Defining and Measuring Quality of Care in Rare Disease

An Assessment of the Rare Disease Quality Landscape

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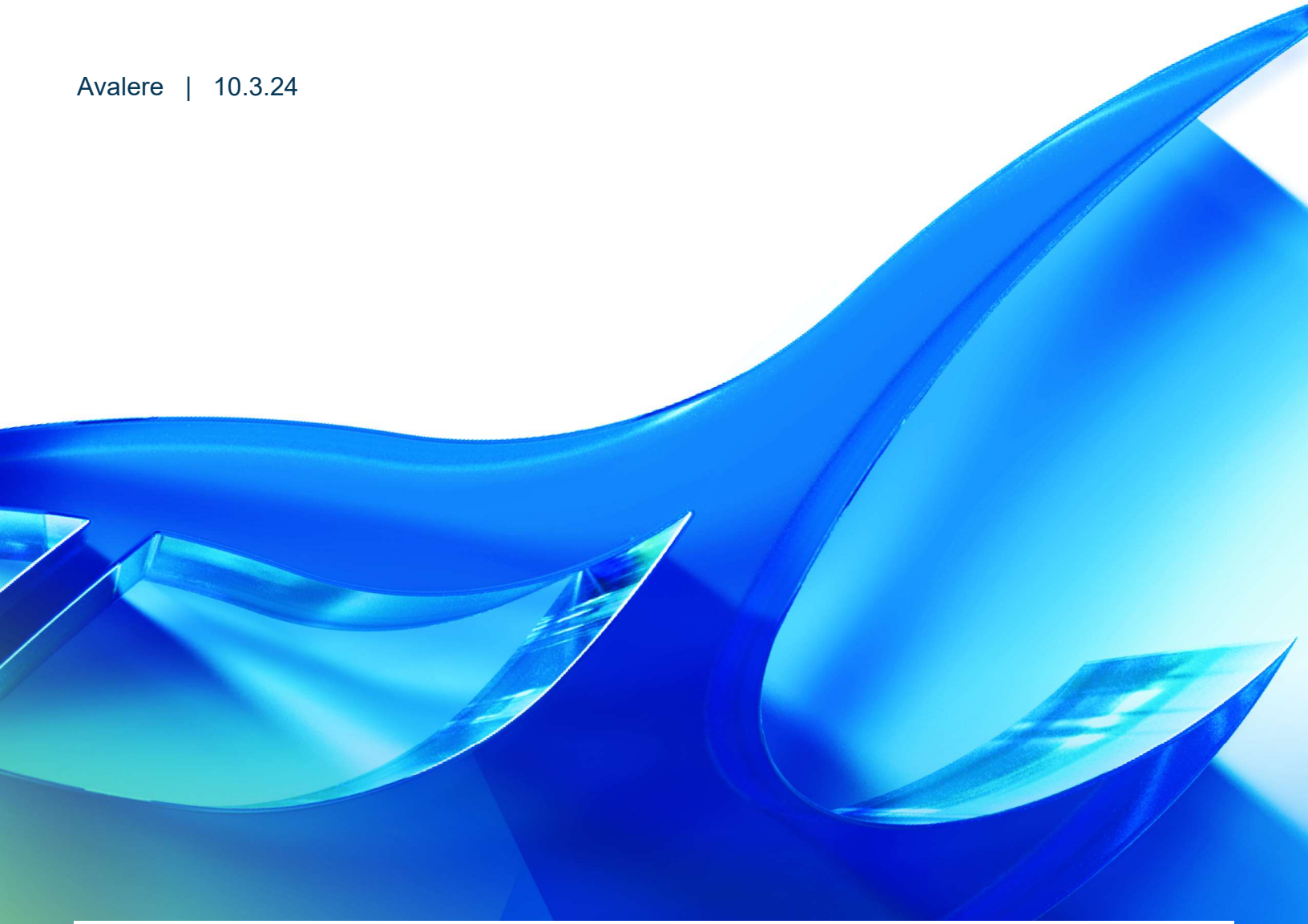

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Background

There are more than 7,000 rare diseases collectively affecting an estimated 25–30 million Americans,[1] a population size rivaling those of the most common chronic conditions. Individuals with rare disease face unique clinical circumstances that may put them at increased risk for poor health outcomes and adverse events compared to individuals with non-rare chronic diseases like diabetes or hypertension.

In a healthcare system optimized for "horses" rather than "zebras,"[2] individuals with rare disease wait four to five years on average for a correct diagnosis, though longer periods also occur.[3,4] During this time, patients may experience misdiagnosis, unnecessary procedures, emotional distress, and clinical deterioration. Initiation of proper treatment may be delayed, and in most cases treatment may not exist. In fact, only 5% of the over 7,000 known rare diseases have a Food and Drug Administration (FDA)-approved, disease-specific medication.[5,6] Even in cases where treatments are available, there are few clinical practice guidelines focused on rare diseases, and existing ones often rely on limited evidence.[7]

With such limited evidence on how best to deliver care, providers typically refer patients to highly specialized providers who have experience treating the condition. However, those specialized providers may only be available at major academic medical centers, which can be a significant barrier to accessing appropriate care.[8] And while all patients face exacerbated risks for poor outcomes during transitions of care, such as when moving from hospital to post-acute or ambulatory settings, these risks can be greater for individuals with rare conditions, especially because a lack of provider familiarity with their condition could lead to treatment interruptions or inappropriate treatment.[4] This can also occur when seeking treatment for other health needs unrelated to the individual's rare condition. If the provider is less familiar with the patient's rare condition, care decisions for other health needs may not consider the impact on the rare disease's exacerbation or progression.

These factors create unique challenges for achieving optimal quality; this is, care that is safe, effective, efficient, equitable, timely, and patient-centered.[9] With health systems held

1 Tisdale, A., Cutillo, C.M., Nathan, R. et al. The IDeaS initiative: pilot study to assess the impact of rare diseases on patients and healthcare systems. Orphanet J Rare Dis 16, 429 (2021). https://doi.org/10.1186/s13023-021-02061-3
2 Michael, Wes. (2020). Zebras Do Exist: The Diagnostic Odessey of Rare Disease Patients. Rare Patient Voice. https://rarepatientvoice.global/zebras-do-exist-the-diagnostic-odyssey-of-rare-disease-patients/
3 Salova M, Buch L, Kyei-Baffour B (2023). Shortening the Diagnostic Odyssey: Benefits, Barriers, and Solutions. Avalere. https://avalere.com/insights/shortening-the-diagnostic-odyssey
4 Willmen T, Willmen L, Pankow A, Ronicke S, Gabriel H, Wagner AD. Rare diseases: why is a rapid referral to an expert center so important? BMC Health Serv Res. 2023 Aug 23;23(1):904. doi: 10.1186/s12913-023-09886-7.
5 Research, C. for D. E. and. (2022). Rare Disease Cures Accelerator. FDA. https://www.fda.gov/drugs/regulatory-science-research-and-education/rare-disease-cures-accelerator
6 Fermaglich, L. J., & Miller, K. L. (2023). A comprehensive study of the rare diseases and conditions targeted by orphan drug designations and approvals over the forty years of the Orphan Drug Act. Orphanet journal of rare diseases, 18(1), 163. https://doi.org/10.1186/s13023-023-02790-7
7 Gittus, M., Chong, J., Sutton, A. et al. Barriers and facilitators to the implementation of guidelines in rare diseases: a systematic review. Orphanet J Rare Dis 18, 140 (2023). https://doi.org/10.1186/s13023-023-02667-9
8 NORD. (2020). Barriers to rare disease diagnosis, care and treatment in the US. National Organization for Rare Diseases (NORD). https://rarediseases.org/wp-content/uploads/2020/11/NRD-2088-Barriers-30-Yr-Survey-Report_FNL-2.pdf
9 Agency for Healthcare Research and Quality (AHRQ). (2022). Six Domains of Healthcare Quality. https://www.ahrq.gov/talkingquality/measures/six-domains.html

accountable for improving quality based on measures such as hospital readmissions or avoidable emergency department use, the collective impact of prioritizing the needs of rare disease patients presents an opportunity to improve the delivery system to reduce the incidence of adverse events and enhance quality of care. However, the fact that each rare disease population is very small, and the broader rare disease patient population is heterogeneous can obscure these commonalities and may complicate efforts focused on measuring quality, delivering high-value care, and achieving health equity for these individuals.

To determine whether and to what degree the core commonalities of rare disease care needs are addressed by existing quality improvement efforts and to identify opportunities to enhance rare disease care quality, Avalere conducted a landscape analysis of the existing quality measures, value-based care programs, and quality improvement initiatives aimed at rare disease.

Methods

Avalere conducted a targeted search to identify major features of the quality landscape specific to rare diseases such as quality measures, improvement programs, and evidence-based care guidelines. To ensure a comprehensive assessment, Avalere employed various tools:

- The Avalere Quality Measure Navigator® (QMN) tool, to identify both current and historical quality measures relevant to rare diseases and care transitions.
- UpToDate®, an evidence-based clinical decision support resource, to identify pertinent clinical guidance documents published after 2015.
- Publicly available resources such as PubMed, Google Scholar, and others to conduct a targeted search spanning the past eight years to uncover quality improvement initiatives, patient registries, and value-based care programs associated with rare diseases.

Results

From this analysis, Avalere identified 34 active quality measures, 17 quality improvement programs, and 26 evidence-based care guidelines focused on rare diseases. For context, there are over 2,500 fully developed quality measures in the QMN® database. Although there is not a straightforward method to count the total number of evidence-based care guidelines and quality improvement programs in existence, the Up-to-Date database alone has more than 850 disease-specific care guidelines.[10] Detailed results can be found in **Tables 1–3** of the Appendix.

Avalere found that patient advocacy groups led the few existing quality improvement programs and patient registries for rare disease. Among these programs, the predominant focus was on expediting time to diagnosis for individuals with rare diseases, achieved through initiatives like physician education. Such tools seek to enhance the recognition of diagnostic criteria (e.g., the thinkALS toolkit[11]). Other improvement efforts focused on establishing specialized treatment centers designed to mitigate geographic barriers to treatment. For example, the National Organization for Rare Diseases (NORD) Centers of Excellence[12] operates a network of US hospitals and medical institutions dedicated to the treatment and research of rare diseases, such as the Center for Rare Disease Therapy at the University of Pittsburgh Medical Center, which specializes in treatment for children with rare inherited metabolic disorders.

Despite efforts to expand rare disease-related measures, quality measures developed for rare diseases are not widely used or found in high-profile quality payment programs. Many of the rare disease measures identified have either been discontinued or are not integrated into Centers for Medicare and Medicaid Services (CMS) reporting programs. A high proportion of the measures identified focused on neurologic conditions in rare diseases; certain therapeutic areas are more likely to be championed by professional societies that prioritize quality initiatives, like the American Academy of Neurology (AAN).

Although few quality measures are directly focused on rare disease populations, it is notable that many commonly used, high-profile quality measures like readmissions, total cost of care, excess days in acute care, and emergency department utilization are indirectly impacted by rare disease outcomes. For instance, atypical hemolytic uremic syndrome (aHUS) can lead to poor outcomes in renal disease, which is a clinical domain that has multiple quality measures and value-based care initiatives such the Kidney Care Choices Model.

These findings indicate an overall lack of quality measurement and improvement programs focused on rare disease, as quality and value initiatives tend to focus on conditions that individually affect larger populations. The unintended effect is that diseases with smaller patient populations are excluded from quality assessments and initiatives focused on improving outcomes, despite the large collective burden of rare conditions.

10 Wolters Kluwer. https://assets.contenthub.wolterskluwer.com/api/public/content/8108df0df756450baf13586b815ae241?v=13d13b1d

11 Haendel, M., Vasilevsky, N., Unni, D., Bologa, C., et al. (2020). How many rare diseases are there?. Nature reviews. Drug discovery, 19(2), 77–78. https://doi.org/10.1038/d41573-019-00180-y

12 NORD Rare Disease Centers of Excellence. https://rarediseases.org/center-of-excellence/

Discussion

Given the challenges of ensuring high-quality care and improving outcomes for patients with rare diseases, concerted efforts are needed to understand, measure, and improve quality of care for these patients. Although measuring quality or developing quality-focused initiatives for such a large number of individual rare diseases may seem complex, nearly all individuals with rare diseases have similar care needs and challenges. Thus, there is a clear opportunity for stakeholders to consider rare diseases collectively rather than individually. Referencing existing campaigns (e.g., NORD's "Alone we are rare. Together we are strong") in a strategy for advancing quality could increase the likelihood of investment and adoption by major stakeholders. Such a strategy could include assembling evidence-based approaches to accelerating diagnosis, increasing access to specialized care, adopting rare disease-tailored care coordination, and improving communication between a patient's providers and rare disease quality programs, certifications, and payment models.

The advancement of quality measures is another strategy that is relevant for multiple stakeholders, especially considering recent prioritization of achieving health equity across CMS programs.[13] Quality measures are powerful tools for incentivizing care transformation. Use of quality measures in payment programs (e.g., federal pay-for-performance, value-based payment) has shown to positively influence care transformation and drive care quality and patient outcomes. Quality measures for common conditions (e.g., heart failure, pneumonia) that address care coordination, such as readmissions measures, are among the most closely watched and incentivized measures. Care coordination is especially relevant for individuals with rare diseases, as their specialized medical needs require care from specialists and practitioners across different healthcare settings, often extended over a lifetime. In addition, over half of all individuals with rare diseases are children, creating complexity and risk when transitioning from pediatric to adult healthcare. Analyzing the health outcomes of individuals with rare disease for existing quality measures (e.g., readmissions, healthcare resource use), in addition to indirectly related quality measures (e.g., patient-reported outcomes, patient experience) could shed light on disparities and support the design of effective interventions and care models for these populations.

Deriving real-world evidence (RWE) from registries presents another opportunity to advance care quality. In addition to serving as a foundation for designing quality measures, RWE from registries can support consensus-building and the establishment of evidence-based care guidelines for high-quality care of rare disease patients. Identified rare disease clinical guidelines are focused on individual diseases, may be based on limited evidence, and tend to rely on the professional experience of providers. With better data on the extent of the quality gap and evidence for what models and interventions work best, stakeholders can develop evidence-based improvement plans, toolkits, and resources to help providers deliver optimal care for all rare patients.

13 "CMS Framework for Health Equity." CMS.gov, July 2023. https://www.cms.gov/priorities/health-equity/minority-health/equity-programs/framework.

Areas for Further Research

This landscape analysis uncovered gaps in defining quality standards and quality measurement for rare disease and offers an opportunity for advocates to band together across rare diseases to advance care quality.

In addition, research is needed to understand how delays in diagnosis impact patient outcomes, quality of care, and patient safety. While it is known that diagnostic delays can lead to treatment delays, clinical deterioration, irrecoverable loss of function, and/or potentially direct harm from misdiagnosis, retrospective analysis of large cohorts has proven challenging due to difficulty pinpointing the onset of symptoms in standard data sets. Delayed and missed diagnosis also means that our understanding of the true prevalence of rare diseases is limited. Improving the diagnostic process is an important element in improving care quality, as patients cannot benefit from high-quality rare disease care until they have an official rare disease diagnosis.

These actions can drive a foundational understanding of quality outcomes in rare disease, the evidence-based best practices to improve those outcomes, and the specific quality measurement gaps in rare disease. The development of a unifying framework for rare disease quality could prove transformative for the millions of Americans living with rare disease who may be struggling to manage their conditions in a healthcare environment that is not designed to care for their unique needs.

Appendix

Below are quality measures, quality improvement programs, and evidence-based care guidelines identified by Avalere's search, conducted in 2023. This list is not intended to be exhaustive.

Table 1: Quality Measures Focused on Rare Disease

Measure Title	Measure Status	Regulatory/Accreditation/Payment Program
Quality ID #386: Amyotrophic Lateral Sclerosis (ALS) Patient Care Preferences	Active	Merit-based Incentive Payment System (MIPS) 2023
ALS Multidisciplinary Care Plan Developed or Updated	Inactive	N/A
Patients with DMD Prescribed Appropriate Disease Modifying Pharmaceutical Therapy	Inactive	N/A
Falls screening (aggregation of AAN disease specific falls measures)	Active	N/A
Quality of Life Outcome for Patients with Neurologic Conditions	Active	MIPS Qualified Clinical Data Registry (QCDR)/Axon Registry 2023
Transcranial Doppler Ultrasonography Screening Among Children with Sickle Cell Anemia	Active	N/A
Antibiotic Prophylaxis Among Children with Sickle Cell Anemia	Active	N/A
Hydroxyurea Use Among Children with Sickle Cell Anemia	Active	N/A
Inappropriate Use of Antiviral Monotherapy for Bell's Palsy (Inverse Measure)	Active	N/A
Bell's Palsy: Inappropriate Use of Magnetic Resonance Imaging or Computed Tomography Scan	Active	MIPS QCDR/American Academy of Otolaryngology – Head And Neck Surgery Foundation Reg-Ent Registry 2023
Hematology: Myelodysplastic Syndrome (MDS) and Acute Leukemias: Baseline Cytogenetic Testing Performed on Bone Marrow	Active	N/A
Quality ID #67: Hematology: Myelodysplastic Syndrome (MDS) and Acute Leukemias: Baseline Cytogenetic Testing Performed on Bone Marrow	Active	N/A
Hematology: Myelodysplastic Syndrome (MDS): Documentation of Iron Stores in Patients Receiving Erythropoietin Therapy	Active	N/A
Quality ID #68 (NQF 0378): Hematology: Myelodysplastic Syndrome (MDS): Documentation of Iron Stores in Patients Receiving Erythropoietin Therapy	Active	N/A
Incorporating results of concurrent studies into Final Reports for Bone Marrow Aspirate of patients with Leukemia, Myelodysplastic syndrome, or Chronic Anemia	Active	MIPS QCDR/MSN Healthcare Solutions LLC 2023
MD Multidisciplinary Care Plan Developed or Updated	Inactive	N/A
Scoliosis Evaluation Ordered	Inactive	N/A
Patient Queried about Pain and Pain Interference with Function	Inactive	N/A
Nutritional Status or Growth Trajectories Monitored	Inactive	N/A

Measure Title	Measure Status	Regulatory/Accreditation/Payment Program
Quality ID #268: Epilepsy: Counseling for Women of Childbearing Potential with Epilepsy	Active	MIPS 2023
Counseling for Women of Childbearing Potential with Epilepsy	Active	N/A
267 Epilepsy: Documentation of Etiology of Epilepsy or Epilepsy Syndrome	Inactive	N/A
Measure #266 Epilepsy: Seizure Type(s) and Current Seizure Frequency(ies)	Inactive	N/A
Depression Outcome for Patients with MS	Active	N/A
Multiple Sclerosis (MS) Diagnosis	Active	N/A
Comparison MRI Within 24 Months of MS Diagnosis	Active	N/A
Current MS Disability Scale Score	Active	N/A
Fall Risk Screening for Patients with MS	Active	N/A
Maintained or Improved Baseline Quality of Life for Patients with MS	Active	N/A
Cognitive Impairment Testing for Patients with MS	Active	N/A
Fatigue Outcome for Patients with MS	Active	N/A
Exercise and Appropriate Physical Activity Counseling for Patients with MS	Active	MIPS QCDR/Axon Registry 2023
Screening for Psychiatric or Behavioral Health Disorders	Active	N/A
Idiopathic Intracranial Hypertension: Improvement of mean deviation or stability of mean deviation	Active	N/A
Quality of Life Outcome for Patients with Epilepsy	Active	N/A
Assessment and Management of Muscle Spasticity—Inpatient	Active	N/A
Management of Muscle Spasticity--Outpatient	Active	N/A
Adherence to Non-Infused Disease- Modifying Agents Used to Treat Multiple Sclerosis (MS)	Active	2023 URAC Pharmacy Benefit Management
Quality of Life Outcome for Patients with Neurologic Conditions	Active	MIPS QCDR/Axon Registry 2023
Comprehensive Epilepsy Care Center Referral or Discussion for Patients with Epilepsy	Active	MIPS QCDR/Axon Registry 2023
Patient reported falls and plan of care	Active	MIPS QCDR/Axon Registry 2023
Closing the Referral Loop - Critical Information Communicated with Request for Referral	Inactive	N/A
Quality ID #374: Closing the Referral Loop: Receipt of Specialist Report	Active	MIPS 2023

Table 2: Rare Disease Quality Improvement Programs

Program/Initiative Name	Organization	Focus
NORD Rare Disease Centers of Excellence	NORD	Diagnosis, care coordination
Myasthenia Gravis Foundation of America (MGFA) Global Patient Registry	MGFA	Research
Axon Registry	AAN	Research
Rare Disease Registry Program	National Center for Advancing Translational Sciences	Research
Newborn Screening Quality Assurance Program	Centers for Disease Control	Diagnosis

Program/Initiative Name	Organization	Focus
National Pediatric Cardiology Quality Improvement Collaborative (NPC-QIC)	NPC-QIC	Transitions of care
RARE Toolkit	Global Genes	Diagnosis, patient education
ThinkALS Toolkit	ALS Association	Diagnosis
Genetic Disorder of Mucociliary Clearance Consortium	National Center for Advancing Translational Sciences	Diagnosis
Cystic Fibrosis Foundation Care Centers	Cystic Fibrosis Foundation	Care coordination
Congenital Heart Defects Toolkit	Centers for Disease Control's Congenital Heart Public Health Consortium	Care coordination, transition of care
ACCESS Telemedicine Model	University of New Mexico Health Sciences Center	Value-based care, access to care
MIPS Value Pathway: Supportive Care for Neurodegenerative Conditions	CMS	Shared decision-making
Coordination of Rare Diseases at Sanford	Sanford Health	Research
The Global Paroxysmal Nocturnal Hemoglobinuria (PNH) Patient Registry	The Aplastic Anemia and MDS International Foundation	Research
Congressionally Directed Bone Marrow Failure Research Program	The Aplastic Anemia and MDS International Foundation	Research
LAL-D Registry	Alexion	Research

Table 3: Evidence Based Care Guidelines

Title	Guideline Developer	Guidance Type	Population
An international consensus approach to the management of aHUS in children	HUS International	Consensus Approach	Pediatric
Hypophosphatasia in Adults: Clinical Assessment and Treatment Considerations	American Society for Bone and Mineral Research	Clinical Assessment	Adult
Orbital/Peri-Orbital Plexiform Neurofibromas (OPPN) in Children with Neurofibromatosis type 1: Multi-disciplinary Recommendations for Care	OPPN Working Group	Consensus Approach	Pediatric
When does a PNH clone have clinical significance?	American Society of Hematology	Practice Guidelines	Pediatric and adult populations
Current Updates on the Management of AL Amyloidosis	N/A	Update to Clinical Guidelines	Pediatric and adult populations
Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria	The American Society of Hematology	Update to Clinical Guidelines	Pediatric and adult populations
International consensus diagnostic criteria for neuromyelitis optica spectrum disorders	AAN	Consensus Approach	Pediatric and adult populations
International Consensus Guidance for Management of Myasthenia Gravis	AAN	Consensus Approach	Pediatric and adult populations

Title	Guideline Developer	Guidance Type	Population
Practice advisory: Thymectomy for myasthenia gravis (practice parameter update)	AAN	Practice Guidelines	Pediatric and adult populations
Myasthenia gravis: Association of British Neurologists' management guidelines	Association of British Neurologists	Practice Guidelines	Pediatric and adult populations
Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation	N/A	Consensus Approach	Pediatric
Health Supervision for Children With Neurofibromatosis Type 1	American Academy for Pediatrics	Clinical Report	Pediatric
Initial assessment and ongoing monitoring of lysosomal acid lipase deficiency in children and adults: Consensus recommendations from an international collaborative working group	N/A	Consensus Approach	Pediatric and adult populations (excluding infants)
Paroxysmal Nocturnal Hemoglobinuria	N/A	Continuing Education Activity	Pediatric and adult populations
ISTH guidelines for the diagnosis of thrombotic thrombocytopenic purpura	International Society on Thrombosis and Haemostasis	Practice Guideline	Pediatric and adult populations
Treatment of mucopolysaccharidosis type II (Hunter syndrome): a Delphi derived practice resource of the American College of Medical Genetics and Genomics (ACMG)	ACMG	Practice Resource	Pediatric and adult populations
Bone Densitometry in Children and Adolescents	American Academy of Pediatrics	Clinical Report	Pediatrics patients with bone demistronomy
Nutrition management guideline for propionic acidemia: An evidence- and consensus-based approach	Southeast Regional Genetics Network, Genetic Metabolic Dieticians International	Consensus approach	Pediatric and adult populations
Nutrition management guideline for very-long chain acyl-CoA dehydrogenase deficiency: An evidence- and consensus-based approach	Southeast Regional Genetics Network, Genetic Metabolic Dieticians International	Consensus Approach	Pediatric and adult populations
Management of metastatic retroperitoneal sarcoma: a consensus approach from the Trans-Atlantic Retroperitoneal Sarcoma Working Group (TARPSWG)	TARPSWG	Consensus Approach	Pediatric and adult populations
Dyskeratosis Congenita and Telomere Biology Disorders:	Dyskeratosis Congenita Outreach, Inc	Practice Guideline	Pediatric and adult populations

Title	Guideline Developer	Guidance Type	Population
Diagnosis and Management Guidelines			
Good practice statements for the clinical care of patients with thrombotic thrombocytopenic purpura	International Society of Thrombosis and Hemostasis	Practice Guideline	Pediatric and adult populations
Consensus guidelines for newborn screening, diagnosis and treatment of infantile Krabbe disease	N/A	Consensus Approach	Newborn infants
Challenges in the diagnosis of hemophagocytic lymph histiocytosis: Recommendations from the North American Consortium for Histiocytosis (NACHO)	NACHO	Practice Guideline	Pediatric and adult populations
The Mayo Clinic Histiocytosis Working Group Consensus Statement for the Diagnosis and Evaluation of Adult Patients With Histiocytic Neoplasms: Erdheim-Chester Disease, Langerhans Cell Histiocytosis, and Rosai-Dorfman Disease	The Mayo Clinic Histiocytosis Working Group	Consensus Approach	Pediatric and adult populations

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