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Subjective Toxicity Profiles of Children in Treatment for Cancer: A New Guide to Supportive Care?

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Abstract

Context.—Children and adolescents with cancer experience treatment-related, subjective adverse events (AEs). Identifying distinct groups of patients who predictably experience higher prevalence of AEs could guide patient care.

Objectives.—Study aims were to 1) identify groups of children and adolescents reporting AEs using the Pediatric Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (Ped-PRO-CTCAE); 2) determine whether demographic and clinical characteristics predict AE group membership; and 3) examine whether AE group membership was related to the distal outcome of psychological stress.

Methods.—Four hundred seventy-seven patients self-reported AEs via the Ped-PRO-CTCAE at T1 (beginning of treatment) and the PROMIS Pediatric Psychological Stress measure at T2 (7–28 days later). Latent class analysis was conducted to identify groups of patients and the relationships of the groups with demographic and clinical characteristics, and with stress.

Results.—Three distinct a priori unknown AE groups were identified (high AE prevalence, moderate AE prevalence, and low AE prevalence). Females, blacks, patients with high psychological stress, and patients more recently diagnosed were more likely to be in the high AE prevalence group. Gender, age, race, and time since diagnosis were associated with psychological stress.

Conclusion.—Children with cancer are heterogeneous in experiencing subjective AEs. Gender, race, and time since diagnosis were significantly associated with higher subjective AE prevalence that may lead to psychological stress.

Keywords

Pediatric oncology; latent class analysis; symptom cluster; PROMIS; PRO-CTCAE

Introduction

Children with cancer experience multiple symptoms throughout treatment[1–3] but most do not report subjective, treatment-related toxicities unless directly asked by clinicians.[4] When questioned, most pediatric oncology patients report the presence of five or more subjective adverse events (AEs)[5] while those receiving myelosuppressive chemotherapy report on average 10.6 subjective AEs.[6] Because AEs are experienced concurrently and synergistically, they exert an exponential effect[4,7] on patients' overall symptom burden, quality of life, and psychological stress.[8–11] The established relationship between number of AEs and patients' psychological stress can serve to validate a new application of a statistical

method to measure the impact of subjective AEs on pediatric oncology patients' quality of life.

Two different data reduction statistical approaches have been applied to patient-reported subjective AE data. The first is a variable-centered symptom cluster approach that groups symptoms based on clinical observation of symptom co-occurrence, research hypotheses, findings of qualitative data analysis, or statistical modeling (e.g., factor analysis).[11–17]

The second approach, finite mixture model, includes latent class analysis (LCA),[18] latent profile analysis (LPA), and latent transition analysis (LTA).[19] These approaches are person-centered and group patients by patterns of symptoms. These approaches yield distinct profiles of children with subjective symptom suffering or AEs during cancer treatment, thereby helping to place a child within a profile and perhaps allowing clinicians to tailor supportive care to match a specific child's symptom profile.

Previously, our research team applied latent profile analysis and latent transition analysis to data from the PROMIS (Patient-Reported Outcomes Measurement Information System) Pediatric Fatigue, Pain Interference, Anxiety and Depressive Symptom measures reported by pediatric oncology patients aged 8 to 18 years and identified two to four profiles of subjective symptom suffering.[18,19] Dominant profiles included high and low symptom groups. In those previous studies, we did not include a clinically relevant, distal outcome of the symptom groups that could have helped to validate the groups. In the present study, we employed LCA with AEs using the newly validated Pediatric Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (Ped-PRO-CTCAE) and we included psychological stress as a distal outcome.

The objectives of our study were to 1) identify groups of children and adolescents with cancer experiencing similar patterns of subjective AEs, 2) determine whether demographic and clinical characteristics predict AE group membership, and 3) examine whether AE group membership was associated with the distal outcome of psychological stress.

Methods

Participants

Eligible patients were 7–18 years, receiving frontline cancer therapy (chemotherapy, surgery, radiation, or combination), had completed at least one month of therapy, were three to six weeks from surgery, able to read and understand English, not experiencing clinically significant cognitive impairments, and agreed to participate. Parents/caregivers gave consent for self and permission for their child to participate. Exclusion criteria were patients participating in any phase I trial, treated with surgery alone or receiving end-of-life care.

Settings

Nine oncology centers participated: Children's Healthcare of Atlanta, Children's Hospital Los Angeles, UPMC Children's Hospital of Pittsburgh, Children's National Hospital (Washington, DC), Dana-Farber Cancer Institute/Boston Children's Hospital, Duke Cancer Institute/Duke University (Durham, NC), the Hospital for Sick Children (Toronto, Ontario,

Canada), St. Jude Children's Research Hospital (Memphis, TN), and the University of North Carolina at Chapel Hill.

Ethics

The study was approved by the institutional review boards at each site in accord with an assurance approved by the Department of Health and Human Services.

Design

Patients self-reported 15 "core" (i.e., frequently occurring) AEs via the Ped-PRO-CTCAE using a tablet at a time when fewer subjective AEs (T1) were anticipated. The psychological stress measurement was purposefully administered at a time that more subjective AEs (T2) were anticipated to determine if AE group membership at T1 predicted psychological stress at T2. T1 occurred within 72 hours of beginning a course of treatment; T2 occurred 7 to 17 days later for patients receiving chemotherapy and four weeks later for patients receiving radiation.

Measures

Demographic Forms.—Parents/caregivers completed two sociodemographic questionnaires, one for themselves (birthdate, gender, ethnicity/race, relationship status, highest completed grade, occupational status, and household income) and one for their child (birthdate, gender, ethnicity/race, current and highest completed school grade).

Pediatric-PRO-CTCAE (Ped-PRO-CTCAE).—The Ped-PRO-CTCAE is a validated set of items to determine the presence, severity, and interference with daily activities of subjective cancer treatment AEs as reported by children aged 7–18 years.[20–24] Items use a seven- day reference period with 4 response options per item consistent with CTCAE grading. Clinicians select AEs from the Ped-PRO-CTCAE library for inclusion in a clinical trial or for assessing clinical concerns. For this study, patients completed items for the 15 most frequently occurring AEs. Presence was measured as a dichotomous variable of the AE symptom (1 – if the symptom was present; 0 – otherwise).

PROMIS Pediatric Psychological Stress Measure.—This measure, developed from literature and interviews with children, parents, and health professionals, assesses children's cognitive, psychological, and somatic states.[25] Psychometric testing established strong reliability and construct validity of the child-report items of perceived stress during the past seven days in pediatric oncology patients aged 7 to 18 years (those reporting anxiety or depression reported higher stress and were more likely to be taking medicines to treat mood)[23] and in children and adolescents experiencing chronic pain (those with higher pain reported higher stress).[26] The 5-point Likert response options range from never[1] to always;[5] higher scores indicate higher stress.[27] Computerized-adaptive testing (CAT) methods were used to tailor data collected from each child.

Analysis.—We used LCA[28–31] to identify groups of patients with respect to presence of the 15 AEs at T1. We estimated and compared several LCA models with an increasing number of groups (e.g., 2, 3, 4). We used information criterion indices (for example,

Akaike's information criterion, Bayesian information criterion, and the adjusted Bayesian information criterion) and likelihood ratio (LR) tests (for example, the Lo-Mendell-Rubin likelihood ratio [LMR LR] test, the adjusted LMR LR [ALMR LR] test, and the bootstrap likelihood ratio test] for model fit comparisons. A smaller information criterion index indicates better model fit; a significant LR test ($P < 0.05$) indicates that the higher group number (e.g., 3 groups) model fit data better than the model with fewer groups (e.g., 2 groups). The relationship of group membership with demographic factors (age, gender, education, race) and clinical measures (time since diagnosis, hemoglobin) was assessed. Finally, we examined the effects of demographic and clinical variables on psychological stress and assessed whether such effects were moderated by group membership.

We applied a 3-step method to examine relationships between the latent groups, covariates, and stress and to minimize measurement error.[32] Associations of latent group membership with demographic and clinical variables were examined with automatic implementation of the 3-step method.[33] The effects of demographic and clinical variables on the distal outcome (i.e., stress score at T2) were examined by group simultaneously in an auxiliary structural equation model where the 3-step method was performed manually.[32,34]

Results

Sample

Mean age among the 477 participants was 13.5 years (SD = 3.4); the majority were male (n = 253, 53.7%), white (n = 268, 56.2%), and receiving leukemia treatment (n = 264, 55.1%). Almost all (n = 437, 91.2%) received chemotherapy (Table 1). Most parents had completed at least some college education (78%).

Descriptive Findings

Ped-PRO-CTCAE.—The highest prevalence AEs at T1 were fatigue (68.3%), insomnia (52.6%), and pain (50.7%) (Table 2). The remaining 12 AEs were reported at rates from 22.4% (vomiting) to 45.9% (nausea). Nearly all participants (97%) experienced ≥ 1 of the core AEs and 66% experienced ≥ 5 AEs (Table 2).

PROMIS Pediatric Psychological Stress.—The mean score of the PROMIS Pediatric Psychological Stress measure was 46.2 (SE = 9.6).

LCA Model Fit Findings.—All information criterion indices and LR tests support the 3-group model (Appendix Table 1) as did interpretability from a clinical perspective. Classification probabilities for high, moderate, and low AE prevalence groups were 0.90, 0.92, and 0.87, respectively, with an entropy statistic of 0.75, indicating adequate classification quality.

The AE groups denoted by the 3-group model showed distinct patterns of presence of subjective AEs (Fig. 1). Patterns were consistent in sensitivity analyses that excluded patients who received radiation treatment (N = 33) or bone marrow transplant (N = 9). We labeled the AE groups as high prevalence, moderate prevalence, and low prevalence. Approximately 22.6% of patients were classified into high prevalence, 51.4% into moderate

prevalence, and 26.0% into low prevalence. In the high prevalence group, patients (n = 108) reported an average of 11 AEs (SD = 1.6; range, 8 to 15 AEs); moderate prevalence (n = 245) an average of 6.3 AEs (SD = 1.7, range, 3 to 11); and low prevalence (n = 124) an average of 1.8 AEs (SD = 1.1, range, 0 to 4) (Table 2).

Demographic and Clinical Characteristics.—Mean age and hemoglobin values were similar across groups (Table 3). Parent education level, race/ethnicity composition, and time since diagnosis varied slightly across groups. Gender composition was significantly different across the 3 groups (Table 4). The percentage of males was lower in the high prevalence group (37.0%), compared with moderate prevalence (57.6%) and low prevalence (58.1%) groups. Patients with shorter time since diagnosis were more likely to be in the high prevalence group (Table 4).

LCA and PROMIS Pediatric Psychological Stress.—The mean psychological stress score was highest in the high prevalence group (53.7), followed by moderate prevalence (46.4), and lowest in the low prevalence group (40.1) (Table 5). The mean score in the high prevalence group is in the median percentile for this measure; the other two mean scores are below the median percentile.[35] The effects of demographic and clinical measures on stress vary by group (Appendix Table 2). The stress score was higher ($\beta = 12.98$, $P < 0.01$) in black patients than other racial groups in the high prevalence group. However, a race effect was not statistically significant in the other two AE prevalence groups. Age and gender had significant effects on stress only in the moderate prevalence group, that is, older patients reported higher stress ($\beta = 0.59$, $P = 0.03$) and males reported lower stress ($\beta = -3.83$, $P <$ 0.0.48). More time since diagnosis had a significant positive effect on stress in the moderate group ($\beta = 3.75$, $P = 0.02$) (Appendix Table 2).

Discussion

In this large pediatric oncology sample, 477 children and adolescents on therapy self-reported core subjective AEs using the Ped-PRO-CTCAE at two time points: before a scheduled treatment course (T1), and the PROMIS Pediatric Psychological Stress measure later (T2) when symptom burden was expected to be higher. Most (65.8%) reported ≥ 5 AEs, similar to reports of pediatric oncology patients experiencing multiple, concurrent subjective AEs even during periods of expected stability.[1–7,12–17] We identified three distinct groups of pediatric oncology patients according to their reports of subjective treatment toxicities which indicated that the study sample was heterogeneous with respect to the 15 AEs. The finding of three distinct patient groups based on prevalence of subjective AEs is significant, as it is similar to previous findings from similar patient groups but based on more established (well validated) pediatric symptom and function measures. Importantly, the number of prevalence groups was not determined a priori but derived from statistical results.

In our group's previous cross-sectional study of 200 pediatric patients who completed four PROMIS Pediatric measures during chemotherapy (n = 97) or in survivorship (n = 103), four latent groups emerged.[18] Similarly, in our prior longitudinal study involving 96 pediatric patients assessed before and during a chemotherapy cycle, three distinct groups emerged with high and low symptom suffering subgroups dominating.[19] In the two prior studies, a

limited number[4] of subjective symptoms were studied, whereas in this study, the much larger sample of pediatric oncology patients on active therapy reported on 15 AEs with three distinct groups emerging.

The number of groups identified across these three studies using LCA and patient-reported outcomes is consistently small (three to four).[18,19] This suggests that the number of clinically meaningful groups of pediatric oncology patients experiencing subjective AEs is limited and therefore translatable into clinical care guidelines specific to each subgroup. Clinicians could be alerted to the patient's group membership to help trigger use of group-specific support resources and inform personalized symptom management. Perhaps most importantly, across studies, there exists a group of high symptom suffering or high AE prevalence that can be identified.[18,19]

High AE Prevalence Subgroup

Our study identified 22.6% of patients in the high prevalence group; our prior two studies found 16%–45.8% of patients in the high symptom suffering group at T1.[18,19] The high symptom suffering group is relatively small across studies and may even decrease during therapy. This group is distinct in terms of probabilities of AEs (Fig. 1), raw number of AEs (8 to 15 AEs per group member compared to 3 to 11 AEs for the moderate group, and 0 to 4 AEs for the low prevalence group) and mean number of AEs (11.0 [SD = 1.56] compared with 6.3 [SD = 1.74] and 1.8 [SD = 1.15] in the moderate and low AE groups]. Identifying patients in this smaller, high suffering group may be especially relevant as this group includes patients likely to need enhanced supportive care.

Moderate AE Prevalence Group

This group at 51.36% was nearly twice the size of the other two groups. Its AE pattern (Fig. 1) was similar to that in the high prevalence group but its prevalence rates were half that of the same AE in the high prevalence group. Insomnia was the exception as it is similar in prevalence between the two groups. These patients' subjective AE experience cannot be discounted given that each reports 3 to 11 AEs.

Low Prevalence AE Group

In each study using the PROMIS Pediatric measures, a low-symptom burden, and in some studies, a high-functioning cohort emerged.[12,18,35] A proportion of children in this current study reported experiencing no (3.1%),1 (8.2%), or 2 (6.5%) AEs at T1. Insomnia and pain were reported by about half (52.6% for insomnia and 50.7% for pain), while over two-third of patients reported fatigue. The possibility that there may be a select cohort of patients for whom symptom burden starts low and remains low across treatments has been demonstrated in one study across a one-month period.[19] Longer-term examination of the groups throughout treatment is merited.

Influence of Gender and Race

A limited number of differences related to gender and race are noted, including a greater proportion of females and a greater proportion of blacks reporting higher stress levels in the high AE prevalence group compared to the other two groups (Table 5). Females in the

moderate prevalence group reported significantly higher levels of psychological stress than males (Appendix Table 2). However, similar to previous studies, these patient characteristics and other demographic variables are rarely found to influence psychological and other outcomes in pediatric oncology patients.[18,19,35–37] When measured, it may be socioeconomic status more than race or gender that is associated with such outcomes.[36] Although gender and racial differences in AE prevalence as well as cultural, clinical, or biological etiologies for these differences need further exploration, the concurrent measurement of socioeconomic status is recommended.

Influence of Time

More time since diagnosis was associated with lower levels of psychological stress in the moderate AE group only. Prior studies of pediatric patient reports during chemotherapy indicate the symptom burden decreased over time.[1,3] Whether this is because children adapt over time, receive more intense therapies earlier, or access personalized supportive care interventions over time is an underexplored but important research question.

Limitations

We did not study the existence, size, and distinctive features of patient groups by diagnosis and oncologic treatment across extended time periods to observe AE patterns of prevalence, interference, and AE severity. We also did not study pediatric self-reported measurements of function (i.e., physical, cognitive, social) but doing so would provide important dimensions to clinical meaningfulness.

Conclusion

Co-occurring subjective AEs occur during pediatric oncology therapies. Using different patient-reported items and in a notably large sample of pediatric patients aged 7–18 years with diverse oncologic diagnoses, our study confirms that clinically meaningful groups exist among pediatric oncology patients based on their experiences with AEs. Using direct AE reports to identify membership in an AE subgroup has clinical utility, such as alerting clinicians to the need to enhance or reduce planned symptom management strategies, particularly as they may relate to psychological stress. As such, our findings have important implications for better understanding AE experiences and preparing personalized supportive care approaches for patients.

Disclosures and Acknowledgments

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Appendix

Appendix Table 1

Latent Group Model Fit Comparison (N = 477)

Model	AIC	BIC	aBIC	LMR LR *P*-value	ALMR LR *P*-value	BLRT *P*-value
1-Group	9297.67	9343.35	9292.57	—	—	—
2-Group	8601.74	8735.10	8633.54	<0.0001	<0.0001	<0.0001
3-Group	8526.26	8726.30	8573.95	<0.0001	<0.0001	<0.0001
4-Group	8493.70	8760.42	8557.30	0.4855	0.4902	<0.0001

AIC = Akaike information criterion; BIC = Bayesian information criterion; aBIC = adjusted BIC; LMR LR = Lo-Mendell-Rubin likelihood ratio; ALMR LR = adjusted LMR LR; BLRT = bootstrap likelihood ratio test; — = not applicable.

Appendix Table 2

The Effects of Demographic and Clinical Measures on PROMIS Pediatric Psychological Stress[a] by Latent Group[b]

Covariates	β	*P*-value
High AE prevalence		
Age	−0.39	0.485
Gender		
Female	—	—
Male	−4.24	0.331
Parent education		
< College	—	—
College/university	−5.14	0.640
Postgraduate	0.44	0.959
Race		
Others[c]	—	—
White	−1.07	0.886
Black	12.98	0.005
Time since diagnosis		
≤ Median	—	—
> Median	−4.05	0.292
Hemoglobin	1.82	0.311
Moderate AE Prevalence		
Age	0.59	0.034
Gender		
Female	—	—
Male	−3.83	0.048
Parent education		
< College	—	—
College/university	1.01	0.708
Postgraduate	−0.56	0.822
Race[c]		

Covariates	β	*P*-value
Others	—	—
White	−1.30	0.637
Black	−3.75	0.132
Time since diagnosis		
≤ Median	—	—
> Median	3.75	0.015
Hemoglobin	−0.35	0.453
Low AE prevalence		
Age	0.09	0.633
Gender		
Female	—	—
Male	0.19	0.633
Parent education		
< College	—	—
College/university	−0.82	0.668
Postgraduate	−0.56	0.738
Race[c]		
Others	—	—
White	1.14	0.602
Black	−2.06	0.276
Time since diagnosis		
≤ Median	—	
> Median	0.61	0.429
Hemoglobin	−0.45	0.452

— = reference group.

[a] PROMIS Pediatric Psychological Stress score at T_2.

[b] Estimated by manual 3-step estimation procedure in Mplus 8.4.[33]

[c] Including Hispanics.

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Key Message

Three distinct groups of children and adolescents exist regarding their experience with prevalence of subjective adverse events (AEs) during cancer treatment: high, moderate, and low AE prevalence. Clinicians could be alerted to patients' group membership to help trigger use of specific support resources to personalize AE management.

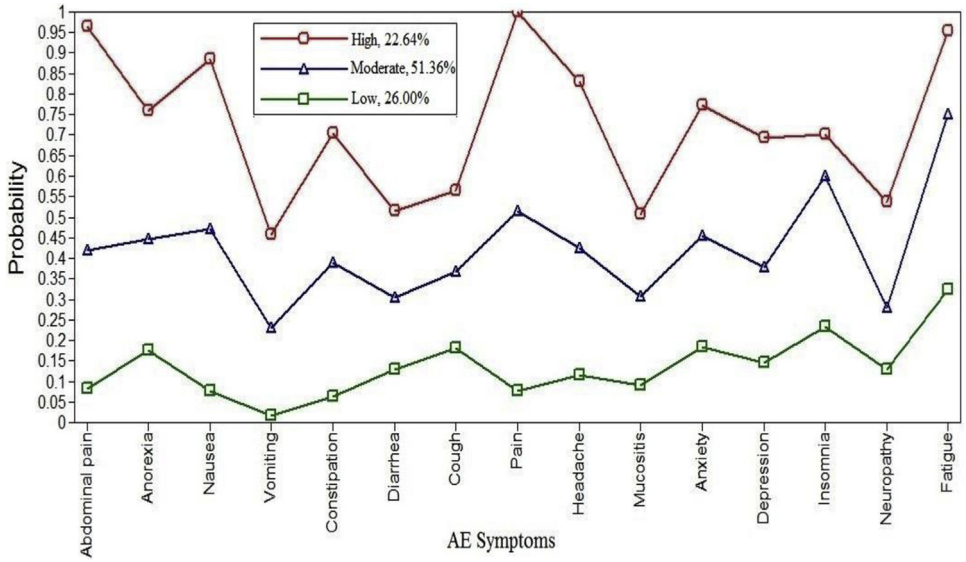

Fig. 1.

Adverse event (AE) subjective symptom groups resulting from the 3-class latent class analysis model.

Table 1

Sample Statistics ($N = 477$)

Variable	Statistics
Child age (yrs)	
Mean (SD)	13.47 (3.4)
Duration since diagnosis	
Mean (SD)	0.44 (0.7)
Hemoglobin (HGB)	
Mean (SD)	10.59 (1.6)
Gender, N (%)	
Male	253 (53.7)
Female	218 (46.3)
Race, N (%)	
White	268 (56.2)
Black	77 (16.1)
Hispanic	65 (13.6)
Others	67 (14.0)
Parent education, N (%)	
Elementary/primary school	6 (1.3)
Secondary/high school	96 (20.5)
Some college/university	125 (26.7)
College/university	169 (36.1)
Postgraduate degree	72 (15.4)
Cancer Type, N (%)	
Leukemia/lymphoma	264 (55.1)
Solid tumor	135 (28.2)
Neuro-oncology	71 (14.8)
Bone marrow transplant (BMT)	9 (1.9)
Cancer treatment, N (%)	
Chemotherapy	437 (91.2)
Radiation	33 (6.9)
Bone marrow transplant	9 (1.9)

Frequencies of some variables may not sum up to $N = 477$ due to missing values.

Table 2

Prevalence of PED-PRO-CTCAE Core AEs at T_1 (N = 477)

AE Symptom	N (%)
Fatigue	326 (68.3)
Insomnia	251 (52.6)
Pain	242 (50.7)
Nausea	219 (45.9)
Anxiety	217 (45.5)
Abdominal pain	216 (45.3)
Anorexia	212 (44.4)
Headache	207 (43.4)
Depression	185 (38.8)
Constipation	178 (37.3)
Cough	173 (36.3)
Diarrhea	145 (30.4)
Neuropathy	142 (29.8)
Mucositis	141 (29.6)
Vomiting	107 (22.4)
Total number of AEs reported	
0	15 (3.1)
1	39 (8.2)
2	31 (6.5)
3	35 (7.3)
4	43 (9.0)
5+	314 (65.8)

An AE toxicity was defined “Yes” if any of its attribute (frequency, severity, or interference) scores was ≥1.

Table 3

Demographic and Clinical Characteristics by Group ($N = 477$)[a]

	Latent Group		
	High Prevalence (N = 108, 22.6%)	**Moderate Prevalence (N = 245, 51.4%)**	**Low Prevalence (N = 124, 26.0%)**
Variable	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Age	13.52 (3.4)	13.52 (3.4)	13.31 (3.5)
		$\chi^2 = 0.341$, $P = 0.843$	
Hemoglobin	10.35 (1.4)	10.67 (1.7)	10.64 (1.5)
		$\chi^2 = 3.131$, $P = 0.209$	
Gender, N (%)			
Female	68 (63.0)	104 (42.5)	52 (41.9)
Male	40 (37.0)	141 (57.6)	72 (58.1)
		$\chi^2 = 14.36$, $P = 0.001$	
Parent education, N (%)			
< College	18 (17.0)	49 (20.4)	35 (28.7)
College/university	69 (65.1)	155 (64.6)	70 (57.4)
Postgraduate	19 (17.9)	36 (15.0)	17 (13.9)
		$\chi^2 = 5.41$, $P = 0.247$	
Race/ethnicity, N (%)			
White	60 (55.6)	136 (55.5)	72 (58.1)
Black	17 (15.7)	33 (13.5)	27 (21.8)
Hispanic	19 (17.6)	35 (14.3)	11 (8.9)
Others	12 (11.1)	41 (16.7)	14 (11.3)
		$\chi^2 = 9.61$, $P = 0.142$	
Time since diagnosis, N (%)			
≤Median (0.30)	72 (66.7)	137 (55.9)	65 (52.4)
>Median (0.30)	36 (33.3)	108 (44.1)	59 (47.6)
		$\chi^2 = 5.27$, $P = 0.071$	

[a]Sample size slightly varies by variables due to missing values.

Table 4

Effects of Demographic and Clinical Measures on Latent Group Classification[a]

	Latent Group		
Covariate	**High vs. Low Prevalence, β (*P*-value)**	**Moderate vs. Low Prevalence, β (*P*-value)**	**High vs. Moderate Prevalence, β (*P*-value)**
Age	−0.01 (0.838)	−0.00 (0.935)	−0.01 (0.885)
Gender			
Female	—	—	—
Male	−0.78 (0.022)	−0.04 (0.898)	−0.74 (0.024)
Parent education			
<High school	—	—	—
High school	0.58 (0.174)	0.38 (0.286)	0.19 (0.654)
College+	0.99 (0.064)	0.58 (0.257)	0.41 (0.423)
Time since diagnosis			
≤ Median	—	—	—
> Median	−1.46 (0.239)	−0.29 (0.094)	−1.17 (0.357)
Race			
Others[b]	—	—	—
White	−0.53 (0.214)	−0.52 (0.176)	−0.02 (0.968)
Black	−0.87 (0.118)	−1.11 (0.025)	0.24 (0.679)
Hemoglobin	−0.09 (0.444)	−0.01 (0.952)	−0.08 (0.461)

[a]Estimated using AUXILIARY statement with R3STEP option in Mplus 8.4.[33]

[b]Including Hispanics.

Table 5

Mean Score of PROMIS Pediatric Psychological Stress[a] by Group ($N = 477$)[b]

Subgroup	Mean	SE
High ($N = 108$, 22.64%)	53.7	1.5
Moderate ($N = 245$, 51.36%)	46.4	0.8
Low ($N = 124$, 26.00%)	40.1	0.6
	Chi-Square	*P*-Value
Overall test	109.3	<0.001
High vs. moderate	14.8	<0.001
High vs. low	68.3	<0.001
Moderate vs. low	42.1	<0.001

[a]PROMIS Pediatric Psychological Stress score at T_2.

[b]Estimated using AUXILIARY statement with DE3STEP option in Mplus 8.4.[33]