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REVIEW

Parenteral Nutrition in Pediatric Patients with Neurodisability: Current Perspectives

Emily White[1], Mohamed Mutalib[1,2]

[1]Department of Paediatric Gastroenterology, Evelina London Children' Hospital, London, UK; [2]Faculty of Life Sciences and Medicine, King's College London, London, UK

Correspondence: Mohamed Mutalib, Department of Paediatric Gastroenterology, Evelina London Children' Hospital, London, SE1 7EH, UK, Email Mohamed.mutalib@gstt.nhs.uk

Abstract: Pediatric neurodisability describes functional limitations in children with varied severity and complexity often attributed to brain or neuromuscular abnormalities. The life expectancy of children with neurodisability is improving, but many will require significant medical support. The gastrointestinal tract is usually affected in children with neurodisability and can lead to a wide range of symptoms. In gastrointestinal (GI) dystonia, a newly coined term, feeding will trigger a distressing dystonia and symptoms can improve with cessation of feed. Parenteral nutrition (PN) is often viewed as a viable option in severe GI dystonia or when enteral feeding does not support sufficient nutrition. The use of PN in children with severe neurodisability is complex. It involves an intricate interplay between medical, psychological and ethical factors. In the absence of a universally agreed guidance on the use of PN in this cohort, paediatricians should maintain the individual need of the child at the centre of the decision-making process and work closely with families and other healthcare professionals before initiating or withholding PN in children with severe neurodisability. In this article, we discuss the complex and multifaceted approach to the use of PN in children with severe neurodisability and aimed to explore the medical, psychological and ethical aspect dilemmas facing clinicians looking after children with declining gut function who may require PN support.

Keywords: pediatric, neurodisability, parenteral nutrition, medical ethics

Introduction

Neurodisability as a term describes a group of conditions (with or without a specific diagnosis) that are attributed to brain and/or neuromuscular system impairment and creates functional limitations with broad range of severity and complexity.[1] The impact of neurodisability may include difficulties with movement, cognition, communication, emotion, and behaviour. Due to advances in medical care, the life expectancy of children with severe neurodisabilities is improving albeit with heavy morbidity burden.[2] The gastrointestinal (GI) system is often affected in children with neurodisability and a multitude of symptoms are routinely reported, directly impacting survival and quality of life for both children and their families.[3]

The complex interplay between the central and enteric nervous systems can partly explain some of the GI manifestations in children with neurodisability, but the pathophysiological processes driving the GI complaints are often complex and multifaceted. Medications used in the treatment of neurological conditions can directly induce GI symptoms and the simultaneous intake of multiple medications (polypharmacy) may adversely affect the gut function.[4] GI motility disorders can lead to some of the most distressing symptoms, often characterised by vomiting, feed intolerance, abdominal pain, constipation, and/or diarrhoea.[5] GI dystonia, an emerging and poorly understood phenomenon is increasingly reported in children with complex motor disorders when feed appears to trigger a cascade of distressing dystonia. In practice, cessation of enteral feeding will often improve both the GI symptoms and the dystonia.[6]

Parenteral nutrition (PN) is currently regarded as a standard of care in most health-care systems. There are robust clinical guidelines advising clinicians on the use of short- and long-term PN and a steady decline in PN-related complications.[7,8] Our improved knowledge on the direct impact of nutrition on health and disease and the readily

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available standardised PN bags has allowed the safe initiation and maintenance of nutrition in almost all clinical settings. Although traditionally PN has been used in the context of intestinal failure (IF), it is frequently used in children with non-GI-related disorders such as in reversing and/or preventing metabolic decompensation, trauma and supporting recovery from serious illnesses.[9] Home PN is also recognised as a safe long-term treatment. Children receiving PN at home for GI-related intestinal failure are often in full-time education and are increasingly reporting improved quality of life despite a heavy care burden.[7] In children without neurodisability, IF (defined as the reduction of functional gut mass below the minimal amount necessary for digestion and absorption adequate to satisfy the nutrient and fluid requirements for growth)[10] remains the leading indication for paediatric PN. Short bowel syndrome, congenital enteropathies and paediatric intestinal pseudo obstruction are the commonest causes of IF in children.[11] On the other hand, the medical literature is acutely short of evidence-based articles in the area of PN use in children with neurodisability. In this article, we attempt to provide a balanced overview on the usage of PN in children with neurodisability and the complex interplay facing healthcare professionals and carers when considering PN in children with severe neurodisability.

GI Function in Children with Neurodisability

Many conditions can affect the gut function in children with neurodisability; some can directly lead to IF, but many can result in a sustained state of chronic nutritional inadequacy.[12] The overall clinical picture is complicated by the absence of a standard nutrition assessment tool for children with neurodisability.[13] The causes of declining gut function in children with neurodisability can be summarised into:

(a) conditions that lead to increased GI losses such as vomiting (or gastrostomy losses) and/or diarrhoea,
(b) conditions leading to reduced intake such as feed intolerance, pain with feeding and GI dystonia,
(c) major GI motility disorders such as intestinal pseudo obstruction,
(d) the natural decline of gut function associated with severe neurodisability.

Management of GI complaints in children with neurodisability has vastly improved over time through a streamlined multidisciplinary approach, improved management of extra intestinal systems (in particular epilepsy and respiratory therapies), increased provision of gastrostomy/gastrojejunostomy tubes and the ready availability of nutritionally complete liquid feeds have contributed to the overall improvement of nutrition and wellbeing of children with neurodisability.[14] GI specific investigations and management strategies have also evolved and improved. Endoscopies and various motility investigations allowed an accurate identification of GI conditions and facilitate individualised management plans. New drugs (prokinetics, laxatives and neuropathy management agents) are offering additional options for refractory GI disorders and alleviate some of the distressing symptoms commonly experienced by children with neurodisability.

Parenteral Nutrition Use in Paediatric Neurodisability

Small but increasing numbers of children with neurodisability are presenting with frank IF or IF-like disorders resistant to standard medical management. Some children are presenting with pain and/or severe dystonia upon using the GI tract and symptoms are often reported to abate with gut rest.[6,12] Short and infrequent periods of gut rest and intravenous hydration are usually well tolerated, but prolonged or frequent cessation of feed may lead to significant nutritional deficits and starvation. In this setting, PN becomes the only viable option, particularly if the child is not on an end-of-life pathway. A handful of papers (mostly case reports and small case series) have reported on the successful use of short- and long-term PN in children with severe neurodisability and many centres are increasingly offering PN at home.[12,15,16]

PN is expensive, resource intense and can be associated with serious adverse events, but the benefits of using PN in the right clinical context far outweigh the risks and the use of short-term PN is regarded as a standard clinical care in most countries. The costs and risks are exponentially increased with long-term and Home PN.[17] Home PN has significantly improved children's quality of life and allowed participating into many childhood activities but it is mostly regarded as a temporal measure with a long-term goal of achieving enteral autonomy.[7,18] Intestinal transplantation is often considered in patients on Home PN who are unable to achieve intestinal rehabilitation.

Initiating PN to support an acute event in children with neurodisability is regarded as routine practice in many clinical settings and will generate no controversy. However, many clinicians will feel uncertain about starting long-term and/or Home PN in children with severe neurodisability[14] due to combinations of medical, ethical and psychosocial factors as explored below.

Medical Factors Affecting PN Utilisation in Neurodisability

Diagnostic Uncertainty

Many children with severe neurodisability will reach the point of long-term PN after a protracted and often difficult period of ongoing GI symptoms. Most would have been extensively investigated and considerations would have been made for treatable and reversible causes of gut decline. In the neurologically able child, the indications for long-term PN has been stretched to cover some poorly understood conditions (such as paediatric intestinal pseudo obstruction) and are also extended to cover an ever-expanding non-GI-related conditions such as malignancies, trauma, supporting major surgeries and organ transplant.[19,20] A common theme in all these conditions is the presence of a clear diagnostic pathway and a defined exit point (enteral autonomy from PN or intestinal transplantation).

The clinical dilemma in the case of children with neurodisability can arise from the absence of definitive aetiological causes for their GI symptoms and the unsuitability of the existing investigations for this group of children. GI dystonia is yet to be defined as a clinical entity. It has no pathognomonic symptoms or diagnostic tools. GI motility disorders (dysmotility) are commonly used to explain heterogeneous GI symptoms in children with neurodisability[21]; however, it is generally a non-specific umbrella term which covers a range of disorders.[22] GI motility investigations are used to study the motility of different parts of the GI tract and to ascertain symptom correlation. Proxy symptom reporting, as is the case in most nonverbal children, will produce inaccurate symptom association in some tests (such as multichannel intraluminal impedance and pH studies (MII pH)) and currently, there are no normal values for MII pH to cover children on gastrostomy or gastrojejunostomy feeding.[23] Standard protocol oesophageal manometry will require oral intake and a certain level of patient cooperation and understanding, limiting its yield in severe neurodisability.[5] Antroduodenal and colonic manometries are invasive and only available in few specialised centres; furthermore, the interpretation of results and their utilisation in altering clinical patient care is yet to be fully explored.[24] Other specialised GI motility investigations such as breath test, MRI and wireless motility capsule are challenging to perform in children with severe neurodisability.

It is worth noting that, in different clinical settings, the presence of diagnostic uncertainty or the lack of evidence did not hinder the usage of PN in paediatrics. On the contrary, the recognition of the vital role of nutrition has resulted in expanding the use of PN to cover many disorders that adversely affect nutritional intake as detailed above.[25] The evidence often follows by retrospectively researching the outcomes of PN usage in a particular patient cohort.

No Clear Exit Point

Long-term PN and Home PN are often used with the long-term goal of eventually reinstating enteral feeding and stopping PN. In certain circumstances, this may have a clear time frame, e.g. pre/post major surgery, cancer care and organ transplant.[26] While in others, the duration of PN usage is less relevant, but the aim remains certain, such as full enteral autonomy in cases of short bowel syndrome or intestinal transplantation in cases of congenital enteropathies.[27,28] The presence of a clear objective may help children and their families to engage with the heavy burden of Home PN and the social restrictions that are associated with it. The support of intestinal rehabilitation teams and the multidisciplinary approach has led to significant improvement in the outcomes of children receiving PN at home.

In children with severe neurodisability, achieving the goal of full enteral autonomy from PN may become less certain and it might not be possible to stop, or indeed even wean long-term PN. This is partly due to the lack of understanding of the pathological process causing the decline in gut function in children with neurodisability or the fact that such deteriorating may represent a process of pre-terminal regression.

However, the picture has not always been that clear even for children without neurodisability. In the first few decades of the universal uptake of Home PN, it was not certain if children with ultra-short bowel syndrome would ever wean

down PN, nor was it possible to confidently predict the survival of children with severe congenital enteropathies. Prior to the success of intestinal transplantation, there was no defined exit point for children with irreversible IF. Continuing provision of Home PN allowed improved understanding of the natural history of these once evolving conditions and bought vital time for medical research to produce and trial novel treatments and therapies.[27,29]

It can be argued that IF in children with severe neurodisability is an evolving disorder and the use of long-term PN will support children through the natural progression of the condition. Nevertheless, the provision of PN in this setting should still be safeguarded with outlining clear goals and objective. This will enable clinicians to successfully work in partnership with families on regular reviews of the agreed outcome measures. If the outcomes are not achieved, the discussion should include the value of continuing the provision of PN.

Ethical Factors Affecting PN Utilisation in Neurodisability

The ethics around invasive nutrition in children with severe neurodisability is convoluted and complex. Medical ethicists have long argued the definition of good medical ethics. The long-held belief of the four principle approach encompassing beneficence, non-maleficence, respect for autonomy and justice is often criticized and regarded to be in need for overhaul.[30,31] However, in the absence of a universally agreed alternative ethical approach, the four principles provide a reasonable moral and ethical analytic framework upon which an argument can be constructed on the use of PN in children with neurodisability.

Beneficence

Beneficence, or simply to do good is the most easily understood principle when discussing advanced nutrition in children with neurodisability. The benefits of nutrition in maintaining health and the role of malnutrition in driving frailty are well documented in medical literature.[32] Long-term PN is deeply ingrained in the palliation of terminally ill patients, without which, these patients will cruelly die of starvation and malnutrition rather than the pre-existing terminal condition.[33]

In gastrointestinal dystonia, a neologism of feed-induced dystonia in children with severe neurodisability, feeding becomes a distressing experience, triggering painful muscle spasms and often a sleep disruption. Although some children were reported to improve with jejunal feeding,[6] the majority will reach symptom respite with gut rest. To combat the extended periods of starvation, often associated with increased energy expenditure secondary to muscle spasms, PN is usually initiated and has been reported to achieve positive clinical outcome in relieving dystonia and maintaining adequate nutrition.[6] Some children are unable to return to full enteral nutrition and the number of children with severe neurodisability on Home PN is gradually increasing.[15]

There is no universal agreement that gastrointestinal dystonia is a terminal or a pre-terminal event and the condition is actively being studied. An argument can be made to sustain the life of the affected individual until medical research can achieve a better understanding of the pathophysiology and treatment of this disorder.

Non-Maleficence

To do no harm, clinicians must exercise extreme caution when the balance of an intervention is tilted towards causing damage. Long-term usage of PN can be associated with central venous catheter-related bloodstream sepsis, liver disease, thromboembolic phenomenon, and loss of vascular access.[34] There is an improvement in the trends of all these complications due to medical advances and the proactive multidisciplinary approach to PN care.[34] Nonetheless, these are serious complications and some children with neurodisability may have a pre-existing predisposition to certain PN-related complications. In this scenario, PN usage should be carefully considered and the risk/benefit balance meticulously scrutinised.

On the other hand, from an ethical standpoint, withholding PN from children with neurodisability who are unable to feed due to prolonged episode of gastrointestinal dystonia can directly cause harm through the negative impact on their nutritional status.[32] Uncontrolled starvation (outside the context of palliative care) can lead to malnutrition and will significantly increase the incidence of multisystem morbidity and mortality.[35]

Respect for Autonomy

Respect for autonomy often generates a vigorous debate among ethicists as it can be perceived to contradict the other pillars of four principle biomedical ethics.[30,36] An autonomous patient can request a particular treatment or make a poor decision based on informed choice, but doctors have a firm moral obligation to benefit their patients, particularly if such a request countervails the principle of do no harm. Respect for autonomy does not equate to giving patients whichever treatment or intervention all they may want. It is rather a deliberation and not a simple choice. Autonomy should also be viewed in equal weighting to the other three of the four principles of medical ethics.

Children with severe neurodisability might not be able to express independent autonomous views on PN. Their parents' opinions are often interpreted to represent the child's best interest. Clinicians should work with families to explore the impact of PN on the individual child. They should assess the desired benefits of symptom control against the medical risks and the restrictions brought about by the long-term use of PN, such as the increased in the frequency of medical interactions and the limitation to activities during infusion time. An independent review is often thought to advocate for the child's view in the events of disagreement between parents and healthcare professionals and many organisations routinely rely on a dedicated ethical committee to provide an impartial review.[14]

Justice

Justice involves a non-discriminatory fair distribution of resources. Long-term PN is an expensive and resource intense intervention, it should be used appropriately after careful patient selection to avoid wasting resources. The benefits of adequate nutrition and the risks of inadequate nutrition are unequivocally proven in medical literature and are universally regarded as essential medical intervention.[32] In the absence of clear harm (to individual or resources), the use of long-term PN in children with severe neurodisability should be diligently considered for each child based on their individual medical circumstances.

Psychosocial Factors Affecting PN Utilisation in Neurodisability

The burden of raising a child with severe neurodisability should not be overlooked during the consideration of long-term PN. Although the primary focus of any medical intervention should solely be on the child, the complexity and subjectivity of symptoms around feeding should also be acknowledged. Distress in children with severe neurodisability can have multiple causes, and it may prove difficult to ascertain a correlation to the gastrointestinal tract.[37] Pain in children with communication difficulties is also directly associated with high level of parental stress, which in turn will impact on their ability to care for their child or work in harmony with healthcare professionals.[38] The level of depression in parents of children with neurodisability can be high and mental health struggles should be explored and supported during the process of PN consideration.[39] Any ambiguity regarding the origin of the child distress or the association with feeding should be clarified and the symptoms objectively assessed and verified. In some instances, this may require a period of direct observation by healthcare professional before invasive nutritional interventions are considered.

It must also be said that raising a child with severe neurodisability will undoubtedly bring positive feelings in many families, and many parents work in congruence with healthcare professionals.[40] The association between feeding and a child's distress can also be very clear due to the evident relief brought about by cessation of feed.

In many developed countries, initiating long-term PN in children with neurodisability will be supported by various packages of care and may not be a burdensome undertaking for parents. However, there may be a huge variation in the level of support provided to these families and therefore a detailed scrutiny of responsibilities should be a routine part of assessment for suitability of Home PN for children with neurodisability.

Finally, the psychosocial impact of long-term PN on children with neurodisability should not be overlooked. PN bags and tubing should be protected from light and should ideally be infused overnight to additionally minimise the disruption to daytime activities. It must be considered that overnight infusions may affect sleep quality and prolonged infusion times may severely limit the child's schooling, leisure and personal interactions.

In conclusion, providing long-term PN to children with severe neurodisability can be complex and multifaceted and will require meticulous considerations, discussions and planning. The process can raise many ethical and practical

hurdles but healthcare professionals should maintain the child's best interest and wellbeing at the centre of all decision-making. The decision whether to initiate or not initiate long-term PN should be tailored to the individual child and their family. Clinicians should also acknowledge the limitation of medical evidence in this area and should consider an impartial ethical review in cases of uncertainty.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Morris C, Janssens A, Tomlinson R, Williams J, Logan S. Towards a definition of neurodisability: a Delphi survey. *Dev Med Child Neurol*. 2013;55(12):1103–1108. doi:10.1111/dmcn.12218
2. Strauss D, Shavelle R, Reynolds R, Rosenbloom L, Day S. Survival in cerebral palsy in the last 20 years: signs of improvement? *Dev Med Child Neurol*. 2007;49(2):86–92. doi:10.1111/j.1469-8749.2007.00086.x
3. Del Giudice E, Staiano A, Capano G, et al. Gastrointestinal manifestations in children with cerebral palsy. *Brain Dev*. 1999;21(5):307–311. doi:10.1016/S0387-7604(99)00025-X
4. Philpott HL, Nandurkar S, Lubel J, Gibson PR. Drug-induced gastrointestinal disorders. *Frontline Gastroenterol*. 2014;5(1):49–57. doi:10.1136/flgastro-2013-100316
5. Keller J, Bassotti G, Clarke J, et al. Expert consensus document: advances in the diagnosis and classification of gastric and intestinal motility disorders. *Nat Rev Gastroenterol Hepatol*. 2018;15(5):291–308. doi:10.1038/nrgastro.2018.7
6. Mordekar SR, Velayudhan M, Campbell DI. Feed-induced dystonias in children with severe central nervous system disorders. *J Pediatr Gastroenterol Nutr*. 2017;65(3):343–345. doi:10.1097/MPG.0000000000001543
7. Hill S, Ksiazyk J, Prell C, Tabbers M. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: home parenteral nutrition. *Clin Nutr*. 2018;37(6Pt B):2401–2408. doi:10.1016/j.clnu.2018.06.954
8. Mihatsch WA, Braegger C, Bronsky J, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition. *Clin Nutr*. 2018;37(6Pt B):2303–2305. doi:10.1016/j.clnu.2018.05.029
9. Mantegazza C, Landy N, Zuccotti GV, Köglmeier J. Indications and complications of inpatient parenteral nutrition prescribed to children in a large tertiary referral hospital. *Ital J Pediatr*. 2018;44(1):66. doi:10.1186/s13052-018-0505-x
10. Goulet O, Ruemmele F, Lacaille F, Colomb V. Irreversible intestinal failure. *J Pediatr Gastroenterol Nutr*. 2004;38(3):250–269. doi:10.1097/00005176-200403000-00006
11. Duggan CP, Jaksic T, Ingelfinger JR. Pediatric Intestinal Failure. *N Engl J Med*. 2017;377(7):666–675. doi:10.1056/NEJMra1602650
12. Wahid AM, Powell CV, Davies IH, Evans JA, Jenkins HR. Intestinal failure in children and young people with neurodisabling conditions. *Arch Dis Child*. 2017;102(5):475–476. doi:10.1136/archdischild-2016-311387
13. Andrew MJ. Nutrition in children with neurodisability. *Paediatr Child Health*. 2019;29(10):436–440. doi:10.1016/j.paed.2019.07.004
14. Romano C, van Wynckel M, Hulst J, et al. European Society for Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for the evaluation and treatment of gastrointestinal and nutritional complications in children with neurological impairment. *J Pediatr Gastroenterol Nutr*. 2017;65:2. doi:10.1097/MPG.0000000000001646
15. Cernat E, Puntis JW. How many children with severe neurodisability are being sent home on parenteral nutrition? *Arch Dis Child*. 2021;106(5):518. doi:10.1136/archdischild-2020-319623
16. Mutalib M. Parenteral nutrition in children with severe neurodisability: a panacea? *Arch Dis Child*. 2021;106(8):736–738. doi:10.1136/archdischild-2020-319278
17. Canovai E, Ceulemans LJ, Peers G, et al. Cost analysis of chronic intestinal failure. *Clin Nutr*. 2019;38(4):1729–1736. doi:10.1016/j.clnu.2018.07.032
18. Lezo A, D'Eusebio C, Riboldi L, Baldini L, Spada M. HPN standard of care and long-term outcomes of CIF pediatric patients: twenty-eight years' experience in a reference center. *Front Nutr*. 2022;9:868273. doi:10.3389/fnut.2022.868273
19. Diamanti A, Capriati T, Gandullia P, et al. Pediatric chronic intestinal failure in Italy: report from the 2016 Survey on behalf of Italian Society for Gastroenterology, Hepatology and Nutrition (SIGENP). *Nutrients*. 2017;9(11):1217. doi:10.3390/nu9111217
20. Gandullia P, Lugani F, Costabello L, et al. Long-term home parenteral nutrition in children with chronic intestinal failure: a 15-year experience at a single Italian centre. *Digest Liver Dis*. 2011;43(1):28–33. doi:10.1016/j.dld.2010.04.012
21. Werlin SL. Antroduodenal motility in neurologically handicapped children with feeding intolerance. *BMC Gastroenterol*. 2004;4(1):19. doi:10.1186/1471-230X-4-19
22. Deane AM, Chapman MJ, Reintam Blaser A, McClave SA, Emmanuel A. Pathophysiology and treatment of gastrointestinal motility disorders in the acutely ill. *Nutr Clin Pract*. 2019;34(1):23–36. doi:10.1002/ncp.10199
23. Hobbs P, Gyawali CP. The role of esophageal pH-impedance testing in clinical practice. *Curr Opin Gastroenterol*. 2018;34(4):249–257. doi:10.1097/MOG.0000000000000441
24. Rao SS, Camilleri M, Hasler WL, et al. Evaluation of gastrointestinal transit in clinical practice: position paper of the American and European Neurogastroenterology and Motility Societies. *Neurogastroenterol Motil*. 2011;23(1):8–23. doi:10.1111/j.1365-2982.2010.01612.x
25. Cohran VC, Prozialeck JD, Cole CR. Redefining short bowel syndrome in the 21st century. *Pediatr Res*. 2017;81(4):540–549. doi:10.1038/pr.2016.265
26. Braga M, Ljungqvist O, Soeters P, Fearon K, Weimann A, Bozzetti F. ESPEN guidelines on parenteral nutrition: surgery. *Clin Nutr*. 2009;28(4):378–386. doi:10.1016/j.clnu.2009.04.002
27. Das B, Sivagnanam M. Congenital tufting enteropathy: biology, pathogenesis and mechanisms. *J Clin Med*. 2020;10:1. doi:10.3390/jcm10010019

28. DeLegge M, Alsolaiman MM, Barbour E, Bassas S, Siddiqi MF, Moore NM. Short bowel syndrome: parenteral nutrition versus intestinal transplantation. Where are we today? *Dig Dis Sci*. 2007;52(4):876–892. doi:10.1007/s10620-006-9416-6
29. Carter BA, Cohran VC, Cole CR, et al. Outcomes from a 12-week, open-label, multicenter clinical trial of teduglutide in pediatric short bowel syndrome. *J Pediatr*. 2017;181:102–111.e5. doi:10.1016/j.jpeds.2016.10.027
30. Gillon R. Defending the four principles approach as a good basis for good medical practice and therefore for good medical ethics. *J Med Ethics*. 2015;41(1):111–116. doi:10.1136/medethics-2014-102282
31. Kong WM. What is good medical ethics? A clinician's perspective. *J Med Ethics*. 2015;41(1):79–82. doi:10.1136/medethics-2014-102302
32. Druml C, Ballmer PE, Druml W, et al. ESPEN guideline on ethical aspects of artificial nutrition and hydration. *Clin Nutr*. 2016;35(3):545–556. doi:10.1016/j.clnu.2016.02.006
33. Bükki J, Unterpaul T, Nübling G, Jox RJ, Lorenzl S. Decision making at the end of life—cancer patients' and their caregivers' views on artificial nutrition and hydration. *Support Care Cancer*. 2014;22(12):3287–3299. doi:10.1007/s00520-014-2337-6
34. Hartman C, Shamir R, Simchowitz V, Lohner S, Cai W, Decsi T. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: complications. *Clin Nutr*. 2018;37(6Pt B):2418–2429. doi:10.1016/j.clnu.2018.06.956
35. Hiesmayr M, Schindler K, Pernicka E, et al. Decreased food intake is a risk factor for mortality in hospitalised patients: the NutritionDay survey 2006. *Clin Nutr*. 2009;28(5):484–491. doi:10.1016/j.clnu.2009.05.013
36. Campbell AV. The virtues (and vices) of the four principles. *J Med Ethics*. 2003;29(5):292–296. doi:10.1136/jme.29.5.292
37. Parkinson KN, Gibson L, Dickinson HO, Colver AF. Pain in children with cerebral palsy: a cross-sectional multicentre European study. *Acta Paediatr*. 2010;99(3):446–451. doi:10.1111/j.1651-2227.2009.01626.x
38. Parkes J, Caravale B, Marcelli M, Franco F, Colver A. Parenting stress and children with cerebral palsy: a European cross-sectional survey. *Dev Med Child Neurol*. 2011;53(9):815–821. doi:10.1111/j.1469-8749.2011.04014.x
39. Scherer N, Verhey I, Kuper H, Manzoli L. Depression and anxiety in parents of children with intellectual and developmental disabilities: a systematic review and meta-analysis. *PLoS One*. 2019;14(7):e0219888. doi:10.1371/journal.pone.0219888
40. Beighton C, Wills J. How parents describe the positive aspects of parenting their child who has intellectual disabilities: a systematic review and narrative synthesis. *J Appl Res Intellect Disabil*. 2019;32(5):1255–1279. doi:10.1111/jar.12617