Charting the Territory: Symptoms and Functional Assessment in Children With Progressive, Non-Curable Conditions*

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Abstract

Background: Children with progressive, non-curable genetic, metabolic, or neurological conditions require specialized care to enhance their quality of life. Prevention and relief of physical symptoms for these children needs to begin at diagnosis, yet, little is known about their patterns of symptoms and functional abilities.

Aim: To describe these children's symptoms, as well as how the children's condition affects them physically.

Design: Cross-sectional, baseline results from an observational, longitudinal study, *Charting the Territory*, that followed 275 children and their families.

Setting/participants: Seven tertiary care children's hospitals in Canada, 2 in the USA. Families were eligible based on the child's condition. A total of 275 children from 258 families participated.

Results: The 3 most common symptoms in these children were pain, sleep problems, and feeding difficulties; on average, they had 3.2 symptoms of concern. There was a pattern of underreporting of children's symptoms for clinicians compared with parents. Regardless of use of associated medications, pain, feeding, and constipation symptoms were often frequent and distressing. Children with a G/J tube had a higher total number of symptoms, and respiratory problems, pain, feeding difficulties, and constipation were more likely to occur. They also tended to have frequent and distressing symptoms and to need extensive mobility modifications, which in turn was associated with higher numbers of symptoms.

Conclusions: These children experience multiple symptoms that have been previously documented individually, but not collectively. Effective interventions are needed to reduce their symptom burden. Future longitudinal analyses will examine which disease-modifying interventions improve, or not, symptom burden.

Children with progressive genetic, metabolic, or neurological conditions for which there is no cure (PNCs) and their families require specialized care to enhance their quality of life. In Canada, about half of the annual 2500 childhood non-traumatic deaths occur because of PNCs.[1,2] These diagnoses account for more than 50% of children who receive pediatric palliative care in North America.[1,3,4] Though individual conditions are rare, they have been broadly categorized within a single group because of their unifying problem: they involve impairment/injury of the central nervous system and are progressive.[5,6] These children typically display problems seen with such impairment, e.g., pain, seizures, and loss of mobility,[7] therefore prevention and relief of physical symptoms needs to begin at diagnosis. Yet, little is known about the patterns of symptoms or possible correlations with functional abilities.

Research in pain and symptom management is a priority in pediatric palliative care,[8] and families of children with PNCs report symptoms and issues around medications as two important milestones in a child's illness trajectory.[6] Common symptoms reported by clinicians include: pain, breathing problems, feeding difficulties, alertness/interaction changes, sleep problems, seizures, and constipation.[3,7,9-22] There is a need to research children's symptoms, but information about symptoms is not always documented even in patient records[4] and the co-occurrence of symptoms is rarely explored. Children may be prescribed multiple medications,[3,20-24] but little is published about the specific types of medications commonly used by clinicians and whether or not the prescribed medications alleviate symptoms.

These children usually experience developmental delays and functional losses that increase over time.[6,9,25] There is some evidence that pain behaviour may be different for children with neurodegenerative conditions,[25] but the literature is inconsistent regarding

whether functional levels affect pain expression.[26,27] The relationships between functional levels and other symptoms remain unclear, yet loss of mobility and needing modifications/equipment are significant milestones in this population.[6]

Many children with PNCs receive enteral feeds, e.g., via gastrostomy or jejunal (G/J) tubes.[6,24] Improved nutrition can lead to improved quality of life for the child and family,[28] but G/J feeding can result in complications such as aspiration pneumonia, site infection, and reflux.[22,28] Consequently, the children may have related symptoms, e.g., pain, feeding or respiratory problems, but little is known about correlations between G/J feeds and symptoms. Further, clinical experience suggests that children with G/J tubes often have restricted mobility, which may contribute to increased symptoms. Exploration of this anecdotal evidence is warranted.

Overall, there is a paucity of research on which to base best practices for care of children with PNCs.[3,29] Much of the fairly limited literature focuses on specific conditions.[9-15,30,31] Discussion is often about the treatment of one symptom such as seizures.[9,16] A majority of the research is retrospective[13,14,30] and often the sample sizes are small.[9,10,15] Though some information has been published, there is little to describe the natural progression of this group as a whole, particularly from a prospective approach. Little information exists about differences in symptoms by physical functioning, e.g., by the need for mobility modifications or presence/absence of a G/J tube.

This paper reports baseline results about 275 child participants (from 258 families) in a multisite, longitudinal study, *Charting the Territory*, that followed children with these conditions, and their families. The focus is on symptoms reported, and differences in selected symptoms by use of medications, G/J tube presence, and/or level of mobility modifications.

METHODS

The larger study was developed to determine the child's clinical trajectory including symptoms, and the associated emotional, social, physical, and spiritual experiences of the family over time. It used quantitative methods, with established instruments and record reviews. Children (0-19 years) and their families were followed for 18-48 months, depending on when they entered the study. Data collection began at baseline and continued through bereavement or until the end of study.[1]

Recruitment

Families were recruited from July 2009 till October 2012, mostly through referrals from hospital clinics (49%) and hospice/palliative teams/services (43%). Eligibility was based on the child's condition (Appendix A, Web only). Of 385 families evaluated for eligibility, 93 did not meet criteria or declined further contact, 34 could not be contacted, leaving 258 families.

Data Collection

To facilitate continuity and reduce the likelihood of inter-rater discrepancies, parents identified a 'designated' parent in their family to answer questions about the child. Designated parents completed baseline questionnaires in-person, by mail, or a combination thereof and, subsequently, reported on their child's symptoms monthly via the Internet or, for a few, by telephone. Parents who chose the online method needed to have an existing email account and access to the Internet. The software included an email component every month to prompt parents to visit the secure website and complete the symptom questionnaire. A Research Assistant (RA) called telephone responders to obtain answers.

Record review

After enrollment, the site RA collected baseline information regarding the child's diagnosis, clinical condition, medications, and procedures undergone. Disease diagnoses were characterized according to a scheme developed in an iterative process by one of the authors (HS) and 2 study collaborators from Biochemical Diseases/Genetics and Pediatric Neurology.

Clinical symptoms

Information about 7 common symptoms in this population was collected at baseline and then monthly. Parents were given definitions for each symptom - pain, respiratory/breathing problems, feeding difficulties, alertness/interaction changes, sleep problems, seizures, and constipation - prior to completing the baseline assessment (Appendix B, Web only).

The instrument takes 6 to 10 minutes to complete and was designed by the research team in consultation with other experienced clinicians, families linked to a pediatric palliative care hospice program, and a psychometrician. It is a modification of the PediQUEST symptom recording tool and the revised Memorial Symptom Assessment Scale (7-12 years of age) developed for symptoms in children with cancer.[32] Symptoms are tracked for timing of onset (symptom latency[15]), frequency in last week, change since first appeared (or since previous month), and extent of distress. Face and content validity were evaluated prior to the start of the study with the assistance of parents of children who received palliative care, and the instrument was pilot tested in clinical practice (HS).

Annual functional assessment: Pediatric Evaluation of Disability Inventory (PEDI©)

The PEDI©[33,34] was used to assess the children's function at baseline, then annually. It yields information under Parts I (Functional Skills), II (Caregiver Assistance), and III (Modifications) in the domains of self-care, mobility, and social function. Scores are summarized into composite scores. Raw scores from Parts I and II can be converted to normative standard

scores as well as scaled scores for comparison against norm-age values. Raw scores are reported for this study because children with PNCs tend to have significant disabilities; therefore, it was deemed unreasonable to compare them to 'norms'. Appendix C (Web only) provides details about the reliability and validity of the PEDI©, procedures for administering it, and steps taken to ensure RAs were competent in using the instrument.

Data Analysis

Data were entered into a database for preprocessing, data cleaning, and determination of scale composites according to the appropriate procedures for the standardized measures. Missing data for outcome measures were linearly imputed, if possible, according to standard procedures for the specific tool. Analyses were performed using the Statistical Package for the Social Sciences (SPSS®), Version 20, with statistical significance at $p<.05$.

Demographics and outcome measures were summarized using descriptive statistics: frequencies and % for categorical variables, means and SD for continuous variables. Two-tailed comparison tests included: χ^2, two-sample t-test, Spearman's Rho and Pearson r correlations, 1-way and 2-way ANOVA.

Ethics approval for this bi-national (Canada/USA) study was obtained from 9 study settings plus the 4 universities where the researchers were affiliated. The University of British Columbia and Children's & Women's Health Centre of BC (Certification #H08-00124) approved the central site in Vancouver. On behalf of themselves and their child(ren), parent participants signed a consent form; the ill children were unable to sign consent/assent forms due to their health conditions.

RESULTS

Sample Characteristics

Few meaningful differences were detected by study site across all analyses, therefore, results are reported for the whole sample. On average, the 258 families had 2.5 (SD 1.4) living children, range 1-10; 283/574 of the total number of children had a PNC, with two such children enrolled from 17 families. Prior to baseline, a total of 20 children in 16 families had died, 50% from a PNC; of the remainder, 5 were miscarriages. Most families (n=169, 65.5%) received some form of palliative care.

Families had been engaged with the medical system for over 6 years on average (table 1). They typically waited almost a year between bringing the child to a physician and receiving a diagnosis; though many children still did not have a diagnosis (n=48, 17.5%). About 30% of parents learned prenatally (n=33) or perinatally (n=51) that the child had a problem. Others initiated investigation because of concerns such as the child not meeting developmental milestones (n=54, 19.6%). The child's average age at which parents began the diagnostic process was 12.1 months (SD 25.5). Clinicians typically employed multiple methods for confirming diagnoses.

Records indicated that all children underwent at least one surgery or interventional radiology procedure (table 2). Most had multiple assessments and many took several types of medications (mean 3.5, SD 2.3). Sixty-one percent (n=168) received nourishment other than orally and 13.1% (n=36) used a ventilator. Many children (n=125, 45.5%) had an abnormal EEG.

As detailed in table 3, symptoms were common, with about half of the children experiencing any of the symptoms except for difficulties with alertness. Parents reported an average of 3.2 (SD 1.9) symptoms at baseline, whereas clinicians documented fewer (mean 2, SD 1.7). Correlations between parental and clinician reports of symptoms were positive, and weak to moderately strong; all were statistically significant (p=<.001).

Parents reported frequency and change for symptoms, as well as the distress they ascribed to the child (table 4). Only two symptoms showed statistically significant differences by conditions: change in seizures (χ^2=35.79, p=.02), and distress from feeding difficulties (χ^2=38.26, p=.03).

The only statistically significant difference between 4 selected symptoms and their associated medication use (table 5) was frequency for seizures (χ^2=11.71, p=<.01), though distress was present for the majority who were receiving seizure medications. Regardless of whether medications were used, parents also reported children experiencing and being distressed by pain, feeding difficulties, and constipation.

Children with G/J tubes had more symptoms (mean 3.67, SD 1.74) than children without (mean 2.68, SD 2; p=<.001). Differences were seen in breathing, pain, feeding, and constipation symptoms depending on G/J tube presence (table 6). Despite mostly statistically insignificant results, G/J tube presence was generally consistent with higher levels of symptom frequency and distress (table 7).

Table 8 shows that average functional levels were all on the low end of the respective subscales, indicating that children could provide little self-care (mean 14.7, SD 19.6), had difficulty in getting around (mean 14.6, SD 19.2), and were limited in social function (mean 16.9, SD 17.8). All Functional and Caregiver Assistance subscales showed statistically significant differences by conditions (p=≤.001).

As shown in table 9, children who scored lower on functional skills had a higher total number of symptoms; children with G/J tubes were more likely to require extensive mobility modifications; and both G/J tube presence and level of mobility modification were associated with higher numbers of symptoms, though their interaction was not statistically significant.

DISCUSSION

Results from this study are supported by the literature in a number of ways, including the plethora of medications given to these children.[3,16,17] One of the most striking findings is the children's large symptom experience. The children had, on average, just over 3 symptoms of concern and almost every symptom appeared in at least half of the children. This finding in children with metabolic, chromosomal, or neurological conditions parallels findings about symptom burden in children with cancer.[35,36]

Symptom management is a hallmark of pediatric palliative care and it is not surprising that many of the children were being treated for multiple symptoms. However, symptoms were often not well-controlled and children frequently experienced and were distressed by symptoms, whether or not they were receiving associated medications. Where children were receiving an indicated medication, the treatment was often not effective. These findings highlight the difficulties in managing symptoms in this population, especially seizures, and suggest that further research is needed to identify optimal management.

Though there were significant correlations between parent and clinician reports of children's symptoms, there was a pattern of underreporting for clinicians compared with parents, a finding that is consistent with some pediatric palliative care literature.[7,21,37,38] There are many potential reasons for this finding, including missing documentation.[4] One reason may be that neurological symptoms especially are difficult to deal with in this population.[23] Another is that clinicians sometimes report only those symptoms that they feel confident in treating[7] or they do not assess for a symptom because of the child's impaired cognition,[21] and, finally, sometimes clinicians disbelieve parents, especially if a child is non-verbal.[38] Clinicians whose approach is to question why they should <u>not</u> believe a parent rather than why they should and

who view symptoms as multidimensional experiences that have meaning for patients and their families rather than simply as side effects may be less likely to underreport.[7,38] Also, many anxieties/difficulties accompany parents dealing with PNCs.[6]. If a symptom causes parental concern then parents may report it more frequently.[39] Therefore, clinicians should ask parents why a symptom is of concern so they can address the parents' needs. From a clinical perspective, it is equally important to be cognizant of both the frequency and the severity of symptoms as each may lead to a different understanding of the nature of a symptom, and, therefore, may contribute to identifying the most appropriate intervention.

The increased pattern of symptom burden when a G/J tube is present and/or when there are extensive mobility modifications indicates that clinicians need to be alert to assessing and managing symptoms in these children. We do not know whether feeding devices or mobility tools increase symptoms directly, but both interventions are indicative of children with more severe conditions and, consequently, more symptom burden. Therefore, extra attention to symptoms in children with feeding devices and/or mobility modifications is warranted.

Limitations

A main limitation of this report is its cross-sectional, primarily descriptive nature. But these are only the first results from a longitudinal study. Future analyses of data, for example examining correlations among variables and over time, will provide a better understanding of changing outcomes as the child's illness trajectory unfolds. Another limitation is that parents reported on behalf of their child. However, this population of children with PNCs is typically non-communicative and parents usually speak for their child in everyday situations. Therefore, it may be reasonable to expect parents rather than these children to provide information.

A limitation of the PEDI© in a population with a high level of neurological impairment is that it does not indicate other functional limitations that can impact health, such as respiratory decline and earlier death correlating with a child's inability to hold his head up when prone. However, an important point to note is that a functional assessment can highlight a child's deterioration over time or it can point out when an intervention may be warranted. Routine evaluation of functioning over time would not only document a condition's trajectory, but would also identify places for clinical intervention, as well as provide comparative data about an individual child over time.

CONCLUSIONS

Pediatric palliative care is an expanding field, yet the paucity of research means that clinicians have little evidence on which to base their practice. This baseline report from a unique longitudinal study offers detailed information about symptoms in children with progressive, non-curable genetic, metabolic, or neurological conditions. The large sample size lends credence to findings and provides a solid foundation for understanding trajectories over time. Future longitudinal analyses will examine which disease-modifying interventions improve, or not, symptom burden.

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We appreciate that the terminology is not settled regarding the most appropriate term to use when reporting on children with the types of conditions in this study. Various terms, such as life-threatening, life-limiting, life-shortening, and complex medical problems, have all been proposed and often one is preferred over another depending on one's country. For the purposes of this paper, we have used the term 'progressive, non-curable conditions' because it reduces ambiguity and is acceptable to this journal.

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What is known about this topic:

- Progressive, non-curable genetic, metabolic, or neurological conditions involve impairment/injury of the central nervous system.
- Children often have multiple symptoms associated with such impairment, e.g., pain, seizures, and loss of mobility, and need appropriate interventions.
- These children often rely on enteral nutrition, e.g., via G/J tube, and require mobility modifications.

What this study adds:

- The 3 most common symptoms in these children are pain, sleep problems, and feeding difficulties; on average, they have 3 symptoms of concern.
- Regardless of medication use, seizure, pain, feeding, and constipation issues may be frequent and distressing to these children.
- Children with G/J tubes, lower levels of function, or extensive mobility modification requirements have a higher total number of symptoms.

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Licence for Publication Statement

Contributor Statement

Gail Andrews: Ms. Andrews conceptualized and designed the study, analysed and interpreted the data, revised the resubmitted manuscript, and approved the resubmitted manuscript.

Susan Cadell: Dr. Cadell conceptualized and designed the study, revised the resubmitted manuscript, and approved the resubmitted manuscript.

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Rose Steele: Dr. Steele conceptualized and designed the study, analysed and interpreted the data, drafted and revised the resubmitted manuscript, and approved the resubmitted manuscript.

Table 1: Selected Demographic Information at Baseline About 275 Children With Progressive, Non-Curable Conditions (PNCs)

Demographic	Ill Children
Gender	
Female	139 (50.5)
Male	136 (49.5)
Age (years) on entry to study	6.6 ± 5.2[a]; 0 to 19
Age (months) at initiation of diagnostic evaluation (n = 261)	12.1± 25.5; -5.8 to 183.5[a,b]
Age (years) at diagnosis (n = 203)	2.2± 3; -0.4 to 15.7[a,b]
New vs. Pre-existing condition (n = 258)	
New (<6 weeks)	3 (1.2)
Pre-existing (≥6 weeks)	255 (98.8)
Top concerns that brought parent to MD[c]	
Not meeting developmental milestones	54 (19.6)
Perinatal: diagnosis or problem noted	51 (18.5)
Seizures	47 (17.1)
Change in muscle tone	34 (12.4)
Prenatal: diagnosis or problem noted	33 (12)
Feeding difficulties	30 (10.9)
Breathing difficulties	21 (7.6)
Losing developmental milestones	21 (7.6)
Weeks since parent first sought medical treatment (n = 261)	315.2± 248.9; 7.9 to 980[a]
Weeks since child's diagnosis (n = 203)	269.6 ± 231.3; 0 to 903.7[a]
Months from initial diagnostic evaluation to confirmation of diagnosis (n = 197)	11.9± 23.6; 0 to 177.9[a]
Diagnostic methods[d]	
Molecular	192 (69.8)
Clinical	178 (64.7)
Biochemistry	142 (51.6)
Anatomic pathology	61 (22.2)
Primary condition	
Multi-organ congenital abnormalities	57 (20.7)
Severe neurological impairment - not yet diagnosed	48 (17.5)
Epileptic encephalopathy/neurodegenerative disease	44 (16)
Lysosomal/peroxisomal leukodystrophy	43 (15.6)
Mitochondrial encephalo-/myopathy	29 (10.5)
Structural CNS abnormalities	18 (6.5)
Small molecules diseases	13 (4.7)
Neuromuscular diseases	10 (3.6)
Other inborn errors of metabolism	6 (2.2)
Congenital disorders of glycosylation	4 (1.5)
Other conditions not otherwise specified (NOS)	3 (1.1)

Values are number (%) unless otherwise indicated.

[a] Plus-minus values are means ± SD; followed by minimum to maximum.
[b] Negative values reflect prenatal evaluations and diagnoses.
[c] Some responses not reported in table; overall, numbers totaled more than sample size because some parents provided multiple responses.
[d] Numbers totaled more than sample size because multiple methods could be documented.

Table 2: Record Review: Assessments, Interventions, and Medications Prior to Baseline for 275 Children With Progressive, Non-Curable Conditions

Assessments, Interventions, and Medications	Ill Children
Assessments	
PT/OT (n = 274)	249 (90.5)
Dietician (n = 248)	246 (89.5)
Home nurse (n = 270)	198 (72.8)
Selected interventions	
Gastric or jejunal tube	148 (53.8)
Oxygen by nasal cannula or mask	29 (10.6)
Limits of care/Do not attempt resuscitation orders	42 (15.3)
Routine suctioning	50 (18.4)
Non-invasive ventilation	23 (8.4)
Clinical trial	20 (7.3)
Total parenteral nutrition	4 (1.5)
Nasogastric tube	16 (5.8)
Invasive ventilator	13 (4.7)
Complementary/alternative modalities	7 (2.5)
Complementary/alternative medications	6 (2.2)
Surgery or interventional radiology procedures	275 (100)
Total number prior to baseline	11.4± 5.5; 6-41[a]
Used with surgery or interventional radiology procedures	
General anesthesia	170 (61.8)
Total number of times anesthesia used	3.23± 4.8; 0-36[a]
Sedation	61 (22.2)
Total number of times sedation used	0.6± 1.6; 0-11[a]
Electroencephalography (EEG) prior to baseline	149 (54.2)
Total number of EEGs	2.6 ± 4.1; 0-30[a]
Abnormal EEG prior to baseline	125 (45.5)
Medications	
Total number of different drug categories	3.5 ± 2.3; 0-12[a]
Anticonvulsants	152 (55.5)
Antacids	125 (45.6)
Metabolic	118 (43.1)
Anxiolytic	111 (40.7)
Other	108 (39.4)
Laxatives	97 (35.4)
Acetaminophen/NSAIDs	52 (19)
Melatonin/hypnotic	48 (17.5)
Pro-kinetics	43 (15.8)
Cardiac	27 (9.9)
Antispasticity	27 (9.9)
Neuroleptic	21 (7.7)
Opiates	21 (7.7)
Antiemetics	12 (4.4)
Anesthetics	3 (1.1)

Values are number (%) unless otherwise indicated.

[a] Plus-minus values are means ± SD; followed by minimum to maximum.

Table 3: Symptoms Present at Baseline for 275 Children With Progressive, Non-Curable Conditions

Symptom	Reported by Parents[a]	p[b]: conditions	Reported by Clinicians in Children's Records[c]	p[d]: conditions	Months Since Birth for Symptom to Appear[e]	p[f]: conditions
Pain	149 (55.2) r_s = .34, <.001	.78	67 (26)	.13	45.7±59.3[g]	<.001
Sleep problems	136 (50.2) r_s = .33, <.001	.28	75 (29.1)	.<01	31.4 ±50.4[g]	.02
Feeding difficulties	130 (48) r_s = .38, <.001	.24	108 (41.7)	.42	29.9 ±49.3[g]	<.001
Constipation	127 (47) r_s = .28, <.001	.33	72 (27.9)	.30	30.7 ±43.1[g]	<.001
Respiratory or breathing problems	126 (46.5) r_s = .28, <.001	.37	66 (25.6)	.57	46.7 ±60.3[g]	<.001
Seizures	109 (40.2) r_s = .65, <.001	<.001	110 (42.5)	<.01	34 ±49[g]	.001
Alertness and interaction changes	94 (34.7) r_s = .24, <.001	.03	42 (16.3)	.61	55.4 ± 61.5[g]	<.001
Total number of symptoms	3.2±1.9[g] r_s = .46, <.001	<.01	2 ±1.7[g]	.02		

Values are number (%) unless otherwise indicated.

[a] % for parents calculated based on number of parents who responded to the question; r_s is the Spearman's Rho result for bivariate correlations between parental and clinician reports, followed by p-value.
[b] χ^2 test was used for categorical variables and 1-way ANOVA was used for the continuous variable to test by children's conditions.
[c] % for clinicians calculated based on number of records reviewed by RA.
[d] χ^2 test was used for categorical variables and 1-way ANOVA was used for the continuous variable to test by children's conditions.
[e] Results predicated on symptom being present.
[f] 1-way ANOVA was used to test continuous variables by children's conditions.
[g] Plus-minus values are means ± SD.

Table 4: Parental Report of Frequency, Change, & Distress for Symptoms Present at Baseline in 275 Children With Progressive, Non-Curable Conditions

Symptom[a]	Frequency[b]	p[c]: conditions	Change[d]	p[c]: conditions	Distress[e]	p[c]: conditions
Pain (n = 149)	4 (2.7); 70 (47.3); 60 (40.5); 14 (9.5)	.31	41 (27.5); 33 (22.1); 52 (34.9); 23 (15.4)	.31	5 (3.4); 64 (43.2); 69 (46.6); 10 (6.8)	.05
Sleep problems (n = 136)	6 (4.5); 39 (29.1); 88 (65.7); 1 (0.7)	.59	30 (22.4); 63 (47); 36 (26.9); 5 (3.7)	.52	34 (25.4); 38 (28.4); 47 (35.1); 15 (11.2)	.14
Feeding difficulties (n = 130)	11 (8.5); 35 (27.1); 81 (62.8); 2 (1.6)	.48	41 (31.5); 43 (33.1); 43 (33.1); 3 (2.3)	.25	26 (20.2); 39 (30.2); 51 (39.5); 13 (10.1)	.03
Constipation (n = 127)	7 (5.5); 48 (37.8); 72 (56.7); 0	.93	34 (27); 63 (50); 29 (23); 0	.37	11 (8.8); 36 (28.8); 66 (52.8); 12 (9.6)	.44
Respiratory or breathing Problems (n = 126)	5 (4); 59 (47.2); 60 (48); 1 (0.8)	.83	40 (32.8); 37 (30.3); 43 (35.2); 2 (1.6)	.81	16 (13); 41 (33.3); 56 (45.5); 10 (8.1)	.20
Seizures (n = 109)	9 (8.3); 45 (41.3); 49 (45); 6 (5.5)	.53	40 (36.7); 27 (24.8); 38 (34.9); 4 (3.7)	.02	22 (20.4); 28 (25.9); 42 (38.9); 16 (14.8)	.39
Alertness and interaction changes (n = 94)	4 (4.3); 57 (62); 27 (29.3); 4 (4.3)	.66	41 (44.1); 22 (23.7); 26 (28); 4 (4.3)	.08	28 (30.1); 22 (23.7); 25 (26.9); 18 (19.4)	.17

Numbers reported as frequency (%).

[a] Sample size for each symptom is the number of times parents reported a symptom was present for their child at baseline.
[b] Frequency of symptom in last week reported as Almost never; Sometimes; Most of the time; Unsure/Can't tell. % calculated based on number of parents who responded to the question.
[c] χ^2 tests used for all variables by children's conditions; for all comparisons.
[d] Change in symptom since symptom first appeared reported as Better; About the same; Worse; Unsure/Can't tell. % calculated based on number of parents who responded to the question.
[e] Extent of child's distress from symptom in last week reported as None or a little bit; Somewhat; A lot; Unsure/Can't tell. % calculated based on number of parents who responded to the question.

Table 5: Relationships Between Use of Associated Medications and Frequency & Distress for 4 Selected Symptoms Present at Baseline in 275 Children With Progressive, Non-Curable Conditions

Symptom[a]	Frequency			P[b]	Distress			P[b]
	Medications	No	Yes		Medications	No	Yes	
Seizures[c] (n = 109)	Almost never:	3	6	<.01	None or a little bit:	5	17	.37
	Sometimes:	8	37		Somewhat:	4	24	
	Most of the time:	1	48		A lot:	3	39	
	Unsure/Can't tell:	2	4		Unsure/Can't tell:	2	14	
Pain[d] (n = 147)	Almost never:	3	1	.17	None or a little bit:	3	2	.1
	Sometimes:	50	19		Somewhat:	52	12	
	Most of the time:	38	22		A lot:	42	26	
	Unsure/Can't tell:	13	1		Unsure/Can't tell:	7	3	
Feeding difficulties[e] (n = 129)	Almost never:	3	8	.26	None or a little bit:	9	17	.27
	Sometimes:	10	25		Somewhat:	18	21	
	Most of the time:	35	46		A lot:	14	37	
	Unsure/Can't tell:	0	2		Unsure/Can't tell:	6	7	
Constipation[f] (n = 126)	Almost never:	4	3	.3	None or a little bit:	8	3	.15
	Sometimes:	29	18		Somewhat:	23	13	
	Most of the time:	34	38		A lot:	29	36	
	Unsure/Can't tell:	0	0		Unsure/Can't tell:	6	6	

Numbers reported as frequency.

[a] Sample size for each symptom is the number of times parents reported on frequency or distress of a symptom for their child at baseline.
[b] χ^2 tests used for all comparisons.
[c] Medications considered to be associated with management of seizures: anticonvulsants.
[d] Medications considered to be associated with management of pain: NSAIDS, Acetaminophen, anesthetics; counted as 'yes' if any of these medications used.
[e] Medications considered to be associated with management of feeding difficulties: antacids, prokinetics, antiemetics; counted as 'yes' if any of these medications used.
[f] Medications considered to be associated with management of constipation: laxatives.

Table 6: Relationships Between Presence of G/J Tube and Presence of Symptoms at Baseline for 275 Children With Progressive, Non-Curable Conditions

Symptom[a]	G/J Tube Present		P[b]
	No	Yes	
Respiratory or breathing problems (n = 270)			
No	84	61	<.001
Yes	41	85	
Pain (n = 270)			
No	67	54	<.01
Yes	58	91	
Feeding difficulties (n = 271)			
No	76	65	<.01
Yes	49	81	
Constipation (n = 270)			
No	76	67	<.05
Yes	48	79	
Seizures (n = 271)			
No	82	80	.07
Yes	43	66	
Sleep problems (n = 271)			
No	69	66	.1
Yes	56	80	
Alertness and interaction changes (n = 271)			
No	85	92	.39
Yes	40	54	
Total # symptoms (n = 271)	125	146	<.001

Numbers reported as frequency.

[a] Sample size for each symptom is the number of times parents reported on presence of a symptom for their child at baseline.
[b] χ^2 tests were used for the categorical variables; two-sample t-test was used for the continuous variable.

Table 7: Relationships Between Presence of G/J Tube and Frequency & Distress for Symptoms Present at Baseline in 275 Children With Progressive, Non-Curable Conditions

Symptom[a]	Frequency			P[b]	Distress			P[b]
	G/J tube Present	No	Yes		G/J tube Present	No	Yes	
Respiratory or breathing problems (n = 125)	Almost never:	2	3	.84	None or a little bit:	7	9	<.05
	Sometimes:	20	39		Somewhat:	16	25	
	Most of the time:	18	42		A lot:	10	46	
	Unsure/Can't tell:	0	1		Unsure/Can't tell:	6	4	
Pain (n = 148)	Almost never:	1	3	.36	None or a little bit:	4	1	<.05
	Sometimes:	31	39		Somewhat:	27	37	
	Most of the time:	19	41		A lot:	20	49	
	Unsure/Can't tell:	7	7		Unsure/Can't tell:	6	4	
Feeding difficulties (n = 129)	Almost never:	3	8	.86	None or a little bit:	13	13	<.05
	Sometimes:	13	22		Somewhat:	19	20	
	Most of the time:	32	49		A lot:	12	39	
	Unsure/Can't tell:	1	1		Unsure/Can't tell:	5	8	
Constipation (n = 127)	Almost never:	3	4	.89	None or a little bit:	6	5	.16
	Sometimes:	17	31		Somewhat:	17	19	
	Most of the time:	28	44		A lot:	23	43	
	Unsure/Can't tell:	0	0		Unsure/Can't tell:	2	10	
Alertness and interaction changes (n = 93)	Almost never:	3	1	.25	None or a little bit:	12	16	.25
	Sometimes:	27	30		Somewhat:	13	9	
	Most of the time:	8	19		A lot:	10	15	
	Unsure/Can't tell:	2	2		Unsure/Can't tell:	5	13	
Sleep (n = 134)	Almost never:	3	3	.51	None or a little bit:	13	21	.37
	Sometimes:	19	20		Somewhat:	3	25	
	Most of the time:	33	55		A lot:	20	27	
	Unsure/Can't tell:	0	1		Unsure/Can't tell:	9	6	
Seizures (n = 109)	Almost never:	4	5	.62	None or a little bit:	7	15	.44
	Sometimes:	20	25		Somewhat:	13	15	
	Most of the time:	16	33		A lot:	18	24	
	Unsure/Can't tell:	3	3		Unsure/Can't tell:	4	12	

Numbers reported as frequency.

[a] Sample size for each symptom is the number of times parents reported on frequency or distress of a symptom for their child at baseline.
[b] χ^2 tests used for all comparisons.

Table 8: Outcome Measure Results for 275 Children With Progressive, Non-Curable Conditions: Pediatric Evaluation of Disability Inventory

PEDI©: Parts I, II, & III and domains	Ill Children[a]	p[b]: conditions	p[c]: gender
Functional skill: Self-care (n = 270)	14.7 ± 19.6	<.001	.23
Functional skill: Mobility (n = 270)	14.6 ±19.2	<.001	.65
Functional skill: Social function (n = 270)	16.9 ±18	<.001	.44
Caregiver assistance: Self-care (n = 270)	4.7 ±9.7	<.001	.11
Caregiver assistance: Mobility (n = 269)	6.5 ±11.1	<.001	.63
Caregiver assistance: Social function (n = 270)	4.1 ±6.8	<.001	.62
Modifications: Self-care (n = 270)			
No modifications	3.9 ±2.2	<.01	.55
Child-oriented (non-specialized) modifications	3.0 ±2	<.01	.49
Rehabilitation equipment	0.4 ±0.8	.22	.05
Extensive modifications	0.7 ±1.1	.05	.14
Modifications: Mobility (n = 270)			
No modifications	4 ±2.3	.001	.26
Child-oriented (non-specialized) modifications	1 ±1.6	.01	.51
Rehabilitation equipment	0.6 ±1.2	.30	.68
Extensive modifications	1.4 ±2.2	.001	.67
Modifications: Social function (n = 270)			
No modifications	4.5 ±1.2	<.01	.65
Child-oriented (non-specialized]) modifications	0.1 ±0.4	.33	.62
Rehabilitation equipment	0.2 ±0.8	.04	.25
Extensive modifications	0.2 ±0.7	.42	.89

[a] Plus-minus values are means ± SD.
[b] 1-way ANOVA was used for all continuous variables to test by children's conditions.
[c] Two-sample t-test was used for all continuous variables to test by gender.

Table 9: Relationships Between Functional Skills, Presence of G/J Tube, Highest Level of Mobility Modification Required, and Total Number of Symptoms Present at Baseline in 275 Children With Progressive, Non-Curable Conditions

PEDI©-G/J Tube Variables	Test Statistics	P
Functional skills – Self-care (Raw score)[a] (n = 271)	Total # symptoms; r = -.287	<.001
Functional skills – Mobility (Raw score)[a] (n = 271)	Total # symptoms; r = -.297	<.001
Functional skills – Social function (Raw score)[a] (n = 271)	Total # symptoms; r = -.21	.001
PEDI©: Highest level of mobility modifications[b,c] (n = 270)	G/J tube present No Yes None: 30 31 Child: 39 28 Rehab: 27 13 Extensive: 27 75 $\chi^2 = 27.39$; df = 3	<.001

Interaction of Highest level of mobility modifications & G/J tube present or not[d]	Total # symptoms;
	F = 1.686; df = 3,258
		.17

PEDI©: Highest level of mobility modifications[d]	Total # symptoms;
	F = 13.654; df = 1,258
		<.001

G/J tube present or not[d]	Total # symptoms;
	F = 4.866; df = 3,258
		<.01

Numbers reported as frequency.

[a] Pearson correlation between functional skills and total number of symptoms at baseline.
[b] Highest level determined by presence of a positive response on at least one of the PEDI modification questions, where None is lowest level possible and Extensive is highest level possible.
[c] χ^2 test used for comparison between highest level of mobility modifications and presence of G/J tube at baseline.
[d] 2-way ANOVA with highest level of mobility modifications and presence of G/J tube as the 2 factors, and total number of symptoms as the response variable.