REVIEW

Recommendations for the Management of Initial and Refractory Pediatric Status Dystonicus

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ABSTRACT: Status dystonicus is the most severe form of dystonia with life-threatening complications if not treated promptly. We present consensus recommendations for the initial management of acutely worsening dystonia (including pre–status dystonicus and status dystonicus), as well as refractory status dystonicus in children. This guideline provides a stepwise approach to assessment, triage, interdisciplinary treatment, and monitoring of status dystonicus. The clinical pathways aim to: (1) facilitate timely recognition/triage of worsening dystonia, (2) standardize supportive and dystonia-directed therapies, (3) provide structure for interdisciplinary cooperation, (4) integrate advances in genomics and neuromodulation, (5) enable multicenter quality improvement and research, and (6) improve outcomes. © 2024 International Parkinson and Movement Disorder Society.

Key Words: dystonia; status dystonicus; childhood-onset movement disorders; deep brain stimulation; clinical pathway

Introduction

Dystonia is a hyperkinetic movement disorder characterized by sustained or intermittent muscle contractions leading to repetitive twisting movements, abnormal postures, or both.[1,2] Dystonia severity often fluctuates along a spectrum from mild and tolerable to severe and life-threatening. Status dystonicus (SD), the most severe

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Relevant conflicts of interest/financial disclosures: A.F. has received grants/research support from Boston Scientific, DMRF – Canada, and Medtronic, and honoraria/consultation fees from Abbott, Boston Scientific, Ipsen, Medtronic, and Merz. D.E.-F. has received speaker honoraria from The Movement Disorders Society and the Taiwan Society of Child Neurology, and consulting fees from Guidepoint LLC, the University of Texas, the Telethon Foundation, and the German Center for Neurodegenerative Diseases (DZNE). C.G. has received honoraria/consultation fees from Medtronic and Ipsen.

Received: 3 November 2023; **Revised:** 7 March 2024; **Accepted:** 11 March 2024

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.29794

form of dystonia, is a medical emergency with significant morbidity, including metabolic derangement, respiratory/bulbar dysfunction, fractures, and pain.[3,4] Children in SD often require care in the intensive care unit (ICU) for sedative infusions, airway management, and other lifesaving procedures. Up to 12.5% of severe cases of SD result in death.[5]

Although SD is more common in pediatric dystonia, precise data on its prevalence and incidence in children are lacking.[3,6] Previous literature distinguished SD as dystonia in which the child cannot tolerate lying still or sleeping, and displays end organ changes (eg, rhabdomyolysis and acute kidney injury).[7,8] SD may emerge insidiously from a precursor entity, termed pre–status dystonicus (pre-SD; Table 1), which involves worsening dystonia without end organ involvement or airway compromise.[8,9] Refractory SD is distinguished as SD that persists despite attempted drug therapy and displays one or more life-threatening complications. SD is frequently observed in children with pre-existing dystonia secondary to neurodevelopmental syndromes, ranging from acquired causes (eg, dyskinetic cerebral palsy) to monogenic disorders (eg, DYT-*TOR1A*, *GNAO1*-related disorder,[10] *KMT2B*-related disorder,[11] or *ARX*-related disorder).[12] SD often ensues in the setting of triggers, including intercurrent illness, fever, dehydration, pain, and discomfort.[6,7] Rarely, SD can present as the first significant movement disorder manifestation of a variety of conditions, including genetic forms of dystonia, inherited metabolic disorders (eg, glutaric aciduria type 1,[13] Lesch–Nyhan syndrome,[14] pantothenate kinase–associated neurodegeneration),[15] or infectious/inflammatory central nervous system disorders (eg, infectious or autoimmune encephalitis).[16]

Worsening dystonia can be difficult for clinicians to recognize and treat. Even once established, it is often challenging to swiftly implement the next steps in management. Despite previous publications that provide tools for assessing severity and recommendations for general management,[7,8,17] there is still a need for comprehensive and systematic guidelines to treat SD in children. To address this unmet need, interdisciplinary working groups at The Hospital for Sick Children (Toronto, ON, Canada) and Boston Children's Hospital (Boston, MA, USA) undertook a literature review, evaluated institutional experiences, and developed clinical pathways. These pathways underwent a multistep consensus process, refining them based on multidisciplinary input provided by relevant teams, stakeholders, and patient safety and quality improvement initiatives (Supporting Information Data S1).

We present the resultant pathways designed to guide the evaluation and management of pre-SD, SD, and refractory SD in both inpatient and ICU settings. We sequentially outline our consensus recommendations, with the goals of (1) facilitating timely recognition and triaging of patients to a suitable level of care, (2) standardizing supportive and dystonia-directed therapies, (3) establishing structured monitoring protocols, (4) incorporating recent advances in genomics and deep brain stimulation (DBS), (5) enabling quality improvement initiatives and (6) enhancing patient outcomes.

TABLE 1 *Definition of relevant terminology in the spectrum of status dystonicus*

Term	Definition
Pre–status dystonicus	A child demonstrating worsening dystonia but without end organ involvement or airway compromise. They may be able to achieve intermittent sleep in this phase; however, it could be fragmented or easily disrupted by dystonia. Generally grades 2–3 on the DSS.
Status dystonicus	Worsening dystonia over 20 min, characterized by discomfort, tachycardia, and diaphoresis, with the presence of one or more end organ metabolic decompensations (hyperthermia, major electrolyte abnormalities, renal failure, myoglobinuria, or elevated serum CK level). Generally grade 4 on the DSS.
Refractory status dystonicus	Status dystonicus that persists despite attempted drug therapy and displays one or more life-threatening complications (bulbar weakness, compromised upper airway patency, exhaustion/pain, metabolic imbalances, renal or respiratory failure). Refractory status dystonicus generally requires care in the ICU setting. Generally grades 4–5 on the DSS.
Resolution of status dystonicus	Dystonia that has improved to grade 1 or 2 on the DSS for a sustained period of time (eg, >24 h), in the absence of infusions. Often this allows for de-escalation from ICU level of care.

Note: Major electrolyte abnormalities are defined as hyperkalemia >5.5 mEq/L. Renal failure is defined as serum creatinine >1.5× baseline and urine output <0.5 mL/kg/h for 6–12 h. Respiratory compromise is defined as the need for respiratory support in the form of continous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) or intubation/mechanical ventilation.
Abbreviations: DSS, dystonia severity scale; CK, serum creatine kinase level; ICU, intensive care unit.

Recommendations for Pediatric SD

Tools for Assessing and Monitoring Dystonia Severity

Managing SD hinges on two key principles: (1) early recognition and (2) prompt treatment. Early recognition

facilitates timely management, effective communication within the care team, and appropriate triaging. This aspect aligns with other acute neurological emergencies, such as stroke or status epilepticus. The unique challenge in SD lies in its gradually worsening and fluctuating initial phase, distinguishing it from more binary presentations such as seizures. In addition, we acknowledge that there are nuances in the phenomenology of SD and other hyperkinetic movement disorder emergencies (eg, complex hyperkinetic crises in *GNAO1*-related disorder or *N*-methyl-D-aspartate receptor encephalitis, which can also encompass severe chorea). Our approach applies broadly because first steps are the same before treatment, which can later be tailored toward the leading phenomenology and etiology. Accurate assessment and close monitoring of dystonia severity are crucial to gauge progression, guide treatment decisions, and evaluate response to interventions. Beyond video recordings and informal reports from families, we propose two standardized strategies: the Dystonia Severity Scale (DSS) and the sleep–wake dystonia diary.

Dystonia Severity Scale (DSS)

The assessment of dystonia severity commonly relies on the use of the DSS, previously published by Lumsden et al in 2013.[7,8] For the purpose of the current consensus recommendations, we have adapted a modified version of the DSS, with appropriately mapped treatment guidelines, in Figure 1. The use of the DSS facilitates clinical decision-making among members of the care team. A common theme in prior literature has been the lack of clearly defined criteria for when a patient is in "pre-SD," "SD," or "refractory SD." We recognize that because of the fluctuating nature of the condition, this is a continuum rather than discrete stages. For ease of communication, we developed definitions of when a patient should be considered in each of these categories (Table 1).

Sleep–Wake Dystonia Diary

To streamline tracking of SD, we recommend a sleep–wake dystonia diary. Although a previous version of this listed five stages,[7,8] our clinical experience suggests that this poses a challenge for families and nursing staff to maintain. Instead, we propose simplifying the patient's state to three categories: (1) asleep, (2) awake and settled, and (3) awake and unsettled (Supporting Information Data S2). The diary is kept bedside and reviewed during rounds, akin to seizure count charts in epilepsy monitoring units. The diary may become integrated into the electronic medical record, allowing prompt correlations with vital signs and the medication administration record. The diary provides valuable information for assessing effects of medications/sedatives and escalation or de-escalation of care. Finally, the tool fosters cooperative care alliances by empowering caregivers.

Acute Dystonia Clinical Pathway

Next, we outline key components of the Acute Dystonia Clinical Pathway, a comprehensive approach to pre-SD or SD (DSS grades 3 and 4) across outpatient, emergency department, and inpatient ward settings (Fig. 2).

Step 1: Determine Dystonia Severity

The initial approach focuses on triaging dystonia severity based on the DSS (Fig. 1) and on conducting a focused history/physical examination (Supporting Information Data S3). If there is respiratory distress and/or significant metabolic derangement, a critical care team evaluation should be prioritized. Next, management along the "ABCD" mnemonic should be initiated without delay and should be revisited frequently: *a*ddress triggers, *b*egin supportive care, *c*alibrate sedation, and administer *d*ystonia-specific medications.[18] These steps should be implemented concurrently.

Step 2: Understand Baseline Dystonia; Search for and Address Triggers for Worsening Dystonia

This step builds on the focused history to identify the underlying etiology of dystonia and acute triggers, performing a comprehensive physical examination, and ordering relevant laboratory tests to identify triggers (Fig. 1, Supporting Information Data S3). Identifying triggers is vital, because about two thirds of SD cases are triggered by common factors, many of which occur in a hospital setting.[4,6,19,20] The history should also include asking about any personalized dystonia action plan and pertinent details about prior medications, including medications that may worsen dystonia (eg, neuroleptics) and recent medication changes.

Step 3: Initiate Supportive Measures

Supportive care should be initiated concurrently with the patient's evaluation (Fig. 2).[8,18] Multiple factors can worsen dystonia, which may lead to an unfortunate cycle where dystonia triggers pain, hyperthermia, dehydration, and metabolic compromise, provoking further dystonia and causing ongoing decompensation. Repeated evaluation of metabolic markers (creatine kinase level, renal function) and search for infection/musculoskeletal pain/constipation and ongoing triggers are important. Care should be taken to position the patient optimally and minimize handling that may exacerbate dystonia. Antipyretics, analgesics, and antimicrobial therapy should be provided as appropriate.

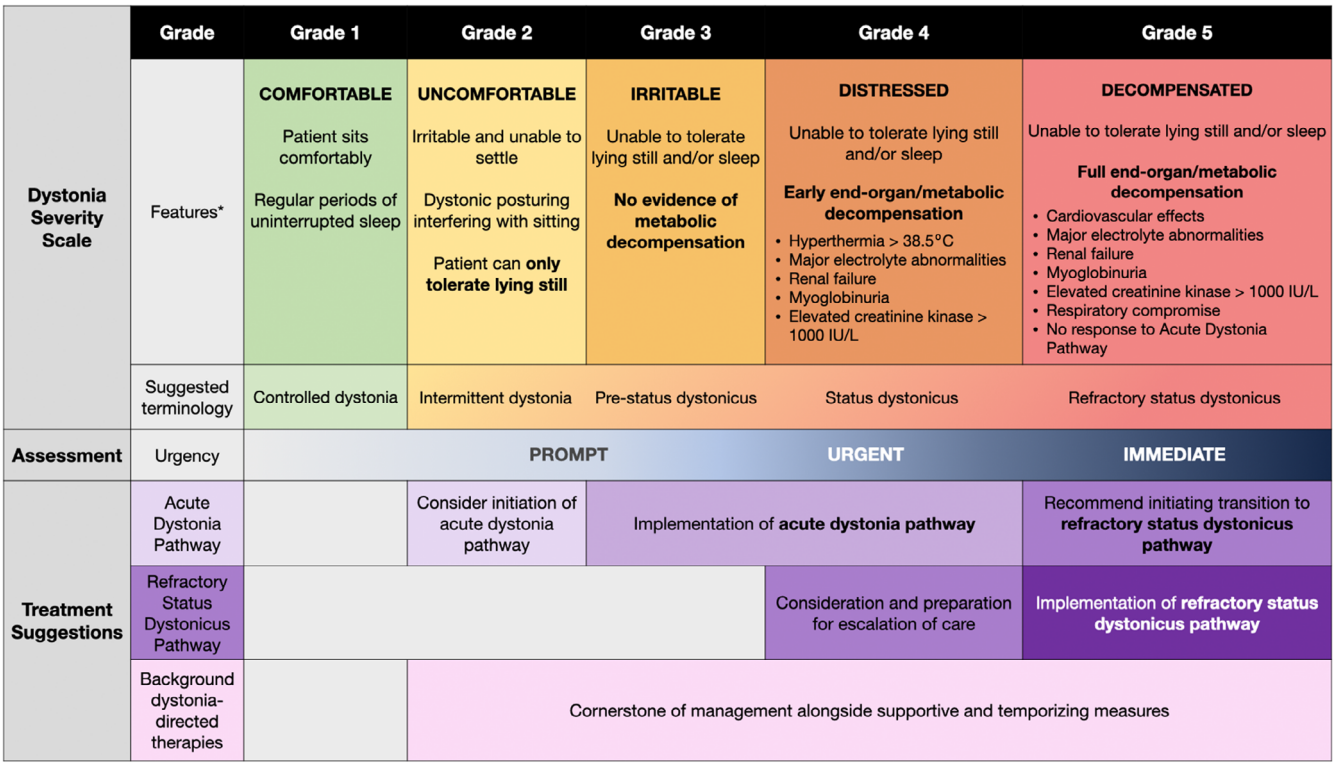

FIG. 1. Dystonia severity scale. The scale is used as a supplemental tool to determine severity of dystonia for the purposes of triaging pathway initiation. We have added additional parameters to indicate when the acute dystonia pathway versus refractory status dystonicus pathway (or escalation of care) should be considered, as well as when clinicians should consider modifying maintenance medications. Major electrolyte abnormalities are defined as hyperkalemia >5.5 mEq/L. Renal failure is defined as serum creatinine >1.5× baseline and urine output <0.5 mL/kg/h for 6–12 hours. Respiratory compromise is defined as need for respiratory support in the form of continous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) or intubation/mechanical ventilation. This scale was adapted from Lumsden et al (2013, 2017).[7,18] [Color figure can be viewed at wileyonlinelibrary.com]

Ensuring adequate intravenous hydration and enteral or parenteral nutrition are of great importance.

Step 4: Initiate Pharmacologic Measures

In addition to supportive care, pharmacological intervention is usually needed. This involves the administration of medications to reduce dystonia and promote sedation/sleep (Table 2). We propose a stepwise approach, starting from least to most sedating medications.

Diphenhydramine is recommended as the initial medication in the pathway. It has rapid availability and a favorable safety profile (Table 2). It is used as a rescue therapy for acute dystonic reactions secondary to antidopaminergic agents and, therefore, is familiar to nonneurologists.[21] If dystonia persists for 10 minutes after intravenous administration or 20 minutes after oral administration of diphenhydramine, the next medication should be administered. Diphenhydramine should not be repeated.

As the second/third-line pharmacological interventions, we suggest enteral diazepam or clonidine (without regard to order). Diazepam is an intermediate-duration benzodiazepine that is commonly used to treat dystonia. Clonidine is a nonrespiratory depressant sedative that acts as a central α_2-receptor agonist and is often effective in controlling or preventing breakthrough dystonia.[18,22-24] If the response remains insufficient after the first dose, we propose moving on to whichever one was not tried (either diazepam or clonidine) as step 3. If available, a fourth-line option is chloral hydrate (Fig. 2, Table 2). Chloral hydrate is the most potent sedative in the acute dystonia pathway and is administered enterally or rectally.[25] Response should be reevaluated after 10–20 minutes, and if dystonia remains inadequately controlled (ie, DSS grade 3), both clonidine and diazepam (as well as chloral hydrate, if applicable) should be repeated as outlined in Figure 2. The pathway can be repeated from the beginning if dystonia returns after 6 hours.

After these acute treatments, a decision regarding the level of care and the need for further treatment escalation should be made. For patients with a presentation consistent with DSS grade 2 (pre-SD, Fig. 1), conservative management may be continued. For patients with DSS grade 3 (SD, Fig. 1), management on the general ward is appropriate unless medical comorbidities,

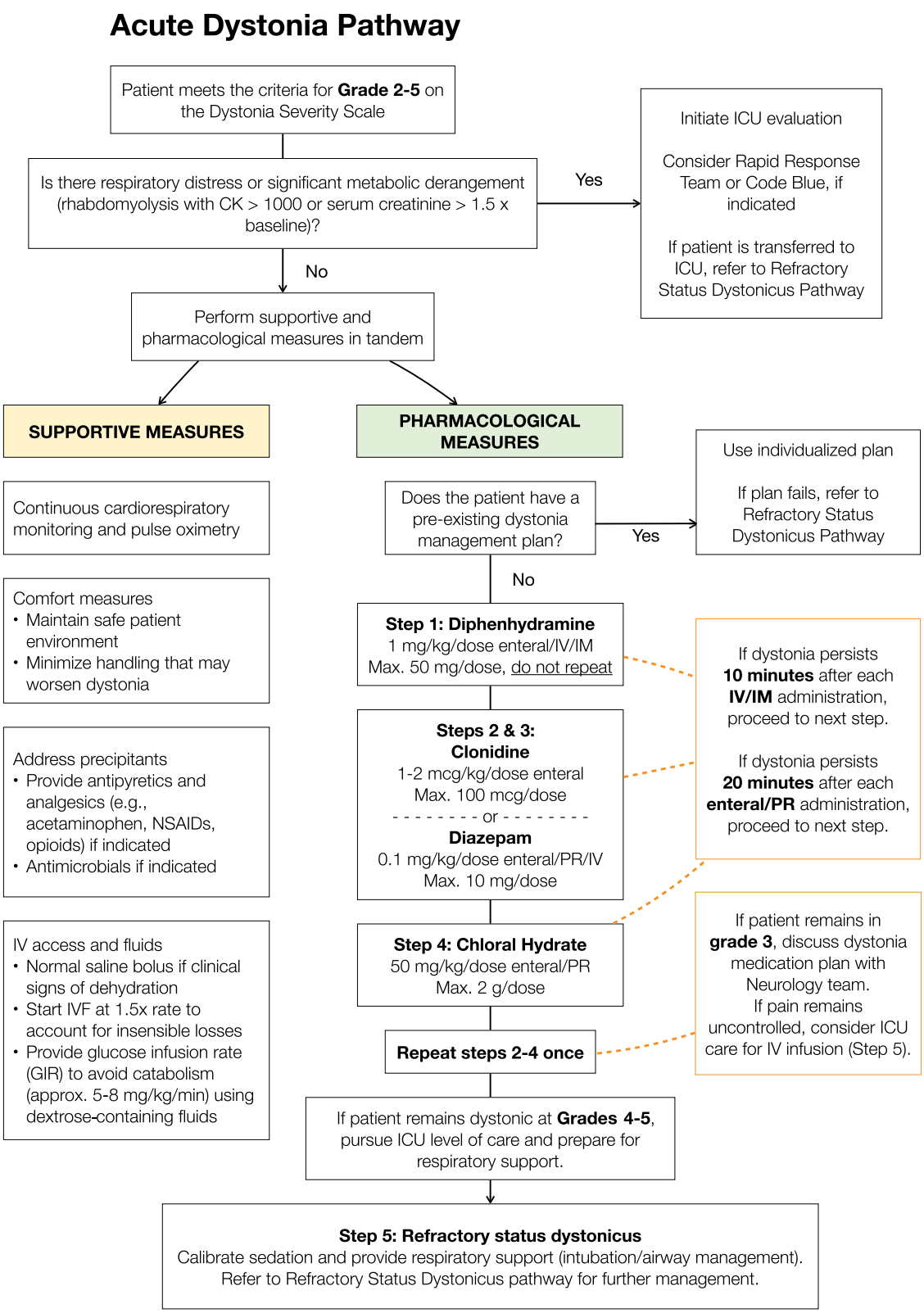

FIG. 2. Acute dystonia pathway. Acute Dystonia Clinical Pathway is a comprehensive approach to pre–status dystonicus and status dystonicus across outpatient, emergency department, and inpatient ward settings. Critical treatment steps should progress along "ABCD" mnemonic and should be revisited frequently: *a*ddress triggers, *b*egin supportive care, *c*alibrate sedation, and administer *d*ystonia-specific medications. These steps should be implemented concurrently. CK, serum creatine kinase level; ICU, intensive care unit; IV, intravenous; IVF, intravenous fluid; NSAID, nonsteroidal anti-inflammatory drugs; PR, per rectum. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 *First-line medications*

Agent and Recommended Dosing (Route)	Mechanism of Action	Duration of Action	Maximal Doses in 24 h[a]	Safety Concerns with Short-Term Use	Comments
Diphenhydramine, 1 mg/kg/dose (max. 50 mg), (enteral, IM)	Anticholinergic and sedative effects via inverse agonism of central H1 receptors	4–6 h	Do not suggest repeated doses	Anticholinergic effects, agitation and delirium, paradoxical excitation	Suggested because of its widespread availability and good safety profile.
Clonidine,[b] 1–2 μg/kg/dose (max. 100 μg) (enteral)	Nonrespiratory sedative via agonism of central α_2-adrenergic receptors	3–5 h	6–12	Hypotension, bradycardia, sedation	Titrate to effect/side effect. More frequent dosing, ie, every 2 h, can be advantageous. Once a stable dose is reached, can be converted to transdermal patch. IV clonidine is available in some regions of the world.
Diazepam, 0.1 mg/kg/dose (max. 10 mg) (enteral, PR, IV)	Sedative and muscle relaxant via GABA-A receptor agonism	60–120 min for sedation, despite long biological half-life	4–6	Cardiorespiratory depression with high doses, paradoxical reactions (rare), drooling	Titrate to effect. Enteral to IV conversion is 1:1.
Chloral hydrate, 50 mg/kg/dose (max. 2 g) (enteral, PR)	Sedative effects because of its active metabolite trichloroethanol via unknown mechanism	4–8 h	4	Excessive somnolence, dependency with chronic use	Not available in the United States.
Dexmedetomidine, 0.5 μg/kg/h (max. 2 μg/kg/h) (IV)	Anesthetic and sedative effects via agonism of α^2-adrenergic receptors	60–240 min after continuous infusion	N/A as continuous infusion	Cardiorespiratory depression, hypotension, tachyphylaxis, withdrawal after prolonged use	Titrate to effect.
Midazolam, 0.1 mg/kg/h (max. 2 mg/kg/h) (IV)	Sedative and muscle relaxant effects via GABA-A receptor agonism	N/A as continuous infusion	N/A as continuous infusion	Cardiorespiratory depression, paradoxical reactions (rare)	Titrate to effect.

Note: All medications listed are used off-label in children.
[a]Maximum number of doses per day is meant as a guide only. Individualized treatment plans are based on patient response, dosing of any existing maintenance medications, and usual safe daily maximum doses of each medication.
[b]Intranasal dexmedetomidine may also be used if clonidine is not available.
Abbreviations: max., maximum; IV, intravenous; IM, intramuscular; N/A, not applicable; PR, rectal.

nursing needs, or uncontrolled pain dictate a higher level of care. Patients who remain at DSS grade 4 or 5 meet the criteria for refractory SD, and care should be escalated. At this point, treatment should follow the Refractory Status Dystonicus Pathway presented later and in Figure 3.

Step 5: Developing an Individualized Dystonia Action Plan

Because patients may respond differently to various medications, and many patients with SD have significant medical complexities and a history of prior medical trials, we encourage the creation of an individualized

"Dystonia Action Plan" (Supporting Information Data S4). This includes the medications and specific order of medication that works best for an individual patient, analogous to seizure action plans in children with epilepsy.

Step 6: Adjusting/Initiating Baseline Dystonia-Directed Therapies

If the pathway is being used repeatedly, it is prudent to initiate or modify existing dystonia-directed therapies (Supporting Information Data S5). This often requires individualized approaches and should be guided by movement disorder specialists. Available agents often take days to weeks to take effect and therefore are added with the acute dystonia pathway acting as a bridge. This usually involves medications that are commonly recalled by another ABCD mnemonic: *a*nticholinergics (trihexyphenidyl), *b*aclofen, *c*lonidine/*c*lonazepam and other benzodiazepines (eg, diazepam), and *d*opamine (dopaminergic medications such as levodopa, versus tetrabenazine and other dopamine-depleting agents).[19,24,26] Medications should be chosen based on etiology/phenomenology, potential side effects, comorbidities, or other medications (Supporting Information Data S5).

Finally, efforts should be made to determine the underlying cause of dystonia if not already well established. This includes relevant biochemical studies, neuroimaging (including DBS planning sequences to establish feasibility of this possible treatment early on), as well as genetic investigations (commonly dystonia multigene panels or whole-exome/genome sequencing). Determination of the precise etiology can have profound implications for treatment and serves as a starting point for counseling, anticipatory guidance, and research. Although a consideration of DBS is appropriate for any patient in SD or any patient with severe or recurrent worsening dystonia despite medical therapy, we highlight that some forms of monogenic dystonia or hyperkinetic movement disorders with prominent dystonia display a superior response to DBS, indicating that it should be pursued early and rapidly in this setting (Fig. 3).[27]

Refractory Status Dystonicus Pathway

Refractory SD is characterized by a DSS grade of 4 to 5 with an inadequate response to initial pharmacological measures, namely, the acute dystonia pathway (Fig. 2), or the patient's personalized dystonia action plan (Supporting Information Data S4). The proposed management of refractory SD is constructed using the same ABCD principles discussed previously (Fig. 3). If not done previously, it is important to interrogate any intrathecal baclofen pump or deep brain stimulator to rule out withdrawal or hardware malfunction. The treatment should then progress along three axes: (1) calibration of sedating medications as a temporizing measure to control dystonia and prevent secondary complications, (2) initiation of dystonia-directed therapies, and (3) optimization of ICU supportive care.

Step 1: Calibrate Sedative Infusions

Sedative infusions provide relief and mitigate life-threatening risks of refractory SD. When administering sedative infusions, it is crucial to closely monitor and support the patient's cardiorespiratory status, and intervene if necessary. As such, this should be done in an intensive care setting. For first-line infusion, we propose dexmedetomidine (Fig. 3). A continuous infusion of dexmedetomidine allows for rapid titration with a relatively low risk of hypotension and other cardiovascular side effects.[28] Intravenous clonidine can be used as well, if available, and has shown to be safe in this setting.[22] If dexmedetomidine or intravenous clonidine prove insufficient, we recommend escalation to a continuous intravenous infusion of midazolam. Midazolam possesses muscle relaxant effects, and its short half-life expedites titration to effect. In rare cases, if dystonia continues to be refractory, a temporary initiation of nondepolarizing paralytics should be considered. In addition, a short course of propofol infusion (<12 hours to mitigate the risk of propofol infusion syndrome) may be considered as a second temporizing measure.[29]

In addition to continuous infusions, children with SD often undergo periodic worsening, which may be related to pain, discomfort, or the fluctuation of their underlying condition. In these cases, we propose reverting back to the patient's own dystonia action plan or the acute dystonia pathway. We suggest administering as needed medications (clonidine and diazepam) if the patient shows generalized dystonic posture/movements lasting more than 15 minutes, with associated discomfort/pain, and autonomic changes such as hyperthermia, tachycardia, or diaphoresis (Fig. 3).

The duration of sedation and intubation should be determined through periodic evaluations while simultaneously initiating and titrating dystonia-directed therapies. This approach allows for the gradual adjustment of sedation and ventilation based on the patient's response to treatment. The use of the acute dystonia pathway, along with the dystonia sleep–wake diary, can inform the appropriate adjustment of maintenance medications. If the patient requires continuous sedative infusions for a prolonged period of time, a "bridge" to intermittently scheduled enteral forms, commonly clonidine and diazepam, should be pursued. These agents have a synergistic effect with the aforementioned infusions and can gradually replace them over time.

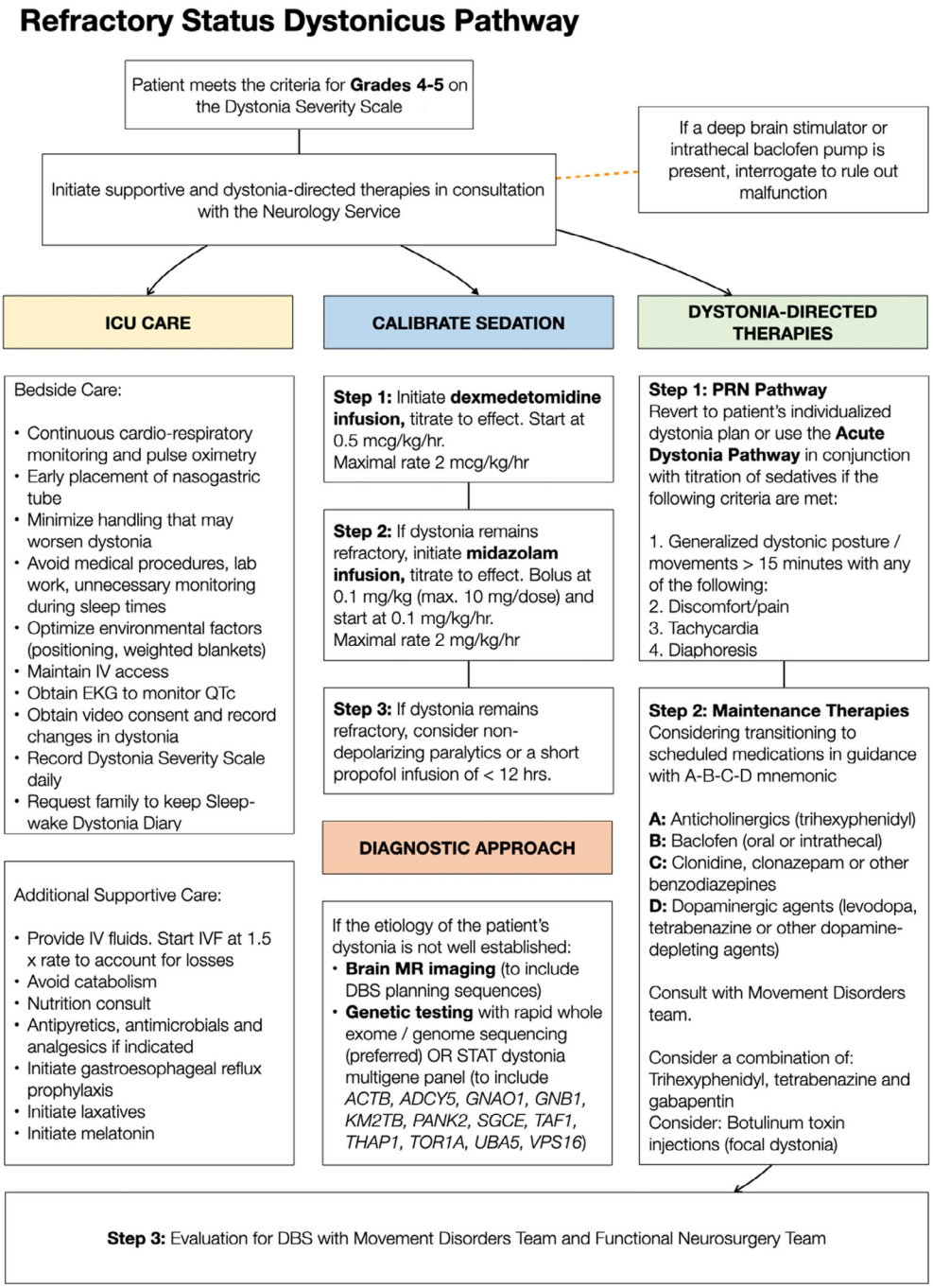

FIG. 3. Refractory Status Dystonicus Pathway. Refractory status is characterized by a Dystonia Severity Scale grade of 4 to 5 with an inadequate response to the acute dystonia pathway or the patient's personalized dystonia action plan. Treatment should then progress along three axes: (1) calibration of sedating medications as a temporizing measure to control dystonia and prevent secondary complications; (2) initiation of dystonia-directed therapies; and (3) optimization of intensive care unit supportive care. IV clonidine, where available, may be considered in place of IV dexmedetomidine. DBS, deep brain stimulation; EKG, electrocardiogram; IV, intravenous; IVF, intravenous fluid; MR, magnetic resonance; PRN, as needed. [Color figure can be viewed at wileyonlinelibrary.com]

Step 2: Dystonia-Directed Therapies

Although dexmedetomidine and midazolam may effectively control SD, such infusions are not suitable for long-term care and impede transfer out of the ICU. Thus, we recommend a transition to scheduled medications with antidystonic effects. This may involve a transition to bolus dosing of enteral clonidine/diazepam or the addition of other maintenance medications with antidystonic properties (Supporting Information Data S5). These medications may be personalized and should be guided by movement disorder specialist consultation, with pharmacy support, accounting for the

nature of the patient's underlying condition and existing medication regimen/side effects. In addition to the medications highlighted in Figure 3, another medication to consider is gabapentin as a nonopioid analgesic. Members of our group have found success with a combination of trihexyphenidyl, tetrabenazine, and gabapentin to leverage multiple mechanisms. It is important to note that children generally tolerate significantly higher doses (per body weight) of antidystonia medications than adults, and higher doses may be required to achieve symptom relief. Careful monitoring for significant anticholinergic side effects (ie, severe constipation, urinary retention, hyperthermia) or cardiac complications (ie, QTc-interval prolongation) is important (Supporting Information Data S5). Following the intensive treatment phase, sedative medications can be weighted toward higher evening doses to support sleep–wake cycle improvement.

Step 3: Supportive Care

Supportive care remains an important pillar throughout the management of acute dystonia, including refractory SD. Careful monitoring of vital signs and laboratory values is crucial, as well as maintenance of vascular and enteral access. Assessment of hydration/nutritional status should be conducted carefully to address deficiencies. Appropriate medications, if indicated, should be provided to manage fever, infections, gastroesophageal reflux, constipation, and pain. Care should be taken to avoid procedures during sleep times. Optimizing environmental factors, such as maintenance of a day–night schedule, positioning, and the use of weighted blankets, can help alleviate symptoms, avoid delirium, and provide comfort to the patient. A relatively long ICU course should be anticipated, and social work support should be provided.[30,31]

Step 4: Integration of Neuroimaging and Rapid Genomic Testing

As discussed earlier, if the etiology of the patient's dystonia is not well established, it is crucial to pursue both expedited genetic testing and neuroimaging (Fig. 3).

Step 5: Consideration of DBS and Other Surgical Measures

Although DBS was traditionally considered a last resort treatment for SD, we advocate for early consideration of DBS within 3 to 5 days of requiring intravenous infusions or once refractory SD is established. Before proceeding with DBS, it is important to conduct family and team meetings to provide counseling and build consensus. Relative exclusion criteria for DBS include young age, low weight, high risk for infection, medical instability, concerns regarding adequate follow-up, or unrealistic caregiver expectations. It is noteworthy that DBS is increasingly performed safely in young children, even as young as 2 to 3 years of age. In most cases, bilateral stimulation of the globus pallidus pars internus is the preferred target; however, subthalamic nucleus stimulation has been performed when globus pallidus pars internus stimulation is unsuccessful or not feasible because of anatomic restrictions.[31] We recommend a one-stage procedure for DBS implantation (implantation of brain electrodes and pulse generator in the same surgery) with stimulation initiated within 24 hours. Specific details regarding programming in this setting have been published recently.[31] Generally, this involves a monopolar review to ensure absence of adverse effects and then delivering double or single monopolar stimulation with the ventral contacts acting as the cathode, at set parameters of 60 μs for pulse width, 130 Hz frequency, and 2 mA or 2 V amplitude. Settings should be optimized every 1 to 3 days depending on the response. The effects of DBS may become evident within a few days, although the full benefit may take several weeks to manifest.[31] DBS has largely supplanted ablative procedures, such as pallidotomy or thalamotomy, for the treatment of refractory SD. If an intrathecal baclofen pump is already in place, bolus dosing or rate adjustments should be considered. If not, insertion of a spinal intrathecal baclofen pump or even intracerebroventricular baclofen therapy can be evaluated.[32] The decision to proceed to DBS versus intrathecal/intraventricular baclofen therapy is institution and patient dependent.

Educating and Empowering Multidisciplinary Teams

As part of the implementation of this guideline, our teams have employed educational outreach. Combined with the publication of the clinical pathways, this has anecdotally heightened awareness and increased confidence in management of dystonia in all care settings. We observed that the pathways enable clinicians to promptly recognize and initiate treatment without awaiting a neurology consultation, akin to what is established for other neurological emergencies, for example, status epilepticus.

Discussion

SD is a life-threatening movement disorder emergency. The condition is often first managed by pediatricians, emergency physicians, or intensive care providers who may have limited background in identifying and treating dystonia. Subsequently, these patients are cared for by many teams (neurologists, intensivists, movement disorder specialists, palliative care physicians, physical medicine and rehabilitation physicians, and

neurosurgical teams, as well as pharmacists, dieticians, physical/occupational/speech therapists, and social workers). To address a lack of systematic clinical recommendations and clear defining criteria for SD, we have proposed a stepwise approach to the assessment and treatment of worsening dystonia. We anticipate that this will standardize assessment/triage, provide guidance to the team looking after these patients, and improve outcomes.

The supportive therapies listed in our guideline expand prior publications.[7,8,18] Given that high-quality studies in the acute pharmacological management of pediatric dystonia are lacking, our guideline is based largely on expert consensus, previous literature/reported use, side effect profiles, and institutional factors. We recognize that this means that the pathway may require adjustment over time as evidence develops. In addition to making consensus recommendations for a general treatment approach, we also advise against other interventions that have been proposed previously, such as the use of haloperidol, dantrolene, or prolonged treatment with propofol. The interventions suggested in the pathway are generally familiar to pediatric providers and neurologists alike. We hope that, with appropriate education, families would be able to adopt some in the home setting (analogous to rescue medications for seizures). We acknowledge that not all the medications proposed in our pathway, and in the specific order, will work for all patients. There may be nuances in choice of medication depending on local availability and the goal of therapy. The medical team, patients, and families should therefore opt to create a personalized dystonia action plan over time (Supporting Information Data S4–S7).

As knowledge about various genetic forms of dystonia evolves, personalized therapies may move into focus. International collaborations will allow better tracking of the natural history of SD in these disorders, as well as their response to medications and DBS. For a growing list of monogenic hyperkinetic movement disorders with significant dystonia, including DYT-*TOR1A*,[33] DYT/CHOR-*GNAO1*,[34] or DYT-*KMT2B*,[11] we strongly recommend consideration of DBS early in the course of the disease. DBS should also be considered in any patient with refractory SD, regardless of the etiology.

The most striking limitation of our guideline is the scarcity of evidence in the field, which necessitated the reliance on expert consensus rather than evidence. We acknowledge that the proposed pathways assume a healthcare setting typical of large academic pediatric hospitals in North America. Although many suggestions and principles will be applicable to healthcare systems around the world, some may not. Accessibility to the recommended medications and DBS may pose a hurdle. In resource-limited settings, additional medications or interventions, such as carefully dosed phenobarbital or a pallidotomy, will have a different relative importance. The pathway offers room for customization to accommodate patient-specific needs and variations in resource availability.

Finally, the guideline primarily focuses on acute therapy, with limited guidance on transitioning to maintenance regimens and the specific strategies to employ during this phase. This omission is attributed to the highly individualized nature of such transitions, which depend on factors such as the patient's clinical condition, triggers (eg, infections), availability of enteral feeding and medications, prior and concurrent medications, medication interactions, and the distribution of dystonia. In the latter instance, adjunct therapies such as botulinum toxin injections should be considered. Given the lack of evidence in this domain, it is crucial to develop and assess outcome measures to track the impact of the proposed interventions. We hope this guideline will spark international, collaborative, prospective multicenter initiatives. Potential metrics to measure the pathway's effectiveness include the setting in which the pathway is used (usage in emergency department, ward, and ICU), initiation and supportive care measures on the first day of admission, effective tracking of sleep–wake dystonia diary by family and nursing staff, number of times the pathway is used and length of time between subsequent steps, peak creatine kinase level, length of hospital stay (divided into ward/ICU, respectively), admission to the ICU, need for intubation, need for intravenous sedative infusions, need for paralytic agents, time to completion of genetic testing, differences of effectiveness of the guideline based on the underlying etiology (patients with acquired cerebral palsy vs. inherited etiologies), number of cases referred for DBS, changes in baseline dystonia medications, and disease severity (resolution of SD vs. death, pre-SD baseline vs. post-SD severity using Burke-Fahn-Marsden Dystonia Rating Scale[35]). Alongside this, it will be important to document diagnoses, prior instances of SD, baseline medications, and whether the creation of an individualized dystonia action plan prevents recurrence of SD.

Conclusion

This review presents a comprehensive consensus approach to managing the challenging spectrum of pre-SD to refractory SD in children. Over the past two decades, SD has gained increasing recognition as a neurological emergency associated with significant morbidity and mortality. Recognizing the dearth of evidence in this domain, the proposed recommendations draw on expert consensus, emphasizing the importance of swift interventions and medications while minimizing side

effects. The overarching goal is to expedite the recognition and treatment of SD in children by enhancing the quality of care provided and establishing standardized terminology. Adopting a unified approach will facilitate multidisciplinary collaboration, ultimately contributing to evidence that can lead to improved care for children with SD.

Acknowledgments: We thank our colleagues of the Neurocritical Care Consult Service at Boston Children's Hospital for feedback, as well as those at SickKids who contributed to the development of the local pathway, including those from pediatrics (Dr. Shawna Silver, Dr. Catherine Diskin, Dr. Tanvi Agarwal, Kathleen Andres) and intensive care (Dr. Gail Annich). We also thank nurse practitioner Meena Kadiwal for providing a prior version for the dystonia action plan.

Data Availability Statement

Data are available from the corresponding author upon reasonable request.

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Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.

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Author Roles

Conception and design of the study: C.G. and D.E.-F. Acquisition and analysis of data/feedback: L.M.V., Z.Z., G.T., K.Y., L.W., R.S., A.T., E.E., S.M., A.F., W.T.N., S.S., M.M., H.G., B.M., M.K., K.L.L., C.G., and D.E.-F. Drafting a significant portion of the manuscript or figures: L.M.V., K.Y., V.Q., C.G., and D.E.-F. Editing the manuscript: all authors.

Financial Disclosures

Darius Ebrahimi-Fakhari. Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: University of Texas Southwestern, German Center for Neurodegenerative Diseases, and Guidepoint LLC. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: Speaker honoraria from The Movement Disorders Society and the Taiwan Society of Child Neurology. Royalties: Cambridge University Press. Patents: US Patent No. 63/503,262, Compounds for treating hereditary spastic paraplegia. Grants: D.E.-F. has received research grants from National Institutes of Health, National Institute of Neurological Disorders and Stroke, CureAP4 Foundation, CureSPG50 Foundation, Spastic Paraplegia Foundation, Tom Wahlig Foundation, Un raggio di Sole per Martina, Manton Center for Orphan Disease Research, BCH Office of Faculty Development, and BCH Translational Research Program and Astellas Pharmaceuticals. Other: None. Elicia Estrella: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Alfonso Fasano: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: Honoraria/consultation fees from Abbott, Boston Scientific, Ipsen, Medtronic, and Merz. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: A.F. has received grants/research support from Boston Scientific, DMRF – Canada, and Medtronic. Other: None. Hernan Gonorazky: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Carolina Gorodetsky: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: Medtronic and Ipsen. Royalties: None. Patents: None. Grants: None. Other: None. Monica Kleinman: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Kerri L. LaRovere: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Shannon Manzi: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Brian McAlvin: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Mahendranath Moharir: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Weston T. Northam: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other:

None. Vicente Quiroz: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Rasha Srouji: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Scellig Stone: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Amy Tam: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Gabriel Tse: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Lindsey M. Vogt: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Laura Wang: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Kathryn Yang: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None. Zainab Zaman: Stock Ownership in medically-related fields: None. Intellectual Property Rights: None. Consultancies: None. Expert Testimony: None. Advisory Boards: None. Employment: None. Partnerships: None. Inventions: None. Contracts: None. Honoraria: None. Royalties: None. Patents: None. Grants: None. Other: None.