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EMPIRICALLY DERIVED PATTERNS OF PAIN, STOOLING, AND INCONTINENCE
AND THEIR RELATIONS TO HEALTH RELATED QUALITY OF LIFE AMONG YOUTH
WITH CHRONIC CONSTIPATION

by

Kimberly L. Klages

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Abstract

Chronic constipation is associated with pain, stress, and fecal incontinence, which negatively impact health-related quality of life (HRQoL); however, it is unclear if patterns of pain, stool frequency, and incontinence are differentially associated with HRQoL in youth with chronic constipation. Four hundred and ten caregivers completed a demographics and symptoms form, the Parental Opinions of Pediatric Constipation, Pediatric Symptom Checklist, and the Functional Disability Inventory. Stooling patterns were derived using Latent Variable Mixture Modeling. A three-class model emerged: *withholding/avoiding (WA)*, *pain*, and *fecal incontinence (FI)*. The *pain* class reported the greatest amount of disease burden/distress, greatest impairments in illness related activity limitations, more psychosocial problems, and, along with the *FI* class, elevated levels of family conflict. The *FI* class reported the greatest amount of parental worry of social impact. Youth with chronic constipation who experience pain or fecal incontinence may be at a greater risk for specific HRQoL problems such as illness related activity limitations, psychosocial issues, disease burden and worry, and family conflict.

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Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life among Youth with Chronic Constipation

Chronic constipation is a common pediatric gastrointestinal disorder with prevalence up to 29.6% in the general population and is often associated with infrequent defecation, hard and large stools, pain while stooling, abdominal pain, and distress (Bongers, van Dijk, Benninga, & Grootenhus, 2009). In the United States alone, constipation is responsible for more than 2.5 million physician consultations, 92,000 hospitalizations, and several hundred million dollars per year for medication costs (Lembo & Camilleri, 2003). Although several definitions of constipation exist, the Rome III criterion is most widely used in medical settings (Kaugars et al., 2010). According to Rome III criteria, the diagnosis for functional constipation requires at least two or more of the following for one month or more in infants and children under 4 years of age and least once per week for two months or more in children 4 and up prior to diagnosis: two or fewer defecations per week, at least one period of fecal incontinence per week after acquiring toileting skills, history of retentive posturing or excessive volitional stool retention, history of painful or hard bowel movements, presence of a large fecal mass in the rectum, and/or a history of large diameter stools which may obstruct the toilet ("Guidelines--Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders," 2006). Up to 84% of children with chronic constipation experience frequent episodes of fecal incontinence, or the passage of whole bowel movements in their underwear (Cunningham & Banez, 2006). Although most children with chronic constipation respond to medical treatment within one year, approximately one third of patients experience symptoms into adulthood (Bongers, Benninga, Maurice-Stam, & Grootenhuis, 2009).

Biopsychobehavioral Model of Chronic Constipation

Cox and colleagues (1998) proposed a biopsychobehavioral model of chronic constipation with fecal incontinence in which constipating events lead to fecal impaction and the buildup of large and hard bowel movements that are difficult to pass. Children with chronic constipation may cope with these painful defecations by withholding stools or avoiding stooling, eventually releasing the bowel movement via overflow incontinence. Avoiding stooling or withholding bowel movements exacerbates constipation, and, in turn, leads to greater fecal incontinence, thus maintaining a maladaptive pattern of stooling (Luxem, Christophersen, Purvis, & Baer, 1997). Subsequent fecal incontinence episodes may lead to peer and family conflict, which may culminate in poor self-esteem and poor self-worth (Cox, Sutphen, Borowitz, Kovatchev, & Ling, 1998). Furthermore, parents may use punishment to reduce fecal incontinence accidents; however, punitive techniques are likely to cause more guilt, poor self-esteem, and anxiety in a child and thus significantly impacting HRQoL in youth with chronic constipation experiencing fecal incontinence (Landmark, Rappaport, Fenton, & Levine, 1986; Nolan & Oberklaid, 1993; Owens-Stiverly, 1987).

Pain and Health-Related Quality of Life among Youth with Chronic Constipation

Past research has shown that youth with chronic constipation experiencing increased symptomatology, such as abdominal pain and pain while stooling, reported lower levels of health related quality of life (HRQoL) when compared to youth experiencing fewer symptoms (Rajindrajith, Devanarayana, & Benninga, 2013). Furthermore, Rajindrajith and colleagues (2013) found a negative correlation between HRQoL and general somatic symptoms (such as aches, pains, and altered body functioning) in youth with chronic constipation. The severity of these somatic symptoms significantly impacted the youth's ability to perform daily activities, thus contributing to lower perceived HRQoL (Rajindrajith et al., 2013). It is currently unclear exactly which somatic symptom patterns exist among youth with chronic constipation and how these symptoms contribute to HRQoL. Youssef and colleagues (2005) assessed HRQoL in children with chronic constipation and compared them to children with other chronic gastroenterology conditions and healthy controls. The impact of chronic constipation on HRQoL

of affected children was similar to children with inflammatory bowel disease, a chronic health condition associated with inflammation of the gastrointestinal tract (Youssef, Langseder, Verga, Mones, & Rosh, 2005). Similar to IBD, youth with chronic constipation often experience bloating, abdominal pain, and pain while stooling that significantly impacts HRQoL (Benninga, Voskuijl, & Taminiau, 2004). In youth with very infrequent stooling, the evacuation of large stools is usually preceded by complaints of abdominal pain and this pain has been reported as the most distressing consequence of constipation (Benninga et al., 2004; Freeman, Riley, Duke, & Fu, 2014).

Internalizing and Externalizing Behaviors among Youth with Chronic Constipation

Youth with chronic constipation with fecal incontinence may be at an increased risk for more problematic externalizing and internalizing behaviors that negatively impact child and family HRQoL (Bongers, van Dijk, et al., 2009; Joinson, Heron, Butler, & van Gontard, 2006; Kaugars et al, 2010; Youssef et al., 2005). Regarding behavioral difficulties, Cox, Morris, Borowitz, and Sutphen (2002) found both mothers and teachers of children with fecal incontinence reported higher rates of aggressiveness, attention problems, and withdrawn behaviors when compared to a sample of children without fecal incontinence. Furthermore, Joinson and colleagues (2006) also noted that parents of children with frequent fecal incontinence reported increased attention and activity problems, obsessions and compulsions, and oppositional behaviors when compared to children who soil occasionally or not at all. Children with chronic constipation are also to be perceived by their parents as more stubborn, defiant, disobedient, and resistant to following instructions than children without (Burket et al., 2006). Khan et al. (2006) found that children with higher levels of fecal incontinence (more episodes and longer duration) also had poorer long-term outcomes such as increased family conflict and difficulties with peer relationships as adults. These internalizing and externalizing behaviors that are often associated with chronic constipation with fecal incontinence have been shown to contribute to poorer HRQoL (Bongers, van Dijk, et al., 2009).

Peer Relations among Youth with Chronic Constipation

The troublesome nature of constipation may cause social embarrassment and rejection by peers. Peers often develop negative stereotypes about youth with fecal incontinence, often labeling them as “dirty” or “stinky” and therefore reject these individuals (Campbell, Cox, & Borowitz, 2009). Bongers, van Dijk, et al. (2009) reported that youth with constipation-associated fecal incontinence reported worrying about experiencing unnoticed fecal incontinence during school and believed that their defecation caused problems at school. These beliefs may lead to feelings of shame, which in turn, can heighten feelings of peer rejection (Nolan & Oberklaid, 1993). Individuals with fecal incontinence may respond to peer rejection with poor self-esteem, hostility, or learned helplessness, which negatively impacts HRQoL (Campbell et al., 2009).

While previous research focused on the individual impact of fecal incontinence, symptom duration, or overall symptom severity on HRQoL (Bongers, Benninga, et al., 2009; Clarke et al., 2008; Youseff et al., 2005), the present study takes a person-centered approach to determine if specific patterns (i.e., latent profiles) of symptoms of constipation, such as stooling (stool size, consistency, frequency, presence of blood in stool, and incontinence), pain (abdominal and while stooling), age, and holding/avoiding stooling exist among youth with chronic constipation. If these latent profiles exist, a second aim of the current study is to determine whether these patterns differentially impact parent report of functional disability, psychosocial functioning, and constipation specific HRQoL (parental burden/distress, family conflict, and parental worry of social impact) in youth with chronic constipation. It was anticipated that three to four distinct patterns would emerge, and the two profiles that were characterized by youth experiencing either pain or fecal incontinence would report the greatest psychosocial issues, increased functional disability, and decreased HRQoL.

Methods

Participants and Procedure

This study was part of a larger, multisite study investigating quality of life in youth with chronic constipation and fecal incontinence. Caregivers of youth with chronic constipation were recruited

from pediatric gastrointestinal clinics at five participating academic medical centers across the United States. A total of 468 caregivers were initially enrolled in the study and 410 had sufficient data and met inclusion criteria (Silverman et al., 2015). The total sample consisted of 122 participants from Children's Hospital of Wisconsin; 154 participants from Nationwide Children's Hospital; 73 participants from Boston Children's Hospital; 39 participants from the University of Texas Southwestern Medical Center; and 22 participants from Children's and Women's Hospital from South Alabama. The study was approved by the respective Institutional Review Board committees at each participating institution. Written informed consent for participation was obtained from adult caregivers and data were collected in pediatric gastrointestinal clinics at each medical center. In order to be included in the study, families needed to be fluent in English and their child had to meet the ROME III criteria for functional constipation or functional constipation with fecal incontinence. Exclusion criteria for the present study included (1) children with a diagnosis of fecal incontinence (without constipation), (2) children with moderate to severe developmental delays, (3) children with associated chronic disease which may have had an impact on quality of life (e.g., cerebral palsy, spine deformity or malformations, severe psychiatric illness, etc.); and (4) children with a diagnosis of irritable bowel syndrome.

Measures

Demographics and Constipation Symptoms Questionnaire. Caregivers of children ages 2-18 completed a demographic questionnaire to report on youth gender, ethnicity/race, age, and diagnosis. Caregivers also reported youth's condition type according to ROME III criteria (i.e., constipation or constipation with fecal incontinence), typical stool size (i.e., small marble, golf ball, tennis ball, or larger than tennis ball), frequency (free response of the number of bowel movements per week) and stool consistency following the Bristol Stool Chart (Type 1, hard lumps to 7, entirely liquid; Heaton & Lewis, 1997). Caregivers rated relevant clinical information regarding abdominal pain, pain while stooling (0 = Never, 1 = Sometimes, 3 = Often 4 = Always), and fecal incontinence using a 4-point Likert scale (0 = Never, 1 = Small amount,

2= Moderate amount, 3 = Large amount). The mean (*SD*) age of youth in the sample was 7.8 (3.5) years and 52% of the sample were male. Seventy-eight percent of participants were Caucasian, 9% African American, 5% Hispanic/Latino, 3.1% Asian/Asian American, and 4% identified as other. Forty-five percent of subjects were categorized as having functional constipation alone and 55% of subjects were categorized as having functional constipation with fecal incontinence.

Parental Opinions of Pediatric Constipation. The Parental Opinions of Pediatric Constipation (POOPC; Silverman et al., 2015) is a 24-item parent report scale that used 5 point anchors (1 = strongly disagree to 5 = strongly agree). The POOPC consists of an overall total score of HRQoL problems and 4 subscales (Burden/Distress, Family Conflict, Difficulties with the Medical Team, and Worry about Social Impact) that assess the effects of pediatric constipation and constipation with fecal incontinence on HRQoL. This measure was developed using qualitative findings, and series of exploratory and confirmatory factor analyses among families seeking constipation treatment in a multidisciplinary clinic (see Kaugars et al., 2010). The POOPC has been found to have internally consistent scales ($\alpha = .79$ to $.90$), good convergent, discriminant, and construct validity, and measurement invariance across ages ranging from 2 to 18 years (Silverman et al., 2015). The Burden/Distress subscale assesses a pattern of caregiver concerns that focus on their child's negative experiences of having constipation (e.g., pain, lack of improvement of symptoms, duration of symptoms, and embarrassment). The Family Conflict subscale assesses a pattern of caregiver concerns focusing on conflicts between family members related to following the constipation treatment regimen (e.g., asking the child to use the toilet, child resisting treatment, worry that the relationship with the child is damaged due to treatment). The Difficulties with the Medical Team subscale measures patterns of caregiver concerns with their child's healthcare provider. The Worry of Social Impact subscale assesses parent concerns related to peer relationships (e.g., child is not asked to play, others finding out about the problem).

Functional Disability Inventory. Caregivers completed the Functional Disability

Inventory (FDI; Walker & Green, 1991; $\alpha = .93$, current study) is a 15-item parent report measure that assesses the child's difficulty in completing daily activities in four domains: home, school, recreational and social domains. Each item is rated on a 5-point Likert scale (0 = no trouble to 4 = impossible). A total score is computed, 0-60 with higher scores indicating greater illness-related disability. Internal consistency reliability of the validation sample ranged from .86 to .91 (Walker & Green, 1991). Validity was supported by significant correlations between child- and parent-report FDI scores with measures of school-related disability, pain, and somatic symptoms.

Pediatric Symptom Checklist. The Pediatric Symptom Checklist (PSC; Gardner et al., 1999) assesses parent report screening measure to identify children and adolescents who may be in need of further evaluation, or as an indicator of psychosocial well-being prior to and following intervention or treatment. The PSC consists of 35 items. Each item is rated as Never = 0; Sometimes = 1; or Often = 2. Higher scores indicate greater psychological impairment in children. The authors report evidence of good sensitivity and specificity, minimal concurrent and moderate convergent validities (Gardner et al., 1999; $\alpha = .93$ for the current study).

Analytic Plan

Latent Variable Mixture Modeling (LVMM) was used to empirically derive patterns of pain, incontinence, and stooling (frequency, consistency, and size) in youth with chronic constipation. LVMM is a person-centered statistical approach (similar to cluster analyses) that classifies individuals into unobserved subgroupings (latent classes) with similar patterns to determine the extent to which these patterns may relate to the variables of interest (Berlin, Karazsia, & Klages, in press; Berlin, Williams, & Parra, 2014; Berlin, Parra, & Williams, 2014). Person-centered approaches are useful when complex interactions may exist between variables of interest (Bergman, von Eye, & Magnusson, 2006; Berlin, Karazsia, & Klages, in press). Person-centered approaches use individuals as the standard unit of the analyses rather than variables (Bauer & Shanahan, 2007; Berlin, Parra, & Williams, 2014; Berlin, Williams, et al., 2014), allowing for intricate patterns among the variables to be identified, thus providing useful descriptive information about the complex patterns among variables. A mix of ordinal (abdominal pain, pain

while stooling, typical stool size, stool consistency, and age), binary (condition type, blood in stool, holding/avoiding stooling), and count (stool frequency) indicators were used in LVMM. A zero inflated negative binomial model was chosen for count data because a sizeable minority of the sample (20%) reported zero bowel movements per week leading to overly dispersed data ($M = 4.56$, $SD = 6.24$). Zero-inflated models result in two variables: 1) a binary variable reflecting membership in a group that is “always zero” vs. a group that can take on values of zero and greater; and 2) the count of bowel movements per week leading among those not always at zero. An exploratory approach was used to establish our model (i.e. additional classes were estimated until a statistically proper and/or practical solution is no longer obtained) and the best fitting model for describing varying classes was selected based on clinical relevance and goodness-of-fit statistics. The model was compared on various forms of fit-statistics including the Bayesian Information Criteria (BIC; Schwarz, 1978) and the Akaike Information Criterion (AIC; Akaike, 1974), where lower values on these indicate a better model fit, and the Lo-Mendell-Rubin test (LMR; Lo, Mendell, & Rubin, 2001) which statistically compares the improvement of adjacent models (e.g., 1 vs. 2, 2 vs. 3, etc.) where a p -value less than 0.05 indicates the best model fit. The entropy statistic was calculated to indicate classification precision, higher values reflecting better accuracy (Berlin, Williams, et al., 2014). Robust full information maximum likelihood was used to account for missing data and for adjustments to the standard errors for non-normality and non-independence across sites (for all models tested, see Table 1).

To determine class differences in HRQoL (POOPC subscales, FDI, and PSC) while controlling for age, a manual BCH procedure was used (Asparouhov & Muthén, 2014). The BCH method can be used to evaluate measurement error weighted intercepts/means across classes and allows for covariates. BCH weighted class intercepts (which reflect the predicted values of the outcome at the average participant age which was mean centered) were compared using the scaled loglikelihood difference test (Muthén & Muthén, 2012). All estimates (intercepts, regression coefficients, variances, etc.) were allowed to vary across classes.

Results

Youth with chronic constipation were empirically assigned to groups, or classes, based on patterns of pain, incontinence, and stooling. The patterns of fit statistics (see Table 1) were mixed suggesting that one (LMR), two (BIC), and three plus (AIC) class models were potentially viable). As such, the class characteristics (uniqueness vs. similarity to each other) and size were considered next. The three-class model provided three profile patterns with clearly differentiated indicator values and distinct characteristics (i.e., distinction of youth experiencing predominately pain and youth experiencing predominately fecal incontinence) while the two-class model provided less of a distinction between class important clinical characteristics (i.e., high/low pain classes with no distinct fecal incontinence class). The four-class model only provided a slight variation of the three-class model in which the pain class was divided into two classes (youth experiencing predominately abdominal pain and youth experiencing predominately pain while stooling; see Table 1 for goodness-of-fit statistics). When considering possible targets of intervention and typical presenting problems, the three-class model was reasoned to be optimal (latent classes are depicted in Figure 1). Univariate entropy indicated that the ordinal variables that contributed most to class formation consisted of pain while stooling (.221) and stool consistency (0.199), followed by age (0.121), stool size (0.087), and abdominal pain (0.082).

Class Characteristics

The largest profile of this three-class model, the *fecal incontinence* (*FI*; $n = 177$, 43.3%) class, was characterized by slightly younger youth ($M = 6.24$, $SD = 0.24$ years of age) experiencing fecal incontinence and loose stools. The *FI* class had relatively low (log) odds ($est. = -3.04$, $SE = 0.62$, $p < 0.01$) of having zero weekly bowel movements ($\approx 4.6\%$ of *FI* class). Among those not always experiencing zero bowel movement per week in the *FI* class, youth experienced an average of 1.8 ($SE = 0.622$, $p < 0.01$) bowel movements per week. The second largest profile, the *withholding/avoiding* (*WA*; $n = 154$, 37.6%) class, was characterized by youth ($M = 7.72$, $SD = 0.31$ years of age) experiencing stool greater stool withholding and stooling avoidance. The *WA* class had the highest (log) odds ($est. = -1.81$, $SE = 0.57$, $p < 0.001$, 14% of *LFS* class) of having zero weekly bowel movements; however, among those not always at zero

bowel movements per week in the *WA* class, youth experienced an average of 1.81 ($SE = 0.06$, $p < 0.001$) bowel movements per week. The smallest profile that emerged, the *pain* ($n = 78$, 19.1%) class, was characterized by youth ($M = 7.62$, $SD = 0.26$ years of age) experiencing large, hard, painful, bloody stools, abdominal pain, and infrequent stooling, and a relatively low (log) odds of zero bowel movements per week ($est. = -3.45$, $SE = 1.94$, $p = 0.076$, $\approx 3.1\%$ of *pain* class). Among those not always experiencing zero bowel movements per week in the *pain* class, youth experienced an average of 0.98 ($SE = 0.114$, $p < 0.001$) weekly bowel movements.

Constipation Specific HRQoL

Significant differences were found between classes for the POOPC subscales when controlling for age differences across classes. Caregivers of youth in the *pain* class reported significantly more disease burden and distress than youth in the *FI* ($est. = 4.02$ vs. $est. = 3.77$; $p < 0.001$; $d = 0.61$) and the *WA* classes ($est. = 3.62$, $p < 0.001$; $d = 1.01$). Caregivers of youth in the *FI* class reported significantly more burden/distress than youth in *WA* class ($est. = 3.77$ vs. $est. = 3.62$; $p < 0.001$; $d = 0.45$). Caregivers of youth in the *WA* class reported significantly less family conflict than *FI* ($est. = 2.47$ vs. $est. = 2.95$, $p < 0.001$; $d = 0.97$) and *pain* classes ($est. = 2.84$; $p < 0.001$; $d = .50$). Caregivers of youth in the *FI* reported significantly more worry of social impact on the POOPC than both *WA* ($est. = 2.77$ vs. $est. = 2.14$, $p < 0.001$; $d = 0.43$) and *pain* youth ($est. = 2.46$, $p = 0.04$; $d = 0.31$). Caregivers of youth in the *pain* class reported significantly more worry of social impact than caregivers of youth in the *WA* class ($est. = 2.46$ vs. $est. = 2.14$, $p < 0.001$; $d = 0.23$). Regarding caregivers' difficulty with the medical treatment team, caregivers of youth in *WA* class reported significantly less difficulty with the medical team than youth in the *pain* class ($est. = 2.10$ vs. $est. = 2.22$, $p < 0.001$; $d = 0.17$).

Functional Disability and Psychosocial Problems

Significant differences (controlling for age) were also found between classes for the PSC and FDI. Caregivers of youth in the *WA* class reported significantly less functional disability when compared to youth in the *pain* class ($est. = 1.53$ vs. $est. = 1.68$, $p = 0.02$; $d = 0.29$). *FI* caregivers reported significantly less, albeit small differences in functional disability than *WA*

(*est.* = 1.49 vs. *est.* = 1.53, $p < 0.001$; $d = 0.07$). Caregivers of youth in the *WA* class reported significantly less psychosocial problems when compared to the *pain* class (*est.* = 1.48 vs. *est.* = 1.58, $p < 0.001$; $d = 0.36$). Caregivers of youth in the *FI* class also reported significantly less psychosocial problems when compared to youth in the *pain* class (*est.* = 1.49 vs. *est.* = 1.58, $p < 0.001$; $d = 0.38$). An overview of all class comparisons and details of the regression model can be found in Table 2 and the online supplemental materials respectively.

Discussion

Using a relatively novel person centered approach, the present study identified patterns of stooling and examined the how these patterns were differentially associated with HRQoL in youth with chronic constipation. Three unique profiles emerged: first, the largest profile, the *fecal incontinence* class, was characterized by youth experiencing symptoms of more frequent stooling and fecal incontinence. The second largest profile, the *withholding/avoiding* class, was characterized by youth experiencing increased withholding stool and stooling avoidance. The smallest profile that emerged, the *pain* class, was characterized by youth presenting with symptoms of abdominal pain, hard, large and painful stools, and infrequent stooling. Overall, caregivers of youth in the *pain* class reported the greatest amount of disease burden and distress, greatest impairments in illness related activity limitations, more psychosocial problems, and, along with the *fecal incontinence* group, elevated levels of family conflict. Caregivers of youth in the *fecal incontinence* class reported the greatest amount of parental worry of social impact. Furthermore, caregivers of youth in the *withholding/avoiding* class reported the least amount of difficulty with the medical treatment team than caregivers of youth in the *pain* and *fecal incontinence* classes.

Pain and HRQoL

These findings are consistent with previous variable centered reports that youth with chronic constipation who experience abdominal pain and fecal incontinence may be at risk for poorer HRQoL relative to affected youth not experiencing these symptoms. Similar to previous variable-centered studies, we found in our person-centered analyses that caregivers in classes

with youth with chronic constipation experiencing abdominal pain and infrequent stooling reported greater illness related activity limitations, and more psychosocial problems, suggesting that the negative symptoms of constipation (i.e., pain, duration of symptoms) significantly impact HRQoL (Cox et al., 1998; Rajindrajith et al., 2013; Youssef et al., 2005). The present study extends this past research by demonstrating distinct symptom patterns are differentially associated with disease specific aspects of HRQoL. More specifically, rather than demonstrating broad problems in HRQoL, this study allowed for a more nuanced examination of the associations between symptom patterns and various facets of HRQoL.

In our person-centered analyses, caregivers in classes of youth experiencing both abdominal and stooling pain reported greater functional disability and more disease burden, distress, and psychosocial problems, suggesting that the negative symptoms of constipation may significantly impact how parents perceive their child's HRQoL. Consistent with previous findings, pain, specifically chronic pain, strongly impacts parent perceived HRQoL (Hunfeld et al., 2001). Furthermore, chronic pain is positively associated with psychological distress and disability (Andrasik et al., 1988; Balagué, Skovron, Nordin, Dutoit, & Waldburger, 1995; Brattberg, 1994). Similarly, Mano, Khan, Ladwig, and Weisman (2011) found that mothers of youth with chronic pain reported low levels of HRQoL and suggested that the type of pain (whether it is abdominal pain or headaches) may have less of an impact on HRQoL than other factors, such as functional disability. Additionally, Warschburger and colleagues (2014) found comparable results in a sample of children with abdominal pain due to functional or organic gastrointestinal disorders, in which abdominal pain greatly contributed to increased levels of psychosocial strain, and in turn, adversely impacted HRQoL.

Fecal Incontinence and HRQoL

Unlike Youssef et al. (2005), we found a significant (medium sized) difference in HRQoL between classes of children with and without a preponderance of fecal incontinence, suggesting that frequent fecal incontinence may differentially impact HRQoL in children with chronic constipation. Since the current study used a disease-specific measure of HRQoL, it is

possible that non-disease specific measures lack sensitivity to assess the impact of fecal incontinence on HRQoL (Bongers, Benninga, et al., 2009). Furthermore, our findings may differ from Youssef and colleagues (2005) because parents of youth with constipation tend to report lower levels of HRQoL for their children when compared to parents of typically developing youth, those with other chronic gastrointestinal diseases, and when compared child self-report. Bongers, van Dijk, et al., (2009) noted that parents of youth with constipation and fecal incontinence tend to be more concerned of the social consequences than their child, as their child may be unaware of the social consequences of their defecation problem.

Peer Relationships

Caregivers of youth in the *fecal incontinence* class also reported greater concerns for peer relationships. Due to the embarrassing nature of the disease, parents of children with fecal incontinence may worry about their child experiencing greater deficits social functioning, such as peer victimization and engaging in antisocial behavior, than parents of children without fecal incontinence (Kaugars et al., 2010). Parents may view their child as unable to adequately clean themselves after experiencing severe fecal incontinence and, therefore, become easy targets for social ridicule and bullying (Clarke et al, 2008). Bongers, van Dijk, et al. (2009) found that 23% of children with fecal incontinence reported regular bullying due to their defecation problem. In contrast, Cox et al. (2003) reported that neither parent nor child indicated peer rejection as an outcome of fecal incontinence. Further research is needed in this area to assess if youth with fecal incontinence experience greater social functioning deficits in comparison to youth with chronic constipation without fecal incontinence.

Withholding/Avoiding Symptoms and HRQoL

Interestingly, caregivers of the *withholding/avoiding* class reported low levels of difficulties with the medical treatment team, functional disability, and psychosocial problems in comparison to the *pain* class and low levels of family conflict in comparison to both the *pain* and *fecal incontinence* classes. Youth in the *withholding/avoiding* of the current study tended to be older in age (which was controlled for statistically) and their caregivers reported intermediate

levels of abdominal pain, pain while stooling, stool consistency, bowel movement frequency per week, and high levels of continence relative to the *pain* and *fecal incontinence* classes. It may be possible that caregivers of youth experiencing high pain who are dissatisfied with their medical treatment team are less likely to adhere to laxative regimens, thus maintaining their child's maladaptive stooling pattern. These findings further suggest that pain, and fecal incontinence may have a larger impact on perceived HRQoL, functional disability, and psychosocial wellbeing than other symptoms; however, more research in this area is needed to establish if pain and incontinence account for these outcomes across the classes.

Clinical Implications of the Current Study

There are several important clinical implications to these findings. The present study provides convergent and discriminant validity (social worry higher in those in the fecal incontinence class, etc.) for the POOPC as a measure of parent perceived HRQoL in youth with chronic constipation. As such, the POOPC may be an invaluable clinical tool for pediatric psychologists to detect specific domains for treatment among youth with chronic constipation and their families (Silverman et al., 2015). Specifically, the POOPC may be potentially sensitive to disease-specific processes and may serve as a helpful tool for determining how to tailor existing interventions or determine whether additional treatment modules are needed in efforts to improve HRQoL in youth with chronic constipation. For example, tailored interventions for youth with similar presenting concerns to those in the pain class might be aimed at enhancing how families cope with the distressing/burdensome nature of functional constipation and improving psychosocial functioning and family conflict. Youth experiencing predominately fecal incontinence may benefit from interventions targeting interpersonal relationships (i.e. peers and family). In contrast, youth experiencing withholding/avoidance may need minimal tailoring of existing evidence based treatments given these patterns of results. The current study also highlights the need for medical providers to be aware of caregiver or patient dissatisfaction with the medical team as it may impact HRQoL. Assessments of family-medical team interactions may be potentially helpful for implementation of interventions focused on improving family

treatment satisfaction, such as active listening and negotiation of behavior change to improve family treatment satisfaction (Kinmonth, Woodcock, Griffin, Spiegel, & Campbell, 1998), and thus, increasing overall HRQoL among patients and caregivers.

Limitations of the Current Study

This study has several limitations that should be acknowledged. First, this sample draws from specialty clinics and participants are likely to have long-standing difficulties with constipation and may represent with the most severe of the clinical cases. This may have biased the response pattern to more severe symptoms and may thus have more negative reporting of HRQoL, psychosocial functioning, and functional disability. Additionally, this study does not have a healthy control group, which may be useful in comparing parent perceived HRQoL between typically developing youth and youth with chronic constipation. Furthermore, given the broad range of youth with chronic constipation in the current study, we relied on parent report, which may impact the current results. In addition, the POOPC was developed for caregiver responses only, and there is not, at this time, a child self-report version. It is important to also note that medication use was not included as an indicator in our LVMM analyses. For example, stool softeners, and osmotic, stimulant laxatives and lubricant laxatives may have potentially impacted youth's symptomology, and thus, class membership. Future research is needed to examine the association between medication use, pain, fecal incontinence, and avoidance.

In summary, the current study examined how specific symptom patterns of pain, stool frequency, and incontinence impact parent perceived psychosocial issues, illness related activity limitations, and disease-specific aspects of HRQoL, including disease burden and distress, family conflict, parental worry of social impact, and satisfaction with the treatment team, among youth with chronic constipation. Overall, we found that caregivers of youth in pain class reported greater levels of illness related activity limitations, more psychosocial issues, increased disease burden and worry, and along with the fecal incontinence class, more family conflict, suggesting that youth with chronic constipation associated with pain or fecal incontinence may be at risk for poorer disease specific HRQoL. Furthermore, varying HRQoL across classes suggest that the

POOPC may be more sensitive to differential levels of family conflict, peer relationships, and disease burden and distress relative to measures of functional disability and psychosocial problems. In addition to addressing gastrointestinal symptoms, targeting family conflict, peer relationships, and coping with the burden and distress of constipation may be helpful to improve HRQoL in youth with chronic constipation. Future research is needed to assess how these patterns of pain, stool frequency, and incontinence associated with HRQoL differentially in youth with chronic constipation using youth self-report and how these initial patterns may predict treatment response.

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Appendix A: Tables and Figures

Table 1

Goodness- of Fit Statistics for 1, 2, 3, and 4 Classes: Information Criteria, Entropy, Likelihood Ratio Tests for LVMMs of Youth with Chronic Constipation

Number of Classes	Log-likelihood	AIC	BIC	Entropy	LMR	LMR-<i>p</i>
1	-4096.636	8255.273	8379.774	NA	NA	NA
2	-3987.978	8099.956	8348.958	0.754	216.158	0.8878
3	-3903.044	7992.089	8365.591	0.770	168.960	1.00
4	-3824.447	7896.894	8394.898	0.798	160.210	1.00

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; LMR = Lo-Mendell-Rubin test; LMR *p* = Lo-Mendell-Rubin test *p*-value.

Table 2

Intercepts, Standard Errors, and Comparisons Across HRQoL Measures for Each Latent Class

Measures	<i>Withholding/ Avoiding, Estimate (S.E.)</i>	<i>Pain, Estimate (S.E.)</i>	<i>Fecal Incontinence, Estimate (S.E.)</i>	Class Comparisons
POOPC Burden/Worry	3.62 (0.028)	4.02 (0.047)	3.77 (0.031)	$P > WA^{**}$ & FI^{**} & $FI >$ WA^{**}
POOPC Family Conflict	2.47 (0.034)	2.84 (0.112)	2.96 (0.042)	$P > WA^{**}$ & FI $> WA^{**}$
POOPC Social Worry	2.14 (0.142)	2.46 (0.101)	2.77 (0.083)	$FI > P^*$ & WA^{**} & $P >$ WA^{**}
POOPC Treatment Team	2.10 (0.075)	2.22 (0.058)	2.18 (0.114)	$WA < P^{**}$
FDI	1.53 (0.042)	1.68 (0.058)	1.49 (0.042)	$P > WA^*$ & $WA > FI^{**}$
PSC	1.49 (0.013)	1.58 (0.041)	1.49 (0.006)	$P > WA^{**}$ & $P > FI^{**}$

Note. $*p < .05$, $**p < .01$. WA = *Withholding/Avoiding* class; P = *Pain* class; FI = *Fecal Incontinence* class.

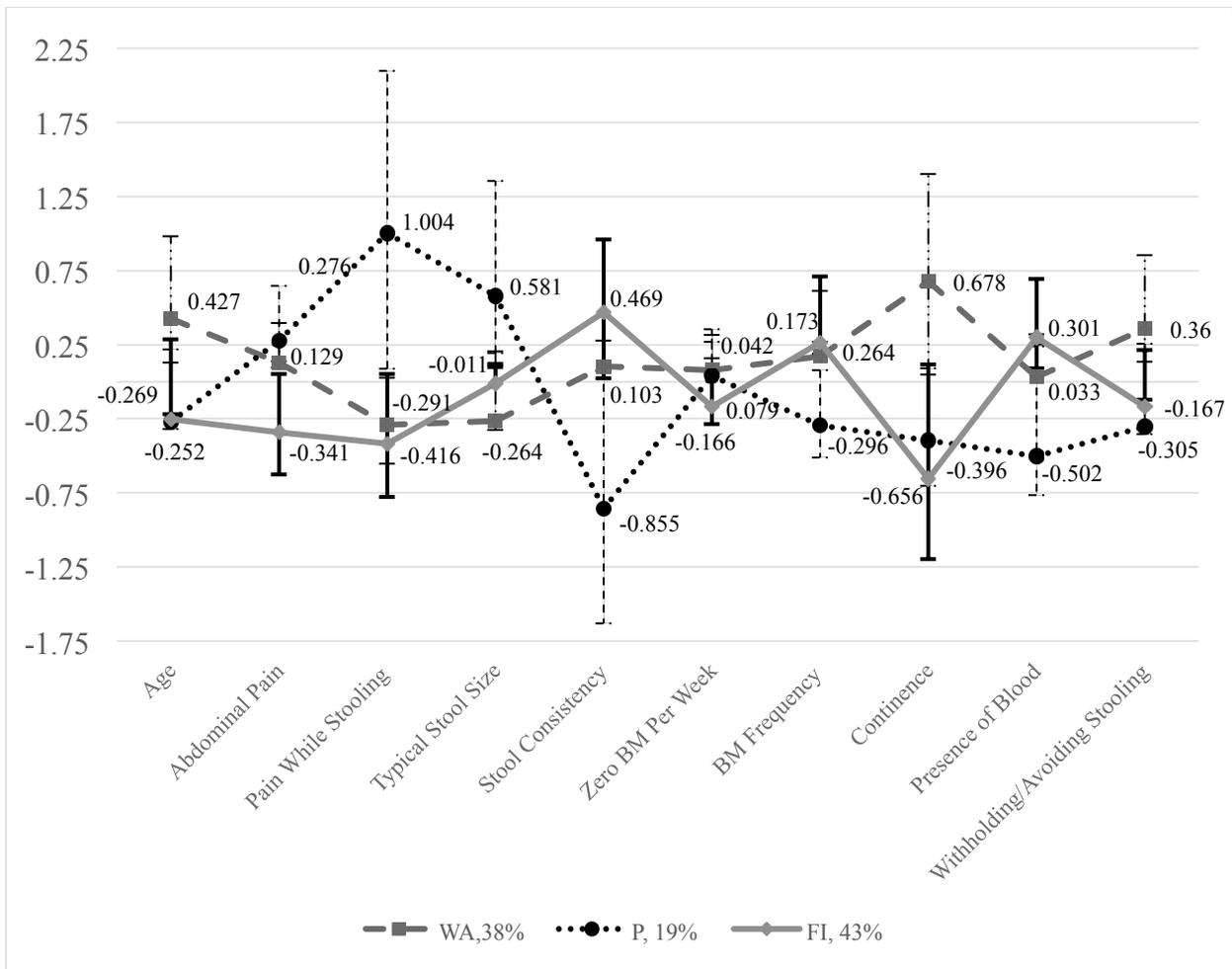


Figure 1. Three-class models of pain, incontinence, and stooling patterns z-scores

Online Supplemental Table

Latent Class Regression Model.

	Estimate	S.E.	Est./S.E.	<i>p</i> -value
<i>Withholding/Avoiding Class</i>				
Child Age ON				
POOPC BW	0.26	0.11	2.43	0.015*
POOPC FC	-0.06	0.17	-0.36	0.716
POOPC MT	-0.20	0.07	-2.80	0.005**
POOPC SO	0.52	0.17	3.13	0.002**
FDI	0.14	0.12	1.18	0.238
PSC	0.18	0.07	2.65	0.008**
Means				
Child Age	0.12	0.02	6.59	<0.001
Intercepts				
POOPC BW	3.62	0.03	128.2	<0.001
POOPC FC	2.47	0.03	72.04	<0.001
POOPC MT	2.10	0.08	27.93	<0.001
POOPC SO	2.14	0.14	15.08	<0.001
FDI	1.53	0.04	36.66	<0.001
PSC	1.48	0.01	117.1	<0.001
Variances				
Child Age	0.10	0.01	17.40	<0.001
Residual Variances				
POOPC BW	0.57	0.05	12.44	<0.001
POOPC FC	0.70	0.04	17.10	<0.001
POOPC MT	0.56	0.05	11.56	<0.001
POOPC SO	1.11	0.08	13.38	<0.001
FDI	0.36	0.04	9.15	<0.001
PSC	0.11	0.01	16.93	<0.001
<i>Pain Class</i>				
Child Age ON				
POOPC BW	0.01	0.13	0.07	0.931
POOPC FC	0.77	0.21	3.60	<0.001
POOPC MT	-0.16	0.21	-0.76	0.448
POOPC SO	1.90	0.21	9.09	<0.001
FDI	0.24	0.26	0.93	0.355
PSC	0.61	0.17	3.53	<0.001
Means				
Child Age	-0.08	0.03	-2.40	0.016
Intercepts				
POOPC BW	4.02	0.05	84.72	<0.001
POOPC FC	2.84	0.11	25.39	<0.001
POOPC MT	2.22	0.06	38.59	<0.001
POOPC SO	2.46	0.10	24.39	<0.001
FDI	1.67	0.06	28.97	<0.001

PSC	1.58	0.04	38.43	<0.001
Variances				
Child Age	0.07	0.01	9.76	<0.001
Residual Variances				
POOPC BW	0.34	0.04	7.86	<0.001
POOPC FC	0.51	0.06	8.55	<0.001
POOPC MT	0.68	0.06	11.92	<0.001
POOPC SO	0.90	0.05	16.92	<0.001
FDI	0.44	0.09	4.82	<0.001
PSC	0.12	0.01	11.85	<0.001

Fecal Incontinence Class

Child Age ON				
POOPC BW	0.11	0.15	0.75	0.452
POOPC FC	0.53	0.30	1.75	0.079
POOPC MT	0.20	0.25	0.78	0.434
POOPC SO	1.36	0.36	3.80	<0.001
FDI	-0.06	0.13	-0.42	0.671
PSC	0.05	0.07	0.66	0.510
Means				
Child Age	-0.07	0.04	-1.73	0.084
Intercepts				
POOPC BW	3.77	0.03	120.3	<0.001
POOPC FC	2.95	0.04	69.56	<0.001
POOPC MT	2.18	0.11	19.12	<0.001
POOPC SO	2.77	0.08	33.25	<0.001
FDI	1.49	0.04	35.40	<0.001
PSC		0.01	248.4	<0.001
Variances				
Child Age	0.06	0.01	7.47	<0.001
Residual Variances				
POOPC BW	0.45	0.04	12.80	<0.001
POOPC FC	0.57	0.04	12.85	<0.001
POOPC MT	0.66	0.08	8.23	<0.001
POOPC SO	1.04	0.10	10.22	<0.001
FDI	0.33	0.04	7.63	<0.001
PSC	0.10	0.003	33.23	<0.001

Note. Child Age was mean centered. POOPC BW = Burden/Worry subscale of the POOPC; POOPC FC = Family Conflict subscale of the POOPC; POOPC MT = Difficulties with the Medical Team subscale of the POOPC; POOPC SO = Worry about Social Impact subscale of the POOPC; FDI = Functional Disability Inventory; PSC-17 = Pediatric Symptoms Checklist. ** $p < 0.01$; * $p < .05$.

Appendix B: Correspondences with *The Journal of Pediatric Psychology*

28-Mar-2016

Dear Miss Klages,

The review of your manuscript entitled, "Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life among Youth with Chronic Constipation" is now complete. Thank you for the opportunity to review your important work and for your kind patience with the review process.

Based on the comments of three expert reviewers and my own careful reading, I am offering you the opportunity to revise and resubmit your paper for further consideration. The key issues that drove my decision are:

1. The statistical aspects of the paper are largely inaccessible to the typical reader of this journal. The paper as written appears in many respects to be directed at statisticians rather than pediatric psychologists. One reviewer has asked for clarification about whether variables that appear to be ordinal in nature were in fact treated as interval-level data in your analyses. I would challenge you to present the statistical approach in a way that can be understood by most readers of this journal. Please be advised that I plan to seek comments from a statistician regarding your revised paper.
2. As raised by Reviewer 3, the fundamental rationale for these specific comparisons is unclear. What clinical, theoretical or methodological gap in the literature does this paper address? What are the clinical implications of the findings?
3. A common theme through all 3 reviews is the absence of key methodological information. It would be very difficult for an interested research to replicate your procedures and this is a fundamental standard for the evaluation of any paper.

If you are able to address these issues and wish to submit a revised manuscript, we would be pleased to consider it. Please submit your revision by April 28, 2016. Your revision would obviously be subject to further review. Please be advised that 180 days from the date of this letter, your manuscript files will be removed from Manuscript Central, so if you intend to resubmit, please do so by the date given in this letter, or communicate your intentions to the journal by emailing us at jpepsy@gmail.com.

To revise your manuscript, log into <https://mc.manuscriptcentral.com/jpepsy> and enter "Author Center", where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision."

Please indicate clearly in your comments to the Editor that it is a resubmitted manuscript. Please also note that along with the manuscript, you should enter your detailed replies to both the reviewers' and associate editor's comments.

Yours sincerely,

Dr Tim Wysocki

Associate Editor, Journal of Pediatric Psychology

Here are the comments of the reviewers:

Reviewer: 1

COMMENTS FOR THE AUTHOR:

Thank you for giving me the opportunity to review the manuscript, “Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life among Youth with Chronic Constipation.” This manuscript describes the use of Latent Variable Mixture Modeling to determine stooling patterns and their effects on quality of life. The manuscript has numerous positive qualities, including the conciseness and quality of writing. However, there are several concerns regarding the manuscript, primarily the clinical significance of findings.

Abstract: It is recommended to slightly expand the Conclusions section so readers understand why youth who experience both high abdominal pain and fecal incontinence are at greater risk for “specific HRQoL problems” since results are different for each pattern. Specifically, why is the FI class included in greater risk for HRQoL problems? It might help to explain the link between parental worry and child’s HRQoL.

Introduction- last paragraph: While a hypothesis is clearly presented, it is unclear if authors are proposing that youth experiencing high pain or high fecal incontinence are considered two distinct groups and if so, how these two groups do not have a high degree of comorbid symptoms.

Methods: Do caregivers rate abdominal pain and pain while stooling on 2 separate items or is this a combined item on the Demographics and Constipation Symptom Questionnaire? I would assume 2 separate items but this needs clarification.

For the measures, please include any statistics of validity or reliability for the POOPC, FDI, or PSC. Statements such as “The authors report evidence of good sensitivity and specificity, minimal concurrent and moderate convergent validities” should have a reference and ideally quantitative data to support such statements.

It is recommended that authors describe how they learned the LVMM approach, especially since one cited article is currently in press.

Can authors describe the theory that was utilized to help select the best fitting model?

What is a manual BCH procedure? Similarly, what does AIC stand for?

I did not see Figure 1?

It would help if authors clearly describe the differences between the 3 groups in terms of symptoms and presentation. It is difficult to visualize the differences between the classes in terms of clinical presentation. For example, what is different about the FI class than the other 2 in terms of symptoms (other than amt of bowel movements per week)? How much less frequent are the stools in the “least frequent stooling class” than the other 2 classes?

Discussion: It doesn't seem that information regarding social functioning was obtained, but it would be interesting to determine if parents worried more about social interactions because the sample actually had more social problems. How can authors conclude that treatment modules could include peer relationships if social functioning among this population is largely unknown?

In general, it is difficult to know how to translate these findings into practice- how would clinicians determine which class a patient is in. More information on assessment or clinical significance of findings would be helpful.

Reviewer: 2

COMMENTS FOR THE AUTHOR:

Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life Among Youth with Chronic Constipation

This manuscript attempts to identify specific, empirically derived patterns of treatment relevant behaviors associated with children who exhibit constipation and soiling. I appreciated the effort to quantify the important variables of pain, frequency of stooling and soiling, toileting avoidance on quality of life measures as this problem affects so many children. The writing style is excellent and has few errors. The general conclusions of the authors seem reasonable and are consistent with the published literature. The authors also acknowledge the limitations of the study in a forthright manner. However, I had a difficult time understanding the statistical methods from my "clinician's" point of view. The following are reactions from closely reading the manuscript.

ABSTRACT: This was clearly and concisely written. No changes suggested.

INTRODUCTION: I agree with the author's use of the Rome III criteria for use in describing GI conditions such as constipation and this is more helpful than the DSM-V. The authors do a good job of reviewing the literature and set up their study logically and in minimal page length.

METHOD: The authors should provide more information about the study sample. I would like to know how many of the subjects were on stool softeners or bowel stimulants. This could explain why subjects ended up in the different categories of FI, LFS and HP and the frequency of important symptoms (i.e., soiling frequency, toileting frequency, abdominal pain, etc.). The inclusion and exclusion criteria were confusing. Explain the difference between non-retentive fecal incontinence (inclusion) and fecal incontinence without constipation (exclusion); and the difference between constipation predominant IBS (inclusion) and IBS – I assume with diarrhea –(exclusion).

On the Demographics and Constipation Symptoms Questionnaire, it would be nice to also list the frequency of soiling.

I would like to see more details of the Parental Opinions of Pediatric Constipation measure. Is it a Likert scale? How do you interpret the data? It is hard to imagine a 24 item measure can produce 4 subscales and a total score without more details. In Table 2, what does a score of 3.62 mean?

I am familiar with the Functional Disability Inventory and the Pediatric Symptom Checklist. These measures are well described.

The only problem I see with measures are that they are all parent report measures.

Analytic Plan: As a clinician, this makes no sense to me. Authors seem to be speaking to the statisticians who will review the manuscript and not the consumers of this manuscript (i.e., clinicians). You'll have to find a way to communicate with the clinician's too. I see that you derived 3 groups and I trust your logic, but I still don't know how you did it. What is "a manual BCH procedure?" Please spell out acronyms.

RESULTS: This section was difficult to follow also. The three groups were a little more recognizable when the authors referred me to Figure 1 and I can see the variability across important subject characteristics. However, when looking at some of the z-scores across the groups it raised questions (again from a clinician's perspective). How does it make sense that the FI group bowel movement per week is essentially the same as the LFS group? How is it that the HP group which experiences the most pain with stooling is least likely to see blood with stooling? Perhaps I should not read too much into Figure 1. There are lots of results presented on the POOPC and I do not know how to interpret the numbers. What is a clinically significant score of the POOPC?

DISCUSSION: The discussion is well written and easy to read. Authors make the statement that the FI group are characterized as having more frequent stooling, and the LFS group is characterized as having infrequent stooling, but the Results and Figure 1 shows no differences (i.e., 1.81 versus 1.8 BMs per week). Need to explain this.

I agree with the conclusions the authors make as I see these with my experience with children with constipation and soiling. It is hard to see how your data fits with these conclusions.

The authors correctly indicate the oversight of not having healthy controls. They explain how this could clarify the results. They also point out that none of the measures used included self-report by the child. These would also help clarify some of the confusing data findings.

REFERENCES: no suggestions.

TABLE 1: This table makes no sense to me as a clinician.

TABLE 2: I like this table as a way of giving me the big picture of the differences between the groups on important variables. But, as previously mentioned, I do not know how to interpret the scores on the POOPC without more details in the manuscript.

FIGURE 1: I like this figure as it shows me the variability among the groups. It would be nice to have some way to represent what differences on the variables are significant and which are not.

Reviewer: 3

COMMENTS FOR THE AUTHOR:

This study attempts to identify distinct symptom patterns in pediatric constipation and fecal incontinence and assess differential associations of health related quality of life. I appreciate the authors attempt to better understand this important population. While some novel findings are presented, I have several concerns about the manuscript in its current state.

Major concerns

-Overall, I do not think the authors present a compelling case as to why these data are important. They have demonstrated statistical significance, but only briefly touch on clinical significance. The clinical implications presented in the Discussion (p. 15) don't seem to directly follow from the main findings, and there is little with regard to future research or theoretical impact. I encourage to the authors to more explicitly articulate the rationale in the Introduction and spend more space regarding implications in the Discussion rather than rehashing the Results.

-There is essentially no description of procedures. How were participants recruited? What settings were they recruited from? The Discussion says speciality clinics, but it is GI clinics? Behavioral Pediatrics clinics? This has strong implications for the generalizability of the data. Where and how were the measures completed?

-What age range was recruited? The description of the Demographics form says 2-18, but the Rome III criteria apply to ages 4 and up. Inclusion criteria are not well described. You also report the demographics before introducing the measure of demographics.

-In several instances, the authors say symptoms patterns "affect" HRQOL. I don't believe these data allow for that conclusion. These patients were not randomly assigned to the symptom profiles, nor is there any evidence of temporal precedence. It's very possible some other variable accounts for the observed relationships and there is no causal relationship here.

Minor concerns

-I am not an expert on LVMM, so I'm not sure of the impact of this, but the authors say abdominal pain, stool size, etc were entered into the model as continuous variables, but the measures describes would seemingly yield ordinal variables. Does this impact the statistical assumptions and thus the results?

-It is unclear what the authors mean by "person centered." This term may have a different connotation under other contexts. Please explain.

-Does it make sense to control for age? Wouldn't an age by symptom interaction seem very possible? High incontinence at age 4 may not cause much psychosocial distress, but certainly it does in adolescence. I may be misinterpreting the statistics here, but I would think assessing different developmental groups separately would yield more useful information. At the very least, this merits discussion.

-There are few typos and some consistent violation of APA style, mostly in the reporting of statistics. These would be easily corrected in the editorial process.

April 28, 2016

Grayson N. Holmbeck, PhD
Professor, Clinical Psychology
Director of Clinical Training
Loyola University Chicago
Department of Psychology
1032 W. Sheridan Rd.
Chicago, IL 60660

Dear Dr. Wysocki and Dr. Holmbeck,

We are pleased that our manuscript entitled “**Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life among Youth with Chronic Constipation**” (JPEPSY-2016-0037) received a review from the *Journal of Pediatric Psychology*. Although the reviewers were positive about the paper, they provided a number of thoughtful comments. These comments have helped us strengthen the paper, and we want to thank them for their time and expertise.

Please see our response to the Reviewers as outlined below. Text that was added to the manuscript is bolded below.

Associate Editor:

1. *The statistical aspects of the paper are largely inaccessible to the typical reader of this journal. The paper as written appears in many respects to be directed at statisticians rather than pediatric psychologists. One reviewer has asked for clarification about whether variables that appear to be ordinal in nature were in fact treated as interval-level data in your analyses. I would challenge you to present the statistical approach in a way that can be understood by most readers of this journal. Please be advised that I plan to seek comments from a statistician regarding your revised paper.*

Thank you for your suggestions. We agree the statistical aspects may be inaccessible to the typical reader of *JPP*; therefore clarification was provided when possible about the variables and the analyses to make it less technical. Unfortunately, in order to accurately describe all the steps in this person-centered approach, some of the more technical language could not be avoided.

2. *As raised by Reviewer 3, the fundamental rationale for these specific comparisons is unclear. What clinical, theoretical or methodological gap in the literature does this paper address? What are the clinical implications of the findings?*

Thank you for bringing this to our attention. The clinical implications section of the manuscript has been expanded to provide more detail regarding the clinical significance of the current study. Specifically, the authors believe that the current study provides several important clinical implications. First, this study demonstrated convergent and discriminant validity (social worry higher in those in the fecal incontinence class, etc.) for the POOPC as a measure of parent perceived HRQoL in youth with chronic constipation (as first published by Silverman et al., 2015). As such, the POOPC may be an invaluable clinical tool for pediatric psychologists to

detect specific domains for treatment among youth with chronic constipation and their families. Specifically, the POOPC may be potentially sensitive to disease-specific processes and may serve as a helpful tool for determining how to tailor existing interventions or determine whether additional treatment modules are needed in efforts to improve HRQoL in youth with chronic constipation. For example, tailored interventions for youth with similar presenting concerns to those in the pain class might be aimed at enhancing how families cope with the distressing and burdensome nature of functional constipation and improving psychosocial functioning and family conflict. Youth experiencing predominately fecal incontinence may benefit increased emphasis on interventions targeting interpersonal relationships (i.e. peers and family). In contrast, youth experiencing withholding/avoidance may need minimal tailoring of existing evidence based treatments given these patterns of results. Overall, the current study provides evidence that current evidence-based treatments for youth with chronic constipation may need to be tailored depending on youths' presenting symptomatology.

3. A common theme through all 3 reviews is the absence of key methodological information. It would be very difficult for an interested research to replicate your procedures and this is a fundamental standard for the evaluation of any paper.

Thank you for bringing this to the attention of the authors. We have provided additional details in the Methods section regarding data collection procedures, inclusion/exclusion criteria, recruitment, and additional information regarding the sample of the current study.

Reviewer One:

1. Abstract: it is recommended to slightly expand the Conclusions section so readers understand why youth who experience both high abdominal pain and fecal incontinence are at greater risk for "specific HRQoL problems" since results are different for each pattern. Specifically, why is the FI class included in greater risk for HRQoL problems? It might help to explain the link between parental worry and child's HRQoL.

Thank you for pointing out this confusion. The conclusion section in the abstract has been expanded to reflect the specific types of HRQoL problems youth with pain or fecal incontinence may face, such as illness related activity limitations, psychosocial issues, disease burden and worry, and family conflict.

2. Introduction: last paragraph, while a hypothesis is clearly presented, it is unclear if authors are proposing that youth experiencing high pain or high fecal incontinence are considered two distinct groups and if so, how these two groups do not have a high degree of comorbid symptoms

Thank you for bringing this confusion to our attention. This sentence in the introduction section has been modified to provide a clearer distinction between the pain and fecal incontinence classes. Error bars have also been added to Figure 1 to demonstrate the presence of comorbid symptoms across the classes.

3. *Methods: do caregivers rate abdominal pain and pain while stooling on 2 separate items or is this a combined item on the Demographics and Constipation Symptom Questionnaire? I would assume 2 separate items but this needs clarification.*

Comma usage was corrected to clarify that these are separate items in the demographics questionnaire: “Caregivers rated relevant clinical information regarding abdominal pain, pain while stooling (0 = Never, 1 = Sometimes, 3 = Often 4 = Always), and fecal incontinence using a 4-point Likert scale (0 = Never, 1 = Small amount, 2= Moderate amount, 3 = Large amount).”

4. *Methods: for the measures, please include any statistics of validity or reliability for the POOPC, FDI, or PSC. Statements such as “The authors report evidence of good sensitivity and specificity, minimal concurrent and moderate convergent validities” should have a reference and ideally quantitative data to support such statements.*

Thank you for your feedback. Cronbach’s alpha for the POOPC, FDI, and PSC and relevant citations have been added to the measures section of the Methods.

5. *It is recommended that authors describe how they learned the LVMM approach, especially since one cited article is currently in press.*

Additional references have been added for those interested in learning more about LVMM as well as relevant citations regarding person-centered statistical approaches. Thank you so much for your feedback regarding the lack citations in this area.

6. *Can authors describe the theory that was utilized to help select the best fitting model?*

Clarity about model selection has been added to the analytic plan section. The best fitting model for describing varying classes was selected based on clinical relevance and goodness-of-fit statistics, now described in more detail in the Analytic Plan section.

7. *What is a manual BCH procedure? Similarly, what does AIC stand for?*

Thank you for your feedback regarding the AIC and BCH procedure. Definitions and relevant detail regarding the statistical approach has been added to the Analytic Plan section.

8. *It would help if authors clearly describe the differences between the 3 groups in terms of symptoms and presentation. It is difficult to visualize the differences between the classes in terms of clinical presentation. For example, what is different about the FI class than the other 2 in terms of symptoms (other than amt of bowel movements per week)? How much less frequent are the stools in the “least frequent stooling class” than the other 2 classes?*

Thank you for providing detailed feedback about the lack of detail regarding how the classes differ in symptomatology. Class names have been modified based on symptom presentation (i.e., pain, fecal incontinence, and withholding/avoiding) and error bars have been added to Figure 1 to show how classes differ (or not differ) in symptom presentations.

9. Discussion: it doesn't seem that information regarding social functioning was obtained, but it would be interesting to determine if parents worried more about social interactions because the sample actually had more social problems. How can authors conclude that treatment modules could include peer relationships if social functioning among this population is largely unknown?

Information regarding caregivers' concerns regarding their child's social functioning has been added to the Discussion section. Specifically, caregivers of youth experiencing predominately fecal incontinence reported greater concern regarding their child's peer relationships. Past research has found that caregivers of youth who experience frequent fecal incontinence worry that their child may become a target for social ridicule and bullying (Kaugars et al., 2010; Clarke et al, 2008). More information regarding peer rejection can also be found in the Introduction section of the current manuscript.

10. In general, it is difficult to know how to translate these findings into practice- how would clinicians determine which class a patient is in. More information on assessment or clinical significance of findings would be helpful.

Thank you so much for your feedback regarding clinical importance of the current findings. The Discussion section has been expanded to include clinical implications, specifically regarding the need for tailored interventions based on youths' presenting symptomatology. In addition, univariate entropy, which reflects which variables contributed most to class formation, has been added to the results section to clarify how classes were formed. Details regarding person-centered statistical approaches have also been added in the Method and Discussion sections to further highlight how these analyses relate to clinical significance.

Reviewer Two

1. The authors should provide more information about the study sample. I would like to know how many of the subjects were on stool softeners or bowel stimulants. This could explain why subjects ended up in the different categories of FI, LFS and HP and the frequency of important symptoms (i.e., soiling frequency, toileting frequency, abdominal pain, etc.).

Thank you for alerting us to this. Medication use was not included as an indicator in our LVMM analyses. A tool softeners, and osmotic, stimulant laxatives and lubricant laxatives may have potentially impacted youth's symptomology, and thus, class membership. As such, this information has been added as a limitation of the current study.

2. The inclusion and exclusion criteria were confusing. Explain the difference between non-retentive fecal incontinence (inclusion) and fecal incontinence without constipation (exclusion); and the difference between constipation predominant IBS (inclusion) and IBS – I assume with diarrhea –(exclusion).

Inclusion and exclusion criteria have been clarified. In order to be in the study, families needed to be fluent in English and their child had to meet ROME III criteria for functional constipation or functional constipation with fecal incontinence. Exclusion criteria included children with a diagnosis of fecal incontinence without constipation, children with developmental delays, children with associated chronic disease, and children with a diagnosis of irritable bowel syndrome (any type). Thank you for pointing out this error regarding exclusion criteria.

3. *On the Demographics and Constipation Symptoms Questionnaire, it would be nice to also list the frequency of soiling.*

Thank you for pointing out this error. Frequency of soiling as part of the demographics and constipation symptoms questionnaire has been added (“Caregivers also reported youth’s condition type according to ROME III criteria (i.e., constipation, constipation with fecal incontinence, or fecal incontinence), typical stool size (i.e., small marble, golf ball, tennis ball, or larger than tennis ball), frequency (free response of the number of bowel movements per week) and stool consistency following the Bristol Stool Chart (Type 1, hard lumps to 7, entirely liquid; Heaton & Lewis, 1997)”.

4. *I would like to see more details of the Parental Opinions of Pediatric Constipation measure. Is it a Likert scale? How do you interpret the data? It is hard to imagine a 24-item measure can produce 4 subscales and a total score without more details.*

Additional details regarding the Parental Opinion of Pediatric Constipation (POOPC), including scale and interpretation information, have been added in the Methods section.

5. *In Table 2, what does a score of 3.62 mean?*

A score of 3.62 is the intercept (or the predicted mean when age is at zero- which in this case it is the sample average when age is mean centered) for the POOPC Burden/Worry subscale for the *withholding/avoiding* class. To provide clarification, Table 2 has been renamed “*Intercepts, Standard Errors, and Comparisons Across HRQoL Measures for Each Latent Class*”.

6. *The only problem I see with measures are that they are all parent report measures.*

Yes, thank you, we agree. This has been added as a limitation in the discussion section. Due to the wide age range, the mean age of the sample ($M_{age} = 7.8$), and that the POOPC is a parent report, the authors determined to solely utilize parent report in the current study.

7. *Analytic Plan: as a clinician, this makes no sense to me. Authors seem to be speaking to the statisticians who will review the manuscript and not the consumers of this manuscript (i.e., clinicians). You’ll have to find a way to communicate with the clinician’s too. I see that you derived 3 groups and I trust your logic, but I still don’t know how you did it. What is “a manual BCH procedure?” Please spell out acronyms*

Thank you for point this out to us. We have edited this section in an attempt to make it more broadly accessible to the readership. Additionally, more information has been provided regarding the BCH procedure in the Analytic Plan section.

8. *Results: This section was difficult to follow also. The three groups were a little more recognizable when the authors referred me to Figure 1 and I can see the variability across important subject characteristics. However, when looking at some of the z-scores across the groups it raised questions (again from a clinician’s perspective). How does it make sense that the FI group bowel movement per week is essentially the same as the LFS group? How is it that the HP group which experiences the most*

pain with stooling is least likely to see blood with stooling? Perhaps I should not read too much into Figure 1. There are lots of results presented on the POOPC and I do not know how to interpret the numbers. What is a clinically significant score of the POOPC?

Thank you for providing detailed feedback about the lack of detail regarding how the classes differ in symptomatology. Class names have been modified to better reflect youths' presenting symptom (i.e., pain, fecal incontinence, and withholding/avoiding) and error bars have been added to Figure 1 to show how classes differ (or not differ) in symptom presentations. LVMM is unique in that analyses allow for fractional membership. This means that youth in the present study may have overlapping symptoms across the classes; however, higher rates of specific symptoms (i.e., pain, fecal incontinence, and withholding/avoiding) largely contributed to class differences. Clinically significant scores on the POOPC were defined as a z-score greater than 1.5.

9. Discussion: the discussion is well written and easy to read. Authors make the statement that the FI group are characterized as having more frequent stooling, and the LFS group is characterized as having infrequent stooling, but the Results and Figure 1 shows no differences (i.e., 1.81 versus 1.8 BMs per week). Need to explain this.

I agree with the conclusions the authors make as I see these with my experience with children with constipation and soiling. It is hard to see how your data fits with these conclusions.

Thank you for this feedback. As mentioned in the previous comment, class names have been modified to better reflect youths' presenting symptoms per class. Error bars have also been added to Figure 1 to better reflect symptomology differences across the classes. Conclusions and clinical implications have been modified to better reflect the results of the current study.

10. The authors correctly indicate the oversight of not having healthy controls. They explain how this could clarify the results. They also point out that none of the measures used included self-report by the child. These would also help clarify some of the confusing data findings.

Thank you, yes, we agree. These points remain as limitations of the current study.

11. TABLE 1: This table makes no sense to me as a clinician.

Thank you for this feedback. Table 1 reflects the goodness-of-fit statistics for 1, 2, 3, and 4 class models. Using these fit statistics (the loglikelihood, AIC, BIC, Entropy, and LMR values, all described in the Analytic Plan section) and clinical relevance, the 3 class model was chosen as the best fitting model. Table 1 has been re-named “*Goodness- of Fit Statistics for 1, 2, 3, and 4 Classes: Information Criteria, Entropy, Likelihood Ratio Tests for LVMMs of Youth with Chronic Constipation*” to provide needed clarification.

12. TABLE 2: I like this table as a way of giving me the big picture of the differences between the groups on important variables. But, as previously mentioned, I do not know how to interpret the scores on the POOPC without more details in the manuscript.

Thank you! As mentioned above, more details have been provided about the POOPC in the Methods section.

13. FIGURE 1: I like this figure as it shows me the variability among the groups. It would be nice to have some way to represent what differences on the variables are significant and which are not.

Thank you so much. Error bars have been added to Figure 1 to reflect differences in symptom presentation across the classes.

Reviewer Three

1. Overall, I do not think the authors present a compelling case as to why these data are important. They have demonstrated statistical significance, but only briefly touch on clinical significance. The clinical implications presented in the Discussion (p. 15) don't seem to directly follow from the main findings, and there is little with regard to future research or theoretical impact. I encourage to the authors to more explicitly articulate the rationale in the Introduction and spend more space regarding implications in the Discussion rather than rehashing the Results. How does this study move the field forward given existing findings? Does it add to the biopsychosocial model they refer to?

Thank you so much for your invaluable feedback regarding the clinical implications of the current study. This section of the manuscript has been expanded to provide more detail regarding the clinical significance of the current study. Specifically, the authors believe that the study provides convergent and discriminant validity (social worry higher in those in the fecal incontinence class, etc.) for the POOPC as a measure of parent perceived HRQoL in youth with chronic constipation. As such, the POOPC may be an invaluable clinical tool for pediatric psychologists to detect specific domains for treatment among youth with chronic constipation and their families (Silverman et al., 2015). Specifically, the POOPC may be potentially sensitive to disease-specific processes and may serve as a helpful tool for determining how to tailor existing interventions or determine whether additional treatment modules are needed in efforts to improve HRQoL in youth with chronic constipation. For example, tailored interventions for youth with similar presenting concerns to those in the pain class might be aimed at enhancing how families cope with the distressing and burdensome nature of functional constipation and improving psychosocial functioning and family conflict. Youth experiencing predominately fecal incontinence may benefit increased emphasis on interventions targeting interpersonal relationships (i.e. peers and family). In contrast, youth experiencing withholding/avoidance may need minimal tailoring of existing evidence based treatments given these patterns of results. These findings and clinical implications relate back to the biopsychobehavioral model of chronic constipation (Cox et al., 1998) in that youth presenting with specific symptoms (i.e., pain, fecal incontinence, withholding/avoiding stooling) may actually from distinct interventions that target different HRQoL domains (i.e., family conflict, peer relationships, psychosocial wellbeing, ect.).

2. What settings were they recruited from? The Discussion says specialty clinics, but it is GI clinics? Behavioral Pediatrics clinics? This has strong implications for the generalizability of the data. Where and how were the measures completed?

Thank you for pointing out this lack of clarity. Data were collected from gastrointestinal clinics at participating medical institutions. Because the sample was drawn from specialty clinics, participants are likely to have long-standing difficulties with constipation and may represent with the most severe of the clinical cases. This may have biased the response pattern to more severe symptoms and may thus have more negative reporting of HRQoL, psychosocial functioning, and functional disability. These implications have been added as a limitation of the current study.

3. What age range was recruited? The description of the Demographics form says 2-18, but the Rome III criteria apply to ages 4 and up. Inclusion criteria are not well described. You also report the demographics before introducing the measure of demographics.

Caregivers of youth 2-18 years were invited to participate in the current study. Thank you for pointing out this error; ROME III criteria for children under 4 years of age has been added to the introduction. Additionally, demographic information has been moved; it is now included in the demographic measure paragraph, following a description of the measure.

4. In several instances, the authors say symptoms patterns "affect" HRQOL. I don't believe these data allow for that conclusion. These patients were not randomly assigned to the symptom profiles, nor is there any evidence of temporal precedence. It's very possible some other variable accounts for the observed relationships and there is no causal relationship here.

Thank you for pointing this out to us. We have changed this language as to not suggest causal relations.

5. I am not an expert on LVMM, so I'm not sure of the impact of this, but the authors say abdominal pain, stool size, etc were entered into the model as continuous variables, but the measures describes would seemingly yield ordinal variables. Does this impact the statistical assumptions and thus the results?

We have edited this section to provide clarity to readers. Ordinal variables were used as indicators in our analyses rather than continuous. Thank you for pointing out this error. Statistical assumptions and results of the current study remain unchanged.

6) It is unclear what the authors mean by "person centered." This term may have a different connotation under other contexts. Please explain.

A more detailed description regarding person centered statistical approaches have been added to the Analytic Plan and Discussion sections. Specifically, Person-centered approaches are useful when complex and reciprocal relations exist between variables of interest (Bergman, von Eye, & Magnusson, 2006; Berlin, Karazsia, & Klages, in press). Person-centered approaches use individuals as the standard unit of the analyses rather than variables (Bauer & Shanahan, 2007; Berlin, Parra, & Williams, 2014; Berlin, Williams, & Parra, 2014), allowing for intricate patterns among the variables to be identified, thus providing useful descriptive information about the complex patterns among variables. Person-centered analyses help identify patterns that are

highly linked to specific problems, such as identifying the link between specific constipation symptomology patterns and HRQoL, psychosocial, and functional disability problems. Thank you so much for your feedback.

7. Does it make sense to control for age? Wouldn't an age by symptom interaction seem very possible? High incontinence at age 4 may not cause much psychosocial distress, but certainly it does in adolescence. I may be misinterpreting the statistics here, but I would think assessing different developmental groups separately would yield more useful information. At the very least, this merits discussion.

Thank you for this feedback. It is for this reason that we included age as an indicator of the latent classes. The withholding/avoiding class was found to be significantly older and the pain class was found to be significantly younger than the sample average. Age was controlled since the classes carried by age and we sought to address this confound (e.g., differences in outcomes could be due to age rather than class membership). By using the BCH procedure, the independent association of age on outcomes can be determined (which also varies by class). These details are provided in the supplemental table, in which we present how age differently predicts outcomes per class. Given the complexity of these analyses and the scope of the present work, we chose to deemphasize these findings, but they are available to those who are interested.

8. There are few typos and some consistent violation of APA style, mostly in the reporting of statistics. These would be easily corrected in the editorial process.

Thank you! The authors have attempted to correct these violations.

14-Jun-2016

Manuscript ID: JPEPSY-2016-0037.R1

Title: Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life among Youth with Chronic Constipation

Dear Miss Klages,

The reviews of your manuscript are now in hand for Journal of Pediatric Psychology, and can be found at the foot of this e-mail. We will be pleased to accept your paper for publication pending some revisions.

As you will see below, all three reviewers felt that your paper is substantially improved and that you had been very responsive to the earlier critiques. At the same time, two reviewers raised additional points for your attention. I would ask you to attend to each of these comments in your revision of this paper and I intend to review your revised paper myself rather than sending it back to the original reviewers.

To revise your manuscript, log into <https://mc.manuscriptcentral.com/jpepsy> and enter "Author Center", where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision." Please return your revised paper via Manuscript Central by July 14, 2016.

Please also note that along with the manuscript, you should enter your detailed replies to the reviewers' and my comments.

If you are unsure of your User ID and Password, please use the "password help" feature located on the login page of the site. The information will be sent to you immediately by email.

We are pleased to be able to publish your work, and look forward to receiving the revised version of your paper.

Yours sincerely,
Dr Tim Wysocki
Editor, Journal of Pediatric Psychology

Here are the comments of the reviewers:

Reviewer: 1

COMMENTS FOR THE AUTHOR:

The authors have made a good effort to respond to the reviewers' concerns and the manuscript is much improved. The more thorough description of methods and expansion of the Discussion. My remaining comments are meant as suggestions to improve the readability of the manuscript for the readership.

Introduction:

- While the Introduction contains pertinent information, it is somewhat lacking in organization. It reads a bit like a list of citations rather than a narrative. For example, the introduction of the biopsychosocial

model on page. 4 seems out of place, as it interrupts a series of paragraphs about different domains of QoL impact. It would fit better nearer the beginning of the Intro.

- For the naive reader, some more space could be given to explicitly stating the rationale of this study. Page 5 line 25 states "Presently, it is unclear if patterns of symptoms associated with constipation and incontinence exist or are differentially associated with parent report of their child's HRQoL and biopsychosocial functioning." I'm sure it will be apparent what is meant by this to many readers. The previous paragraph is full of citations for relationships between symptoms and HRQoL. These are "patterns" to an extent, though perhaps not exactly in the way the authors are using the term. Could the authors elaborate some on the shortcomings of the existing research and how that informs the rationale of this study? e.g., previous research looked at overall symptom severity vs this more nuanced approach. Perhaps even the limitation of those group-based (vs patient centered) statistical approaches. Doing so will help readers understand the usefulness of this study.

Discussion

- thought RE: Pain group and medical team dissatisfaction - Perhaps these patients are less likely to adhere to laxative regimens, thus experience more pain? Do the authors have any recommendations for facilitating family-medical team interactions?

Overall

- I strongly recommend the authors consider use of subheadings throughout the paper in order to improve organizational flow and readability.

Reviewer: 2

COMMENTS FOR THE AUTHOR:

The majority of my concerns raised in my first review were addressed in this revised version of this manuscript. At this point, my main recommendation is for a revision of the last paragraph of the introduction to increase clarity of the study's purpose. In particular, the last sentence of that paragraph of the introduction could use clarification as it states that the purpose is to determine profiles, then discusses 2 profiles of pain and fecal incontinence. The first sentence of that paragraph could also benefit from revision since "patterns of symptoms" is vague.

Reviewer: 3

COMMENTS FOR THE AUTHOR:

I enjoyed reviewing the manuscript.

June 27, 2016

Grayson N. Holmbeck, PhD
Professor, Clinical Psychology
Director of Clinical Training
Loyola University Chicago
Department of Psychology
1032 W. Sheridan Rd.
Chicago, IL 60660

Dear Dr. Wysocki and Dr. Holmbeck,

We are pleased that our manuscript entitled “**Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life among Youth with Chronic Constipation**” (JPEPSY-2016-0037) received a review from the *Journal of Pediatric Psychology*. Although the reviewers were positive about the paper, they provided a number of thoughtful comments. These comments have helped us strengthen the paper, and we want to thank them for their time and expertise.

Please see our response to the Reviewers as outlined below. Text that was added to the manuscript is bolded below.

Associate Editor:

- As you will see below, all three reviewers felt that your paper is substantially improved and that you had been very responsive to the earlier critiques. At the same time, two reviewers raised additional points for your attention. I would ask you to attend to each of these comments in your revision of this paper and I intend to review your revised paper myself rather than sending it back to the original reviewers.*

Thank you so much for your feedback. I have responded to the additional points of the reviewers below.

Reviewer One:

- Introduction: while the Introduction contains pertinent information, it is somewhat lacking in organization. It reads a bit like a list of citations rather than a narrative. For example, the introduction of the biopsychosocial model on page. 4 seems out of place, as it interrupts a series of paragraphs about different domains of QoL impact. It would fit better nearer the beginning of the Intro.*

Thank you for this feedback. The structure of the introduction has been changed; the biopsychosocial model and impact of pain on HRQoL have been moved to improve the organization of the manuscript.

- For the naive reader, some more space could be given to explicitly stating the rationale of this study. Page 5 line 25 states "Presently, it is unclear if patterns of symptoms associated with constipation and incontinence exist or are differentially associated with parent report of their child's HRQoL and*

biopsychosocial functioning." I'm sure it will be apparent what is meant by this to many readers. The previous paragraph is full of citations for relationships between symptoms and HRQoL. These are "patterns" to an extent, though perhaps not exactly in the way the authors are using the term. Could the authors elaborate some on the shortcomings of the existing research and how that informs the rationale of this study? e.g., previous research looked at overall symptom severity vs this more nuanced approach. Perhaps even the limitation of those group-based (vs patient centered) statistical approaches. Doing so will help readers understand the usefulness of this study.

Authors of the current study agree. The last paragraph of the introduction has been modified to provide clarity regarding rationale of the current study. A statement regarding previous research has been included in the beginning of the last paragraph.

3. Discussion: thought RE: Pain group and medical team dissatisfaction - Perhaps these patients are less likely to adhere to laxative regimens, thus experience more pain? Do the authors have any recommendations for facilitating family-medical team interactions?

These two suggestions have been added to the Discussion section of the manuscript. The first suggestion can be found under the heading "Withholding/Avoiding Symptoms and HRQoL" and the second under "Clinical Implications of the Current Study." Thank you for these suggestions.

4. Overall: I strongly recommend the authors consider use of subheadings throughout the paper in order to improve organizational flow and readability.

Subheadings have been added throughout the manuscript to improve the organizational flow and readability.

Reviewer Two

1. The majority of my concerns raised in my first review were addressed in this revised version of this manuscript. At this point, my main recommendation is for a revision of the last paragraph of the introduction to increase clarity of the study's purpose. In particular, the last sentence of that paragraph of the introduction could use clarification as it states that the purpose is to determine profiles, then discusses 2 profiles of pain and fecal incontinence. The first sentence of that paragraph could also benefit from revision since "patterns of symptoms" is vague.

The last paragraph of the introduction has been modified to provide clarity regarding the rationale of the current study. Thank you so much for your suggestions and feedback throughout this process.

28-Jun-2016

Manuscript ID: JPEPSY-2016-0037.R2

Title: Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life among Youth with Chronic Constipation

Dear Miss Klages,

The reviews of your manuscript are now in hand for Journal of Pediatric Psychology, and can be found at the foot of this e-mail. We will be pleased to accept your paper for publication pending two quite minor revisions. Both of these relate to what I say as somewhat awkward wording in a few places:

1. Page 4, line 27: Does "high abdominal pain" mean high levels of abdominal pain or upper abdominal pain? Please rewrite to clarify.
2. Page 5, line 12 "poorer externalizing and internalizing behaviors" could probably better be expressed as "more problematic externalizing and internalizing behaviors".

I ask that you resubmit by July 28, 2016. Along with the revised manuscript, please send a detailed cover letter indicating how and where in the manuscript each of the changes was made. I will not be sending your manuscript out again for review, but will review it myself.

To revise your manuscript, log into <https://mc.manuscriptcentral.com/jpepsy> and enter "Author Center", where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision."

Please also note that along with the manuscript, you should enter your detailed replies to the reviewers' and my comments.

If you are unsure of your User ID and Password, please use the "password help" feature located on the login page of the site. The information will be sent to you immediately by email.

We are pleased to be able to publish your work, and look forward to receiving the revised version of your paper.

Yours sincerely,

Dr Tim Wysocki

Editor, Journal of Pediatric Psychology

June 29, 2016

Grayson N. Holmbeck, PhD
Professor, Clinical Psychology
Director of Clinical Training
Loyola University Chicago
Department of Psychology
1032 W. Sheridan Rd.
Chicago, IL 60660

Dear Dr. Wysocki and Dr. Holmbeck,

We are pleased that our manuscript entitled **“Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life among Youth with Chronic Constipation”** (JPEPSY-2016-0037) received a review from the *Journal of Pediatric Psychology*. Thank you for providing additional suggestions for this manuscript.

Please see our response to the Reviewers as outlined below. Text that was added to the manuscript is bolded below.

Associate Editor:

1. Page 4, line 27: Does "high abdominal pain" mean high levels of abdominal pain or upper abdominal pain? Please rewrite to clarify.

Thank you so much for your feedback. “High” was eliminated from this sentence to provide clarification.

2. Page 5, line 12 "poorer externalizing and internalizing behaviors" could probably better be expressed as "more problematic externalizing and internalizing behaviors".

Thank you for this suggestion. This sentence has been modified per your suggestion above.

30-Jun-2016

Manuscript ID: JPEPSY-2016-0037.R3

Title: Empirically Derived Patterns of Pain, Stooling, and Incontinence and their Relations to Health Related Quality of Life among Youth with Chronic Constipation

Dear Miss Kimberly Klages:

I am pleased to report that your manuscript has been accepted for publication in the Journal of Pediatric Psychology without revision. You should hear from our Production Department in due course regarding page proofs, an offprint order form, and a request to complete the License to Publish form, which will be completed on line.

Also, if you haven't already sent us signed copies of the mandatory author forms please go to: http://www.oxfordjournals.org/our_journals/jpepsy/for_authors/index.html for the Certification of Compliance with APA Ethical Principles and Conflict of Interest Statement, listed under the section: "Information for Authors" on the left hand side as separate bullets. Please also have each author fill out the Author Contribution form, which can be found on the same site. Please sign and return the forms by email (jpepsy@gmail.com<<mailto:jpepsy@gmail.com>>) or by regular mail to the Editorial Office address at the bottom of this email as soon as possible.

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We look forward to seeing your manuscript published in Journal of Pediatric Psychology.

Yours sincerely,

twysocki@nemours.org<<mailto:twysocki@nemours.org>>

Editor, Journal of Pediatric Psychology