RARE DISEASE IMPACT REPORT

Rare Disease Impact Report:
Insights from patients and the medical community

Shire

April 2013

This report was commissioned by Shire and developed in collaboration with an external advisory board.

Table of Contents

Foreword

At Shire, patients are at the heart of everything we do. We are dedicated to researching, developing, and marketing novel products that enhance the quality of life of patients suffering from rare diseases. However, despite the progress that has been made over the past few decades to help improve the quality of life and care for patients with rare diseases, there is still an urgent need to better understand the unique challenges of rare diseases so that appropriate measures can be taken to address any gaps in care.

This is why Shire, in collaboration with an expert global panel of patient advocates, physicians, and policy experts in the rare disease field, conducted survey research in the United States (US) and United Kingdom (UK) to determine the health, psycho-social, and economic impact of rare diseases among patient and medical communities.

Key findings published in this Rare Disease Impact Report identify and quantify the impact of rare diseases based on survey responses from a multi-stakeholder audience of patients/caregivers, physicians, payors, and thought leaders. We hope this report will serve as a sustainable tool that will drive a dialogue about the future of research, patient care, and access so as to improve the lives of people living with rare diseases and the families that care for them.

Flemming Ørnskov, MD, Chief Executive Officer Designate, Shire

"This new report from Shire highlights and confirms the issues faced by patients affected by rare diseases. The inclusion and comparison of clinicians', payors' and patients' experiences demonstrate the importance of working together, as a community, to tackle the issues faced by patients. It also highlights the importance of working with the international rare disease community in order to share best practices and information for all those affected."

Alastair Kent, Director, Genetic Alliance UK

"This Impact Report brings to light the specific barriers to quality care that exist for patients with rare diseases, particularly the challenges in getting an accurate diagnosis, adequate information and ongoing care."

Nicole Boice, Founder and CEO, Global Genes | RARE Project

Acknowledgments

We would like to thank our external advisory board who contributed significantly to the development of this Report: Nicole Boice, Founder and CEO, Global Genes | RARE Project; Dr. Priya S. Kishnani, Division Chief, Medical Genetics, Duke University Medical Center; Tomas Philipson, Daniel Levin Professor of Public Policy Studies, The University of Chicago; Alastair Kent, Director, Genetic Alliance UK; Dr. Christian J. Hendriksz, Clinical Lead, Adult Inherited Metabolic Disorders, Salford Royal NHS Foundation Trust; and Mike Drummond, Professor of Health Economics, University of York.

We would also like to thank Joel Middleton, Assistant Professor of Applied Statistics, New York University, who contributed to the survey questionnaire design and survey analysis.

Introduction: Uncovering the Impact of Rare Diseases

Globally, some 7,000 rare diseases have been identified.[1] Compared to widespread conditions that strike hundreds of millions of people, rare diseases can lack similar levels of interest amongst the general public and medical/research communities. Most of these individual diseases receive little attention because they affect only thousands – or sometimes only hundreds – of patients worldwide.[2]

Yet looking at rare diseases as a collective entity, we are able to realize their expansive impact. Collectively, there are approximately 30 million people living with a rare disease in the US and another 3.5 million in the UK.[3,4] Around the globe, the rare disease community is estimated to include 350 million people.[5] And rare diseases touch more than just the patient. These conditions also impact families, friends, caregivers, physicians, payors, and society as a whole.

There is an urgent need to understand the state of rare diseases and the current gaps in care and support. To address this need, in January 2013, Shire conducted online surveys over a four-week period among US/UK rare disease patients and their caregivers, physicians treating patients with rare diseases, payors who handle reimbursements for healthcare plans and government/institutions, and thought leaders in the rare disease space. Surveys were fielded through market research agency ORC International and also distributed by advocacy group partners Global Genes and the Genetic Alliance UK.

Based on survey responses from a multi-stakeholder audience sample, the overarching concerns centered on several key themes:

- There are a lack of resources and information to address these less common illnesses
- The economic impact of diagnosing and managing rare diseases is significant
- Rare diseases take a major emotional toll on patients/caregivers

Patients, physicians, and payors alike cited the extensive time it takes to diagnose a rare disease along with the uncertainty of treating many of them as the two key drivers of both cost and emotional stress. The entire care journey for many patients is characterized by misdiagnosis, conflicting medical opinions and stress.

Report Findings Call for the Following:

1. ***Greater collaboration among physicians and access to specialists with expertise in rare diseases.*** **Patient and physician responses point to the need for increased awareness, more educational programs, and additional networking opportunities or platforms connecting general practitioners and patients with appropriate specialists. This may help to expedite the lengthy process to a correct diagnosis.**
2. ***Additional resources for patients and caregivers to navigate the emotional impact of rare diseases, particularly for those where the treatment outlook is limited.*** **There is a tremendous amount of emotional burden involved with finding credible information and qualified specialists as patients and their caregivers fight and pay for care for an uncommon ailment. Resources or care coordinators that help to navigate this process or ease the emotional burden are warranted.**
3. ***A need for more research to expand the current rare disease body of knowledge.*** **Additional academic and clinical research will ultimately offer patients increased options, and provide physicians with more tools to diagnose patients, all while equipping payors with evidence-based guidelines upon which to base coverage decisions.**

> "These survey findings suggest that whether in the US or UK, more research, information and education could help to alleviate some of the obstacles we see in getting patients the care they need."
>
> *Dr. Christian J. Hendriksz, Clinical Lead, Adult Inherited Metabolic Disorders, Salford Royal NHS Foundation Trust*

Methodology: The Data Collection

Patient/Caregiver Sample

While there are approximately 7,000 different types of rare diseases and disorders worldwide, the survey aimed to look at the commonalities in health, financial, and psycho-social experiences shared by those living with a rare disease and their loved ones.

- A total of 144 patients and 132 caregivers responded in the US. In the UK, 487 patients and 124 caregivers responded
- A total of 466 rare diseases were represented by the survey respondents (178 in the US, 288 in the UK)
- The types of rare diseases represented by the sample varied in prevalence and included blood, neurologic, immune, chromosome, metabolic disorders, and rare cancers
- Rare diseases ranged between those where treatment is available (defined as approved drugs, biologics, or devices that help to manage or control the disease) and those where there are no treatments. A majority of patients surveyed (60% in the US, 71% in the UK) said there was an existing treatment for their rare disease. More than half of caregivers surveyed reported their loved one suffered from a rare disease for which there was no treatment (56% in the US, 51% in the UK)

Physician Sample

The survey looked at physician experiences treating and managing patients with rare diseases.

United States

Respondents included 50 US physicians with the following classifications:

- Internal medicine/general practice physicians (66%), pediatricians (8%), cardiologists (8%), hematologists (6%), nephrologists (6%), allergists (4%), and a neurologist (2%)
- Worked in private practice (56%)
- Belonged to a group practice with at least three physicians (34%)
- Had a full or part ownership in the practice (48%)
- Were board certified in a given specialty (94%)
- Less than 10% of physicians' patient bases had a rare disease (92%)

United Kingdom

Respondents included 50 UK physicians with the following classifications:

- Pediatricians (50%), cardiologists (16%), hematologists (12%), internal medicine/general practitioners (10%), neurologists (8%), a nephrologist (2%), and an OB/GYN (2%)

Hannah Ostrea, child who suffered from Gaucher disease type 2/3

- Belonged to a specialist register (78%), followed by cardiologists (16%), and hematology specialists (12%)
- Had a hospital-based practice (94%)
- Less than 10% of physicians' patient bases had a rare disease (78%)

Payor Sample

The survey looked into payor perspectives providing coverage and services for rare disease patients.

United States

Respondents included 20 payors with the following classifications:

- Worked for a government health insurance provider (70%), private insurance providers (30%)
- Held director-level positions (60%) while the remainder held higher than a director-level position (40%)

United Kingdom

Respondents included 20 payors with the following classifications at the time of fielding (of note, the National Health Service (NHS) is currently reorganizing and classifications may change):

- Worked at a Primary Care Trust (10%) or other Care Trust (65%), which combines national and local health agencies; the Department of Health (15%); and the Strategic Health Authority (10%)
- Held a management position (60%)

Thought Leader Sample

The survey looked into thought leaders' perspectives (e.g., policymakers, researchers, advocates) on the key issues/challenges facing the rare disease community in areas such as diagnosis, scientific understanding, treatment options, and social services.

Respondents included 11 thought leaders in the US and five thought leaders in the UK. Feedback from these surveys was used to help support and reinforce the key rare disease gaps/ issues identified within the other surveys.

Combined Summary of Key Findings

THEME 1: There is a Lack of Resources and Information to Address Rare Diseases

Physicians (both primary care and specialists) have limited resources and information to properly diagnose/manage patients with rare diseases as compared to more common diseases seen.

According to physicians surveyed, as compared to their experience in managing more common diseases:


92% in the US


88% in the UK

The majority of physicians reported it is more difficult to address the needs of a rare disease patient in a typical office visit.


98% in the US


96% in the UK

Nearly all physicians stated more office visits are required to diagnose a rare disease patient.


92% in the US


88% in the UK

The majority of physicians said it takes more office visits to adequately address symptoms.


46% in the US


50% in the UK

Around half of physicians said that medical professional organizations do not give enough attention to rare diseases.


54% in the US


62% in the UK

More than half of physicians stated there aren't enough opportunities to network with other physicians who treat rare diseases.


76% in the US


88% in the UK

While it may be necessary to coordinate with other physicians when managing a patient with a rare disease, **the majority of physicians** said they found it difficult to do so.

According to patients and caregivers surveyed:


60% in the US


50% in the UK

Around half of patients with a rare disease and their caregivers stated they received conflicting information from different healthcare professionals about treatment options.


67% in the US


62% in the UK

More than half of patients and caregivers stated they needed to provide their healthcare professionals with information on their rare disease.

Delays in Diagnosis

According to patients surveyed, it takes:

on average **7.6 years in the US**

on average **5.6 years in the UK** for a patient with a rare disease to receive a proper diagnosis

According to patient/caregiver respondents, in order to get a proper diagnosis, a patient typically visits up to

8 physicians: 4 primary care and 4 specialists

and receives **2** to **3** misdiagnoses

THEME 2: The Economic Impact of Diagnosing and Managing Rare Diseases Is Significant

The costs associated with rare diseases are rising:

- The journey to diagnosis and beyond comes with a steep price tag for many coping with a rare disease. This long road, which frequently includes numerous tests and physician visits, can become financially overwhelming, particularly for those in the US. Payor respondents cited several factors as contributing to the higher costs of care for rare disease patients, as compared to more common diseases, including:
  - More diagnostic tests (100% in the US, 80% in the UK)
  - More costly diagnostic tests (100% in the US, 90% in the UK)
  - More visits to specialists (95% in the US, 95% in the UK)
  - More mental health support needed (90% in the US, 75% in the UK)
- **Nearly all payors** surveyed reported that treatment for patients with rare diseases is relatively more expensive compared to treatments for other patients with more common diseases (95% in the US, 100% in the UK) and costs are also rising more rapidly (90% in the US, 85% in the UK)
- The cost of medical care and the multitude of services associated with managing the disease place a greater financial burden in the US than the UK
- Although 90% of patients surveyed had health coverage in the US:

55% in the US

18% in the UK

55% of US respondents incurred direct medical expenses not covered by insurance compared to 18% in the UK not covered by the National Health Service.

37% in the US

21% in the UK

37% borrowed money from family and/or friends to pay for expenses in the US compared to only 21% in the UK.

Payors find it difficult to determine how rare diseases should be covered due to the lack of standards and guidelines:

- Almost all payors surveyed indicated there is less information/data available to help determine the standards of care for rare diseases (95% in the US, 90% in the UK) and that it is more difficult to decide what coverage to provide for patients (90% in the US, 85% in the UK)

THEME 3: Rare Diseases Take a Major Emotional Toll on Patients/Caregivers

Rare diseases have a considerable emotional impact on patients and caregivers, particularly for those where the hope of treatment is minimal.

According to physicians surveyed, as compared to their experience in managing more common diseases:

Rare disease patients reported their disease caused:

- Depression (75% in the US, 69% in the UK)
- Anxiety and stress (86% in the US, 82% in the UK)
- Isolation from friends/family (65% in the US, 57% in the UK)
- Less interaction with friends/family (70% in the US, 68% in the UK)
- Worry based on future outlook of disease (90% in the US, 91% in the UK)
- Worry based on lack of information available on disease (83% in the US, 81% in the UK)

Caregivers of rare disease patients felt similar psycho-social concerns and feelings of:

- Depression (72% in the US, 65% in the UK)
- Anxiety and stress (89% in the US, 88% in the UK)
- Isolation from friends/family (64% in the US, 54% in the UK)
- Less interaction with friends/family (55% in the US, 45% in the UK)
- Worry based on future outlook of disease (97% in the US, 94% in the UK)
- Worry based on lack of information available on disease (87% in the US 84% in the UK)

For those rare disease patients where treatment options are limited, overall they worry more, feel more depressed, interact less, and feel more isolated from family and friends compared to patients with rare diseases for which there are available treatments.

The health-related quality of life is significantly lower for patients suffering from a rare disease compared to patients who are otherwise healthy; the quality of life is even lower for those where there is no treatment available.

According to survey results, health-related quality of life for patients with a rare disease is estimated to be about half of what it would be if the patients were healthy.

44% in the US

50% in the UK

The health-related quality of life is significantly lower for those with rare diseases for which there is no treatment.

58% in the US

60% in the UK

The Mills sisters, both diagnosed with CADASIL syndrome

Patient/Caregiver Findings

Key Insights

In the past few decades, increased awareness and the advent of programs specifically designed to encourage the development of treatments for rare diseases has led to some improvements in diagnosis, treatment, and overall care. Despite this progress, there is still an urgent need to better understand the obstacles patients and caregivers within the rare disease community face, so appropriate measures can be taken to address gaps in care. Challenges extend beyond the disease itself. These challenges, which can at times be overwhelming, include the following:

- Finding appropriate medical care during the many years it often takes to receive a correct rare disease diagnosis and locating hard-to-find specialists post-diagnosis
- Handling the financial aspects of a rare disease, which can be exacerbated by bills for special care, travel to find specialists and, for some, the inability to work while managing their disease
- Coping with the emotional challenges a rare disease presents, which include feelings of isolation and uncertainty about the future

> "Finding a doctor that can treat me is the most difficult part. I have traveled to many states looking for a qualified doctor."
>
> *US patient with Multiple Hereditary Exostosis, a rare disease that causes noncancerous bone tumors that can later become cancerous*

Survey Results

Long, Slow Road to Diagnosis

For many, being diagnosed with a rare disease isn't the beginning of their journey. Often the journey began years earlier with a symptom, an unyielding pain, or a constellation of signs that could not be explained. Multiple doctor visits often accompanied by ad-hoc Internet research direct a path for the rare disease patient that is usually far from linear.

Sometimes there's no GPS signal.

When relatively few people have a disease, information is frequently scarce, forcing many patients to navigate with little guidance. This leaves many patients and their caregivers alone in a maze of roadblocks and detours, which includes difficulty finding a knowledgeable specialist, dealing with financial burdens, as well as handling emotional difficulties.

At times the directions are conflicting.

General practitioners may miss the indicators of a rare disease because they may have never seen a particular rare disease before or the disease presents the signs and symptoms of a more common disease. This misdirection can lead to a missed rare disease diagnosis or to misdiagnosis.

Road conditions lead to further delays.

Often the healthcare system doesn't allow doctors to easily share information or collaborate with each other, even with a patient's consent. A test taken at one center or an observation from one physician may not make its way to the next medical professional.

As a result of these challenges, on average, it takes 7.6 years in the US and 5.6 years in the UK for a patient with a rare disease to receive the proper diagnosis, based on survey results. Along the way, the average patient visits four primary care doctors and four specialists and receives two to three misdiagnoses. Those who care for people with rare diseases also reported delays and missteps. In both the US and in the UK, caregivers surveyed said diagnosis took an average of 3 years after seeing a total of seven or eight doctors.

"Getting a correct diagnosis was so difficult, stressful and humiliating at times. I found that doctors did not like to listen to my take on things, they did not like my asking relevant questions or expressing concerns, looked only at specific test results and if these were not fitting into the categories of their particular expertise or discipline, they would dismiss me. ...There was also a lot of 'passing' me from doctor to doctor without an overall coordinator of care."

UK patient with Mixed connective tissue disease, an autoimmune rare disease which has the signs and symptoms of lupus, scleroderma, polymyositis, and rheumatoid arthritis

Patients and Caregivers Reported that They Must Wear Many Hats

Often, when dealing with a rare disease, patients and caregivers find themselves wearing multiple hats and juggling several roles in an effort to receive optimal care. These include playing multiple roles:

Researcher. A lack of information about many rare diseases is a major obstacle. Often, to obtain answers, the role of the researcher falls on those dealing with the disease or their caregiver, as they scour the Internet for assistance with diagnosis, possible treatments, specialists, and information on studies as they seek support from others fighting a similar battle. In fact, in both the US and UK, more than 60% of patients and caregivers surveyed responded that they needed to provide health care professionals with their own information on their rare disease (67% in the US, 62% in the UK). When it comes to a disease that very few patients have, doctors often can't provide answers to the many questions that arise, such as:

67% in the US

62% in the UK

- What causes this disease?
- Is this something that I could pass along to my children?
- Is this symptom related to the disease?
- What treatments are available to help with symptoms?
- How will the disease progress?
- Are there treatments that can slow the disease progression?
- Will it help to alter my diet or other activities?
- Is there a support group in my area?
- Is there an organization online for this disease?
- How can I participate in a research study?

Care Coordinator. Managing multiple appointments, taking detailed notes during appointments, and relaying information from one medical professional to another often falls on the patient or caregiver. When a disease is unfamiliar, there will be many questions. Keeping records of the answers, planning the next steps, and handling conflicting advice can feel like a full-time job and can quickly become overwhelming. Within the survey, 60% of US patients/caregivers and 50% of UK patients/caregivers said they received conflicting information from different healthcare professionals about treatment options for their rare disease.

60%
in the US

50%
in the UK

Hannah Ostrea, child who suffered from Gaucher disease Type 2/3, and her care team

Advocate. When there's no clear roadmap, the patient or caregiver must often chart his or her own course. This frequently involves seeking additional medical opinions from various healthcare professionals, appealing to payors for unconventional care, resolving billing issues, and becoming a self-advocate as well as an advocate for others suffering from a similar ailment. The role of advocacy is particularly crucial in the rare disease community. Because of the small number of people living with a particular disorder, patients and caregivers feel the added pressure to educate others about the disease, often times including medical professionals. At times, this advocate role will involve lobbying government for care or organizing a support group for others with a similar rare disease.

Significant Financial Costs of Care

> "I had to end my career as a paralegal as the pain and medication associated with the disease made it impossible for me to work a full-time job. I was forced onto disability, causing financial hardship."
>
> *US patient with Wegener's granulomatosis, a rare disease that causes blood vessels to inflame making it difficult for blood to flow*

The lengthy journey to diagnosis and ongoing disease management create a significant financial burden for patients and caregivers coping with a rare disease. This is particularly true in the US, according to the survey findings. Medical costs and services were considered a "major burden" by half of those in the US, double the rate reported in the UK.

On each financial question included within the survey, patients and caregivers in the US fared significantly worse than those in the UK:

Financial Consequences	US	UK
Had to use savings to pay for medical expenses	53%	31%
Incurred direct medical expenses not covered by insurance/National Health Service	55%	18%
Borrowed money from family and/or friends to pay for expenses	37%	21%
Sought help from charity or public assistance	34%	18%
Negatively impacted credit score	32%	10%
Used retirement funds to pay for expenses	23%	10%

These financial outlays occurred despite the fact that 90% of patients/caregivers in the US have insurance or another program that pays for all or part of the medical expenses associated with the rare disease.

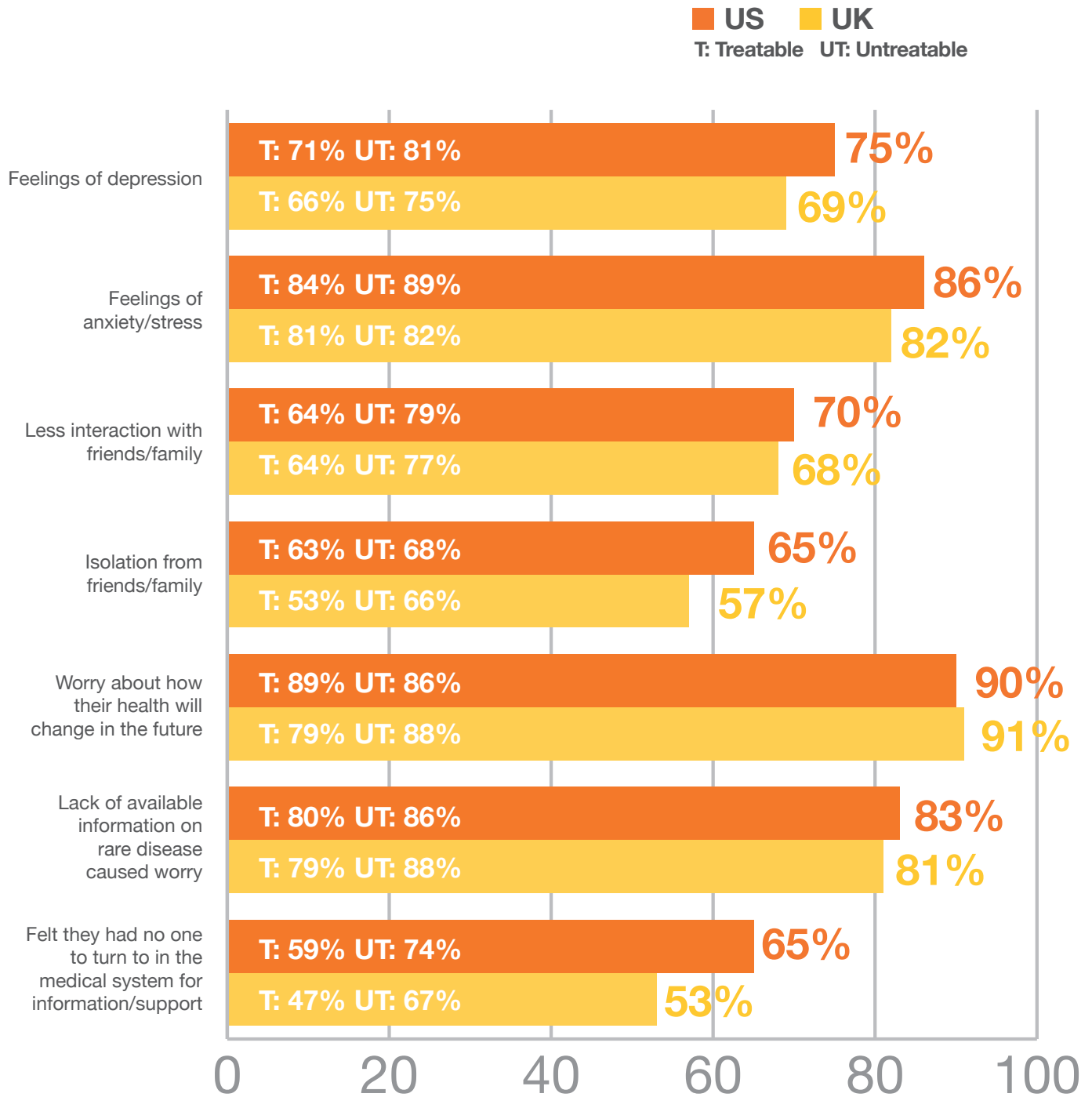
The Emotional Toll on Patients and Caregivers

> "The most difficult experiences have been my anxiety, depression, the inability to cope with stressful situations, and physical complaints associated with my disorder."
>
> *US patient with Late-onset congenital adrenal hyperplasia, a rare genetic disease that can result in excessive hair growth, absent periods, infertility, and hair loss in women and early beard growth, small testes, and short stature in men*

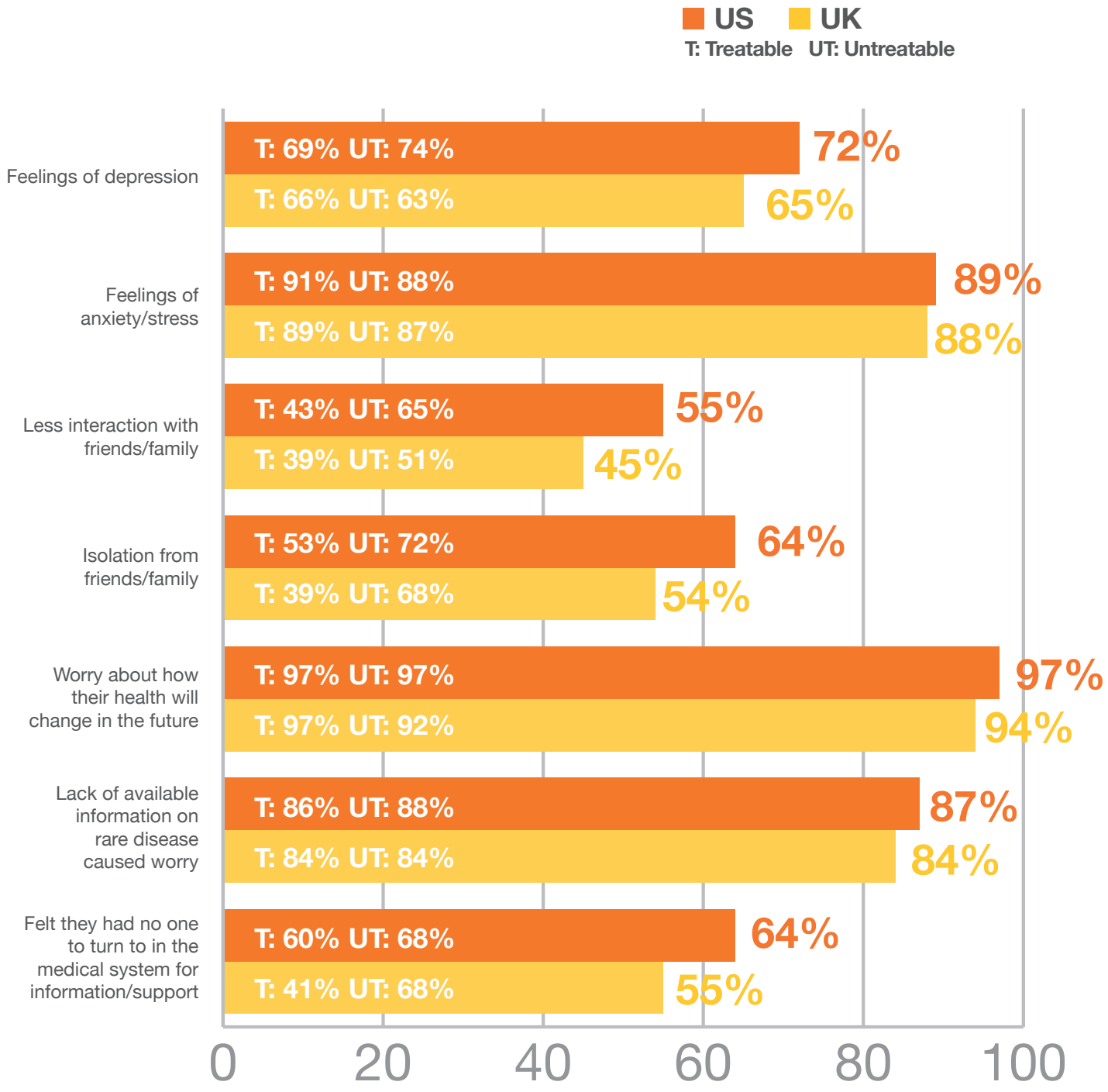
As with any illness, there are added emotional burdens, such as worry, stress, and anxiety. These burdens are compounded by uncertainty, the lack of available information and resources, economic strain, and added responsibilities for many patients with rare diseases and their caregivers. Patient and caregiver respondents reported the following emotional difficulties as a result of having to manage or take care of a loved one with a rare disease.

As illustrated, the highest emotional burden can be seen in those with a rare disease where there are no available treatments. Overall, compared to patients with rare diseases where there are available treatments, patients with a rare disease with no treatment worry more, feel more depressed, interact less with friends and family, and feel more isolated from friends and family.

Emotional Impact of Rare Disease on Patients



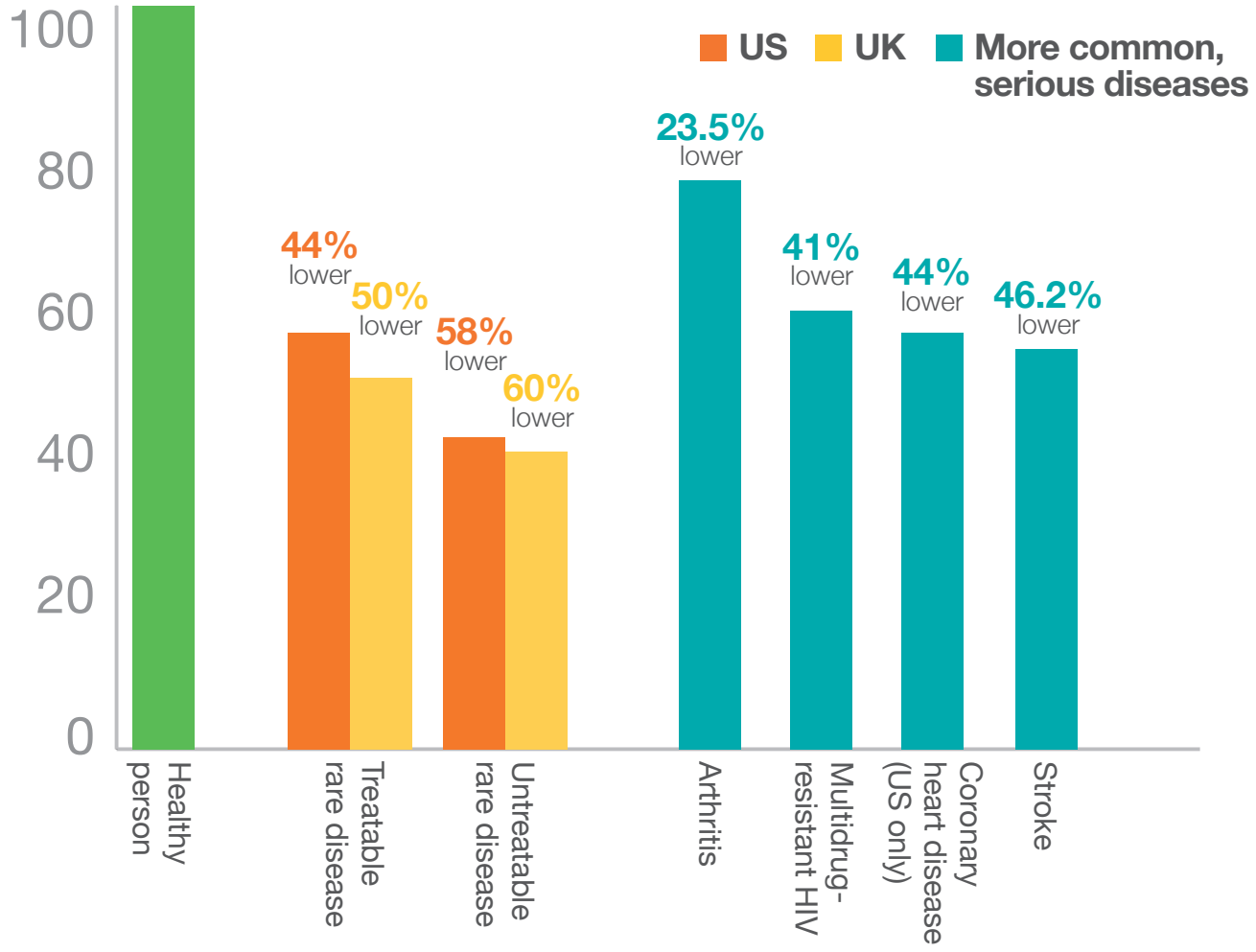
Emotional Impact of Rare Disease on Caregivers



Health-Related Quality of Life*

Patients with a rare disease and those who care for them reported that their overall quality of life was lower when compared to those who are healthy. Some of the most dramatic differences on quality of life were observed among patients with rare diseases for which there are no treatments available. This is the case when compared to an otherwise healthy person and even when compared to those with more common, serious diseases such as coronary heart disease, HIV, stroke, or arthritis.

Quality of Life of Rare Disease Patient When Compared to Healthy Subject and More Common, Serious Diseases



**To measure health-related quality of life, a scale called the Health Utilities Index™ (HUI) was used. By rating vision, hearing, speech, walking, dexterity, happiness, cognition, and pain, the scale calculated a score, that can be compared to someone in perfect health. For example, a score of 1.0 is for someone with optimal health, 0.0 would represent death and a score of 0.60 suggests a quality of life that is 40 percent lower than they would have if not for their health issues.*

"Clearly, there are substantial financial and emotional burdens of rare diseases on patients and their families. A largely unrecognized issue is the inordinate amount of time it takes to establish a clear diagnosis for patients with rare diseases and the stress that this causes. Patients often consult with a wide range of clinical practitioners over a period of years before receiving the appropriate information about their condition."

Mike Drummond, Professor of Health Economics, University of York

Jeff, Renee, and Matthew Wuchich (diagnosed with Alternating hemiplegia of childhood) and Dr. Mohamad Mikati (pediatric neurologist) at Duke Children's Hospital

Physician Findings

Key Insights

When it comes to assessing the needs of the rare disease community, physicians have a unique vantage point. As medical professionals, they encounter a range of conditions and symptoms while treating numerous patients. On the front line of care, doctors must stay abreast of current research while serving as the delivery point and, at times, as an intermediary between patients and payors.

Given the complexity and inherent challenges of diagnosing and managing rare diseases, it is important to grasp the physician perspective – across the spectrum from primary care physicians to specialists. A key issue many physicians face when treating patients with rare diseases includes the limited resources and information to properly diagnose and manage patients with rare diseases when compared to more common diseases:

- Rare disease patients require longer and more frequent visits with their physician(s), making it difficult to provide needed care in the allotted appointment time
- Physicians feel that medical professional organizations do not provide sufficient attention to rare diseases and do not have enough opportunities to network with other physicians who treat rare diseases
- To treat rare disease patients, doctors must coordinate more often with other treating specialists and healthcare providers

> "Rare diseases require a great deal of time, financial cost, and patient education. Additional research funding is sorely needed."
>
> *US physician*

Survey Results

Top Barriers Reported to Offering Quality Care to Patients with Rare Diseases

Barriers	Percentage of US physician respondents that agreed with statement	Percentage of UK physician respondents that agreed with statement
More difficult to address the needs of a rare disease patient in typical office setting	92%	88%
More office visits are required to diagnose	98%	96%
More office visits needed to adequately address symptoms	92%	88%
Medical professional organizations do not give enough attention to rare diseases	46%	50%
Aren't enough opportunities to network with other physicians who treat rare diseases	54%	62%
Difficult to coordinate with other physicians when managing a patient with a rare disease	76%	88%
Adequate and effective treatments are less available once patient is diagnosed	86%	90%

Lack of Time for Diagnosis and Care

"These kids and families have tremendous needs. … It is difficult to spend the needed time to address all of the needs of children with complex medical conditions. … More patients need to be seen in a day and this limits the time available for all patients including those with rare diseases."

US physician

Because physicians see those suffering from rare diseases infrequently, they find themselves faced with more questions, yet fewer answers. Compared to patients with diseases that are as serious, but more common, rare disease patients require:

- More office visits to receive an accurate diagnosis and proper care
- Longer office visits, as there is less available information and more need for patient education
- Additional support services, such as patient education services, mental health services and referrals to support organizations

Once a correct diagnosis is finally made – which patients reported can take more than five years – physicians reported that adequate and effective treatments are less available, which also adds to the time doctors spend trying to find solutions for their patients.

Rare Disease Treatment Requires More Resources

Resources, like time, are finite. Many physicians stated their practices must dedicate more of their limited resources when managing a patient with a rare disease. Providing these extra support services increases the strains on their time.

28% in the US

42% in the UK

28% of US physicians and 42% of UK physicians surveyed report that their practice must use their non-physician staff, such as nurses, counselors or other healthcare professionals to educate rare disease patients on managing their disease.

44% in the US

42% in the UK

44% of US physicians and 42% of UK physicians surveyed provide written materials to patients that explain guidelines for recommended care. These wellness services were particularly common among doctors who work at large institutions, such as medical schools and hospitals.

66% in the US

82% in the UK

Most physicians in both the US and in the UK agreed that it is often more labor intensive to administer claims and to code office visits and procedures for rare disease patients.

> "There is a lack of local experience, therefore patients have to travel long distances to see someone with the expertise that is needed to treat them."
>
> *UK physician*

More Coordination Needed Throughout Medical Community

In many cases, patients with a rare disease need to see multiple physicians before getting correctly diagnosed and also need to obtain care from multiple practitioners simultaneously, in order to address all the symptoms/complications associated with their disease. These factors all require communication and coordination among the medical professionals on a patient's care team.

However, a majority of physicians who responded to the survey stated that they find it more difficult to coordinate with other providers who are all managing the same patient with a rare disease (76% in the US, 88% in the UK).

> "It's hard to coordinate care for patients with specialists due to time constraints."
>
> *UK physician*

More Awareness and Support Needed

Because of the nature of the category, many physicians (both primary care and specialists) see rare disease patients – especially those with the same disorder – infrequently. Therefore, individually, they seldom amass sufficient experience in all phases of diagnosis, treatment, and supportive care to become experts on a specific disorder. This leads them to call for an increase in education and support throughout the medical community to assist in gathering and sharing rare disease information with each other. However, fewer than half of physicians surveyed thought that medical professional organizations provide sufficient attention to rare diseases (46% in the US, 46% in the UK). Likewise, fewer than half thought that there were enough opportunities to network with other physicians who treat rare diseases (46% in the US, 38% in the UK).

The challenge of staying abreast of rare disease developments and being aware of diagnostic criteria also arose as a concern for physicians surveyed.

> "It is difficult to stay up to date regarding rare diseases that I see infrequently compared with most of my general pediatric practice."
>
> *UK physician*

> "You never see enough of them [patients with rare diseases] to build up the experience."
>
> *US physician*

Payor Findings

Key Insights

Payors are in a unique position as their decisions impact both patients' care and physician treatment decisions. Payors can provide valuable insights into the reasons how and why certain coverage decisions are made. For many rare diseases, evidence-based treatment guidelines may not be adequate and, in some cases, non-existent, which makes it harder for payors to make coverage decisions. Other barriers payors find when making rare disease coverage decisions include the following:

- The lack of standards related to rare disease care
- The costs of care, which continue to rise, leading to uncertainty about future pricing
- The increased level of care rare disease patients need, which also translates to higher costs
- In the US in particular, these high costs strain an already stretched healthcare system

> "There is a reluctance of insurance companies to pay for certain treatments and tests for rare diseases they feel are not proven."
>
> *US payor*

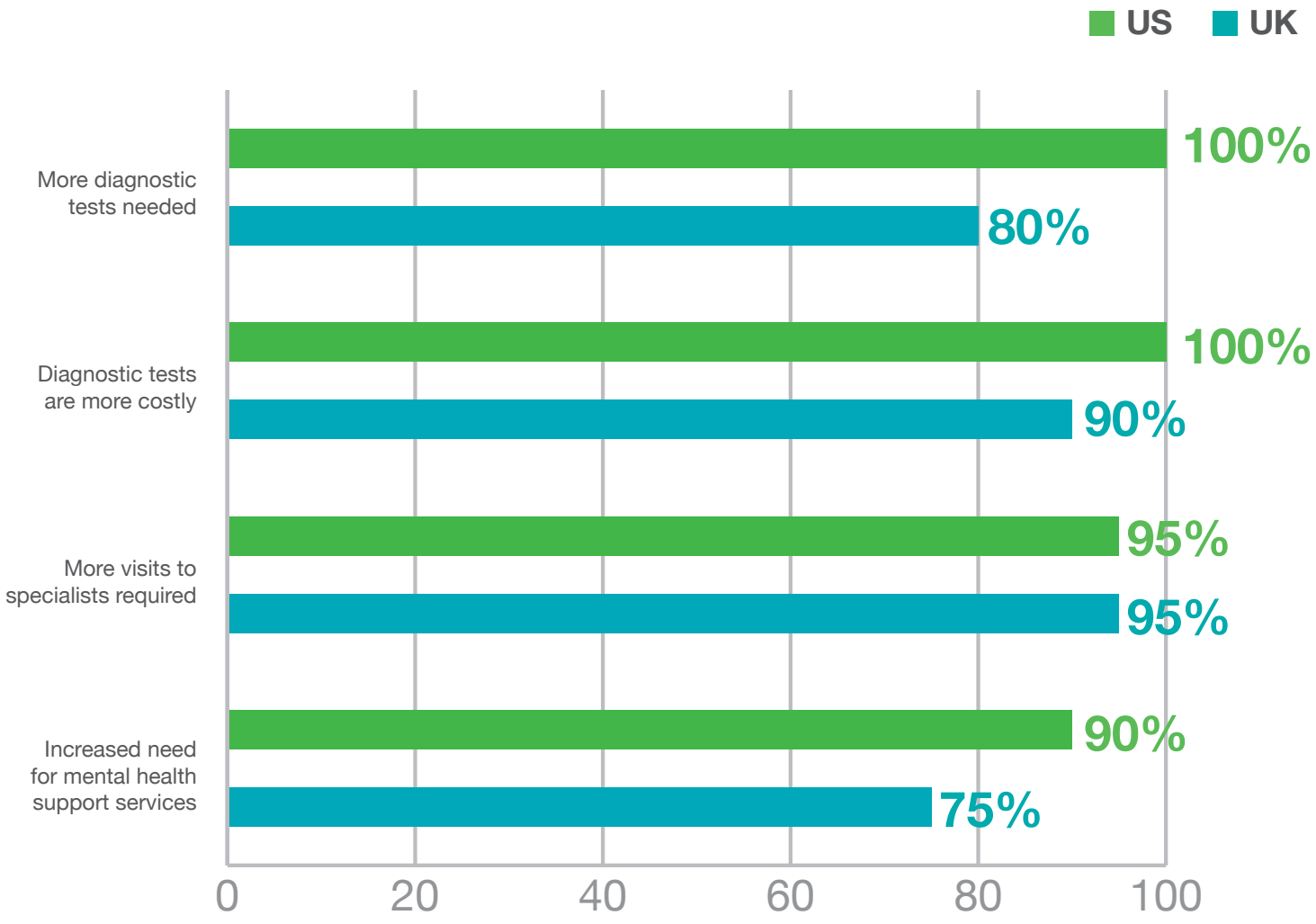
Survey Results

> "It is difficult to predict healthcare costs and what interventions may be required over a lifetime."
>
> *US payor*

Across the spectrum, patients, those who care for them, physicians, and payors all agree that the cost of rare disease care is a major concern and obstacle to care. This was seen in responses from payors in the US, who represented both government and private insurers, as well as those in the UK, who represented the government-sponsored health system.

Despite the vast differences in healthcare systems, payors in the US and UK agreed almost unanimously that compared to treatment of more common diseases of comparable severity, treating those with rare diseases is relatively expensive (95% in the US, 100% in the UK) and costs are rising more rapidly (90% in the US, 85% in the UK).

Payor-Cited Factors Contributing to High Costs of Rare Diseases



US and UK: Different Perspectives

Not surprisingly, because of vastly different healthcare systems, several factors impact US payor decisions more so than those in the UK.

Factors	Percentage of US Respondents that Agreed with Statement	Percentage of UK Respondents that Agreed with Statement
Rare disease patients require more prescription drugs	90%	30%
Rare disease patients have an increased need for customer service support	90%	45%
Rare disease patient care puts a strain on the healthcare system	90%	45%
It is difficult to predict the cost of caring for rare disease patients in the future	95%	70%
Rare disease patients are likely to reach lifetime caps on coverage expenditures (US only)	100%	n/a
Compared to patients with common diseases of comparable severity, rare disease patients are likely to be denied coverage (US only)	90%	n/a

More Awareness and Support Needed

When dealing with one disease that has an impact on so few people, payors often find themselves in uncharted territory. Just as the lack of information confounds patients and doctors, it also leaves payors to make decisions without established guidance.

The shortage of information led almost all payors surveyed to indicate that compared to common diseases of comparable severity, there is less information available to help determine the standards of care for rare diseases (95% in the US, 90% in the UK). They also reported, overwhelmingly, that it is more difficult to decide what coverage to provide for rarely seen diseases (90% in the US, 85% in the UK).

> "The rarity of a disease inevitably means a lack of expertise, a lack of understanding of the needs of patients and no clearly identified treatment pathways or packages of care."
>
> *UK payor*

Appendix

Areas for Future Research

Based on the findings uncovered in this report, below are some areas to consider for future research:

- Additional focus on cultural or regional differences of the impact of rare diseases
- Further research on the impact of rare diseases on patients with treatable rare diseases compared to those ultra-rare conditions where there aren't any treatments available
- Further explore the primary care physician perspective on rare disease diagnosis and management compared to the perspective of specialists to identify major discrepancies and gaps

References

1. U.S. National Library of Medicine, National Institutes of Health website. "Rare Diseases." http://www.nlm.nih.gov/medlineplus/rarediseases.html. Accessed March 18, 2013.
2. World Health Organization website. "Bulletin of the World Health Organization: Coming together to combat rare diseases." http://www.who.int/bulletin/volumes/90/6/12-020612/en/. Accessed March 18, 2013.
3. National Institutes of Health website. "Office of Rare Disease Research." http://rarediseases.info.nih.gov/AboutUs.aspx. Accessed March 18, 2013.
4. Rare Disease UK website. http://www.raredisease.org.uk/. Accessed March 18, 2013.
5. Global Genes website. "RARE Facts and Statistics." http://globalgenes.org/rarefacts/. Accessed March 18, 2013.

List of Rare Diseases

Patients and families affected by the following rare diseases responded to the survey:

US

16p11.2 deletion syndrome
1q21.1 microdeletion syndrome
1q43 chromosome deletion syndrome
22q11.2 duplication syndrome
Addison's disease
Alexander disease
Alopecia, epilepsy, pyorrhea, mental subnormality
Alpha 1-antitrypsin deficiency
Ankylosing spondylitis
Aortic valves stenosis of the child
Asbestosis
Ataxia telangiectasia
Autosomal-Dominant Alport syndrome
Bannayan-Riley-Ruvalcaba syndrome
Basal cell nevus anodontia abnormal bone mineralization
Basilar migraine
Beckwith-Wiedemann syndrome
Behçet's disease
Benign paroxysmal positional vertigo
Birdshot chorioretinopathy
Bone cancer
Bowen's disease
Breast cancer, childhood
Bronchiolitis obliterans
Bicuspid heart valve
CADASIL syndrome
Cancer of the perineum
Carney triad
Caroli disease
Cataract and cardiomyopathy

C. diff
CDKL5
Cerebellar ataxia
Charcot-Marie-Tooth disease type 1A
Chromosome 16q deletion
Chronic inflammatory demyelinating polyneuropathy
Chronic myeloid leukemia
Chronic recurrent multifocal osteomyelitis
Common variable immunodeficiency
Complex regional pain syndrome
Congenital heart block
Cowden's disease
Cutaneous mastocytosis
CVID and MGUS
Cystic fibrosis
Cystic hygroma
Cystinuria
D-2 hydroxyglutaric aciduria
Dandy Walker syndrome/malformation
Desminopathy
Devic disease
Diabetes hypogonadism deafness mental retardation
Diabetes mellitus, transient neonatal
Diabetes persistent mullerian ducts
Diabetic mastopathy
Diamond-Blackfan anemia
DICER1-related pleuropulmonary blastoma cancer predisposition syndrome
Distal chromosome 18q deletion syndrome
Dominant optic atrophy
Duchenne muscular dystrophy
Dysautonomia-like disorder
Ehlers-Danlos syndrome
Eosinophilic esophagitis
Familial periodic paralysis
Fibrous dysplasia
Friedreich ataxia
Gardner syndrome
Gastric duplication cysts
Gaucher disease
Gitelman syndrome
Glycogen storage disease type 2
Granulomatous disease of unknown etiology
Harlequin ichthyosis
Heart defect, tongue hamartoma and polysyndactyly
Hemophilia A, acquired
Hemophilia A, congenital
Hereditary coproporphyria
Hereditary Spastic Paraplegia
Heterotaxy syndrome
Hirschsprung's disease
Homocystinuria
Hyper-IgD syndrome
Hypereosinophilic syndrome
Hyperglycinemia, isolated nonketotic type 1
Hypocalcemia, autosomal dominant
Infantile spasms
Isovaleric acidemia
Joubert syndrome
Joubert syndrome with ocular anomalies
Juvenile dermatomyositis
Juvenile-onset fibromyalgia, Ehlers-Danlos syndrome
Kleefstra syndrome
Klippel-Feil syndrome
Langerhans cell histiocytosis
Late Infantile Batten disease
Late-onset congenital adrenal hyperplasia
Leber's congenital amaurosis
Legg-Calve-Perthes disease
LEOPARD syndrome
Leukoencephalopathy with vanishing white matter
Lupus
Lupus anticoagulant
Mal de debarquement
Maple syrup urine disease
Marfan syndrome

Metastatic extra adrenal paraganglioma and metastatic diffuse sclerosing variant of thyroid cancer
Microscopic polyangiitis
Mitochondrial genetic disorders
Mixed connective tissue disease
Moebius syndrome
Monogenic diabetes (MODY 2)
Morgellons
MPS III (Sanfilippo syndrome)
Mucha-Habermann disease
Mucolipidosis III alpha/beta
Mucopolysaccharidosis
Multiple chemical intolerance
Multiple chemical sensitivity
Multiple hereditary exostoses
Multiple myeloma
Myasthenia gravis
Nephropathic cystinosis
Neuro medulloblastoma
Neurocutaneous melanosis
Neuromyelitis optica spectrum disorder
Neuronal ceroid lipofuscinoses
Non ketotic hyperglycinemia syndrome
Non-Hodgkin lymphoma, childhood
Nonketotic hyperglycinemia
Oculofaciocardiodental syndrome
Ollier disease
Opsoclonus myoclonus ataxia
Opsoclonus myoclonus syndrome
Oral facial digital syndrome
Oral facial digital syndrome 1
Ornithine transcarbamylase deficiency
Pachygyria
Pallister-Killian syndrome
Pelizaeus-Merzbacher disease
Peripheral neuropathy
Phelan-McDermid syndrome
Pheochromocytoma
Pompe disease
Pontocerebellar hypoplasia with spinal muscular atrophy (VRK1 mutation)
Premature ovarian failure, familial
Primary Immunodeficiency Disorder (PIDD)
Progressive pseudorheumatoid chondrodysplasia
Pseudoachondroplasia
Pseudomyxoma peritonei
Pseudotumor cerebri
Pyruvate kinase deficiency
Ramsay Hunt syndrome
Relapsing polychondritis
Rhabdomyosarcoma alveolar
Sanfilippo syndrome A
Sarcoidosis
Schmid-Fraccaro syndrome/Cat Eye syndrome
Sheehan's syndrome
Skin cancer, non-melanoma, childhood
Soft tissue sarcoma
Stiff person syndrome
Systemic mastocytosis
Thyroid cancer, medullary
Trimethylaminuria
Trisomy 18
Tuberous sclerosis
Ulcerative colitis
Unbalanced chromosomal translocation between 7 & 10
Undiagnosed neurometabolic disorder
Unidentified genetic syndrome
Vasovagal reflex
WAGR syndrome
Wegener's granulomatosis
Williams syndrome
Wilms' tumor

UK

3-beta-hydroxysteroid dehydrogenase deficiency
Acoustic neuroma
Acquired angioedema

Acquired C1 esterase deficiency due to autoimmune antibodies
Acrodermatitis
Acromegaly
ACTH + Androgen deficiency
Action myoclonus-renal failure syndrome
Acute articular rheumatism
Acute intermittent porphyria
Addison's disease
Adrenoleukodystrophy X-linked
Aglossia and situs inversus
Alopecia, epilepsy, pyorrhea, mental subnormality
Alpha 1-antitrypsin deficiency (A1AD)
Alström syndrome
Alzheimer disease type 1
Amyotrophic lateral sclerosis
ANCA-negative vasculitis possibly polyarteritis nodosa
ANCA-postive vasculitis
Aniridia
Aplastic anemia
Areflexia, pes cavus, optic atrophy, and sensorineural hearing loss
Ataxia (unknown type)
Atypical hemolytic-uremic syndrome
Autosomal dominant optic atrophy, hearing loss, and peripheral neuropathy
Autosomal dominant spinocerebellar ataxia type 6
Bardet-Biedl syndrome
Barth syndrome
Basilar migraine
Batten disease
Behçet's disease
Birdshot chorioretinopathy
Blood clotting factor deficiency
Bone cancer
Brain tumor, adult
Brittle bone disease
Brown-Vialetto-Van Laere syndrome
C-ANCA positive cerebral vasculitis
C1 esterase deficiency and angioedema (HAE)
C1 protein inhibitor deficiency
Carcinoid syndrome
Caroli disease
Cataract, glaucoma
CDKL5 disorder
Central nervous system vasculitis
Cerebellar ataxia
Cerebellar degeneration
Cerebral vasculitis
Chiari malformation
Cholangiocarcinoma
Chondrosarcoma
Chromosome 10p duplication
Chromosome 12q deletion
Chromosome 13q deletion
Chromosome 15q deletion
Chromosome 15q duplication (partial octasomy of chromosome 15 – believed to be the only one in the world that we know of)
Chromosome 1q21.1 duplication syndrome
Chromosome 9p deletion
Chronic lymphocytic leukemia
Chronic mucocutaneous candidiasis
Chronic myeloid leukemia
Chronic progressive external ophthalmoplegia plus
Churg-Strauss syndrome
CIDP
CNS vasculitis
Cockayne syndrome
Common variable immunodeficiency
Complex regional pain syndrome
Congenital toxoplasmosis
Congenital adrenal hyperplasia
Congenital chloride diarrhea
Congenital myasthenic syndrome – presumed, unknown gene fault
Congenital sideroblastic anemia
Craniopharyngioma

Creutzfeldt-Jakob disease
Cri-du-chat syndrome
Crohn's disease
Cushing's syndrome
Cutaneous necrotizing vasculitis
Cystic fibrosis
Cystinosis
Cystinuria
Dercum's disease
Diabetes insipidus nephrogenic mental retardation and intracerebral calcification
Dopamine-responsive dystonia and vasculitis
Duchenne muscular dystrophy
Dystonia 5, dopa-responsive type
Ectodermal dysplasia
Ehlers-Danlos syndrome
Electrical hypersensitivity
Empty sella syndrome
Esophageal cancer
Essential thrombocythemia/PV (MPN)
Essential thrombocythemia
Fabry disease
Familial cerebellar ataxia
Familial prostate cancer
Friedreich's ataxia
Furunculous myiasis
Gall bladder cancer
Gastrointestinal stromal tumors
Gerstmann syndrome
Giant cell arteritis
Gluten ataxia
Goldenhar syndrome
Gorlin-Goltz syndrome
Greig cephalopolysyndactyly syndrome
Group B strep disease in newborns
H-ABC syndrome
Hailey-Hailey disease
Hairy cell leukemia
Henoch-Schönlein purpura
Hereditary angioedema
Hereditary leiomyomatosis and renal cell cancer (carcinoma) HLRCC fumarate hydratase (FH) gene
Hereditary neuropathy with liability to pressure palsies
Hermansky-Pudlak syndrome
Hilar cholangiocarcinoma
Holt-Oram syndrome
Hyperemesis gravidarum
Hypermobility syndrome
Hypocomplementemic urticarial vasculitis syndrome
Hypogonadotropic hypogonadism
Hypohidrotic ectodermal dysplasia with immunodeficiency – NEMO gene
Hypomelanosis of Ito
Hypopituitarism
Idiopathic bilateral panuveitis
Idiopathic cerebellar degeneration
Idiopathic intracranial hypertension (IIH)
IGA nephropathy
Immune thrombocytopenia (ITP)
Inappropriate sinus tachycardia with ectopic and SVT
Intracranial hypertension
Jansen type metaphyseal chondrodysplasia
Kabuki syndrome
Kallmann syndrome
Kartagener syndrome
Kleefstra syndrome
Klippel-Feil syndrome
Klippel-Trénaunay-Weber syndrome
Langerhans cell histiocytosis
Late onset ataxia
Late onset Tay-Sachs
Laurence-Moon Bardet-Biedl syndrome
Leukocytoclastic vasculitis
Lichen planopilaris and Oral lichen planus
Lichen sclerosus

Lipodystrophy, familial partial, type 2
Lowe oculocerebrorenal syndrome
Lupus nephritis
Lyme Neuroborreliosis
Lymphoma – AIDS related
Macrocephaly-capillary malformation
Maffucci syndrome
Ollie's disease – they are unsure which at moment
Mal de debarquement syndrome
Manifesting carrier of Duchenne muscular dystrophy
MECP2 duplication syndrome
Mesenteric panniculitis
Methylmalonic acidemia and homocystinuria cblC type
Microdeletion 15q11.2
Microdeletion 17q21.31 Koolen-de Vries syndrome
Microscopic polyangiitis
Microscopic polyangiitis with granulomatous
Microtia-Anotia
Mitochondria mutation/disorder
Mitochondrial myopathy with lactic acidosis
Mixed connective tissue disease
Motor neuro-ophthalmic disorders
Mucopolysaccharidosis type II
Multiple chemical sensitivity
Multiple endocrine neoplasia type 1
Multiple joint dislocations metaphyseal dysplasia
Myalgic encephalomyelitis
Myasthenia gravis
Myotonia congenita autosomal recessive
Nail patella syndrome
Narcolepsy
Neurofibromatosis type 1
Neuromyelitis optica spectrum disorder
Neuromyotonia; myasthenia gravis
Niemann-Pick disease
Nonfunctioning pituitary adenoma
Non-Hodgkin lymphoma, childhood
Nonketotic hyperglycinemia
Opsoclonus myoclonus syndrome
Osgood-Schlatters disease
Osteogenesis imperfecta
Palindromic rheumatism
Palmoplantar keratoderma
Panhypopituitarism
P-ANCA vasculitis
Panhypopituitarism
Panhypopituitarism X-linked
Paroxysmal nocturnal hemoglobinuria
PCOS
Pearl syndrome
Pearson's syndrome
Pediatric multiple sclerosis
Periodic hypothermia
Periventricular nodular heterotopia
Permanent neonatal diabetes mellitus
Pernicious anemia
Phelan-McDermid syndrome
Phenylketonuria
Pheochromocytoma
Pitt-Hopkins syndrome
Pituitary dysfunction steroid dependant
Pituitary hormone deficiency, combined 3
Pituitary tumour
Polyarteritis nodosa
Polycythemia vera
Postural orthostatic tachycardia syndrome, platybasia
Primary angiitis of the central nervous system
Primary ciliary dyskinesia
Primary sclerosing cholangitis
Protein S deficiency
Proteus syndrome
Pseudoachondroplasia
Pseudoxanthoma elasticum
Pseudomyxoma peritonei
Psychogenic non-epileptic seizures

Pulmonary vasculitis and membranous glomerulonephritis

Ramsay Hunt syndrome

Rare chromosome disorder

Refsum disease, infantile form Zellweger spectrum disorder

Relapsing polychondritis

Retinitis pigmentosa

Retinopathy aplastic anemia neurological abnormalities

Rheumatoid vasculitis

Rosai-Dorfman disease

Sarcoidosis

Scar 8 ataxia (cerebellar)

Scheuermann disease

Scleroderma (systemic sclerosis)

SDHD

Sertoli-leydig cell tumors

Severe dry eye

Sickle cell anemia

Spina bifida and hydrocephalus

Spinocerebellar ataxia

Spinocerebellar ataxia 2

Spinocerebellar ataxia 3

Spinocerebellar ataxia 6

Spinocerebellar ataxia type 1: SCA1

Stiff person syndrome

Susac's syndrome

Suspected Brown-Violetto-Van Laere syndrome

Sweet’s Syndrome (Acute febrile neutrophilic dermatosis)

Symphalangism familial proximal

Syringomyelia

Systemic vasculitis, mix of diseases

Takayasu’s arteritis

Takayasu’s vasculitis

Tarlov cyst disease

Thyroid eye disease

Transposition of the great arteries

Transverse myelitis

Trigeminal neuralgia

TSHOMA pituitary infarction, enlarged empty sella, postural orthostatic tachycardia syndrome

Ulcerative colitis

Uncategorised vasculitis

Underactive thyroid

Undifferentiated connective disease

Unknown cause ataxia and cervical dystonia

Urticarial vasculitis

Vaginal cancer

Variegate porphyria

Vascular Ehlers-Danlos syndrome

Vasculitis

Vasculitis of the lungs

Vasculitis Wegener’s granulomatosis

Very long-chain acyl-coenzyme A dehydrogenase deficiency

Wagner syndrome

WAGR/11p deletion

Waldenström’s macroglobulinemia

Warburg micro syndrome

Weaver syndrome

Wegener’s granulomatosis

Weil’s disease

Wilson’s disease

Worster-Drought syndrome

X-linked hypohidrotic ectodermal dysplasia

X-linked juvenile retinoschisis

X-linked periventricular heterotopia

Zellweger syndrome