BARRIERS TO RARE DISEASE DIAGNOSIS, CARE AND TREATMENT IN THE US:

A 30-Year Comparative Analysis

November 19, 2020

NORD® RARE INSIGHTS®

For more information, please contact: orphan@rarediseases.org
rarediseases.org

The National Organization for Rare Disorders (NORD®) is the leading independent advocacy organization representing over 25 million Americans affected by a rare disease. NORD is committed to the identification, treatment and cure of the more than 7,000 rare diseases, of which approximately 90% are still without an FDA-approved treatment or therapy.

NORD began as a small group of patient advocates that formed a coalition to unify and mobilize support to pass the Orphan Drug Act of 1983. For more than 37 years, NORD has led the way in voicing the needs of the rare disease community, driving supportive policies and education, advancing medical research and providing patient and family services for those who need them most. NORD is also home to over 350 disease-specific member organizations and their communities and is an active partner with many other organizations on specific causes of importance to the rare disease community.

ABOUT RAREINSIGHTS®

RareInsights® is a NORD initiative to expand public knowledge of rare diseases and translate that knowledge into real-world solutions for patients and families. Through this initiative, NORD is commissioning and undertaking a broad range of projects to collect and analyze empirical data for next-generation advocacy that is patient-centered and data-driven. Information is shared with the community in a variety of accessible formats, including reports, white papers, infographics, fact sheets, and more.

INTRODUCTION

Nearly 1 in 10 Americans lives with a rare disease. While each person's experience is unique, individuals with rare diseases tend to report commonalities, such as a long road to diagnosis, limited treatment options and a need for research to better understand their medical condition.

As part of the effort by the National Organization for Rare Disorders (NORD®) to advance understanding of the rare disease patient experience and generate evidence through data under our RareInsights initiative, we analyzed results from two separate studies aimed at identifying the barriers and facilitators of rare disease diagnosis, care and treatment in the United States. The first study, conducted in 1988 and led by NORD, was published on behalf of the National Commission on Orphan Diseases[1,2], in 1989. Thirty years later, in 2019, a second study was conducted, also by NORD, to comparatively assess how experiences and trends for rare disease patients have changed over time.

THE COMMUNITY RESPONSE AT A GLANCE

The findings reported in 1989 reflected information collected from 801 individuals through a series of voluntary telephone interviews. All individuals were chosen at random from a list of general inquiries received by NORD. The recently conducted 30-year follow-up survey gathered voluntary responses from 1,108 individuals via a secure web-based platform from October 2019 through March 2020. Participants were recruited via NORD social networks, NORD email listservs, the NORD website and in-person conferences. To be eligible, respondents from both surveys were required to live in the US, be 18 or over and report that they were either affected by a rare disease, the caregiver of someone with a rare disease, or a family member of someone with a rare disease.

In 1989, 66% of respondents self-identified as female and 34% as male.[3] This distribution closely tracks to the 74% female, 25% male and 1% gender non-binary reported by respondents in 2019.

TIME TO DIAGNOSIS

NORD's comparative analysis found that in 2019, 36% of respondents had been diagnosed with a rare disease within the first year, compared to 51% in 1989. Likewise, in 2019, 28% said it took seven or more years, while 15% reported six years or longer in 1989. Additionally, 38% of people in 2019 received a misdiagnosis during their diagnostic journey, with some (3%) still undiagnosed at the time of completing the survey.

Despite scientific advancements and increased information sharing, particularly through online resources in recent years, the challenges to timely and accurate diagnosis persist. According to the 2019 survey, 50% of patients and caregivers attributed diagnostic delays to a lack of disease awareness, and 42% believed that delays were caused by limited medical specialization. In the open-ended responses, numerous participants raised the following reasons, echoing one another's experiences that: doctors did not connect the dots between symptoms, particularly across different organ systems; the wait times to see specialists were long; patients needed more testing; the

[1] US Department of Health and Human Services. Office of the Assistant Secretary of Health. *Report Of The National Commission On Orphan Diseases*; 1989. https://rarediseases.info.nih.gov/files/report_of_the_national_commission_on_orphan_diseases_february_1989.pdf. Accessed October 26, 2020.

[2] Institute of Medicine (IOM). *Rare Diseases And Orphan Products: Accelerating Research And Development*. Washington, DC: The National Academies Press; 2010. https://www.ncbi.nlm.nih.gov/books/NBK56189/pdf/Bookshelf_NBK56189.pdf. Accessed October 26, 2020.

[3] Previously unpublished survey data from the 1989 survey.

main symptoms of their rare disease were also common in other conditions, adding complexity to the pathway to accurate diagnosis; and pediatricians attributed rare disease symptoms to developmental delays, advising that children would eventually meet age appropriate milestones. Slightly more respondents reported sourcing information about their rare disease diagnosis from internet searches (74%) than from physicians (69%), followed by patient advocacy communities (40%), NORD's Rare Disease Database (34%) and medical journals (27%) (Figure 1). These findings indicate that greater awareness of rare diseases among health care professionals and more coordinated care may improve the rate of diagnosing rare diseases.

While rare diseases can be difficult to diagnose, diagnostic delays can have devastating effects. An accurate diagnosis is the first step in managing a rare disease appropriately and identifying specific resources and interventions for the best possible clinical outcome for patients. As time goes on without answers, illnesses may progress, putting patients in a vulnerable position with their condition, with more complexity and greater severity of disease. This is on top of the toll to mental and emotional health that patients and caregivers experience while devoting resources, concern, costs, time and energy to the diagnostic journey.

To help understand what measures can facilitate rare disease diagnoses, NORD examined the impact of newborn screening and genetic testing in the 2019 survey. An association was found between newborn screening and time to diagnosis. When respondents received newborn screening (13%), 44% were diagnosed within 0-6 months, compared to 27% of all survey participants. When individuals received genetic testing (41%), 24% were diagnosed within 0-6 months. (N.B.: No statistical association was found between genetic testing and time to diagnosis; however, the survey did not ask respondents to specify when genetic testing was administered.)

Newborn screening and genetic testing expanded significantly over the 30-year period between NORD's surveys. Newborn screening began in the 1960s, yet some states still screened for as few as four conditions as recently as 2002.[4] As of 2018, however, most states[5] were screening for more than 30 conditions and advocacy efforts for the continued expansion of newborn screening are ongoing. Genetic testing, on the other hand, has been advancing rapidly following the development of new genomic technologies and the completion of the "Human Genome Project" in 2003.[6] A type of genetic testing known as whole exome sequencing yields about a 25-68% success rate in diagnosing inherited rare diseases.[7,8] Though genetic tests can be critical to the diagnosis of many rare genetic conditions, there is still significant variability in clinical evaluations that may suggest benefit from ordering a genetic test, and the cost of these tests may be expensive–particularly if they are not covered by health plans. Despite these challenges, these advances reflect some of the changes to the rare disease landscape over time. Given that 80% of rare diseases are genetic in origin, opportunities for further progress exist.

As increased opportunities to utilize diagnostic genetic testing come into focus, potential barriers must be addressed to ensure equitable access for patients, including: filling knowledge gaps to empower patients and health care professionals with information regarding clear diagnostic criteria and when and what type of genetic testing is appropriate; addressing insurance barriers and long wait times for appointments; and overcoming shortages of trained geneticists.[9]
At the recent 2020 NORD Rare Diseases and Orphan Products Breakthrough Summit®, the Children's Hospital of Pittsburgh presented their service delivery model of an on-site genetics clinic, which has improved access to genetics testing, reduced the time to genetic diagnosis for patients and can serve as a model to be replicated by other medical centers.

Looking to the future, technology is also being leveraged to new heights with the goal to accelerate rare disease diagnoses. The *Global Commission to End the Diagnostic Odyssey for Children with a Rare Disease* discussed a new pilot program, also at the 2020 NORD Summit, that uses artificial intelligence (AI) to recognize symptoms based on medical records, patient-reported data and genetics data, and in testing has resulted in the identification of a diagnosis 79% of the time. As another example, the Rare Disease Institute at Children's National Medical Center is utilizing two pilot mobile applications to speed up diagnoses, one that facilitates consultations between physicians and rare disease specialists on difficult medical cases, and another for patients to organize and share their health information for both diagnostic and data aggregation efforts. NORD will continue to study this topic and leverage its IAMRARE™ patient registry and natural history study program to support the goal of identifying paths that can and will shorten the diagnostic odyssey for people with rare diseases.

ACCESS TO CARE AND TREATMENT

Geographic Barriers

People with rare diseases often face geographic barriers to care. In the case of many rare diseases, there are only a handful of specialists nationwide, or even worldwide, who have expertise in a given rare condition. As a result, patients often travel long distances to access their treating providers. NORD's recent survey shows that 80% of respondents were being treated by at least one specialist.

NORD's 2019 survey (which captured responses before COVID-19 related shut downs took hold) also shows that people had been traveling slightly less to access medical care related to their rare disease compared to 30 years ago. Thirty-nine percent of respondents needed to travel 60 or more miles in 2019, compared to 56% who traveled 50 or more miles in 1989.

At the same time, the results also demonstrate that more people have been permanently relocating to access medical care related to their rare disease. In 2019, 17% of individuals had already relocated or were considering it, compared to 8% in 1989. Further research is needed to better understand individual

[4] US National Institutes of Health (NIH). Brief History of Newborn Screening. www.nichd.nih.gov/health/topics/newborn/conditioninfo/history. Published 2017. Accessed October 26, 2020.

[5] National Organization for Rare Disorders (NORD) Rare Action Network. *State Of The States Report: Fifth Edition*; 2018. https://rareaction.org/ wp-content/uploads/2020/01/NRD-2021-StateOfTheStatesReport_5thEd_FNL.pdf. Accessed October 26, 2020.

[6] Durmaz A, Karaca E, Demkow U, Toruner G, Schoumans J, Cogulu O. Evolution of Genetic Techniques: Past, Present, and Beyond. *Biomed Res Int.* 2015;2015: 1-7. doi:10.1155/2015/461524

[7] National Organization for Rare Disorders (NORD). *Genetic Testing 101 For Rare Diseases [Webinar Slides];* 2018. https://www.youtube.com/watch?v=eEdV2vwz160. Accessed October 26, 2020.

[8] Malinowski J, Miller D, Demmer L et al. Systematic evidence-based review: outcomes from exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability. *Genetics in Medicine*. 2020;22(6):986-1004. doi:10.1038/s41436-020-0771-z

[9] Maiese D, Keehn A, Lyon M, Flannery D, Watson M. Current conditions in medical genetics practice. *Genetics in Medicine*. 2019;21(8):1874-1877. doi:10.1038/s41436-018-0417-6

reasons for relocating, however, one possible explanation may be the impact of the Affordable Care Act (ACA) of 2010, under which eligibility rules for Medicaid differ from state to state.

Separate from this survey, in recent years numerous rare disease patients and their family members have told NORD that they had uprooted their lives and moved across state lines to have better access to medical care.[10] Knowing this, we took a close look at the data around relocation to identify any significant associations. The data shows that respondents earning less than $20,000 per year were more than twice as likely to consider relocating than respondents in any other income category (Figure 2), and 44% of respondents in this income group reported receiving health care through Medicaid.

Medicaid serves an important role to medically vulnerable populations in the US because many rare disease patients have complex needs for care and they or their family member caregivers may struggle to work outside of the home in the formal economic sector to generate income. As a result, Medicaid can provide vital access to health coverage. Across the nation, 48% of children with special health care needs and 45% of nonelderly adults with disabilities are covered by Medicaid.[11] Under the well-documented complexities and differences among state Medicaid programs, the percentage of children with special health care needs covered by Medicaid/CHIP varies by state from 15-67%.[12]

These findings underscore why NORD continues to advocate for Medicaid expansion to help reduce barriers to care and ensure that all rare disease patients have access to high quality and affordable health care coverage when they need it.

Treatment Barriers

Although access to health insurance has increased under the Affordable Care Act (ACA), insurance alone has not necessarily translated into access to health care for rare disease patients. For instance, in 2019, only 29% of respondents had been granted access to treatments that were not approved by FDA for their medical condition. This practice, known as off-label prescribing, is legal and quite common in the US (one in five prescriptions written are for off-label use[13]). People with rare diseases often rely on off-label prescriptions because they have no other treatment options available to them, given that only a few hundred of the 7,000 known rare diseases currently have an FDA-approved treatment.

In cases where new treatments for rare diseases have been developed (i.e. 862 orphan products had been approved by FDA as of March 2020, compared to 46 orphan products at the end of 1989[14]), patients have not always been able to access them. According to NORD's 2019 survey, 61% of patients had been denied or faced delays accessing treatments that required pre-approval from an insurance company (i.e. prescriptions, medical devices or other treatments), and 18% had been denied referral to a specialist. Respondents earning less than $20,000 per year were twice as likely to be denied referral to a specialist than those earning $100,000 or more (Figure 3). Reasons for the delays and denials under different types of health coverage were not collected in this survey and further study is needed to understand the observed differences and any related health disparities.

Another barrier to treatment put in place by payers and observed in this study is the cost-sharing mechanism of specialty tiers. According to NORD's most recent *State of the States Report*,[15] in 2019, 93% of plans in the individual market featured four or more tiers for prescription drugs. Cost-sharing increases with each tier, so that each additional tier represents greater spending by patients. Given that the majority of rare disease treatments in existence are Tier 4 drugs,[16] patients' expenses may become untenable, forcing people to go without their medication or use alternative treatments that are not as safe and effective.

These findings underscore why NORD continues to advocate for all people with rare diseases to have access to comprehensive, affordable health care coverage and timely access to the providers they need to see.

To learn more about NORD's policy work, visit the Policy Issues and Policy Statements sections: bit.ly/NORD-Policy

ACCESS TO RESEARCH

Because the majority of rare diseases still do not yet have an FDA-approved treatment, research is critically important. Fortunately, we have seen progress in rare disease research over the past 30 years, both in terms of new opportunities for patients to participate and in the number of patients who are getting involved.

First, rare disease patients' interest in clinical trials is at an all-time high. Nearly nine out of 10 (88%) people living with a rare disease would consider using an investigational treatment, compared to 62% of respondents 30 years ago. The number of people participating in clinical trials has increased, with 16% reporting that they had already participated in a clinical trial, compared to 12% in 1989. Further exploration of the population demographics of those being served by clinical trials is needed.

An area of research that has grown exponentially in the time between NORD's two surveys is the development and utilization of natural history studies and patient registries. Natural history studies collect longitudinal data to help advance understanding of rare diseases and how they progress over time, helping to facilitate clinical research and the development of new treatments. NORD's recent survey shows that 38% of respondents were aware of existing patient registries or natural history studies for their rare diagnosis and, among those, 78% of individuals had participated. Overall, 80% had not yet participated in a patient registry or natural history study, although more than half (53%) would if one became available for their rare disease state.

[10] Family Moves Across State Lines to Receive Better Access. National Organization for Rare Disorders (NORD). https://rarediseases.org/family-moves-across-state-lines-receive-better-access/. Published 2016. Accessed October 26, 2020.

[11] Medicaid's Role for Children with Special Health Care Needs: A Look at Eligibility, Services, and Spending. *Kaiser Family Foundation (KFF)*. 2019. https://www.kff.org/medicaid/issue-brief/medicaids-role-for-children-with-special-health-care-needs-a-look-at-eligibility-services-and-spending/. Accessed October 26, 2020.

[12] KFF, "*Medicaid's Role*" (see page 6, footnote 11)

[13] Off-Label Drugs: What You Need to Know | Agency for Health Research and Quality. Ahrq.gov. https://www.ahrq.gov/patients-consumers/patient-involvement/off-label-drug-usage.html. 2015. Accessed October 26, 2020.

[14] Search Orphan Drug Designations and Approvals. Accessdata.fda.gov. https://www.accessdata.fda.gov/scripts/opdlisting/oopd/. Accessed October 26, 2020.

[15] NORD, "*State of States*" (see page 4, footnote 5)

[16] Quintiles IMS Institute. *Orphan Drugs In The United States: Providing Context For Use And Cost*; 2017. https://rarediseases.org/wp-content/uploads/2017/10/Orphan-Drugs-in-the-United-States-Report-Web.pdf. Accessed October 26, 2020.

The patient-driven data in natural history studies provides a more comprehensive understanding of rare diseases, captures what matters to patients and allows for collaboration with clinicians and researchers. Then the knowledge generated may be used to reshape clinical trials and product development processes, providing treatments that are truly meaningful to the community. Through this type of platform, patients are empowered to drive and influence research for their rare diseases, an opportunity for patient engagement that did not exist 30 years ago.

Janet Woodcock, MD, Director of the Center for Drug Evaluation and Research at FDA, has called registries, "an exciting new tool researchers are using to study rare diseases."[17] Adding to the momentum, technology platforms, such as the Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP), a partnership between the Critical Path Institute and NORD, are aggregating rare disease datasets with the goal of speeding up the development of new therapies for many rare diseases.[18,19]

To learn more about NORD's research work, visit: bit.ly/NORD-IAMRARE

FINANCIAL BURDEN

The financial burden of having a rare disease in the US is significant. According to NORD's 2019 survey, 76% of all respondents had experienced financial challenges due to their own or their family member's rare diagnosis. Thankfully, the number of people experiencing extreme or great financial burden has decreased over the last 30 years, from 43% to 30%. Increased access to health coverage under the ACA may be a potential factor in the decreased extreme financial burden among respondents. Only 2% of respondents did not have health insurance in 2019, versus 9% in 1989. However, among those without health insurance in 2019 (n=21), more than half (62%) cited its high cost as their reason for not having it.

If you are struggling financially because of a rare disease, NORD might be able to help – visit our patient assistance webpage: bit.ly/NORD-PAP

Several associations in the data suggest inequalities exist in the rare disease community related to household income. First, participants with lower household incomes reported greater financial burdens due to having a rare disease (Figure 4). Second, participants earning less spent greater percentages of household income on rare disease care than those earning higher incomes (Figure 5). Third, respondents in the highest income category were significantly more likely to have the highest levels of out-of-pocket costs (Figure 6). Considered in parallel with the increasing prevalence of payers' cost-sharing specialty tiers, the data suggests that two individuals who have the same rare disease but different levels of income may have dissimilar and unequal access to health care. NORD will continue to research this topic and advocate for approaches that address health disparities that exist in the rare disease community.

[17] "The more we know about rare diseases, the more likely we are to find safe and effective treatments." U.S Food & Drug Administration (FDA). 2014. https://www.fda.gov/news-events/fda-newsroom/fda-voices?feed=rss.

[18] Innovative Platform Built To Accelerate Drug Development for Rare Diseases. *Technology Networks*. 2019. https://www.technologynetworks.com/drug-discovery/news/innovative-platform-built-to-accelerate-drug-development-for-rare-diseases-324212. Accessed October 30, 2020.

[19] National Organization for Rare Disorders (NORD). *RDCA-DAP First Year Milestones Highlighted At Virtual Workshop*; 2020. https://rarediseases.org/rdca-dap-first-year-milestones-highlighted-at-virtual-workshop/. Accessed November 5, 2020.

FURTHER IMPACTS

Over the past 30 years, more people reported being unable to attend work or school for a period of time due to their rare disease. In 1989, only 5% were unable to attend school and 23% were unable to attend work due to the impact of their rare disease. In recent years, these numbers have skyrocketed, with 26% reporting an inability to attend school and 62% unable to attend work, according to the 2019 survey. These figures speak to some of the toll and reality of rare diseases outside of the medical setting—where the challenges patients and their families face cause disruption to daily and family life.

CONCLUSION

When the results of NORD's 1989 survey were published initially,[20] government leaders identified the prognosis of people with rare diseases as "very uncertain." In the three decades since, we have seen significant changes to the rare disease landscape that have reduced patients' barriers to diagnosis, care and treatment, yet more work remains to be done.

Advocacy efforts and new technologies are focused on advancing rare disease diagnoses. Newborn screening has expanded over the years and is an effective tool for diagnosing many rare diseases. Genetic testing has also expanded and is being increasingly utilized to help diagnose adults and children with rare diseases, the majority of which are genetic in origin. NORD continues to focus advocacy efforts on these topics, to ensure that diagnostic tools are well understood by both patient and medical communities, effectively utilized by health care professionals, and equitably implemented.

As a patient, knowing your diagnosis and any genetic variation related to your medical condition can help you participate in research, connect with others in similar situations and know what therapies are safe to take. Alternately, any delays in diagnosis may not allow for patients to get the maximum benefit from available treatments, or may cause patients to miss a treatment window entirely, and can slow our collective ability to drive progress and cures.

Excitingly, we may be approaching a tipping point in rare diseases where we will start to see the rate of diagnosis and new treatments begin to accelerate. Recent efforts to collect and aggregate patient-driven data through natural history studies and patient registries are enabling stronger disease-specific and cross-disease research. Our expanded knowledge of genetics and new applications of AI and other technologies are changing what we know about rare diseases on a near-daily basis. Rare disease patients are more interested than ever in participating in clinical trials. Safe, novel treatments, including life-altering gene therapies, are being developed by drug developers and being approved by FDA. The majority of rare diseases are without an FDA-approved treatment, yet each year we are seeing first-ever treatments for individual rare diseases become available, and this progress is expected to continue.

Many advancements in health care policy over the past 30 years have helped reduce barriers to care for people with rare diseases. Access to health insurance has increased, in part due to the passage of the ACA, yet challenges still remain. Without universal Medicaid expansion we are seeing patients and families in the

[20] US Department of Health and Human Services, *"Report Of"* (see page 3, footnote 1)

rare disease community uproot their lives and move across state lines to have better access to medical care over the long-term. Insurance providers are also having an impact in that more than half of respondents have been denied or faced delays accessing treatments, and nearly one-fifth have been denied referrals to specialists. Cost-sharing measures put in place by payers have meant that patients are not always able to afford treatments for their condition.

The number of people reporting extreme or great financial burden due to their rare disease is significant, but thankfully has decreased over the 30-year period of this study, perhaps linked to the impact of the ACA. Despite this progress, several associations in the data were observed between household income and access to care. Further research is needed to understand these disparities and to ensure health equality for people with rare diseases.

NORD's studies also show that rare diseases continue to significantly affect patients and their families outside of medical settings. More people have reported being unable to attend work or school for a period of time due to their rare disease. People with rare diseases often have complex and costly needs for care, which can affect families' resources as well as family dynamics throughout the diagnostic odyssey and beyond.

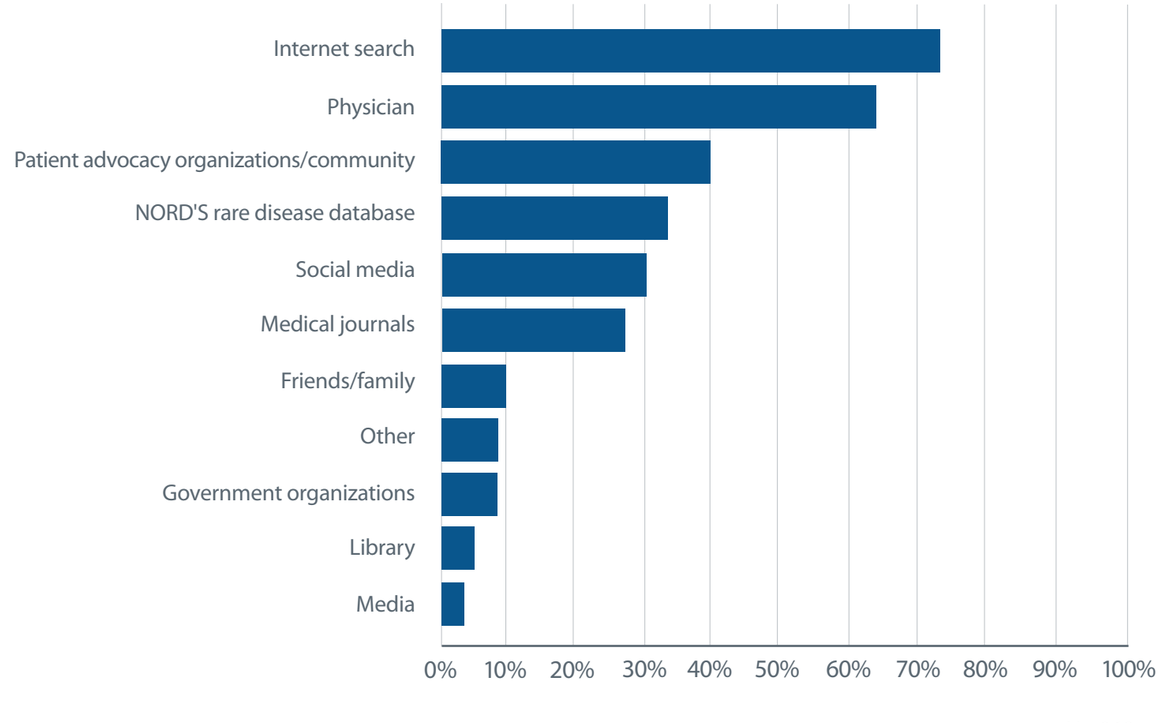
The landscape in rare diseases and health care has and continues to shift with current events. In ways that many could not have been anticipated, the COVID-19 health emergency in 2020 has brought about a rapid increase in access to telehealth[21] that, if made permanent, could help to further reduce barriers that people with rare diseases traditionally have faced. This month, the US Supreme Court is hearing arguments on the whether the ACA is constitutional, in whole or in part, and is expected to rule on the matter by June 2021.

The findings from NORD's 30-year comparative analysis underscore why NORD continues to advocate to eliminate barriers for all people with rare disease. As new challenges and opportunities arise, we have the power to drive change and create progress. We are stronger when we work together for everyone in the rare disease community.

[21] National Organization for Rare Disorders (NORD). *Ensuring Access to Telehealth for Rare Diseases*; 2020. https://rarediseases.org/wp-content/uploads/2020/10/NRD-2098-RareInsights-Telehealth-Report.pdf. Accessed October 26, 2020.

FIGURES

Figure 1. Sources of information for rare disease diagnosis (es)



N= 968

Figure 2. The association between relocating for care and household income

Linear-by-linear association (P= .001) N= 986

NOTE: While the survey was open from October 2019-March 2020, participants were asked to report on their 2018 annual household income.

Figure 3. The association between being denied referral to a specialist and household income

Linear-by-linear association (P= .002) N= 989

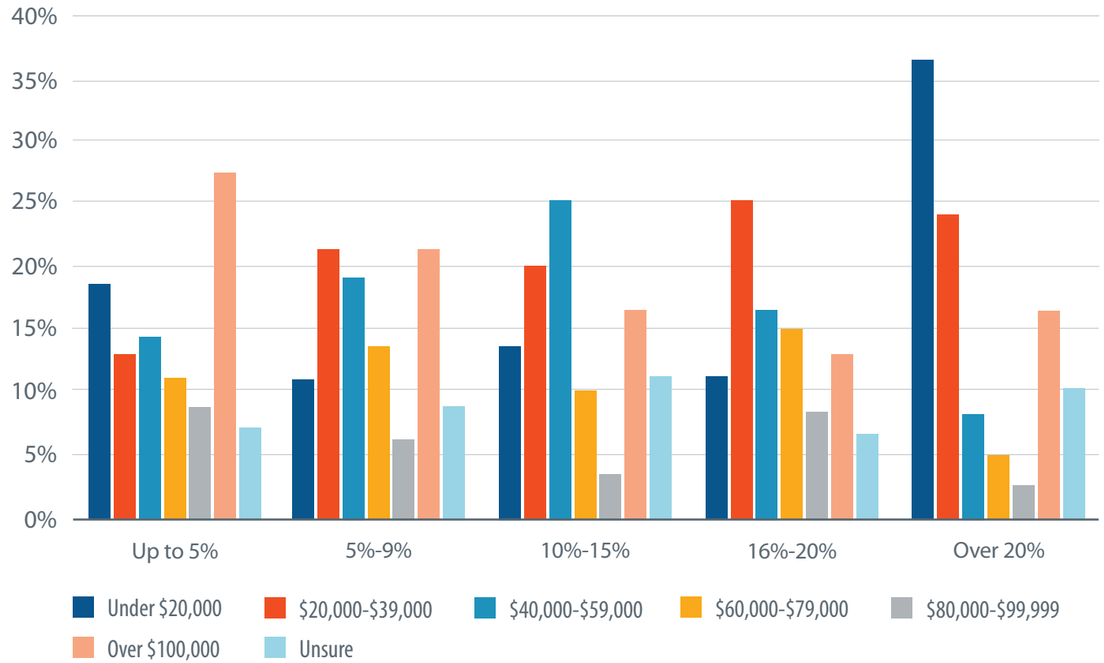
NOTE: While the survey was open from October 2019-March 2020, participants were asked to report on their 2018 annual household income.

Figure 4. The association between financial burden due to rare disease diagnosis and household income

Pearson Chi-Square (P= .001) N= 992

NOTE: While the survey was open from October 2019-March 2020, participants were asked to report on their 2018 annual household income.

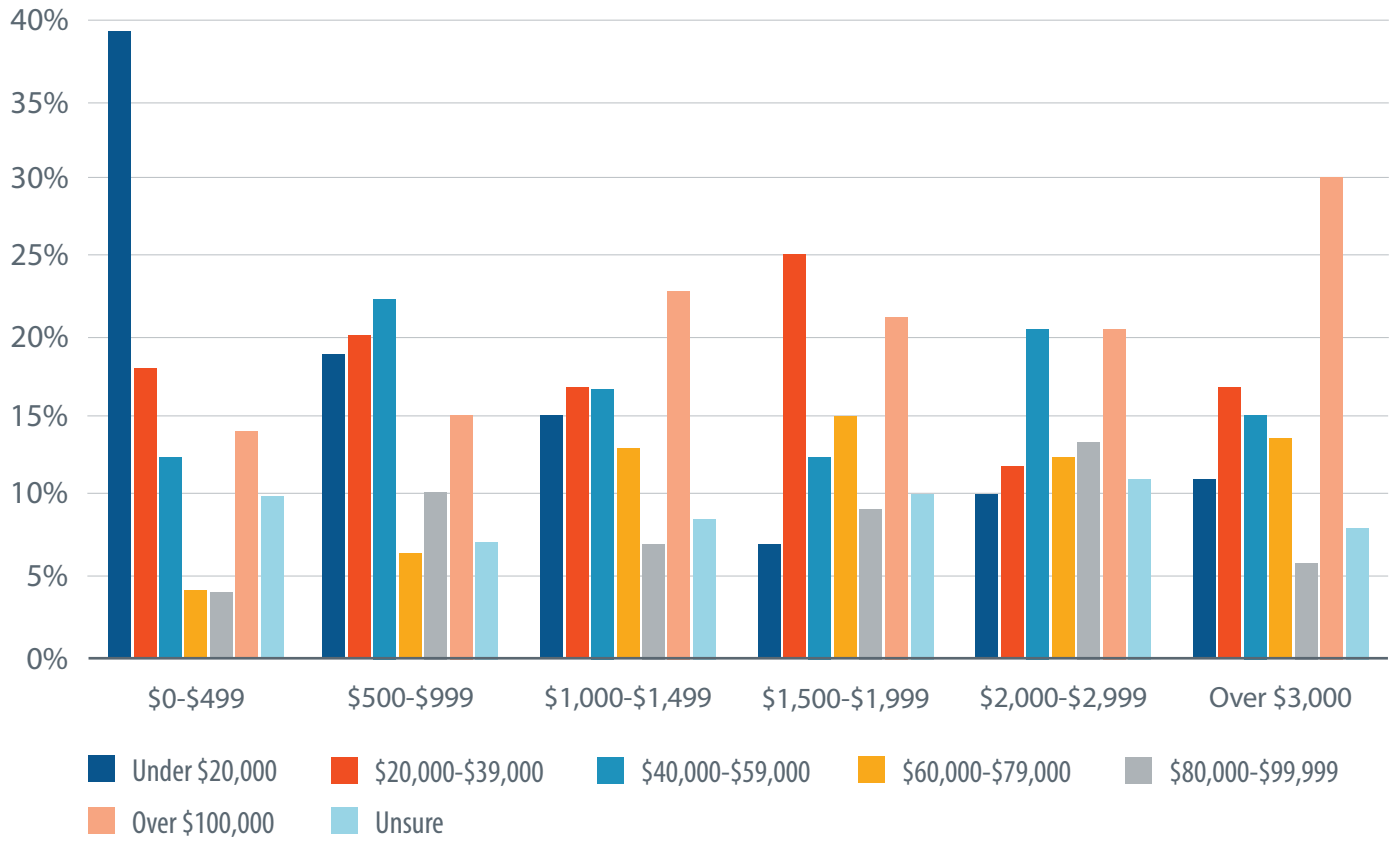
Figure 5. The association between the percentage of household income used toward rare disease care and household income reported



Pearson Chi-Square (P= .001) N= 975

NOTE: While the survey was open from October 2019-March 2020, participants were asked to report on their rare disease health care expenditure in relation to their annual household income from 2018.

Figure 6. The association between the amount paid in out-of-pocket health claims and household income



Pearson Chi-Square (P= .001) N= 978

NOTE: While the survey was open from October 2019-March 2020, participants were asked to report on their 2018 annual household income.

RESOURCES

NORD's lines are always open.

rarediseases.org

orphan@rarediseases.org

203.744.0100

ACKNOWLEDGEMENTS

Thank you to the rare disease patients, families, caregivers and patient advocates for participating in these surveys.

NORD® National Organization for Rare Disorders