Ethical decision-making for children with neuromuscular disorders in the COVID-19 crisis

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Neurology® 2020;95:260-265. doi:10.1212/WNL.0000000000009936

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Abstract

The sudden appearance and proliferation of coronavirus disease 2019 has forced societies and governmental authorities across the world to confront the possibility of resource constraints when critical care facilities are overwhelmed by the sheer numbers of grievously ill patients. As governments and health care systems develop and update policies and guidelines regarding the allocation of resources, patients and families affected by chronic disabilities, including many neuromuscular disorders that affect children and young adults, have become alarmed at the possibility that they may be determined to have less favorable prognoses due to their underlying diagnoses and thus be assigned to lower priority groups. It is important for health care workers, policymakers, and government officials to be aware that the long-term prognoses for children and young adults with neuromuscular disorders are often more promising than previously believed due to a better understanding of the natural history of these diseases, benefits of multidisciplinary supportive care, and novel molecular therapies that can dramatically improve the disease course. Although the realities of a global pandemic have the potential to require a shift from our usual, highly individualistic standards of care to crisis standards of care, shifting priorities should nonetheless be informed by good facts. Resource allocation guidelines with the potential to affect children and young adults with neuromuscular disorders should take into account the known trajectory of acute respiratory illness in this population and rely primarily on contemporary long-term outcome data.

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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Glossary

COVID-19 = coronavirus disease 2019; **DMD** = Duchenne muscular dystrophy; **QALY** = quality-adjusted life year; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2; **SMA** = spinal muscular atrophy.

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread across the globe, straining resources in many countries, especially hospitals in general and critical care services in particular. Many people have abruptly had to confront the possibility that resource shortages may occur or are already occurring[1] and that painful, troubling decisions may need to be made on the spot and without warning in clinical care settings. Although the illness burden of COVID-19 is largely borne by adults, resource allocation issues nonetheless affect children and young adults, by virtue of the need to reallocate resources such as intensive care unit beds, ventilators, health care professionals, and personal protective equipment to adult care and by the abrupt ramp down of non–COVID-19 clinical efforts in medical centers around the country.[2] Additional stressors that have emerged for chronically ill children and young adults during the pandemic include restricted access to home health services and physical therapy.[3] Health care workers, policymakers, and government officials are all seeking ways in which ethical decisions can be made in a consistent, transparent, and equitable manner. These discussions are leading to the creation or updating of policies and guidelines by individual health systems and governments. Consideration of scarce resource allocation for children and young adults raises unique and vexing ethical challenges.

A broad spectrum of chronic neuromuscular disorders affects both children and adults. The diagnosis of inherited neuromuscular disorders with specific genetically defined subtypes has proliferated since the landmark discovery of *DMD* as the gene associated with Duchenne muscular dystrophy (DMD) in 1986[4]; scores of different genes are now associated with subtypes of disease categories such as muscular dystrophy and Charcot-Marie-Tooth disease. There is some predictability in the natural history for individual gene-specific disease subtypes, but significant variations in outcomes occur even among patients with mutations in the same gene. A classic example is Becker muscular dystrophy, which by definition is associated with milder mutations in *DMD* than DMD, but has a very broad range of motor outcomes ranging from loss of ambulation in early adulthood to ambulation throughout life.[5] Several other factors contribute to the complexity of assessing the clinical status and prognosis for an individual patient with a chronic neuromuscular disorder, especially in childhood and early adulthood, such as the integration of multidisciplinary care models and new molecular therapies that have significantly altered the natural history of some of these diseases, with more advances on the horizon.

To address the ethical considerations involved in the complex issues surrounding resource allocation affecting patients with neuromuscular disease in the setting of a pandemic, we assembled an ad hoc group of specialists with expertise in the following relevant fields: pediatric neurology, neuromuscular medicine, biomedical ethics, pediatric anesthesia/critical care, neonatology, and genetics.

COVID-19 and neuromuscular disorders

COVID-19 has rapidly spread throughout all corners of the globe, including every state in the United States (arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6).[6] Respiratory complications are serious and common in COVID-19, raising concerns about the impact of this disease on patients with chronic neuromuscular disease. We do not know whether children and young adults with underlying neuromuscular disease are especially vulnerable to respiratory complications of COVID-19; however, there are significant concerns as these individuals are generally at a high risk of acute and chronic superimposed respiratory illnesses.[7] For example, children and young adults with neuromuscular disease are at a higher risk of respiratory failure in the setting of influenza infection.[8] Little is known to date regarding the clinical course of symptomatic COVID-19 infection for such patients, including duration of mechanical ventilation and convalescence, but they require particular vigilance in light of their suspected risk profiles.[9] What is known, however, is that in general, children and young adults with chronic neuromuscular disease will often survive critical care admissions and recover without the need for continued invasive ventilation.[10]

In recent years, implementation of respiratory care guidelines for children and young adults with chronic neuromuscular disease has relied heavily on noninvasive ventilatory options, including bilevel positive airway pressure through mask interfaces and cough assist devices, often deferring the need for tracheostomy.[11–14] However, there are concerns about noninvasive ventilatory support in patients with COVID-19 due to a risk of aerosolization and viral spread.[15] Furthermore, emerging evidence suggests that the use of invasive ventilators should also be used judiciously in patients with COVID-19, especially in the setting of resource limitations.[16] These realities call attention to the importance of preventive infection control precautions in children and young adults with underlying neuromuscular disease, prompt evaluation of suspected COVID-19 infection in such individuals, and implementation of parallel isolation measures when additional respiratory support becomes necessary.

The long-term prognosis of children and young adults with neuromuscular disorders

In years past, the long-term prognosis of children and young adults diagnosed with chronic neuromuscular disorders was generally considered to be grim. Until the late 20th century, only comfort care was recommended and available for infants with spinal muscular atrophy type I (SMA I, previously known as Werdnig-Hoffman syndrome), and the offering of therapeutic and supportive interventions for children with DMD was fairly restrained. The life expectancy for affected children without any interventions is less than 2 years for SMA I and adolescence for DMD. However, multidisciplinary and interprofessional care with aggressive monitoring and treatment for the manifold complications of these diseases, particularly expanded options for respiratory support, has extended the life expectancy of affected children for years in the case of SMA I and into the 4th decade and beyond for DMD. Thus, the long-term prognosis for such diseases changed dramatically in the early 21st century, even before sophisticated new molecular therapies became available, to the point where an increasing number of affected patients survive well into adulthood.

The life expectancies and quality of life of individuals with SMA have also significantly improved in the context of supportive care that has become increasingly sophisticated and multidisciplinary in recent decades.[17] More recently, 2 novel therapies for SMA have been approved, one based on an antisense oligonucleotide approach[18] and the other on gene replacement delivered via an adeno-associated virus vector.[19] These new treatments have dramatically changed the outcomes of these patients by offering opportunities for palpable disease modulation. Children with SMA I who would otherwise die or progress to long-term around-the-clock ventilator support within a couple of years can now be expected to have marked improvement in respiratory function and motor abilities, far past that age.

The natural history of certain childhood neuromuscular disorders is not necessarily predictable by their initial presentations, and some infants who appear quite ill at birth may improve spontaneously with adequate supportive care and live well into adulthood. A classic example is congenital myotonic dystrophy. These infants often require respiratory and nutritional support at birth, but within a few weeks, many will improve to the point where such support is no longer needed.[20]

Granular genetic diagnostic capabilities have helped clinical investigators identify small molecule therapies that have changed the course of certain neuromuscular disorders dramatically. A prime example is congenital myasthenic syndrome, which now has been associated with over a dozen different genes whose protein products localize to the neuromuscular junction.[21] Certain genetic subtypes respond well to small molecule medications such as pyridostigmine, an acetylcholinesterase inhibitor, whereas the same drug worsens the symptoms of other subtypes. As respiratory distress and respiratory failure are cardinal manifestations of some congenital myasthenic syndrome subtypes, genetic diagnosis followed by appropriate drug treatment has had a significant impact on the outcomes of affected children; for example, pyridostigmine can prevent or mitigate apneic episodes in choline acetyltransferase deficiency.[22]

It is important for key decision-makers and policymakers to be aware of current developments and prognoses for children and adults with rare diseases such as inherited neuromuscular disorders so that individual patient decisions and policies are grounded by accurate clinical information. It is also important to remember that the able-bodied and usually developing frequently underestimate the health-related quality of life experienced by those with chronic medical disorders,[23] indicating the need for caution in using subjective estimates of future quality of life in developing institutional or public health policies. In principle, quality-adjusted life years (QALYs) are generated using patient-reported outcomes and thus take into account the perspective of patient stakeholders,[24] but the need for parental interpretation of quality of life for young and noncommunicative patients introduces opportunity for underestimating quality of life[25]; QALY determinations are subject to additional limitations[26] and are generally meant to be used for cost-effectiveness analysis, not resource allocation decisions in a public health crisis.[27]

An ethical approach to children and young adults with neuromuscular disorders in resource-limited settings

As recently as 2019, guidelines have made specific note of pediatric neuromuscular disorders with poor prognoses as a disease category that may be assigned a lower priority for critical care resource allocation in the setting of shortages.[28] The exclusion of large categories of patients from scarce resources due to underlying diagnoses fundamentally violates the ethical principle of justice, as such exclusions arbitrarily carve out some patients a priori for additional scrutiny, rather than equitably and empirically identifying markers of poor prognosis among all patients vying for that resource.[1] Some previously proposed triage protocols focus on short-term prognosis, i.e., likelihood of survival to hospital discharge.[29] One widely used scale that has been applied to adults in the COVID-19 pandemic is the Sequential Organ Failure Assessment.[30] In principle, such approaches could allay fears of age-related or disability-related bias, as they disregard the utility derived from amortizing investment of resources over more life-years saved and value-driven determinations of societal worth.

During the current COVID-19 pandemic, some guidelines have attempted to individualize decisions by recommending a point system based on a roster of criteria, which allows a single allocation algorithm to be applied over a variety of illnesses, recognizing that not every patient in need of critical care is infected by SARS-CoV-2.[31] Such systems are appealing because they appear to offer an approach to resource allocation that is fundamentally more just and offers a simple, formulaic approach that does not require a triage officer or triage committee to have working knowledge of the patient's specific disease. But a deeper consideration of the implications of such strategies reveals that they do not alleviate existing health disparities or eliminate the potential for value-based bias. Specifically, scores that take into account preexisting comorbidities among the factors that predict short-term survival[28] may put certain patients affected by certain social determinants of health, including chronic disability, at a disadvantage.[32] The desire for like patients to be treated alike by way of clinical scoring systems is understandable, but their intuitive appeal has the potential to be overemphasized in the face of considerable limitations.[33–36] These tools are generally developed as research tools with specific populations or diseases in mind, failing to account for heterogeneity in populations of critically ill children. Sequential iterations of 2 more general scales used in children, the Pediatric Index of Mortality and the Pediatric Risk of Mortality, were originally developed as reference standards for research and quality improvement and have shown widely divergent accuracies regarding mortality risk in various studies.[37,38] Overall mortality rates for acutely ill children are less than 3%, recognizing that mortality rates are higher in certain settings such as pediatric acute respiratory distress syndrome,[39] leading to difficulties in establishing statistically significant or clinically relevant criteria for triage.

Another concerning aspect of triage algorithms developed with a view toward a predominantly adult population of patients with viral respiratory failure is the emphasis on predetermined time points at which the effectiveness of the intervention is assessed. Such a strategy inevitably fails to take into account the natural history of a respiratory viral illness in a child with underlying respiratory insufficiency and introduces the risk that children and young adults with neuromuscular illness will be deemed treatment failures too early in their hospital course. In addition to the risk that lives will be lost unnecessarily, such a strategy has the potential to fuel self-fulfilling prophecies in which a biased impression of mortality in a population drives future decision making and reinforces this bias.[40]

Ethical guidance

We recommend that the following principles be observed both for decisions regarding individual patients and for the composition of policies and guidelines that will be used by hospitals and other health care systems. These principles should apply to children with chronic neuromuscular conditions and may also be adapted and extended for children with other chronic disabilities, along with adults with chronic neuromuscular conditions.

1. Transparency and accessibility of triage algorithms are essential to support a uniform and fair system of resource allocation across institutions and care settings, including home-based life-sustaining services.
2. A plurality of perspectives and expertise should be represented in the development and implementation of resource allocation policies to ensure that these policies are based on contemporary evidence and take into account the priorities of a diverse group of stakeholders.
3. Determination of eligibility for initiation and continuation of a scarce treatment should be based on the known, contemporary epidemiology of an individual patient's condition, including expected duration of illness and likelihood of return to previous baseline health-related quality of life. Limitations of current knowledge, especially in a rapidly emerging pandemic, should be acknowledged to avoid mistaken assumptions.
4. Existing or future disabilities should not be factors in allocation of scarce resources, given the inherent potential for bias and inequity in such value-based determinations.
5. Children and young adults whose underlying conditions impart the risk of more resource-intense treatment or a slower recovery from acute illness than their healthier peers, but nonetheless have similar chances of returning to their previous functional baseline, should not be disadvantaged in triage algorithms.
6. The underlying neuromuscular condition should be considered as a factor only if it imparts poor short-term survival to hospital discharge, in and of itself, comparable to the mortality thresholds for adults and other children, with the current level of support provided (including continuation of any home ventilatory support) and taking into account all available therapeutic options including modern molecular medicines and gene therapies.
7. Given that it is impractical to consider the innumerable complex chronic conditions that affect children and young adults, ad hoc consultation with clinicians with expertise in the relevant condition, but do not have direct responsibilities for care of the patient in question, should be considered to advise triage officers and triage committees for individual resource allocation decisions.

Conclusion

The medical community has partnered with families to make decisions around advanced technologies and other therapies to mitigate morbidities, contribute to longevity, and

normalize activities of daily living for children with chronic neuromuscular disorders. Novel gene-targeted and medical treatments continue to emerge, allowing some affected by neuromuscular diseases to participate in many routine aspects of family and community life throughout childhood and into adulthood. Even in resource-poor settings where advanced diagnostic and therapeutic technologies are not readily available, patients may often be diagnosed at least to the level of neuroanatomic localization and neuromuscular disease category based on a keen observation of clinical features, and this knowledge alone can provide valuable prognostic information that may have a positive influence on triage decisions. An equitable approach to the distribution of resources during times of crisis will ensure that decades of progress in the care of children with chronic neuromuscular disorders and other chronic disabilities will be preserved and extended in the years to come.

Acknowledgment

The authors appreciate early discussions of patient perspectives that one of the authors (PBK) had with Kathryn Bryant, Founding President and CEO of the Speak Foundation.

Study funding

No targeted funding reported.

Disclosure

Dr. Laventhal reports no disclosures. Dr. Graham has consulted for F. Hoffmann-La Roche AG, Biogen Inc., and Audentes Therapeutics and serves as an uncompensated board member for Cure SMA. Dr. Rasmussen has served on advisory committees for the Teva Pregnancy Registry, Solriamfetol Pregnancy Registry, and Gilenya Pregnancy Registry; has consulted for F. Hoffmann-La Roche AG; and receives grant support from the NIH and the Centers for Disease Control and Prevention. Dr. Urion has received honoraria from the American Academy of Pediatrics for contributions to AAP Grand Rounds and Elsevier for contributing chapters to Nelson's Textbook of Pediatrics. Dr. Kang has consulted for AveXis and ChromaDex; served on an advisory board for Sarepta Therapeutics; and received honoraria from the American Association for Neuromuscular and Electrodiagnostic Medicine (speaker at annual meeting), the American Academy of Neurology (speaker at annual meeting), the American Academy of Pediatrics (speaker at annual meeting), Brookes Publishing for a textbook chapter, Fondazione Telethon for serving on a grant review committee, the Institute for Clinical and Economic Review for advisory activities, the National Initiative for Cockayne Syndrome for serving on an advisory board, the NIH for serving on grant review committees, Wiley for serving as associate editor of *Muscle & Nerve*, and Wolters Kluwer for authoring topics for *UpToDate*. He receives grant support from the Centers for Disease Control and Prevention and from the Xtraordinary Joy Foundation. Go to Neurology.org/N for full disclosures.

Publication history

Received by *Neurology* April 27, 2020. Accepted in final form May 22, 2020.

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Naomi T. Laventhal, MD	University of Michigan, Ann Arbor, MI	Designed and conceptualized the study; participated in drafting the manuscript for intellectual content; and revised the manuscript for intellectual content
Robert J. Graham, MD	Boston Children's Hospital, Boston, MA	Revised the manuscript for intellectual content
Sonja A. Rasmussen, MD, MS	University of Florida, Gainesville, FL	Revised the manuscript for intellectual content
David K. Urion, MD	Boston Children's Hospital, Boston, MA	Revised the manuscript for intellectual content
Peter B. Kang, MD	University of Florida, Gainesville, FL	Designed and conceptualized the study; participated in drafting the manuscript for intellectual content; and revised the manuscript for intellectual content

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