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Health-Related Quality of Life Profiles in Adolescents and Young Adults with Chronic Conditions

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Abstract

Purpose: To assess health-related quality of life (HRQOL) among adolescents and young adults (AYAs) with chronic conditions.

Methods: AYAs (N=872) aged 14–20 years completed NIH's Patient-Reported Outcomes Measurement Information System® (PROMIS®) measures of physical function, pain interference, fatigue, social health, depression, anxiety, and anger. Latent profile analysis (LPA) was used to group AYAs into HRQOL profiles using PROMIS T-scores. The optimal number of profiles was determined by model fit statistics, likelihood ratio test, and entropy. Multinomial logistic

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Author Contributions

Conceptualization, methodology, formal analysis, results interpretation, first draft, draft revision, final draft approval

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. The current study was ruled exempt from IRB review by the Duke University Health System.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent to publish

The authors affirm that human research participants provided informed consent for publication.

regression models were used to examine how LPA's HRQOL profile membership was associated with patient demographic and chronic conditions. The model prediction accuracy on profile membership was evaluated using Huberty's I index with a threshold of 0.35 for good effect.

Results: A 4-profile LPA model was selected. A total of 161 (18.5%), 256 (29.4%), 364 (41.7%), and 91 (10.4%) AYAs were classified into Minimal, Mild, Moderate, and Severe HRQOL Impact profiles. AYAs in each profile had distinctive mean scores with over a half standard deviation (5-points in PROMIS T-scores) of difference between profiles across most HRQOL domains. AYAs who were female or had conditions such as mental health condition, hypertension, and self-reported chronic pain were more likely to be in the Severe HRQOL Impact profile. The Huberty's I index was 0.36.

Conclusions: Approximately half of AYAs with a chronic condition experience moderate to severe HRQOL impact. The availability of risk prediction models for HRQOL impact will help to identify AYAs who are in greatest need of closer clinical care follow-up.

Plain Language Summary

Adolescents and young adults (AYA) with chronic conditions may experience impacts on their physical, mental, and social well-being. In addition to their chronic conditions, there may be demographic factors that affect AYA health-related quality of life (HRQOL). This study clustered AYAs into sub-groups based on their HRQOL experiences and identified demographic and health-related characteristics associated with HRQOL group membership. In this study, AYAs (N=872) aged 14–20 years completed self-reported measures of physical function, pain interference, fatigue, social health, depression, anxiety, and anger. A statistical modeling approach called latent profile analysis (LPA) was used to cluster AYAs into different HRQOL sub-groups. We identified four AYA clusters that represented minimal, mild, moderate, and severe HRQOL impact. AYAs who were female or AYAs with chronic conditions such as mental health condition, hypertension, and self-reported chronic pain were more likely to be placed in a cluster with a greater negative impact on their HRQOL. These findings may help identify AYAs who are more likely to be at risk for more severely impacted HRQOL and require closer clinical care surveillance.

Keywords

AYA; HRQOL; LPA; chronic conditions; PROMIS

Introduction

Adolescents and young adults (AYAs) are estimated to account for 15.5% of the total disease burden for all age groups worldwide [1]. Approximately 20–30% of AYAs in western countries have chronic conditions [2]. Chronic conditions may negatively affect AYAs' health-related quality of life (HRQOL), which is a multidimensional construct that generally includes physical, mental, and social domains [3–5]. Prior HRQOL research has typically only focused on either older adults [6–12] or children/adolescents with chronic conditions [13, 14]. AYAs experience significant developmental challenges marked by physical, psychological, and cognitive maturing while they are trying to become independent [3–5]. Considering the developmental and social similarities between adolescents and young

adults, combining them and evaluating their HRQOL could provide a better understanding of their functioning and well-being in this understudied group.

Previous studies have looked at HRQOL in AYAs sampled from a specific disease or a narrow range of conditions such as cerebral palsy, multiple sclerosis, and cancer [13–25]. For example, Nelson et al. (2014) examined 229 adolescents aged 14–19 years with various mental health problems in residential care and found significant impairments in HRQOL compared to an established clinical cutoff [25]. Comparing HRQOL in patients from a disease-specific population with healthy controls is often limited by only comparing across one or two domains, leaving the impact of a full range of domains on HRQOL unknown. Moreover, the results are difficult to be generalized to other disease populations. To bridge this knowledge gap, there is a need to evaluate HRQOL in AYAs across a broad range of chronic conditions.

Also, prior studies examined HRQOL domains one at a time in AYAs [13–16, 18, 19, 21, 22, 26]. For example, Kamp-Becker et al. (2010) reported that AYA patients aged 17–28 years with autism spectrum disorder had significantly lower HRQOL scores in physical health, psychological health, and social relation domains but not in environment domain compared to healthy controls [21]. Patients who have HRQOL deficits across the board may not be identified in the domain-by-domain HRQOL evaluation. Moreover, patients with different HRQOL domains impacted at different levels cannot be directly compared if only one domain is evaluated at a time. There is a lack of studies that have incorporated multiple HRQOL domains as a single outcome to identify which AYAs are at greater risk for poorer HRQOL.

Latent Profile Analysis (LPA) is a model-based approach that can be used to group individuals into distinct profiles based on similar experiences across several HRQOL domains [27–33]. Unlike factor analysis methods, which typically aim to explore dimensions underlying observed variables (i.e., clustering of HRQOL indicators) [34, 35], our focus is on classifying AYAs into distinct subgroups (i.e., profiles) based on their HRQOL impacts (i.e., scores). This approach provides insight into the heterogeneity of HRQOL experiences among this AYA population with chronic conditions. Importantly, this classification approach deviates from other analytic methods that focus on the average HRQOL experiences that could obscure those AYAs who may be suffering and benefit from greater clinical care.

The findings from the approach used in this study may have important clinical implications. Using LPA methods, our study will identify AYAs who are experiencing high HRQOL impact from their disease or treatment and identify demographic and clinical factors associated with worse HRQOL experiences. This will enhance clinicians' awareness of the heterogeneity within the patient population and what conditions or patient characteristics are signals for the clinicians that someone may be suffering. In addition, future studies may develop prediction models based on this and other study findings that can be integrated into the electronic medical systems to alert clinicians which patients may be at additional risk for poor HRQOL [36–41]. This knowledge can inform treatment planning and personalized care. For instance, interventions can be designed to address the particular aspects of

HRQOL that are comparatively lower in certain subgroups, thereby tailoring care to their specific needs [41–43]. Moreover, each subgroup may benefit from specific educational materials, self-management strategies, or support groups tailored to their particular HRQOL challenges. This can enhance patient empowerment, self-care, and coping skills, leading to improved HRQOL outcomes [44–47]. Furthermore, the identification of HRQOL impact subgroups allows longitudinal monitoring of patient progress [36, 48, 49]. Clinicians and AYA patients can utilize these subgroups to establish personalized goals based on AYA patients' initial HRQOL levels, helping AYA patients and their families set realistic expectations and measure patients' progress in a meaningful way [50, 51].

This study investigates the HRQOL impact in a diverse sample of AYAs with a range of chronic conditions. An innovative aspect of this study is that we use LPA to cluster AYAs into different groups based on their disease burden across physical, mental, and social domains. Further, this study will examine chronic conditions and demographic factors that are associated with membership in different HRQOL profiles. Identified risk factors associated with poorer HRQOL may help clinicians identify AYAs with additional need for clinical care or active surveillance.

Methods

Participants and Data Collection

This study is a secondary analysis of data collected as part of an NIH-funded research study to provide linking between pediatric and adult versions of the Patient-Reported Outcome Measurement Information System® (PROMIS®) measures in AYAs. The current study was ruled exempt from IRB review by the Duke University Health System. A total of 874 AYAs aged 13–20 years with "special healthcare needs" enrolled in the study. AYAs had to be able to read and write English and have access to the internet. As described by Reeve et al. (2016), "special healthcare needs" was defined as AYAs who have or are at an increased risk of a chronic physical, developmental, behavioral, or emotional condition and who also require health care or related services beyond what patients generally require [52]. The participants were recruited using a convenience sampling approach from two sources: public health insurance programs (Medicaid and the Children's Health Insurance Program (CHIP) in Florida, U.S.) and the Opinions for Good (Op4G) panel. For the Medicaid/CHIP cohort, special healthcare need status for an individual was defined by the Clinical Risk Groups criteria [53]. Participants were randomly sampled from the Medicaid/CHIP databases. Medicaid/CHIP patients completed surveys between April 1, 2012 and May 31, 2013 and received a $20 gift card. For the Op4G cohort, special healthcare need status was determined by a screener [54]. Op4G participants completed surveys between August 1, 2013 and September 30, 2013 and earned $25 they could donate to nonprofit organizations. Approximately 73% of this study's participants were from the Op4G panel.

Participants completed a demographic form including their age, gender, race and ethnicity, and a checklist of chronic conditions and health-related characteristics including chronic conditions, blindness, deafness, and whether they required assistance to get around. AYAs completed adult versions of the PROMIS measures including the PROMIS SF v1.0 - Physical Function 10a, PROMIS SF v1.0-Pain Interference 8a, PROMIS SF v1.0-Fatigue

8a, PRMIS SF v2.0-Social Health: Emotional Support, PROMIS SF v1.0-Depression 8b, PROMIS SF v1.0-Anxiety 8b, PROMIS SF v1.0-Anger 8a. Previous evidence supports that all PROMIS short forms included in this study were highly reliable across at least 3 standard deviation (30 T-score) units (reliability ≥0.9), and the measures all include the range of mild to severe impairment, where our AYAs with chronic diseases and conditions were expected to be located. Additionally, correlations between scores on the full PROMIS item banks and their respective short forms were strong (0.89 in physical function domain, above 0.9 in other domains) [55]. All PROMIS items have five ordered response options. Physical Function response options are “Not at all”, “Very little”, “Somewhat”, “Quite a lot”, and “Cannot do”. Fatigue and Pain Interference response options are “Not at all”, “A little bit”, “Somewhat”, “Quite a bit”, and “Very much”. Depression, Anxiety, Anger, and Emotional Support response options are “Never”, “Rarely”, “Sometimes”, “Often”, and “Always”. Scores on the PROMIS measures are on a T-score metric, with a mean of 50 and a standard deviation of 10 in the general U.S. population. Higher PROMIS T-scores for symptom domains represent worse symptom burden, and higher PROMIS T-scores for functional domains represent better functioning. In anger, anxiety, depression, fatigue, pain interference domains, PROMIS T-score less than 55 is considered within normal limits, 55–60 is the mild range, 60–70 is the moderate range, and above 70 is the severe range. In physical function and social health domains, PROMIS T-score greater than 45 is considered within normal limits, 40–45 is the mild range, 30–40 is the moderate range, and less than 30 is the severe range [56]. While the adult PROMIS measures are designed for adults 18 years or older, a previous study with this same dataset found no differential item functioning (DIF) for any of the PROMIS items between the adolescents (14–17 years) and young adults (18–20 years) [57].

Statistical Analysis

We used LPA, a posterior membership probability model, to identify subgroups (profiles) of AYAs comprised of individuals with similar levels of symptom severity and functional impairment based on their PROMIS scores. A simple/naïve three-step LPA approach was adopted, where we first estimated the measurement model using the basic latent class model without the external demographic and health condition variables; then assigned AYAs to predicted latent HRQOL impact profiles; estimated the structural models of interest for the latent profiles and external demographic and health condition variables, using the assigned profiles in place of the latent profiles [58]. The optimal number of HRQOL profiles was determined by generating a hierarchically-nested series of LPA models with an increasing number of latent profiles and iteratively comparing the fit of each successive model *k* with the previous (*k*-1) model using Akaike, Bayesian, and sample-size adjusted Bayesian information criterion indices (AIC, BIC, and SABIC, respectively), the Lo-Mendell-Rubin likelihood ratio (LMR LR) test, and the Vuong-Lo-Mendell-Rubin likelihood ratio (VLMR LR) test [59–62]. A significant p value from the LMR LR or VLMR LR test indicates the model with the larger number of groups (*k* classes) should be preferred over the model with the smaller number of groups (*k*-1 classes) [63]. Entropy, which evaluate models with respect to confidence with which individuals have been classified as belonging to one group or another, is compared across profiles [60, 61]. Entropy values over 0.8 indicate a good separation of the latent profiles, and values approaching 1 indicate clear delineation

of profiles [64]. In addition, interpretability of the profiles was a criterion, which was determined by the authors. We classified AYAs into their most likely latent profiles using the highest estimated probabilities being categorized into each of the four profiles and the entropy statistic.

We compared whether the AYA's demographics and health-related characteristics were different across the LPA profiles by using Fisher's exact test. Diseases or conditions with zero patient prevalence in any LPA profile membership were not included as covariates in the following regression models. We examined the association between the HRQOL profile membership and individual patient characteristics including gender, age, race/ethnicity, chronic conditions, patient's parent relation status (married, living together, never together, separated, divorced, or windowed), parent highest education level, and language spoken at home in multinomial logit models. Blindness and deafness were not included in the model because they can be congenital or acquired. Additionally, blindness and deafness could potentially affect some aspects of social and physical function, but they are unlikely to be associated with other domains included in the PROMIS measure. Logit models predicted the patient's HRQOL impact profiles by using the individual patient characteristics described above and their beta coefficients. *Mplus* version 8.7 was used for LPA modeling and R version 4.0.5 was used for logit modeling. We calculated the profile assignment agreement between LPA results and profiles predicted by the logit regression model. Huberty's I index was computed to evaluate the hit rate with a threshold of 0.35 in I index for high effect [65, 66].

To address the uncertainty in LPA profile results incorporated independently in the multinomial regression models in the naïve 3-step approach, we ran the 2-step LPA approach in a sensitivity analysis. We (1) fit the latent profile measurement model on its own; (2) the parameters of the measurement model were held fixed when the structural model is estimated [58, 67]. Additionally, we ran LPA using the bias-adjusted 3-step approach by using the r3step in Mplus with all covariates included in the multinomial regression listed in Table 4. We also examined whether AYAs would be placed in the same HRQOL impact profiles by using one domain at a time (e.g., pain interference) by using LPA or the PROMIS T-score Cut Points in sensitivity analysis.

Results

AYAs' demographics and health-related characteristics

One participant was excluded due to missing PROMIS score data. Another participant was excluded due to violation of the age eligibility criteria (14–20 years). The mean (standard deviation) age is 15.6 (1.19) in adolescents (N=413) and 18.9 (0.75) in young adults (N=459). The remaining 872 AYAs' demographics and health-related characteristics are summarized in Table 1. Attention Deficit Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD) was the most prevalent condition (N=244, 28.0%) followed by mental health condition (N=199, 22.8%), hypertension (N=198, 22.7%), and asthma (N=197, 22.6%). A total of 65 (7.5%) participants did not self-report any chronic conditions listed in Table 1.

HRQOL Profile Identification

The 4-profile classification was selected based on the model fit statistics (see Table 2), with no significant improvement in fit statistics with a 5-profile model according to VLMR LRT ($p = 0.21$) and LMR LRT ($p = 0.22$). The 4-profile model was also favored by the authors because of its ease of interpretation and potential application in clinical settings. The four profiles were named *Minimal HRQOL Impact*, *Mild HRQOL Impact*, *Moderate HRQOL Impact*, and *Severe HRQOL Impact* according to profile functioning and symptom domain score ranges consistent with cut-points recommendations on the PROMIS website [56]. The entropy value was 0.89, suggesting the profile classification was good [64]. A total of 161 (18.5%), 256 (29.4%), 364 (41.7%), and 91 (10.4%) AYAs were classified into the Minimal, Mild, Moderate, and Severe HRQOL Impact profiles, respectively.

The mean HRQOL scores in the adult PROMIS measures for the four profiles are presented in Figure 1. The four profiles differ in their levels of HRQOL impact, with profiles mean score differences of more than five points across all HRQOL domains except social functioning. Five points on the PROMIS T-score metric represents half a standard deviation, a moderate effect size difference according to Cohen [68]. Those in the Severe HRQOL Impact and Moderate HRQOL Impact profiles are far above the U.S. general adult population norm scores of 50 on the PROMIS T-score metric.

In sensitivity analysis, each AYA participant was assigned to the same HRQOL impact profile by using the naïve 3-step, bias-corrected 3-step, and the 2-step LPA approach. When using only pain interference domain T-scores in LPA, only 58% AYAs were placed in the same HRQOL profile compared to the profiles when using the 7 domain T-scores in LPA. Only 43% AYAs were placed in the same HRQOL profile when using the PROMIS T-score cut points thresholds.

AYA Characteristics Associated with HRQOL Profile Membership

The comparison of participants' demographics and health-related characteristics in the four HRQOL Impact profiles is shown in Table 3. We found univariate significant differences in AYAs across HRQOL profiles for gender, race and ethnicity, medication status, parent's highest education level, and language spoke at home. We also found statistically significant differences in HRQOL representation for these chronic conditions: ADHD or ADD, mental health condition, hypertension, self-reported chronic pain, intestinal disorder, and kidney disease.

In the multinomial logistic regression results, covariates with statistically significant odds ratios are presented in Table 4. The full regression model results are presented in supplemental information. A total of eight AYAs were excluded in the model due to missingness in AYAs' gender, on medication status, parent relationship status, or parent highest education level. Male AYAs were less likely to be in the Mild, Moderate, or Severe HRQOL impact profiles compared with female AYAs, with the Minimal HRQOL impact profile as the reference. Older AYAs were more likely to be in the Severe HRQOL impact profile compared to Minimal and Moderate HRQOL impact profiles. AYAs on medication were more likely to be in the Mild, Moderate, and Severe HRQOL Impact profiles compared

to AYAs not on medications. AYAs with chronic conditions of mental health condition, hypertension, self-reported chronic pain and thyroid disease are associated increased odds of being in the higher severity HRQOL impact profiles. For example, the odds ratio of being in Severe vs. Minimal HRQOL Impact profile among patients with self-reported chronic pain is 12.00 (95% CI 4.97 – 28.95). In the sensitivity analysis, the odds ratios (95% CI) were very similar to using the naïve 3-step, bias-corrected 3-step, and the 2-step approach (Supplemental information).

Including all the demographic factors and health-related characteristics, the regression model correctly predicted 442 out of 864 (51.2%) AYAs into profiles assigned from the LPA (Table 5, Figure 2). Together with the probability of being assigned to Minimal, Mild, Moderate, and Severe HRQOL Impact profile obtained from LPA, the hit rate observed was 0.51 while the hit rate by chance was 0.24, which considers both the four profiles and sample size in each profile. The Huberty's I index was 0.36, which was above the threshold of 0.35, suggesting good prediction accuracy.

Discussion

In this study, we used LPA methods to cluster 872 AYAs with a broad range of chronic conditions into Minimal, Mild, Moderate, and Severe HRQOL Impact profiles based on their self-reported scores on adult PROMIS measures of anger, anxiety, depression symptoms, fatigue, pain interference, social health and physical function. The four profiles were at least a half standard deviation apart on the PROMIS T-score metric, suggesting meaningful differences in HRQOL impact on average between profiles.

The methods we used to classify AYAs with chronic conditions into different subgroups (profiles) of HRQOL impact is based on a statistical model of quantitative data collected from a self-reported questionnaire (i.e., the PROMIS measures). These profiles are not based on nor confirmed by qualitative data that could be collected through individual interviews or focus groups with different stakeholders (e.g., AYAs, clinicians). Thus, we don't know the extent that these groupings would be consistent between quantitative and qualitative approaches. However, we can observe that the PROMIS scores across the HRQOL domains within each AYA profile map to different clinical severity thresholds that are established by the PROMIS initiative and featured on the PROMIS website [56]. For example, the Severe HRQOL Impact AYA profile scores are consistent with the "severe" threshold cut-point values suggested by the PROMIS initiative. Similarly, the "Moderate HRQOL Impact", the "Mild HRQOL Impact", and the "Minimal HRQOL Impact" AYA groups have scores consistent with the PROMIS published severity areas of "moderate", "mild", and "within normal limits", respectively. In addition, the distance between each AYA profile in every domain except social health is larger than the PROMIS minimally important difference thresholds of 2–6 points [69]. Future quantitative and qualitative studies could be conducted to confirm these classifications.

We believe that the quantitative distinct HRQOL impact profiles identified in the study are still useful and clinicians can interpret the results focusing on understanding the varying degrees or levels of HRQOL within the AYA with chronic conditions population. Clinicians

can see the quantitative mean score differences between subgroups and the proportion of AYAs in each subgroup, recognizing the heterogeneity of HRQOL levels in AYAs. Some psychological domains including anger, anxiety, depression, and the physical health domain of fatigue were the primary drivers of the differences between the subgroups, while social health shows the least impact. This knowledge could facilitate more efficient clinical resource allocation and care planning, enabling clinicians to develop targeted interventions and/or provide more intensive care to address these mental health domains. Additionally, monitoring changes over time in the HRQOL impact subgroup for an individual AYA can inform disease management and guide interventions.

Consistent with existing evidence, we found that AYAs who were female, older, having chronic conditions including mental health condition, hypertension, self-reported chronic pain, and thyroid disease, and being on medication were associated with higher odds of being assigned to more severe HRQOL impact profiles. AYAs experiencing pain have reported significant impacts on physical, mental, and social well-being [70–74]. Considering hypertension is most often asymptomatic, AYA patients with hypertension may have other co-existing conditions not adequately accounted for in the current data. It is important to note that we did not find statistically significant differences in HRQOL impact membership in the univariate or multivariable models by race and ethnicity group. A strength of this study, compared to other studies, is that we had a relatively larger sample of Hispanic (38%) and Black AYAs (16%). We did not find differences in HRQOL by race or ethnicity which is in contrast to the differences observed across race and ethnic groups in older adult populations, where African American and Hispanic reported lower HRQOL [9–12, 75].

The regression model correctly predicted 51.2% AYAs' HRQOL impact profiles obtained from LPA. The association between chronic conditions and HRQOL impact profiles may be influenced by disease management and social and/or family support. AYAs may adapt to living with chronic conditions over time. For instance, Jorngarden et al. (2007) found that cancer patients' (aged 13–19 years) HRQOL were significantly worse than those of the general population at diagnosis, but the difference gradually disappeared and then were reversed, resulting in cancer patients reporting significantly better HRQOL and lower level of anxiety and depression compared with the general population 1.5 years after diagnosis [23]. Thus, there are likely other variables that could explain variation in HRQOL impact membership not captured in this study, such as socio-economic status, access to care, and detailed disease characteristics such as duration and severity. Overfitting may have occurred because the same dataset was used for both estimating latent profiles and exploring associations between profiles and demographics/clinical characteristics. Future research is encouraged with additional data in the AYA population with chronic diseases to determine if these HRQOL profiles and the factors associated with them are valid. It is interesting to note that the prediction model correctly categorized 295 out of 363 (81%) AYAs in the Moderate HRQOL Impact profile from the LPA results, but only 6 out of 91 (7%) in the Severe HRQOL Impact profile. Thus, the prediction accuracy was better for moderately impacted HRQOL profiles. In the future, more accurate prediction is helpful to estimate the HRQOL of a larger population of AYAs with chronic conditions who do not have PROMIS scores.

There are some important limitations in this study. While the PROMIS computer adaptive tests (CATs) are generally considered to offer advantages in terms of precision and efficiency compared to the short-forms, the current study used the PROMIS short forms with a fixed set of items. This choice was based on the demonstrated reliability of the selected static short forms and their use for the primary study linking the pediatric and adult versions of the PROMIS measures [52, 76]. In addition, the standard errors of the latent trait estimates were not incorporated into the modeling process, and thus, their impact on the results remains unknown."

The prevalence of kidney disease, thyroid disease, rheumatic disease, cancer, cerebral palsy, intestinal disorders, sickle cell diseases, congenital heart disease, and epilepsy or other seizure disorders were low (<5%) within the study sample. This may lead to less accurate effect size estimation in regression models. Additionally, we are missing additional key explanatory demographic and health-related factors (e.g., diet, physical activity level, sleep duration and quality, family relationship, etc.) that would be useful in predicting HRQOL. The study's generalizability is limited by the use of convenience sampling, which involved enrolling AYAs exclusively from two sources. As a result, caution should be exercised when attempting to apply the findings to the broader population of AYAs aged 14–20 years with chronic conditions without additional research. Furthermore, it is important to note that the results may not be applicable to young adults with chronic conditions who fall outside the age range of 14–20 years. To enhance the external validity of the findings, future studies should incorporate a more diverse and representative sample.

CONCLUSIONS

This study presented the strength of LPA methods to accommodate multiple HRQOL domains in the clustering of AYAs in different profiles. With appropriate predictors, prediction models can be generated to identify AYAs at risk for more severe HRQOL impact to allocate resources to provide appropriate care and surveillance. Additional studies should seek to confirm this LPA solution and examine additional explanatory variables, such as disease management and social or family support, in order to capture a more complete picture of patients at risk for more severely impacted HRQOL.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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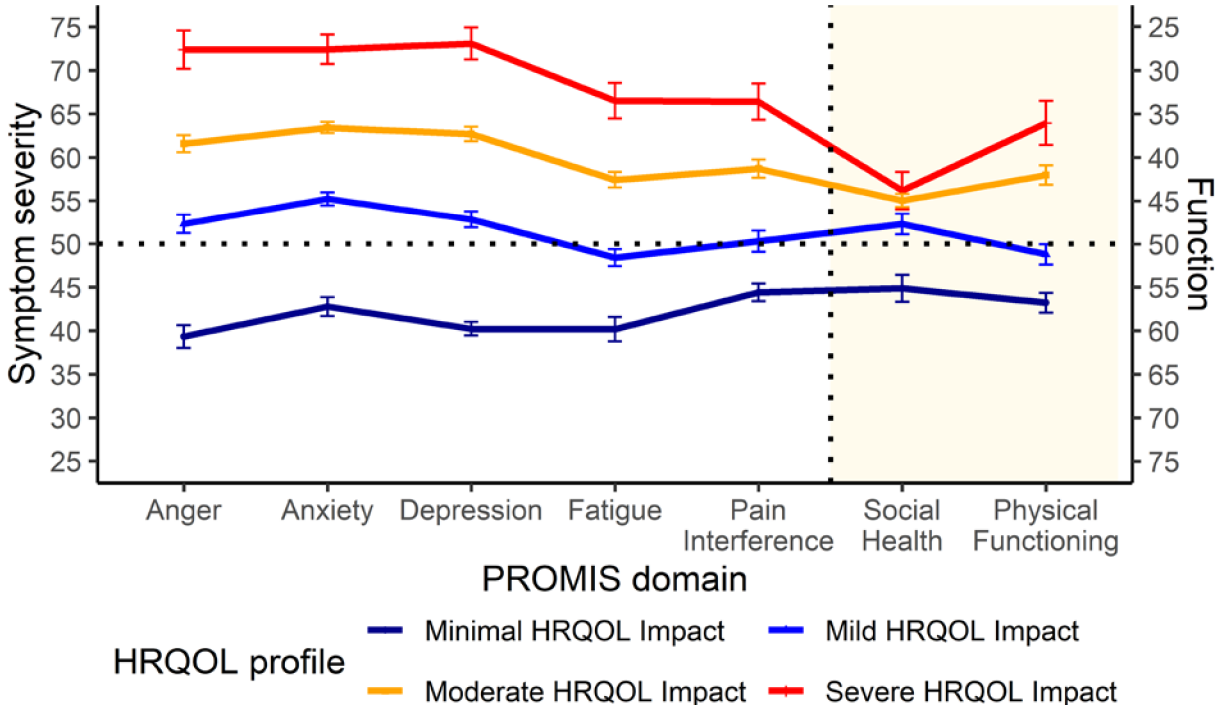

Figure 1.

Mean PROMIS HRQOL domain T-scores of four latent profiles estimated by LPA among 872 AYAs. The 95% confidence intervals were shown. PROMIS scores are on a T-score metric, normed in a reference group to have a mean of 50 and a standard deviation of 10. PROMIS, Patient-Reported Outcomes Measurement Information System; LPA, latent profile analysis. For symptom domains including anger, anxiety, depression, fatigue, and pain interference, higher scores indicate worse symptom burden; for function domains of social health and physical functioning, higher scores indicate better functioning. The dotted vertical line separates symptom severity scores (on the left, clear background color) and functioning scores (on the right, pale yellow background color). The y-axis scales for symptom severity and function are reversed for interpretation.

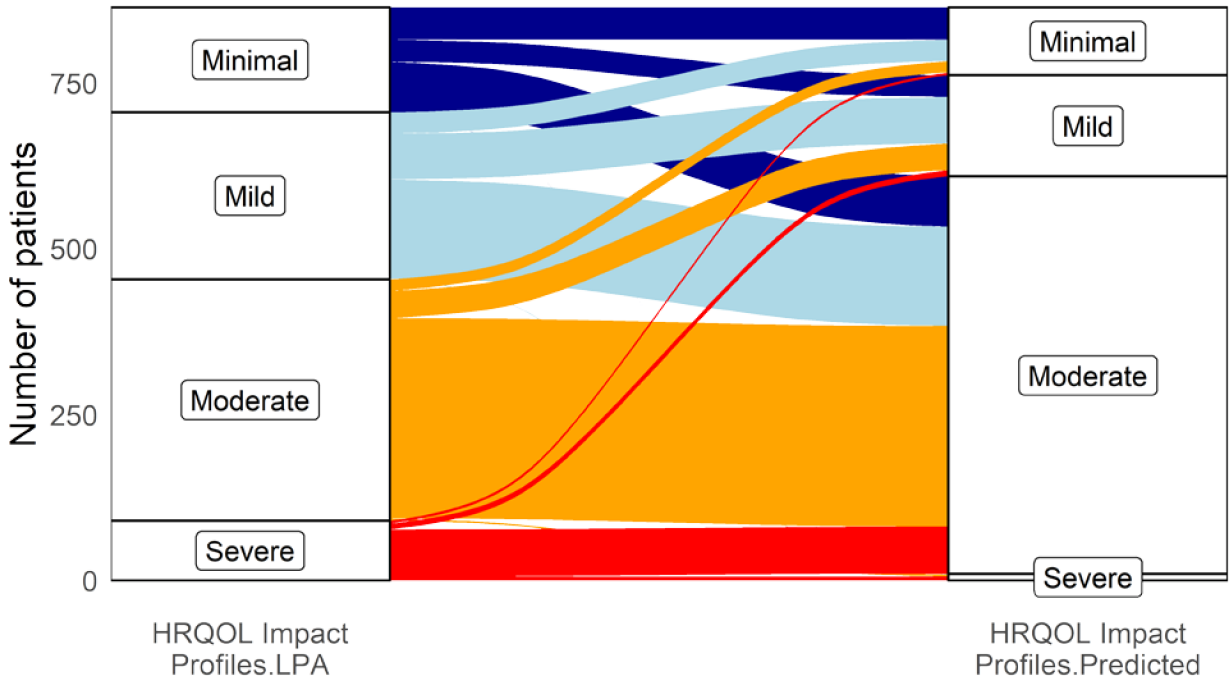

Figure 2.

HRQOL profile membership agreement between profiles assigned by the LPA (on left) and profiles predicted by the regression model (on right). N=442 out of 864 (51.2%) patients were assigned to the same profile by the two methods.

Table 1.

Demographics and clinical characteristics of AYA participants (N=872)

	N (%)*
AYA Characteristics	
Gender: male	406 (46.6%)
Age (years): Mean (SD)	17.4 (1.92)
Race and ethnicity	
Non-Hispanic White	299 (34.3%)
Non-Hispanic Asian	61 (7.0%)
Non-Hispanic Black	137 (15.7%)
Non-Hispanic Other	42 (4.8%)
Hispanic	333 (38.2%)
Language spoken at home: English	768 (88.1%)
On medications	671 (77.1%)
AYA's Health Condition	
ADHD or ADD	244 (28.0%)
Mental health condition	199 (22.8%)
Hypertension	198 (22.7%)
Asthma	197 (22.6%)
Self-reported chronic pain	190 (21.8%)
Allergies	178 (20.4%)
Overweight	151 (17.3%)
Diabetes	88 (10.1%)
Born prematurely	37 (4.2%)
Intestinal disease	36 (4.1%)
Thyroid disease	32 (3.7%)
Epilepsy or other seizure disorders	32 (3.7%)
Kidney disease	31 (3.6%)
Rheumatic disease	25 (2.9%)
Cancer	25 (2.9%)
Deaf or hard of hearing	17 (1.9%)
Congenital heart disease	16 (1.8%)
Sickle cell disease	15 (1.7%)
Requires assistance to get around	14 (1.6%)
Blind	12 (1.4%)
Cerebral palsy	10 (1.1%)
None of the conditions above	65 (7.5%)
Parent Characteristics	
Parent relationship status	

	N (%)*
Married or living together	560 (64.4%)
Single or living as single†	309 (35.6%)
Parent highest education level	
Less than high school	83 (9.5%)
High school degree	185 (21.3%)
College and above	581 (66.8%)
Unknown	21 (2.4%)

Note:

*% based on available data only. N=1 participant had missing information in gender, N=2 participants had missing information on "On medication", N=3 participants had missing information on parent relationship status, N=2 participants had missing information on parent highest education level.

Parent relationship status:

†Other = never together, or separated, or divorced, or widowed.

N, number; SD, standard deviation; ADHD, attention deficit hyperactivity disorder; ADD: attention deficit disorder.

Table 2.

Comparison of different LPA model fit indices using information criterion indices and likelihood ratio tests.

LPA Model	AIC	BIC	SABIC	VLMR LRT (p-value)	LMR LRT (p-value)	Entropy
2-profile	43560.7	43665.6	43595.8	2510.91 (<0.001)	2465.39 (<0.001)	0.90
3-profile	42811.4	42954.6	42859.3	765.24 (0.001)	751.37 (<0.001)	0.87
4-profile	42372.0	42553.3	42432.6	455.47 (<0.001)	447.22 (<0.001)	0.89
5-profile	42157.1	42376.5	42230.4	230.90 (0.21)	226.71 (0.22)	0.88

Note: LPA, latent profile analysis; AIC, Akaike information criterion; BIC, Bayesian information criterion; SABIC, sample size adjusted BIC; VLMR LRT, Vuong-Lo-Mendell-Rubin likelihood ratio test; LMR LRT, Lo-Mendell-Rubin adjusted likelihood ratio test. Both the VLMR-LR and the LMR-LR tests compare one nested LPA model to another model with one additional profile with statistically significant improvement ($p < .05$) suggesting the model with more profiles reflects a better fit. Entropy is a measure of uncertainty in the posterior classifications of the model with higher entropy values reflecting less uncertainty.

Table 3.

Distribution of AYA Demographic and Clinical Characteristics Across Health-Related Quality of Life (HRQOL) Profiles (N=872)

	Minimal HRQOL Impact (N=161)	Mild HRQOL Impact (N=256)	Moderate HRQOL Impact (N=364)	Severe HRQOL Impact (N=91)	Fisher's exact test p-value*
AYA's characteristics					
Gender: male	93 (57.8%)	120 (47.1%)	168 (46.2%)	25 (27.5%)	<.01
Age (years) Mean (SD)	17.2 (1.81)	17.4 (1.93)	17.4 (1.94)	17.7 (1.97)	0.30≠
Race and ethnicity					0.02
Non-Hispanic White	50 (31.1%)	82 (32.0%)	138 (37.9%)	29 (31.9%)	
Non-Hispanic Asian	6 (3.7%)	23 (9.0%)	27 (7.4%)	5 (5.5%)	
Non-Hispanic Black	24 (14.9%)	42 (16.4%)	54 (14.8%)	17 (18.7%)	
Non-Hispanic Other	5 (3.1%)	17 (6.6%)	16 (4.4%)	4 (4.4%)	
Hispanic	76 (47.2%)	92 (35.9%)	129 (35.4%)	36 (39.6%)	
Language at home: English	132 (82.0%)	215 (84.0%)	335 (92.0%)	86 (94.5%)	<.01
On medication	88 (54.7%)	183 (72.0%)	322 (88.5%)	78 (85.7%)	<.01
AYA's Health Condition					
ADHD or ADD	32 (19.9%)	66 (25.8%)	116 (31.9%)	30 (33.0%)	0.02
Mental health condition	11 (6.8%)	59 (23.0%)	102 (28.0%)	27 (29.7%)	<.01
Hypertension	11 (6.8%)	45 (17.6%)	113 (31.0%)	29 (31.9%)	<.01
Asthma	41 (25.5%)	54 (21.1%)	86 (23.6%)	16 (17.6%)	0.46
Self-reported chronic pain	9 (5.6%)	36 (14.1%)	107 (29.4%)	38 (41.8%)	<.01
Allergies	32 (19.9%)	54 (21.1%)	70 (19.2%)	22 (24.2%)	0.73
Overweight	28 (17.4%)	39 (15.2%)	67 (18.4%)	17 (18.7%)	0.75
Diabetes	15 (9.3%)	20 (7.8%)	38 (10.4%)	15 (16.5%)	0.14
Born prematurely	9 (5.6%)	10 (3.9%)	11 (3.0%)	7 (7.7%)	0.17
Intestinal disorders	2 (1.2%)	11 (4.3%)	14 (3.8%)	9 (9.9%)	0.01
Thyroid disease	3 (1.9%)	5 (2.0%)	20 (5.5%)	4 (4.4%)	0.07
Epilepsy or other seizure disorders	5 (3.1%)	6 (2.3%)	14 (3.8%)	7 (7.7%)	0.16
Kidney disease	2 (1.2%)	4 (1.6%)	18 (4.9%)	7 (7.7%)	0.01
Rheumatic disease	1 (0.6%)	6 (2.3%)	14 (3.8%)	4 (4.4%)	0.12
Cancer	2 (1.2%)	4 (1.6%)	13 (3.6%)	6 (6.6%)	0.05
Deaf or hard of hearing	2 (1.2%)	6 (2.3%)	7 (1.9%)	2 (2.2%)	0.89
Congenital heart disease	2 (1.2%)	3 (1.2%)	9 (2.5%)	2 (2.2%)	0.64
Sickle cell disease	0 (0%)	2 (0.8%)	9 (2.5%)	4 (4.4%)	0.06
Requires assistance to get around	0 (0%)	2 (0.8%)	7 (1.9%)	5 (5.5%)	0.03
Blind	0 (0%)	2 (0.8%)	8 (2.2%)	2 (2.2%)	0.33
Cerebral palsy	0 (0%)	0 (0%)	7 (1.9%)	3 (3.3%)	0.43
None of the conditions above	32 (19.9%)	25 (9.8%)	7 (1.9%)	1 (1.1%)	<.01

	Minimal HRQOL Impact (N=161)	Mild HRQOL Impact (N=256)	Moderate HRQOL Impact (N=364)	Severe HRQOL Impact (N=91)	Fisher's exact test p-value*
Parent Characteristics					
Parent relationship status					
Married or living together	109 (68.1%)	159 (62.4%)	227 (62.4%)	65 (71.4%)	0.27
Other†	51 (31.9%)	96 (37.6%)	136 (37.4%)	26 (28.6%)	
Parent highest education level					
Less than high school	93 (58.5%)	171 (66.8%)	253 (69.5%)	64 (70.3%)	0.01
High school degree	37 (23.3%)	45 (17.6%)	83 (22.8%)	20 (22.0%)	
College and above	22 (13.8%)	33 (12.9%)	22 (6.0%)	6 (6.6%)	
Unknown	7 (4.4%)	7 (2.7%)	6 (1.6%)	1 (1.1%)	

Note:

*% based on available data only. N=1 participant had missing information in gender in Mild HRQOL Impact profile, N=2 participants had missing information on "On medication" in Mild HRQOL Impact profile, N=1, 1, 1 participant in Minimal, Mild, Moderate, and Severe HRQOL Impact profiles respectively had missing information on parent relationship status, N=2 participants in Minimal HRQOL Impact profile had missing information on parent highest education level. Parent relationship status:

†Other = never together, or separated, or divorced, or widowed.

N, number; SD, standard deviation; ADHD, attention deficit hyperactivity disorder; ADD: attention deficit disorder. Fisher's exact test was performed on values >0 across profiles.

‡One-way ANOVA was performed on age (years) across profiles.

Table 4

Characteristics Statistically Associated with HRQOL Impact profiles using Multinomial Logistic Regression Model (n=872)

Predictors	Reference (HRQOL Impact)	Response (HRQOL Impact)	OR (95% CI)
Gender: male	Minimal	Mild	**0.62 (0.39 – 0.98)**
	Minimal	Moderate	**0.56 (0.35 – 0.88)**
	Minimal	Severe	**0.24 (0.12 – 0.46)**
	Mild	Moderate	0.9 (0.62 – 1.30)
	Mild	Severe	**0.38 (0.21 – 0.70)**
	Moderate	Severe	**0.44 (0.25 – 0.78)**
Age (years) *	Minimal	Mild	1.05 (0.93 – 1.18)
	Minimal	Moderate	1.05 (0.93 – 1.18)
	Minimal	Severe	**1.19 (1.02 – 1.40)**
	Mild	Moderate	1 (0.91 – 1.10)
	Mild	Severe	1.15 (1.00 – 1.33)
	Moderate	Severe	**1.15 (1.00 – 1.32)**
On medication	Minimal	Mild	**1.76 (1.05 – 2.93)**
	Minimal	Moderate	**3.75 (2.17 – 6.46)**
	Minimal	Severe	**2.85 (1.29 – 6.32)**
	Mild	Moderate	**2.11 (1.30 – 3.42)**
	Mild	Severe	1.59 (0.75 – 3.37)
	Moderate	Severe	0.74 (0.35 – 1.59)
Mental health condition	Minimal	Mild	**3.85 (1.90 – 7.78)**
	Minimal	Moderate	**5.47 (2.72 – 10.98)**
	Minimal	Severe	**5.26 (2.28 – 12.14)**
	Mild	Moderate	1.47 (0.98 – 2.23)
	Mild	Severe	1.44 (0.78 – 2.67)
	Moderate	Severe	0.94 (0.53 – 1.67)
Hypertension	Minimal	Mild	**2.53 (1.21 – 5.28)**
	Minimal	Moderate	**4.96 (2.45 – 10.05)**
	Minimal	Severe	**4.97 (2.14 – 11.51)**
	Mild	Moderate	**1.94 (1.26 – 2.99)**
	Mild	Severe	**1.97 (1.05 – 3.67)**
	Moderate	Severe	1.11 (0.63 – 1.95)
Asthma	Minimal	Mild	0.78 (0.46 – 1.35)
	Minimal	Moderate	1 (0.58 – 1.70)
	Minimal	Severe	0.5 (0.22 – 1.11)
	Mild	Moderate	1.27 (0.81 – 2.00)
	Mild	Severe	0.61 (0.29 – 1.29)

Predictors	Reference (HRQOL Impact)	Response (HRQOL Impact)	OR (95% CI)
	Moderate	Severe	**0.48 (0.23 – 0.99)**
Self-reported chronic pain	Minimal	Mild	**2.69 (1.19 – 6.07)**
	Minimal	Moderate	**7.18 (3.31 – 15.56)**
	Minimal	Severe	**12 (4.97 – 28.95)**
	Mild	Moderate	**2.65 (1.66 – 4.24)**
	Mild	Severe	**4.44 (2.37 – 8.31)**
	Moderate	Severe	1.71 (0.99 – 2.97)
Thyroid disease	Minimal	Mild	0.99 (0.17 – 5.74)
	Minimal	Moderate	3.42 (0.71 – 16.43)
	Minimal	Severe	1.87 (0.27 – 12.66)
	Mild	Moderate	**3.31 (1.05 – 10.49)**
	Mild	Severe	1.76 (0.36 – 8.48)
	Moderate	Severe	0.51 (0.14 – 1.84)
Parent relationship status: other†	Minimal	Mild	1.2 (0.75 – 1.91)
	Minimal	Moderate	1.17 (0.73 – 1.87)
	Minimal	Severe	0.65 (0.34 – 1.26)
	Mild	Moderate	1.04 (0.71 – 1.51)
	Mild	Severe	0.58 (0.32 – 1.05)
	Moderate	Severe	**0.53 (0.30 – 0.94)**

Note: The full regression model adjusted for AYA patient's gender, age (year), race/ethnicity, different health conditions (hypertension, ADHD or ADD, mental health condition, kidney disease, self-reported chronic pain, asthma, thyroid disease, overweight, rheumatic disease, diabetes, intestinal disease, congenital heart disease, epilepsy or other seizure disorders, allergy, on medication or not), parent relationship status (married or living together, other), parent highest education level (less than high school, high school, college and above, unknown), and language spoken at home (English, non-English). Only variables statistically associated ($p<.05$) with the outcome response (HRQOL Impact profile) are presented in this table. The sample size was 864 (out of 872) due to missing values for some covariates.

*Age (years) is a continuous predictor.

†Parent relationship status: reference is married or living together.

HRQOL, health-related quality of life; OR, odds ratio; CI, confidence interval. Results interpretation example, the odds of being in the mild vs. minimal HRQOL impact profile in males is 0.62 times the odds of being in the mild vs. minimal HRQOL impact profiles in females. Odds ratios with 95% confidence intervals which do not contain 0 are bolded.

Table 5.

Health-Related Quality of Life Profile prediction accuracy

Profiles from LPA	Profiles predicted in the regression model				
	Minimal	Mild	Moderate	Severe	Total
Minimal	75	27	56	0	158
Mild	44	66	140	2	252
Moderate	24	41	295	3	363
Severe	2	13	70	6	91
Total	145	147	561	11	864