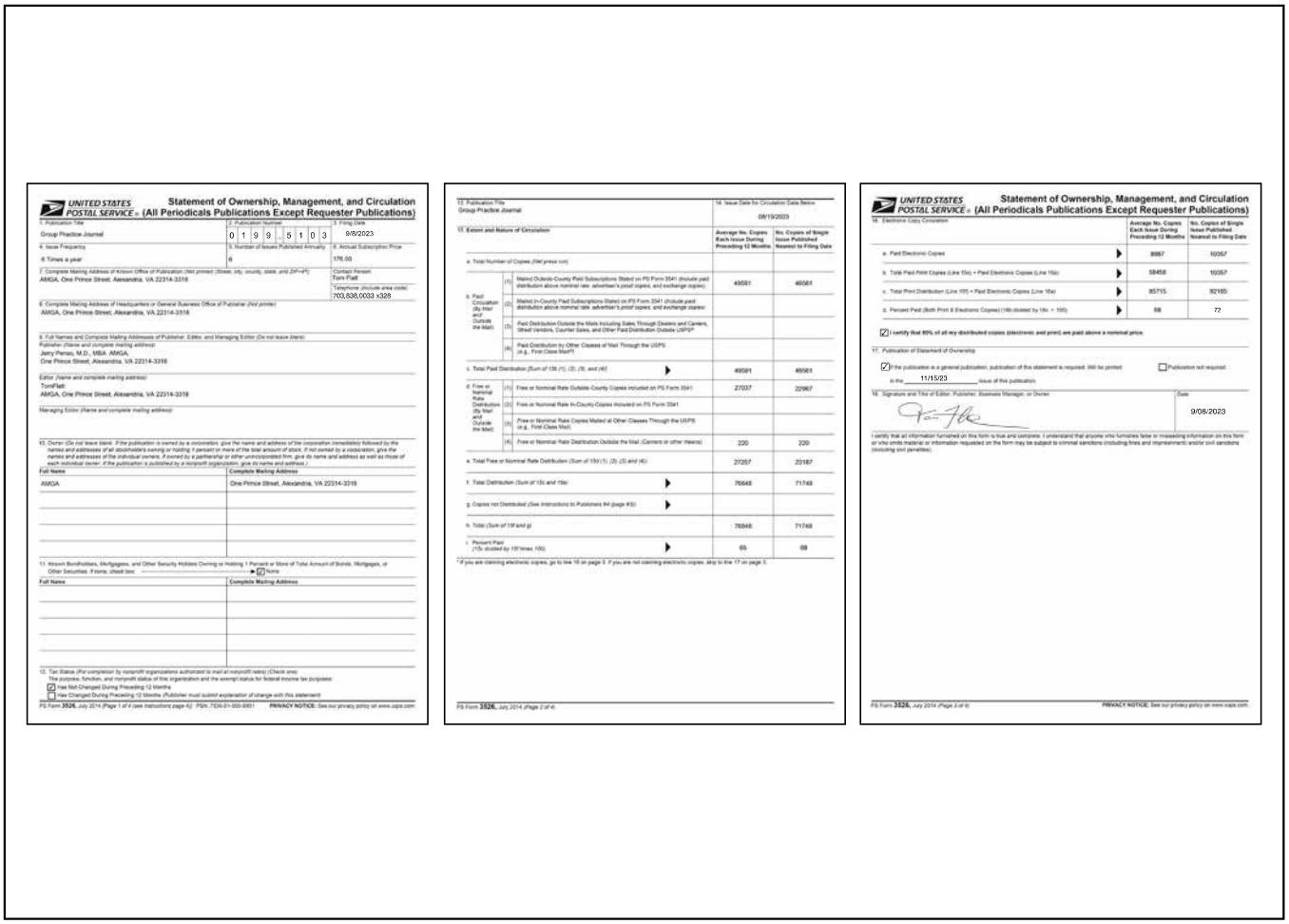
Exclusive drug distribution. Medications for rare diseases may require special handling, such as refrigeration, overnight delivery, and shipment tracking. An SP partner that specializes in rare diseases already uses these techniques to provide uninterrupted therapy. These partners can offer exclusive, national distribution, ensuring patients have access to therapies they need when they need them most. This model can also offer manufacturers significant cost savings.

Technology and communications. SP end-to-end solutions impact the lives of individuals with rare disease and keep the patient as the crucial point of focus. Expert call centers use technology-based communication tools and algorithms to engage patients, break down barriers to communication, and ensure optimal therapeutic outcomes. Ideally, a holistic approach that recognizes personal communication preferences, such as communicating through a mobile app, text, email, or telephone, meet the needs of these vulnerable patients to encourage continuity of care.

Empowering Physicians

Physicians deal with chronic conditions on a daily basis, but experience shows that doctors deal with few patients with rare diseases. More likely than not, doctors do not receive the training and education necessary to recognize symptoms and understand treatment options for these rare diseases.

A 2021 survey by BioNews, Inc., sought to promote understanding of the challenges healthcare providers face in diagnosing and treating rare disease patients.[11] Consistent with small patient populations for each disease, lack of rare disease education and symptom awareness were the most common challenges when addressing patients with rare diseases. Additional challenges included shortages of



More likely than not, doctors do not receive the training and education necessary to recognize symptoms and understand treatment options for rare diseases.

physicians specializing in rare diseases, limited facilities dedicated to rare diseases, and a lack of clinical trials for disease areas. However, increased education for physicians was the most commonly reported factor for improving rare disease diagnosis and treatment over the next five years—cited by more than half of respondents.

Moreover, visits for rare diseases are uncommon in primary care.[12] Future research may help explain whether this low level of rare disease management in primary care practices is consistent with a goal of a broad scope of care. Although most physicians will face the diagnosis or treatment of a rare disease at some point in their professional lives, many conclude that they may never meet a patient with a specific condition. While initiatives are underway for addressing the challenges for patients and stakeholders, research shows that a primary barrier rare disease patients face during medical encounters is medical professionals' low level of knowledge and experience on the diagnosis, treatment, and rehabilitation of rare disease patients.[15]

Despite progress, the economic burden of rare diseases continues. In addition to inpatient costs, a 2022 study in *Health Affairs Forefront* found multiple drivers of direct medical costs, including outpatient care (14.0%), prescription medications (17.7%), outpatient prescription administration costs (10.6%), and other ancillary costs (near 11.0%).[2]

A clear need cries out to increase the standards of medical education in the field of rare diseases and to revise undergraduate and postgraduate training programs that empower clinicians to treat patients. This alone would go a long way toward ensuring access to specialty treatment. GPJ

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