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Special Report

The Spectrum of Caregiving in Palliative Care for Serious, Advanced, Rare Diseases: Key Issues and Research Directions

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Abstract

Rare diseases are often life-limiting conditions, the majority of which require constant caregiving needs. The realization of a spectrum of palliative care throughout the trajectory of rare diseases could ensure individualized and caregiver-focused approaches to the care of patients and families. In June 2015, the National Institute of Nursing Research (NINR), the lead institute at the National Institutes of Health for end-of-life research, in conjunction with the National Center for Advancing Translational Sciences, Office of Rare Diseases Research (ORDR) held an interdisciplinary workshop on the unique challenges of caregiving and palliative care in adult and pediatric rare diseases. The panel identified gaps in current knowledge, and afforded suggestions for research opportunities in palliative care science to improve the care of individuals with serious, advanced, rare diseases and their caregivers. This meeting provided an in-depth opportunity to incorporate new concepts into palliative and end-of-life care for individuals with a range of rare diseases and their caregivers. This report presents a summary of the workshop.

Introduction

In the United States, 30 million individuals are living with a rare disease.[1] By definition, a rare disease is one that affects fewer than 200,000 persons in the United States, yet collectively they present a significant health concern for 8% to 10% of the U.S. population.[2] The impact of rare diseases is far reaching, as they affect more people than both cancer and HIV combined.[3] New rare diseases and disorders are identified every day; the RARE List™[4] currently contains 7000 different rare diseases and disorders. In some cases there may be multiple etiologies that impact individuals across the lifespan. In fields such as cancer and neurology, rare diseases are most common. When combined, rare cancers account for 25% of those diagnosed each year, and 25% of cancer-related deaths.[5] With regard to neurologic rare disorders, De Vivo states, ''In neurology, rare diseases and conditions are not so rare. In fact, they are pretty common.''[1] Rare neurologic disorders can include well-known conditions such as amyotrophic lateral sclerosis (ALS), Duchenne muscular dystrophy (DMD), and Huntington's disease (HD). In these progressive conditions, there are no cures and definitive causes remain elusive.[2]

Due to the many additional challenges involved, a rare disease diagnosis can bring increased burden for individuals and their families/caregivers compared to more common disorders. The functional, physical, emotional, and economic burdens placed on the individual and their families often begin with many extended periods of tension between hope for an accurate diagnosis and uncertainty precipitated by a series of misdiagnoses.[6]

Once a diagnosis is made, the path forward is often filled with an uncertain prognosis, limited treatments, and appropriate resources or assistance, and numerous care challenges. In a few cases, disease-modifying therapies may support a 'normal' lifestyle, yet in most circumstances rare diseases significantly impact the health and lifespan of an individual.[2] According to the 2013 Shire Rare Disease Impact Report, individuals with rare diseases and their caregivers experience significant depression, anxiety, stress, isolation, and worry based on future outlook and a lack of information.[6]

Although no curative treatments are available for approximately 95% of the nearly 7000 identified rare diseases, much can be done to improve quality of life.[3] In the absence of disease-modifying drugs or curative treatments, a palliative care approach prioritizes alleviation of physical suffering, preservation of individual autonomy and dignity, and support for caregivers—all pillars of palliative care.[7,8] However, significant barriers and gaps in the provision of comprehensive palliative and hospice care remain for the rare disease community. Many of these needs require new research to develop

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and test evidence-based approaches that clearly support palliative care. Several reports have emphasized this need for new research. The International Shire Rare Disease Impact Report called for ''additional resources for patients and caregivers to navigate the emotional impact of rare diseases, particularly for those where the treatment outlook is limited'' (p. 3).[6] The Eurordis position paper, Patients Priorities and Needs for Rare Disease Research 2014–2020, emphasized a need for ''broad strategy trials, covering all aspects of patient care'' and further emphasized that such research ''is a relatively unexplored area that deserves immediate and urgent action'' (p. 4). The report also noted, ''Equally as important in this multidisciplinary field of research, are quality-of-life studies, especially on how to manage and cope with a RD [rare disease], and studies on the social consequences of the disease, health economy, communication and culture'' (p. 7).[9]

Palliative care research focused on individuals with rare diseases and their caregivers will supply evidence on which to base palliative and end-of-life care choices, and provide hope for improved quality of life. To address these issues from a palliative care perspective, the National Institute of Nursing Research (NINR), with support from the Office of Rare Diseases Research (ORDR), conducted a one-day workshop, ''The Spectrum of Caregiving and Palliative Care in Serious, Advanced, Rare Diseases'' on June 9, 2015. The workshop brought together a multidisciplinary group of experts to consider, across the lifespan, the palliative care needs of individuals with rare diseases and their caregivers. Discussion focused on how these needs may be unique and/or similar to the needs of other palliative care users, and the availability of vital resources and information. Additionally, attention was given to the most effective strategies to assess and manage constellations of complex symptoms, and optimization of crucial issues such as advance care planning. Panelists included researchers in adult and pediatric palliative and hospice care, family management, symptom management, oncology, geriatrics, medical decision making, ethics, caregiver health, measurement and statistics, genetics, communication, and neurodegenerative diseases. Participants were asked to deliberate on the current state of the science; the knowledge gaps and challenges in the area of building palliative care research within serious, advanced, rare diseases; and the key issues and specific research questions that will address these gaps and build momentum for new science in this area. The following is a summary of the knowledge gained from the workshop discussions.

Knowledge Gaps

Living with uncertainty

Uncertainty pervades all aspects of living with a rare disease. Because the majority of rare diseases are misdiagnosed for years, there is an unclear trajectory with an eventual prognosis that is likely fatal. A typical patient/family visits up to eight physicians (four primary care and four specialists) and receives two to three misdiagnoses.[6] In a European survey of individuals with one of eight rare diseases, 40% of respondents reported their first diagnosis was incorrect, while 25% reported waiting between 5 and 30 years for a correct diagnosis.[10] In some cases an individual's illness may have no definitive diagnosis. Throughout the journey, accurate information on treatment and management is generally limited, and once care needs are identified, proximity to specialists and treatment facilities are a common challenge. This compounding uncertainty often impacts treatment decisions;[11] quality of life; and physical, emotional, and social well-being for individuals and their family caregivers.[12–14] In one study focused on adults with metastatic cancer, uncertainty was found to be a barrier to illness understanding and engagement in advance care planning. More aggressive palliative chemotherapy and palliative radiation were more often prescribed in this population than in individuals with more common cancers, likely due to a dearth of other options.[12]

In the United States, health-related quality of life for those with rare diseases is estimated to be almost half (44%) of what it would be if the person were healthy. The quality of life is even lower in people with rare diseases for which there are no treatment options. Caregivers also experience decreased quality of life due to high levels of physical strain. In fact, the longer an individual cares for a loved one, the more likely they are to rate their health as fair or poor.[6] Loggers and Prigerson reported that rare cancer caregivers were more likely than those caring for individuals with more common cancers to have a decline in health during the final year, and marginally more likely to use mental health services to cope with their loved one's illness.[12]

For individuals and families, particularly families of young children, a lack of information may force them to adopt multiple roles such as care coordinator, researcher, decision maker, and advocate, in efforts to achieve optimal quality care.[6,15] Health providers are often unable to address questions on diagnosis, prognosis, treatment of symptoms, or support and available resources for assistance. Inadequate information from clinicians may lead to fruitless searches for information in the literature and on the Internet. Frequently, caregivers face multiple challenges related to difficult care choices, coordination of a care plan, education of others, decisions to use off-label or experimental drugs, whether or not to enroll in clinical trials, decisions between life-sustaining treatments and comfort care, how to evaluate the effectiveness of therapies and technologies, preparing for the end of life, and planning for the future, while managing the life-limiting aspects of a rare disease. In the United States, 60% of caregivers surveyed indicated that they received conflicting information from different health care professionals about treatment options; in fact, 67% of U.S. patients and families indicated they provided their health care professionals with information on their rare diseases.[6]

Uncertainty is also evident relative to a pervasive insufficiency in caregiver training across all domains, from physical care of the patient to decision making and advance care planning.[16] In addition, caregivers are generally uncertain how to integrate the ill individual and their daily care needs into the overall needs of the family, and this dilemma can negatively impact family functioning.[17] Within the rare disease experience, uncertainty adds a layer of stress to the patient and caregiver that is not as prevalent in individuals with more common illnesses.

Caregiving comes at a price

Across the lifespan, caregivers of individuals with rare diseases share common challenges in managing the care of their loved one. These issues impact work, social interactions,

family structures, and financial stability.[18] Respondents to a U.S. caregiver survey reported emotional difficulties resulting from taking care of a loved one with a rare disease that included depression (72%), anxiety and stress (89%), worry (87%), isolation (64%), and decreased interactions (55%) with friends and family.[6] For caregivers and/or their spouses, the ability to work is often impacted due to the time commitment involved in caring for another, and particularly if travel is necessary to access specialists, which also adds financial strain Anticipatory grief and bereavement following the death of a loved one also have a significant impact on caregiver well-being.[16] The challenges of caregiving can precipitate stress, moral tension, and reduced quality of life, with caregivers reporting difficulties balancing caregiving roles with everyday needs, a deep sense of loneliness, isolation, impaired social functioning, and anxiety.[19]

In the context of caring for a child with a rare neuromuscular disease, parents may seek normality for their child and their family while discovering ways to give voice to their child's and siblings' perspectives. However, some families may view caring for a loved one as a positive experience. When surveyed, parents said they reflected on the 'moral order' of their lives, and for many of these parents, the time spent with and caring for their child along with the constant threat of death brought a deeper appreciation for the value of life. Parents described the experience as enriching and rewarding, and stated that caring for their child resulted in a ''new level of spirituality.''[19]

Frequently, caregivers face significant ethical challenges to their values and preferences for care at various transition points in the disease trajectory, for example, whether to participate in genetic testing, enroll in clinical trials, initiate mechanical ventilation, or withdraw therapies.[19] Decisions of this nature, along with the overall strain of caring for a loved one, can lead to tension between the caregiver and the patient, as well as tensions across family relationships, as they struggle between hope and cure and the eventual fatality.[12, 20]

Caregiver competence or perceived competence in caring for a loved one can affect caregiver quality of life. A caregiver's perceived competence can be affected by many related variables, like family income, their loved one's quality of life, and balancing the demands of other family members. This underscores the importance of comprehensive training for caregivers, not only on caring for the ill individual, but in managing competing responsibilities. The functionality of the primary caregiver affects the ability of the rest of the family to function.[21]

A lifespan framework of family caregiving

The long-term, progressive nature of many rare diseases requires a family-centered lifespan framework of caregiving. With rare disorders that manifest in childhood, parents may live as long-term primary caregivers, even after their child enters adulthood.[21] Although many of the basic care demands are similar to those of children with more common conditions, rare disease caregivers face additional challenges associated with the complexities of care needs, assistance in everyday responsibilities, and fostering psychosocial health for all concerned.[22] There are personal, societal, medical, and institutional challenges that impede transition to independence, and families must work to incorporate these experiences into ongoing family life for years to come.[19,21]

Many family caregivers of children with rare neuromuscular disease find that extended care requires navigating the complex, frustrating, and fragmented array of services associated with transition of care from childhood to adulthood.[19] Family caregivers balance leading a 'normal life' with grieving daily, and the desire to appropriately discuss the future, death, and dying with others. At the same time they are challenged to gain information on and access to trained, compassionate care and services. One study of adult family caregivers of individuals with a primary malignant brain tumor found that a main predictor of caregiver burden was perception of their loved one's suffering, something caregivers often feel they have no control over.[23]

Caregivers of individuals with neurodegenerative diseases like HD face their own unique barriers.[17,24,25] The average age of onset for HD is 25 years and the average age of death is 57 years; there are no curative phases or treatments to slow the progression of the disease and extend life.[26] Therefore, individuals often require assistance for approximately 20 or more years. In prodromal stages, adult caregivers may not discuss the illness with employers, family, friends, and health care providers, to avoid the stigma associated with living with a rare disease.[25] Once diagnosed, care may be provided at home by the family or in a skilled nursing facility; however, most often local long-term care facilities are not flexible in meeting the needs of a person with HD, and may not be prepared to manage the behavioral issues associated with this condition.[20] In fact, in the United States there are only 12 HD Society of America Centers of Excellence dedicated to long-term care, which leaves families searching for appropriate care facilities and/or advocating for appropriate care for their loved ones.

For many rare diseases and conditions, the role of caregiver may extend across family members, with multiple individuals including partners, parents, at-risk siblings, and even at-risk children and teens providing care.[27,28] Teens acting in the caregiver role have a unique set of stresses and needs, and the effect of caregiving on the health of teens is a largely understudied area. The younger the caregiver, the higher the potential level of stress.[17] It is not uncommon for a teen to be caring for a parent or sibling with a heritable disease like HD, where they have the burden of decisional responsibility without the legal authority to enforce these decisions. The experience of caregiving at a young age along with, in some cases, the knowledge that they may also develop the condition, can lead to a high rate of depression and anxiety, and feelings of isolation from peers, as well as negative impacts on their own health.[28]

Genetics and the dilemma of disclosure

Approximately 80% of rare diseases are caused by genetic mutations, and approximately one-third of palliative care patients have conditions related to inherited genetic alterations.[1] For many individuals and family members with a rare disease or condition, genetic testing can be predictive in helping confirm or rule out a suspected genetic condition. Results may also determine a person's chance of developing or passing on a genetic disorder to children, and affect current and future approaches to health. Unfortunately, the use of predictive genetic testing for heritable disorders like HD is much lower than anticipated. Surveys of individuals at risk

for HD reported that 56%–81% would agree to undergo predictive testing.[29] However, 20 years after genetic testing was made available, uptake remained at 10%–20%, [30] although some recent reports suggest that uptake is increasing.[31] Speculation about the reasons for the low uptake of predictive testing for HD includes avoidant coping styles, single versus multipayer health care systems, stigmatization, and lack of legal protections against discrimination.[32]

Some rare diseases are only directly heritable in a small percentage of families, and this is where the opportunity to use predictive genetic testing may be overlooked. For example, 90% of individuals with ALS have no family history of the disorder, and present as an isolated case, termed sporadic ALS (SALS). The remaining 10% of persons with ALS have a close second family member with ALS, which is referred to as familial ALS (FALS). In some cases, FALS is masked and the diagnosis is not determined by a presymptomatic genetic test due to an incomplete family history, such as if the patient is adopted or the patient's parents died at a young age.[33]

Ideally, genetic testing should be conducted when the ill individual is still living, but this rarely occurs, making testing and risk assessment more challenging. Appropriate referral to genetic testing requires vigilance on the part of health care providers, with palliative/hospice care providers having the last opportunity to directly test the individual. However, genetic testing is often not incorporated into these programs due to time constraints, insufficient knowledge of referral pathways, or lack of consideration of referral.[34,35] The lowest rates of referral occur in socioeconomically disadvantaged and minority populations, which is concerning.[36]

Conversations about genetics may present ethical challenges due to the familial nature of genetic information. The benefits of genetic testing extend to the family, and therefore a balance must be struck between the rights of the individual versus the rights of family survivors. Some may see the knowledge generated from genetic testing as valuable information, where others may see it as a threat to their well-being and future. There is little known about how genetic risk affects the palliative care needs of rare disease patients and their families, no clear consensus on best practices for discussions of genetic risk, and little understanding of the most effective communication strategies for these conversations. With the growing need for advance care planning discussions throughout the trajectory of a rare disease, palliative care providers have a unique opportunity to facilitate conversations and reduce barriers. Smith stresses the need for clinicians to engage in meaningful advance care planning discussions, stating, ''If we want to honor our patients' wishes about the type of care they want to receive, we have to first discern those wishes.''[37]

Understanding the benefits of end-of-life and palliative care

Individuals with rare diseases and their families are some of the most vulnerable patients, who could benefit greatly from appropriate and timely palliative and end-of-life care. However, the purpose and goals of palliative care are commonly misunderstood. Lack of education on the palliative care approach may result in patients, families, and even clinicians confusing palliative approaches with end-of-life hospice care and death. Even when individuals are aware of palliative care, many do not seek services due to prohibitive availability or cost; age-appropriateness; or lack of collaboration, training, and education in rare diseases by providers and palliative care specialists. For example, in a survey of families caring for an individual with DMD, 85% of families were unaware of palliative care and its benefits. When available, palliative services were located in skilled nursing facilities, and these attended only half of the DMD individuals surveyed. Additional attendant care and case manager services were received by only 44% of patients, while less than 20% of individuals obtained respite care, transportation assistance, pain management, and hospice services.[38]

Rushton and Geller noted that misunderstandings regarding the meaning of the term 'palliative care' as well as a lack of awareness that palliative care may be provided alongside traditional treatments are major barriers to widespread adoption of palliative care principles. These areas should be the focus of research studies to demonstrate how palliative care principles are aligned with what clinicians already provide. Expanding the repertoire of skills, resources, and services that are offered to individuals and their families is vital.[19]

The lack of information about palliative care, together with the uncertainty inherent in a rare disease diagnosis, can lead to more aggressive treatments and poorer end-of-life and palliative care. Prigerson stated during the workshop, ''Not knowing what to do fuels the approach of doing more.'' For example, a rare cancer diagnosis can accentuate the difficulties of experiencing a life-limiting illness. Rare cancer caregivers were marginally more likely than common cancer caregivers to prefer aggressive treatment and more likely to report a decline in their own health in the final year of their loved one's life.[12] At the same time, rare cancer caregivers were significantly more likely to score higher on a scale of optimism, possibly due to diagnostic ambiguity, an uncertain disease trajectory, and lack of an evidence base; this optimism may explain the reluctance to engage in advance care planning and end-of-life discussions.[12] Research is vital that delineates (1) the factors affecting acceptance of a fatal rare cancer; (2) how to inform, educate, support, and advocate for individual needs; and (3) ongoing practices to improve care and encourage positive outcomes.

Effective communication of information between patients and families regarding all aspects of the illness can alleviate some of the effects of uncertainty. When informed patients discuss end-of-life care, they tend to accept that they are terminally ill, and will therefore possess more realistic survival estimates. Contrary to common belief, engaging in end-of-life discussions does not make ill individuals and their caregivers feel hopeless.[39] During the workshop, Teresi noted a lack of research-driven screening tools and information technologies to identify caregiver status in the context of rare diseases, and the need to develop these evaluations and technologies for education, communication, care coordination, and process and outcome assessment.

Addressing the Gaps

The goal of this workshop was to identify key issues and specific research questions to address knowledge gaps brought forth by the presentations and discussions throughout the day. Overall, there is a need to clarify the differences

between the rare disease experience and the 'common disease' experience. Research must establish what palliative interventions and/or models of care are effective in both situations, and when there is a need for an intervention tailored to a specific rare condition. During the workshop the following gaps and potential research areas were discussed (see Table 1).

Study design

When planning studies involving individuals with rare diseases, researchers may need to move beyond randomized, controlled trials to include other formats more appropriate to their research question, such as multisite pragmatic designs, case methodologies, mixed methods, or studies that consider co-occurring trajectories and/or that focus on mechanisms of action. The method of study can affect the accuracy of outcomes, and no one method will address all of the key issues. Multisite trials and research teams with the expertise to carry out multidisciplinary palliative approaches should be considered. There is also the uniqueness of the rare disease population to consider when designing studies. For example, because there may be a small number of individuals with a particular rare disease in one location, it may be difficult to recruit a sufficient number of study participants. Whether disease states should be combined together to increase power,

Table 1. Research Areas for End-of-Life and Palliative Care Science in Rare Disease Populations

Knowledge gap	*Research area to address gaps*
Study design	Use diverse study designs: multisite pragmatic, case methodologies, mixed methods, studies that consider co-occurring trajectories, and/or that focus on mechanisms of action.
	Address unique challenges of studying a rare disease population (small *n*, distinct groups).
	Establish the correct measures to answer key questions.
Consideration of caregivers	Extend the theoretical understanding of who in the individual's life is impacted by a rare disease diagnosis.
	Create a national definition of caregiver; establish suitability of a general definition for rare disease populations.
	Determine information needs of caregivers to inform design of effective tools and resources to improve their competence and ability to care for their loved one.
	Test integrated palliative care models as standard care for rare diseases.
Do no harm	Prevention of treatment-related adverse events.
	Ethical collection and use of research data.
	Identify situations where the gathering and possession of information may lead to harm for individuals and their families.
Ethnic and cultural differences	Improve understanding of the needs/wishes of ethnically diverse individuals and their families/caregivers.
	Determine the preferences and goals for care at the end of life of different ethnic/cultural groups.
	Develop culturally competent translations of interventions to facilitate individual and family understanding of palliative and end-of-life care.
	Design and test culturally adapted models of end-of-life and palliative care.
	Consider the potential for ethnic bias in study measures.
Communication	Research to improve the communication process and develop decision-making strategies to promote individualized, goal-directed care.
	Determine critical communication components (i.e., who should be involved in care discussions, discussion formats, optimal timing of initiating care discussions).
	Design family-centered decision-making strategies by addressing the communication processes surrounding complex medical needs (i.e., options for care, decisions such as withdrawal of life-sustaining treatment).
	Develop communication strategies to assist clinicians, individuals, and families assess the value of palliative care options, to promote informed decision making.
	Enhance communication processes between individuals, families, and clinicians to improve the understanding of palliative and and-of-life care.
	Fully examine decision making processes of parents and clinicians.
Transitions	Identify the truly important transitions that occur apart from chronological age.
	Determine optimal support strategies for children and their families along protracted disease trajectories.
	Ascertain available services and those that should be developed for children, adolescents, and young adults across different stages of their illness.
	Improve understanding of the dynamisms of decision making and the effect of emotion in parents.
	Develop child-centered interventions tailored by culture and family structure that adapt based on effectiveness at different stages in the disease trajectory.
	Establish how/when to involve children in care decisions and how to help families and clinicians hear the child's voice.
	Determine how to keep clinicians in sync so that patients and families do not receive mixed messages.

or groups studied separately to capture unique characteristics, should be considered.

Another research opportunity is the development and testing of interventions that address coordination and quality-of-care transitions across the palliative care continuum, a particular challenge in rare disease populations. Further, in some cases, appropriate measures may not exist to answer key questions such as, 'How do the needs of patients and families change over time?' 'What is the impact of the quality of care given to individuals with rare diseases?' and 'How should researchers measure the quality of informal caregiving?' Quality indicators of care could be designed that are tailored to caregivers of individuals with rare diseases.

Consideration of caregivers

There is a need to extend the theoretical understanding of who is involved when an individual is diagnosed with a rare disease; immediate as well as extended family caregivers must be considered in addition to the patient. Further, there is a lack of a clear, national understanding of whom and what defines a caregiver, and little information on the suitability of such general definitions for rare disease populations. With respect to support for caregivers, studies are needed to determine essential information for caregivers (i.e., 'What questions should they ask providers?') so that effective tools and resources may be developed to improve their knowledge, competence, and overall ability to care for their loved one. To accomplish this, studies must be carried out that include caregivers, using participatory methods and qualitative as well as quantitative study designs. Due to the distinctive nature of rare disease populations, unique sampling methods may need to be developed, i.e., innovative sampling methodologies and/or use of new technologies. Once interventions to assist caregivers are developed, investigators could determine the best ways to integrate palliative care models into standard care models for individuals with rare diseases.

Do no harm

Individuals with rare diseases that have limited or no known treatment may turn to the use of risky, experimental treatments with unproven benefits along with the unknown side effects.[40] Therefore, within the context of 'doing no harm,' investigators and clinicians must weigh the physical and psychological cost of aggressive or experimental care to individuals and their families. This is relevant both during and following the inevitable conclusion of the disease trajectory. In addition, issues such as the ethical collection and use of research data must be considered, along with situations where gathering and possessing information may lead to harm for the individual or their family. Individuals with heritable, rare disorders and their families should be allowed to choose whether genetic information should be obtained and shared with the individual and their family.

Ethnic and cultural differences

Until recently, research in the United States has been performed primarily in white, middle-class individuals; and as a result, research findings do not always sufficiently reflect the ethnic and cultural diversity of the country.[41,42] When designing studies, researchers should always consider the potential for ethnic bias in study measures. Further, family structures can differ by culture such that there may be dyads, triads, or multiple individuals involved in decision making regarding the care of an individual, and this can affect the needs and wishes of the family.[43,44] A systematic review of studies that evaluated racial/ethnic minority groups facing cancer revealed ''individuals' perceptions and preferences for medical decision making cannot be authentically examined outside the context of family and community—and that this may be especially so among ethnic minority patients.''[45]

Preferences and goals for care at the end of life in ethnically diverse populations are understudied. A recent report showed that non-Hispanic black family members were less satisfied with the end-of-life care of their loved one when compared to non-Hispanic white family members. Areas of difference included patient's pain relief, information provided about prognosis, referrals to specialists, the way treatments were performed, inclusion of the family in treatment decisions, and information given about tests.[46] Research can address gaps through development and testing of culturally adapted models of care. For example, in a study of African Americans coping with cancer, participants reported that an interactive communication intervention which facilitated Afrocentric coping skills such as relying on faith, promoting fictive kin support, highlighting positives, and encouraging flexibility in family roles resulted in significantly improved family member communication and satisfaction.[47] This illustrates the need for culturally competent interventions that facilitate individual and family understanding, so that care can be individualized based on cultural preferences.

Communication

A fundamental component of the palliative and end-of-life experience in individuals with rare diseases is communication within and between families and care teams. Clinical, behavioral, and translational research to inform improved communication processes and decision-making strategies that promote individualized, goal-directed care are needed. Also crucial are investigations to inform best practices for communication, such as who should be involved in discussions of palliative and end-of-life care, how discussions should be carried out, and the optimal timing of initiating communication on topics such as end-of-life wishes. Appropriate methods to measure these elements should also be developed. Findings by Goldsmith et al. further suggest that communication interventions should be guided by caregiver characteristics so that the needs and preferences of different caregiver types are met.[48]

Investigators should also examine the decision-making processes of parents and clinicians, so that communication is synchronized and families do not receive mixed messages. Communication strategies to assist clinicians, individuals, and families assess the value of palliative care options and promote informed decision making should be developed, as well as interventions that enhance the process of communication to improve the understanding of palliative and end-of-life care. In cases where there is an unknown disease trajectory, individuals with rare diseases and their caregivers may need to have multiple, different conversations regarding an advance care plan that incorporates many potential

scenarios. Thus, research focused on the timing and best practices for approaching ongoing conversations across the disease trajectory are needed to inform palliative care practice for this unique population.

Transitions

One element unique to caring for children and adolescents with rare diseases is the need for appropriate transitions of care. Transitions along the disease trajectory create many challenges, and these transitions must then be integrated into supporting the child in living as 'normal' a life as possible. Examples of this type of transition include conversion into the need for a wheelchair, feeding tube, or mechanical ventilation. Transitions may also occur within families, such as when a caregiver can no longer provide care to a loved one and another family member must take over the caregiving role. Research is needed to ascertain what services are available and what services still need to be developed for children and adolescents across different stages of their illness.

Decision support can be improved once it is understood how decisions are made and then remade; along the illness trajectory, the same decision may be made at multiple transition points. Parents of children with rare diseases face unique dilemmas in choosing treatments and care for their child, and weighing the risks and benefits of the choices available to them. There is a need to understand how emotion affects decision making in parents and how dynamic the process of decision making can be. Emotion and moral distress are missed if only the thinking process is studied.

Empowering families to be heard and engage in decision making when clinicians are not ready to hear them sets the situation up for failure. Greater understanding of the decision-making processes of clinicians and development of strategies to keep clinicians in sync with parents are needed to facilitate family-centered decision making across transition points. Further, studies can determine how best to design child-centered interventions that are tailored by culture, socioeconomic status, and family structure. Interventions should be tailored and adapted based on effectiveness at the particular stage in the disease trajectory, with the understanding that needs change as the illness progresses. Moreover, the question must also be answered of how best to involve the child in decisions about their care, as well as how to help families and clinicians hear the child's voice.

Conclusions

The goal of this article is to communicate the key points discussed during the workshop, to bring to the forefront scientific and research priorities for key issues related to palliative care for individuals with serious, advanced, rare diseases and their caregivers. A considerable amount of information was covered, gaps were identified and key issues and specific research questions put forward. The conversation brought to light a need for research to develop, build, and sustain disseminable solutions to the challenges identified in the context of improving palliative and end-of-life care. Individuals with rare diseases and their families and caregivers deserve high-quality end-of-life and palliative care support, and research is an important tool to determine the breadth and depth of the needs of this vulnerable population. The workshop provided a forum to identify research opportunities to move forward and build, over time, a spectrum of palliative care across the trajectory of illness focused on personalized approaches to the care of individuals, caregivers, and families facing rare diseases.

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