Validity and Reliability of the Adolescent Versions of the Migraine Specific Quality of Life Questionnaire and the Headache Disability Inventory

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Abstract

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Evidence from the literature and the current study suggests that disease-specific measures may be more sensitive to variations in the health-related quality of life of adolescents with migraine than general measures. The Migraine Specific Quality of Life Questionnaire, Adolescent form (MSQ-A) and the Headache Disability Inventory, Adolescent form (HDI-A) were designed to specifically assess direct and indirect functional impairment due to migraines, and migraine-related affective distress. There have been only limited attempts to evaluate the psychometric properties of MSQ-A and HDI-A and the current study aimed to examine the factor structure, validity and reliability of these instruments. 97 adolescents (age 11-17) with episodic migraine were recruited to participate in this study. Upon recruitment participants completed MSQ-A and HDI-A and additional validity measures. Participants then recorded their migraine symptoms in an electronic daily headache diary over a four week period. At the end of the four week period, participants were invited to visit the test setting again, submit the electronic diary and complete follow-up MSQ-A and HDI-A.

Confirmatory factor analysis found the proposed three factor model for MSQ-A yielded only marginally good fit to the data. Modification indices suggested that the fit of the three factor model can be improved by the addition of six residual correlations between errors of items within the same subscale. The modified model was good fit to the

data. However, high inter-correlatedness between the three subscales of MSQ-A raised concerns about their discriminant validity. The internal consistency of MSQ-A was adequate at both baseline and follow-up (α = .72-.94), but item-subscale correlations suggested that multiple MSQ-A items relate equally to two or more of its subscales. Similarly, while MSQ-A demonstrated significant relationships in the expected directions with criterion measures in this study, correlations between its subscales with each criterion measures were of similar magnitude, raising questions about the utility of the MSQ-A subscales as separate constructs.

Exploratory maximum likelihood factor analysis of HDI-A did not provide support for any meaningful factor structure of the instrument. Because no meaningful factors were identified, only the reliability and validity of HDI-A total score were explored. The internal consistency of HDI-A was adequate at both baseline and follow-up (α = .89-.92). While significant relationships were found between HDI-A and all validity measures in this study, examination of these relationships provided no evidence that HDI-A is sensitive to migraine-related impairment. Moreover, since as a single factor measure HDI-A was not a good fit to the data, the use of its total score may be problematic.

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Introduction

Epidemiology and Impact of Episodic Migraine

Migraine in adolescence is characterized by episodes of moderate to severe head pain, lasting from one hour to three days, as well as a variety of migraine associated symptoms including gastrointestinal disturbances (i.e. nausea), heightened sensitivity to light (photophobia) and noise (phonophobia) (Headache Classification Subcommittee of the International Headache Society, 2004); see Table 1 for full diagnostic criteria for migraine). Migraine is classified as either episodic (<15 days/month) or chronic (>15 days/month) based on the number of total monthly migraine days. Although chronic migraine is associated with greater individual and socioeconomic burden (Katsarava et al., 2012), in adolescents episodic migraine is considerably more common, affecting up to 23% the population aged 12-18 worldwide (Arruda et al., 2010; Bigal et al., 2007; Fendrich et al., 2007; Lewis, 2009; Linet et al., 1987; Lu et al., 2000; Ozge et al., 2013). Episodic migraine in adolescence has also been found to contribute to significant disruption in daily life, including reduced productivity and missed days of work, school, housework, family and leisure activities. (Andrasik et al., 1988; Kernick & Campbell, 2009; Stovner, 2007; Tkachuk et al., 2003; Powers et al., 2006). Given the high prevalence of episodic migraine in adolescents, and its potential to disrupt multiple areas of functioning, calls have been made to provide assessment tools that would aid the measurement of migraine-related impairment (Kernick & Campbell, 2009). Unfortunately, although there are many assessment options currently available for adults with migraine, relatively few are available for use with adolescents. This lack of assessment options is reflected in clinical settings, where migraine-related impairment is

rarely assessed beyond surveying the frequency, severity and duration of episodes (Kernick & Campbell, 2009).

Quality of Life Assessment in Migraine

In the literature, one construct commonly used to estimate the overall impairment associated with a health condition such as migraine is Health Related Quality of Life (Guyatt, 1989; Hartmaier et al., 2001; Holroyd, 2002). Health Related Quality of Life (HRQL) in migraine patients can be assessed by general or disease-specific measures, and usually a combination of both is recommended (Holroyd, 2002). General questionnaires allow for a direct comparison of disease burden across different conditions. However, general measures also tend to be most sensitive to impairments in quality of life that are stable across time, and less sensitive to the periodic impairments associated with episodic conditions such as migraine where a person is most impaired during and around periods of symptom activity, but might report good overall functioning most of the time. Disease-specific questionnaires can focus on the types of impairment that are associated with a particular disease. Such instruments may detect clinically important changes in the quality of life of patients with episodic conditions including migraine, and may provide information about specific domains of disease impact that can be targeted by domain-specific interventions (Guyatt, 1989; McDowell, 2006). Accordingly, it has been suggested that proper assessment of the impact of health conditions such as migraine should include at least one disease-specific HRQL instrument (Eiser et al. 2001; Holroyd, 2002).

Domains of Migraine-Related Impact on Quality of Life

When assessing the usefulness of a disease-specific quality of life measures, it is important to note whether a measure was designed to include items that assess different domains of impact on quality of life. The majority of migraine research has been done with adults and a review of these studies suggests there are three important domains of migraine-related impact on HRQL that would need to be assessed by a migraine-specific quality of life measure. These include:

(1) direct functional impairment due to migraines - the prevention of participation and decreased participation in daily activities such as work (Brandes, 2009; Breslau & Davis, 1993; Dowson & Jagger, 1999; Davies et al., 1999; Kessler et al., 2010; Radtke & Neuhauser, 2008; Stewart, 2010) family and social functioning (Dahlöf & Solomon, 1998; Lipton, Scher & Stewart, 2003), and self-care (Smith, 1998; Kelman & Rains, 2005) due to the direct effects of a migraine episode;

(2) indirect functional impairment due to migraines – the avoidance and reduced participation in daily activities because it is anticipated that participation might trigger a migraine or worsen an on-going migraine episode (Brandes, 2009; Cady, Schreiber & Farmer, 2004; Dahlof & Dimenas, 1995; Freitag, 2007; Stronks et al., 2004).

(3) migraine-related affective distress - the negative emotions associated with living with migraine (Brandes, 2009; Buse, Rupnow & Lipton, 2009; Dueland et al., 2004; Passchier et al., 1998).

Although few investigators have examined the specific domains of migraine-related impact on adolescents quality of life, evidence from available studies suggests the same three domains identified for adults (direct and indirect functional impairment and

migraine related affective distress) are relevant to adolescents. Because of the pain and associated symptoms during migraine attack adolescents experience direct impairment in their ability to function at school resulting in school absence, decreased extracurricular activities, and poorer academic achievement (Langeveld, Koot & Passchier, 1997). In fact, researchers have estimated that up to one million school days are missed each year in the United States due to the direct effects of migraine (Carlsson, Larsson & Mark, 1995; Linet et al., 1989; Nealis & Miller, 1984).

Data on indirect functional impairment due to migraines is limited, but some evidence suggests that adolescents may restrict activities and experience migraine-related impairment in quality of life during periods of no headaches and no associated symptoms of migraine (Bruni et al., 2004; Cavallini et al 1995; Heng & Wirrell, 2006; Kabbouche & Gilman, 2008). Avoidance or reduced participation in activities such as sports, play and social activities that are anticipated to trigger or worsen migraines is commonly observed and even advised by health professionals. Thus, it is likely that impact on school, social and recreational activities is not limited to the direct effects of migraine, but also includes the indirect effects of migraine, where efforts are made to prevent and avoid future episodes.

Finally, adolescents may worry about whether a migraine will begin or worsen, worry about interference with social and academic life, may experience a loss of control of their daily routines because of their migraines, and feel fed up, frustrated and angry in response to living with migraines (Cavallini et al 1995). The actual extent of the migraine-related affective distress experienced by adolescents remains unclear, possibly due to lack of migraine-specific instruments to assess the impact of migraine on

emotional functioning. Recently authors of two large literature review articles have called for additional efforts to improve the assessment of migraine-related affective distress experienced by adolescents (Antonaci et al. 2011; Bruijn et al., 2009). Previous studies of adolescents with migraines have used general measures to assess for psychological symptoms associated with anxiety, mood or behavioral disorders rather than specifically assess affective distress related to migraine. Results these studies suggest that adolescents with migraine do not differ from healthy controls in terms of rates of psychiatric disorders, and do not experience externalizing behavior problems (i.e. difficulties with attention, aggression and conduct) at a greater rate than healthy controls. However, participants in these studies did consistently report subclinical elevations in somatic complaints and internalizing behavior, including withdrawal, fearfulness, and periods of low mood (Antonaci et al., 2011; Anttila et al., 2004; Bruijn et al., 2009; Just et al., 2003; Powers, Gilman & Hershey, 2006). These results have prompted Bruijn and colleagues (2009) to suggest that sub-clinical elevations in internalizing psychological symptoms reported by adolescents with migraine might reflect affective distress due to living with migraines rather than symptoms of psychiatric disorders. Overall, from the studies discussed above, it follows additional research efforts are necessary to explore quality of adolescents with migraine while taking into consideration the direct and indirect functional impairment due to migraines and migraine-related affective distress.

Disease-Specific Quality of Life Assessment Options for Adolescents with Migraine

A review of the literature indicates that there are currently only two headache- or migraine-specific quality of life instruments available for adolescents, including the Quality of Life Headache in Youth (QLH-Y; Langeveld, Koot & Passchier, 1997;

Langeveld, Koot & Loonen, 1996) and the Pediatric Migraine Disability Assessment Score (PedMIDAS; Hershey et al., 2001). Neither instrument was designed to measure all three dimensions of migraine-related impairment discussed earlier, including the direct and indirect functional impairment due to migraines and migraine-related affective distress. Thus, both measures are less than ideal in the assessment of adolescents with migraine.

The three domains of migraine-related quality of life have been recognized by researchers attempting to improve quality of life assessment for adults. Two widely used HRQL instruments for adults have been designed to include items assessing direct and indirect functional impairment due to migraines and migraine-related affective distress. These are the Migraine Specific Quality of Life Questionnaire (MSQ; Jhingran et al., 1998A; Martin et al., 2000) and the Headache Disability Inventory (HDI; Jacobson et al., 1994).

Migraine Specific Quality of Life Questionnaire.

The Migraine Specific Quality of Life questionnaire (MSQ) contains 14 items that are answered in regards to how frequently within the 4 week period prior to testing a certain migraine-related problem occurs. The MSQ was developed to assess three postulated domains of migraine-related quality of life, termed Role Preventive, Role Restrictive and Emotional Functioning by the authors (Jhingran et al., 1998A; Jhingran et al., 1998B). The Role Restrictive subscale measures indirect functional impairment due to migraines, including the degree to which performance of normal activities is limited by an ongoing migraine or the perception that a migraine might occur (i.e. “5. In the past 4 weeks, how often did migraines *limit* your ability to concentrate on work or daily

activities?"). The Role Preventive subscale measures the direct functional impairment due to migraines, including the degree to which performance of normal activities is prevented or completely interrupted by migraine (i.e. "10. In the past 4 weeks, how often did you have to *stop* work or daily activities to deal with migraine symptoms?"). The Emotional Function subscale measures migraine-related affective distress, including the feeling of frustration and helplessness associated with migraines or the sense that one is a burden on others because of migraines (i.e. "13. In the past 4 weeks, how often have you *felt* like you were a burden on others because of your migraines?"). The instrument was later updated by Martin et al. (2000) and is currently in its 2.1 version (Appendix A).

The three-factor structure of the MSQ has been confirmed by several different studies with adults (Cole, Lin, & Rupnow, 2007; Jhingran et al., 1998B; Loftland et al., 1999; Martin et al., 2000). However, high correlations among factors identified by these studies (r = .81-.89; Cole, Lin, & Rupnow, 2007; Jhingran et al., 1998A) have raised possibility that all 3 types of impairment tend to occur together. The internal consistency and test-retest reliability of MSQ has been deemed acceptable (Cronbach's α = .79-.96; Bagley et al., 2011; Cole, Lin, & Rupnow, 2007; Jhingran et al., 1998A; Martin et al., 2000). The construct validity of the instrument has been examined by comparing the three subscales to previously validated measures of headache-specific impairment (Headache Impact Test-6, r=.60-.92; Bagley et al., 2011, Cole, Lin & Rupnow, 2007; Headache Disability Inventory, r=.69-.92; Cole, Lin & Rupnow, 2007; Migraine Disability Assessment Score, r=.38-.57; Bagley et al., 2011). Smaller relationships have been found between the three subscales of MSQ and general quality of life scales (Short Form-36; r=.19-.38; Cole, Lin & Rupnow, 2007; Martin et al., 2000), suggesting that

general and migraine-specific quality of life are related but distinct constructs. Although scores on MSQ have been found to be consistently correlated with diary recordings of migraine frequency, severity and severity of associated symptoms, the magnitude of these correlations has been found to be small (r=.15-.31; Bagley et al., 2011; Martin et al., 2000). These findings are consistent with authors' intent that MSQ assesses migraine impact as a multi-dimensional construct that is influenced by, but not limited to the effects of migraine frequency and severity (Jhingran et al., 1998A).

Headache Disability Inventory.

The Headache Disability Inventory (HDI, Jacobson et al., 1994) was designed to assess direct (i.e. "I am unable to think clearly because of my headaches"), and indirect (i.e. "I avoid travelling because of my headaches") functional impairment due to headaches and headache-related affective distress in adults (i.e. "I feel irritable because of my headaches"). It contains 25 items where the respondent is asked to rate the frequency of each behavior or feeling on a three-point scale of "yes", "sometimes", or "no" (Appendix A). While the HDI specifies an Emotional Distress subscale, items written to assess direct and indirect functional impairment due to headaches are grouped on a single Functional Impairment subscale.

The authors of HDI provided only a hypothesis about its factor structure and did not perform factor analysis to confirm it (Jacobson et al., 1994; 1995) Tests of the proposed factor structure of the HDI have so far not been supportive of its proposed subscales as separate factors and further investigation of the internal structure of the instrument has been recommended (Holroyd et al., 1999). Apart from the potential problems with the internal structure of HDI, the total score has been found to have good

clinical utility and psychometric properties in studies with adults Jacobson et al., 1994; Jacobson et al., 1995; Mannix et al., 1999). Internal consistency of the total score has been found to be excellent (Cronbach's $\alpha = 0.94$; Jacobson et al., 1994). The test-retest reliability of the HDI also appears strong when measured for short-term (one week, $r = 0.93 - 0.95$; Jacobson et al., 1995) and longer-term testing periods (two months; $r = 0.76 - 0.83$, Jacobson et al., 1994). Scores on the HDI have also shown agreement with the spouse version of the HDI ($r = 0.78$ for total scale, $r = 0.78$ for functional subscale, and $r = 0.71$ for emotional subscale Jacobson et al., 1995). The HDI has demonstrated sensitivity to treatment with guided imagery (Mannix et al., 1999), headache medication, and stress management therapy (Holroyd et al., 2001).

Conclusions

Both MSQ and HDI are limited in their usefulness with adolescents. The two instruments were designed to measure the degree of impact on an adult's daily life activities. An adolescent's day to day life differs considerably from that of an adult (Rosenbaum, Cadman & Kirpalani, 1990; Frisén, 2007). School-related functional impairment is a significant component of adolescent's quality of life. Socialization, including both friends and family based activities is another important component of adolescent quality of life. Age-specific assessment of quality of life in migraine is also recommended because there are important differences between migraines in adolescence and adulthood, including duration and localization of pain, and incidence of migraine-associated symptoms (Linder & Winner 2001; Olesen, 2004; Hershey et al., 2005; Wober-Bingol et al., 1996).

When considering options for age-specific assessment of quality of life, creating options for continuity of assessment over time is important. Episodic migraine frequently worsens in severity during adolescence, or transforms into chronic migraine, continuing to cause disability in adulthood (Mack, 2006; Ozge et al., 2013; Stewart et al.1991; Victor et al., 2010). In longitudinal clinical and research studies, as well as in the context of medical care it helps to be able to compare assessment reports across time and point out trends and transitions (Charles et al. 2009). Developing child, adolescent and adult versions of the same instrument can fulfill this task. Therefore, age-specific adaptation and the further investigation of the construct validity of existing good quality of life instruments is the next logical step in the research, rather than development of new uqlity of life assessment instruments (Frisen, 2007).

Aims

Following the recommendations listed above, adolescent versions of MSQ and HDI have been developed, but are yet to be evaluated psychometrically. The present study aimed to examine the psychometric properties of the Migraine Specific Quality of Life - Adolescent form (MSQ-A) and the Headache Disability Inventory - Adolescent form (HDI-A).

Factor Analysis.

The first goal of the present study was to investigate the internal structure of the adolescent versions of MSQ and HDI. Based on studies with adults, where the factor structure of MSQ has been confirmed, it is hypothesized that the adolescent version of the instrument will have the same factor structure as the adult version, including Role Restrictive, Role Preventive and Emotional Functioning. Because no evidence exists in

the adult literature supporting the factor structure proposed for HDI by its authors, no hypothesis can be formed about the factor structure of the adolescent version of HDI and instead, exploratory factor analysis was used to investigate the internal structure of that instrument.

Reliability Analysis.

The second goal of the present study was to investigate the reliability of the adolescent versions of MSQ and HDI, including internal consistency of total scores and subscales, and item analysis.

Construct Validity Analysis.

The third goal of the study was to investigate the construct validity of the adolescent versions of MSQ and HDI. In the literature construct validity of a new measure is examined by comparing it to previously validated instruments of the same concept or construct. However, no previously validated instruments that assess direct and indirect functional impairment due to migraines and migraine-related affective distress are available for adolescents. Therefore, in the present study, construct validity of the two experimental measures was examined by exploring their relationships with other theoretically relevant constructs. Several hypotheses were formed about relationships between MSQ-A and HDI-A with criterion measures based on previous research. Because of the large number of correlations explored in this study, statistical significance may be an insufficient measure of their clinical relevance. Instead, the effect size of the correlation coefficients obtained was used as a measure of their clinical relevance. Cohen's (1988) rule of thumb about defining small (r=.1), moderate (r=.3) and large

(r=.5) effect size of Pearson's Correlation Coefficient (r) were used in forming hypotheses about correlations between experimental and criterion measures in this study.

Hypothesis I.

It was hypothesized that higher scores on MSQ-A and HDI-A (indicating lower quality of life) would be correlated with greater number of missed/interrupted activities and impaired performance due to the effects of migraines. It was hypothesized that the Role Preventive and Role Restrictive subscales on MSQ-A, which were written to assess direct and indirect functional impairment due to migraines would have correlations of moderate or higher magnitude (r > .3; Cohen, 1988) with previously validated measures of missed/interrupted activities and impaired performance due to the effects of migraines. It was hypothesized that if a Functional impairment subscale is identified for HDI-A by factor analysis, it would also have correlations moderate or higher magnitude (r > .3; Cohen, 1988) with previously validated measures of missed/interrupted activities and impaired performance due to the effects of migraines.

Hypothesis 2.

Greater impairment in quality of life, as measured by the adolescent versions of MSQ and HDI was expected to be related to increased migraine activity, including greater frequency and severity of migraines and greater severity of associated symptoms of migraine. However, MSQ and HDI were designed to assess the impact of migraines on quality of life of adolescents beyond the impact of these migraine characteristics. Consistent with this intent, in the adult literature, correlations between quality of life as measured by MSQ and migraine characteristics have been found to be small (Bagley et al., 2011; Martin et al., 2000). Based on these findings, small positive correlations (r < .3;

Cohen, 1988) were expected for the adolescent versions of MSQ and HDI with migraine frequency and severity reported by participants in this study.

Hypothesis 3.

It was hypothesized that for adolescents with migraine, impairment in quality of life due to migraines is related, but not equivalent to impairment in their general quality of life. Therefore the adolescent versions of MSQ and HDI were expected to be correlated with previously validated measures of general quality of life, but the magnitude of these correlations was expected to be small (r<.3; Cohen, 1988).

Hypothesis 4.

In the literature, it has been hypothesized that the sub-clinical elevations in internalizing symptoms reported by adolescents with migraine in other studies reflect are related to affective distress due to migraines rather than symptoms of psychiatric disorders (Bruijn et al., 2009). MSQ and HDI were written to assess affective distress due to headaches (Jacobson et al., 1994; Jhingran et al., 1998A; Martin et al., 2000) and it was hypothesized that correlations or moderate or larger magnitude (r > .3; Cohen, 1988) would be found for MSQ-A and HDI-A with previously validated measures of internalizing symptoms.

Hypothesis 5.

No evidence from the literature suggests that migraine is associated with externalizing symptoms in adolescents. Therefore, it was hypothesized that elevations in externalizing symptoms reported by participants in this sample would not be related to impairment migraine-related quality of life as measured by the adolescent versions of MSQ and HDI. It was also hypothesized that since previous research supports increased

internalizing symptoms reported by adolescents with migraine, the two experimental measures would have correlations of larger magnitude with measures of internalizing symptoms than with measures of externalizing symptoms.

Methods

Experimental Measures

Migraine-Specific Quality of Life – Adolescent Form.

Using the Migraine Specific Quality of Life questionnaire for adults, version 2.1 as a template, the instrument was adapted for use of adolescents with migraine (Cottrell, Drew & Holroyd, 2006). The items on the MSQ 2.1 were modified by psychologists and a pediatric nurse in an age appropriate language (i.e. "interfered with your leisure time activities such as reading or exercising" became "interfered with fun activities (like hobbies, hanging out with friends, etc.)?") and the instrument itself was renamed Migraine Specific Quality of Life questionnaire -Adolescent form (MSQ-A) in order to reflect the changes in content. The quality of the instrument was then assessed by three focus groups with 25 adolescents who found MSQ-A to be easy to understand, and that all items were relevant and addressed important domains of migraine impact (RTI Health Solutions, 2007). Participants agreed with the 3 domains of migraine-related quality of life measured by the MSQ-A (role-restrictive, role-preventive and emotional function) and no participant indicated that an area of impact was missing from the instrument. Additional information on the focus groups study and other studies that have used MSQ-A is available in Appendix A. Based on the feedback from the focus groups ran by RTI Health Solutions (2007), answer options for each question on MSQ-A were decreased from 6 to 5. The answer option "a good bit of time" was dropped as it was judged by adolescents in focus groups to be too similar to the adjacent response choices to be meaningful. Items 7 and 12 were also re-written based on feedback from the focus groups (RTI Health Solutions, 2007). MSQ-A has been used in several small studies with

adolescents, and results from these studies suggest that the instrument may have good psychometric properties (Cottrell et al. 2006; 2007; 2008; McDonald et al., 2011; Tkachuk et al., 2003; see Appendix A for more information about these studies). Although the factor structure of MSQ-A has not been previously investigated, based on data from studies with the adult version of the instrument (Cole, Lin, & Rupnow, 2007; Jhingran et al., 1998B; Loftland et al., 1999; Martin et al., 2000) and preliminary exploration of the psychometric properties of the adolescent version (Cottrell et al. 2006; 2007; 2008; McDonald et al., 2011; RTI Health Solutions, 2007; Tkachuk et al., 2003) it can be hypothesized that in the present study, MSQ-A would have the same three-factor structure as its adult version.

In its final form, MSQ-A consists of fourteen items, including seven items that are hypothesized to compose the Role Restrictive dimension (Items 1-7), four items for the Role Preventive dimension (Items 8-11), and three items for the Emotional Functioning dimension (Items 12-14). Items are answered based on how frequently given migraine-related behavior occurs on a five-point scale of "None of the time", "A little bit of the time", "Some of the time", "A good bit of the time", "Most of the time", and "All of the time". Consistent with scoring the adult version of MSQ-A, subscale scores were computed by summing up the items for each subscale and transforming the score to a 0 to 100 scale. A total quality of life score was computed from the sum of all items that was then transformed to a 0 to 100 scale. Higher total and subscale scores indicate greater migraine-related impairment. The transformation process was recommended by MSQ's authors (Martin et al., 2000) to allow each dimension score to reflect the percentage of the total possible score achieved (since 100 equals the highest score).

Headache Disability Inventory – Adolescent Form.

The Headache Disability Inventory Adolescent Form (HDI-A) was adapted from the adult version of the Headache Disability Inventory (Jacobson et al., 1994; 1995) for the present study. The HDI-A contains 25 items where the respondent is asked to rate the frequency of given migraine-related behavior or feeling on a three-point scale of "yes", "sometimes", or "no". For the adult version of the HDI, items are used to compute two subscales – Functional (the sum of items 2, 4, 7, 13, 15, 16, 17, 18, 19, 21, 24 and 25, transformed to a 0 to 100 scale) and Emotional (the sum of items 1, 3, 5, 6, 8, 9, 10, 11, 12, 14, 20, 22 and 23, transformed to a 0 to 100 scale). A total quality of life score is also computed from the sum of all 25 items (possible range of 0 to 100). Higher subscale and total scores on the HDI-A indicate greater headache-related impairment. However, because of lack of previous studies supporting the proposed factor structure of HDI, and the fact that the adolescent version of the instrument has not been previously used, no hypothesis can be made about its factor structure.

Criterion Measures

Pediatric Migraine Disability Assessment Score.

The Pediatric Migraine Disability Assessment Score (PedMIDAS, Hershey et al., 2001) was used to assess missed and/or interrupted activities and impaired performance due to migraines. It consists of 6 items that aim to assess the degree to which migraines are affecting day-to-day activity as indicated by days missed or diminished functional status due to headaches. Higher score on PedMIDAS indicates greater migraine-related impairment. No subscales are obtained for the PedMIDAS.

The Pediatric Quality of Life Inventory.

The Pediatric Quality of Life Inventory (PedsQL; Varni, Seid & Kurtin, 2001) was used to assess general health-related quality of life. The PedsQL contains 23 items grouped into two subscales, including Physical (8 items) and Psychosocial (15 items).

Youth Self Report.

The Youth Self Report (YSR) was used to assess externalizing and internalizing symptoms (Achenbach, 1991; 2001). The YSR provides self-ratings of 20 competence items that measure the teen's participation in hobbies, games, sports, jobs, chores, friendship, and activities, and 112 items that are used to compute two subscales called Externalizing (assessing behavioral problems, inattention, aggression, etc) and Internalizing (assessing depression, anxiety and somatic complaints). Higher scores on the Internalizing and Externalizing scales indicate higher number of symptoms. For Externalizing Problems, and Internalizing Problems, T scores less than 60 are considered in the normal range, 60-63 represent borderline scores, and scores greater than 63 are in the clinical range (Achenbach, 1991).

Electronic Daily Diary.

Migraine activity over a 4-week period was assessed through an electronic daily diary (PalmOS; Holroyd & Chen, 2000). The PalmOS is a handheld computer capable of storing the daily entries of the participants and uploading them to centralized database. Entries include start and end time of headache, headache type, severity of headaches and of associated symptoms of migraine, and number of hours where adolescents felt disabled by their migraines. Migraine frequency or number of migraines per 30 days (with the requirement that distinct episodes be separated by 24 hour pain free period), migraine severity (average severity of migraines; range 0-3) and associated symptom severity (the

sum of the three average severity ratings provided for nausea, phonophobia and photophobia provided for each migraine; range 0-9) were computed using data from PalmOS. The PalmOS also assesses headache-related impairment by surveying number of hours teens felt "totally disabled" (unable to perform any school, work or social/recreational activities) and "partially disabled" (at least 50% impaired functioning in above activities). From this data, a total migraine-disability hours score (the sum of hours disabled and .5 x hours impaired) was computed.

Procedure

Data from a larger project was used for the purposes of this study. The primary objective of this project was to assess the scaling properties, reliability and validity of five migraine specific measures for adolescents as well as two corresponding measure for their caregivers. The study also included previously validated measures of migraine characteristics, missed activities and impaired performance due to migraines, general quality of life, psychological symptoms, pain catastrophizing, perceived social support from family and friends, and coping. There have been no previous publications or publications currently in preparation using data from this project. Data from measures not used in the current study was not analyzed for this study's purposes. All questions and hypotheses that are discussed in the current study were obtained from the literature.

IRB approval for this study was obtained from both the Nationwide Columbus Children's Hospital and Ohio University in 2006 and renewed in 2009. Potential participants were identified by treating physicians at the Nationwide Columbus Children's Hospital outpatient headache clinics in Columbus, OH and referred to an onsite member of the study team. Inclusion was based on: 1) pediatric neurologist

diagnosis of episodic migraine with or without aura based on the second edition of The International Headache Classification (Headache Classification Subcommittee of the International Headache Society, 2004); 2) average self-reported migraine frequency of at least 1 migraine per month for each of the last 3 months; 3) ability and willingness of both parent/caregiver and adolescent to give informed consent/assent; 4) English as primary language to ensure subjects' ability to read and comprehend the questionnaires. Because this study aimed to explore Exclusion criteria included: 1) diagnosis of chronic migraine (>15 migraine days per month) 2) diagnosis of medication overuse headache; 3) diagnosis of a pain disorder other than migraine as a primary diagnosis; 4) diagnosis of a medical or psychiatric conditions that in the opinion of the study staff might render the subject unable to participate in the study.

All participants were informed of the aim and purpose of the study before being invited to participate. Written informed consent from the teen and informed assent from the teen's parent or guardian was obtained (see Appendix B). Participants were then administered the first set of questionnaires, including Demographic and Health Questionnaire that inquired about the teen's age and gender; baseline MSQ-A and HDI-A; Pediatric Migraine Disability Assessment Score, Pediatric Quality of Life Scale, and Youth Self Report). Upon leaving the test setting, each participant was provided an electronic daily diary (Palm OS) to record headaches for the next four weeks. After four weeks participants were invited to visit the test setting again, submit the electronic diary and complete follow-up questionnaires (follow-up MSQ-A and HDI-A). For their participation, each adolescent received $20 per assessment visit (total of two visits) and $10 after completing the electronic diary.

Participants

Data from 97 adolescents, age 11-17, was available for the purposes of this study. All adolescents who agreed to participate (N=97) returned at least several questionnaires. However, some adolescents did not complete all study measures, and the number of participants available for each analysis varied across measures. Thus, results from correlational analyses in this study are reported along with total number of participants available for each analysis. Missing values on individual items were replaced with the average score for the overall sample on that particular item.

Results

Data Screening

All variables were examined using SPSS 16 for accuracy of data entry, missing values, outliers, and fit between their distributions and the assumptions of multivariate analysis. Patterns of implausible reporting were checked with a visual scan and none were detected (see Appendix C for additional information about univariate and multivariate outliers screening).

There were more female (73) than male (24) participants in this sample. Such gender distribution is representative of the general population where adolescent girls experience migraine at a greater rate than adolescent boys (Lewis, 2009; Kröner-Herwig, Heinrich & Vath, 2010).

Several of the MSQ-A subscales were positively skewed, indicating that the while the majority of participants reported mild migraine-related impairment, several participants reported severe migraine-related impairment. These subscales included Emotional Functioning at baseline (skewness = .60, standard error = .25), and Role Preventive at both baseline (skewness = .77, standard error = .25) and follow-up (skewness = 1.1, standard error = .26). The distributions of several indexes computed using headache diary data were also positively skewed, including migraine episodes per month (skewness = 1.1, standard error = .30) and migraine disability hours (skewness = 1.7, standard error = .30). In an effort to reduce the impact of skewness, all construct validity analyses were run using both raw scores and a square root transformation of the indexes listed above. Using square root transformation of these indexes resulted in new skewness coefficients that were within the -.50 to .50 range, indicating no significant

skewness of distribution. The distributions of the scores on the rest of the criterion measures in this study were normal.

All correlations run with the transformed indexes differed by less than .05 from correlations run with raw indexes scores. The correlation between MSQ-A Role Preventive at follow-up and associated symptom severity of migraines (Table 10), was marginally significant when raw scores were used, and reached statistical significance when transformed MSQ-A Role Preventive score was used. No other meaningful differences in correlation sizes were noted based on whether raw or transformed scores were used in the analysis. Because using square root transformations of raw scores had minimal effects on the construct validity analysis, only results using the uncorrected scores are presented in the following sections.

Sample Characteristics

The means and standard deviations of MSQ-A and its hypothesized subscales and HDI-A total score at baseline and follow-up are summarized in Table 2. The means and standard deviations of the demographic and criterion measures used in this study are summarized in Table 3.

Mild to moderate migraine-related impairment was reported on average by participants on MSQ-A and HDI-A at both assessment times. Examination of self-reported impaired functioning as measured by both PedsQL and PedMIDAS (Table 3) also indicates that on average, adolescents in this sample experienced relatively mild impairment. Thus, results from all measures that assess impaired functioning used in this study were consistent.

On average, adolescents in this sample reported infrequent migraines (average of 3.4 migraine episodes per 30 days) of moderate severity (average severity of 2 on a 0 to 3 scale) in the four-week period between baseline and follow-up assessment (Table 3). Consistent with adolescents reporting migraines of low frequency and moderate severity, there was a noticeable change in average MSQ-A and HDI-A scores from baseline to follow-up, with follow-up scores indicating improved quality of life (Table 2). A paired samples *t*-test was performed to compare the baseline and follow-up scores for MSQ-A and HDI-A. All follow-up scores were significantly lower than scores obtained at baseline ($p < .05$). This reduction in migraine symptoms and migraine-related impairment may reflect the positive effects of migraine management adolescents received during the 4 week period. It may also be consistent with regression to the mean, where participants in this study initially sought treatment when they were experiencing frequent or severe migraines, and their migraines diminished in frequency and severity over time to reflect the infrequent migraines of mild-to moderate severity that are typical for episodic migraine.

Finally, consistent with expectations and previously reported findings (Antonaci et al. 2011; Bruijn et al., 2009), adolescents in this sample reported higher mean levels of internalizing ($\bar{x} = 55$) than externalizing ($\bar{x} = 48$) symptoms on the Youth Self Report ($p < .05$) (Table 3).

Factor Analysis

Different analyses were conducted to examine the factor structure of MSQ-A and HDI-A. Based on findings from previous research with the adult and adolescent versions of the instruments, confirmatory factor analysis was conducted to examine the factor

structure of MSQ-A, and exploratory factor analysis was conducted to examine the factor structure of HDI-A.

Factor Structure of the Migraine Specific Quality of Life-Adolescent Form.

Based on previous findings, it was hypothesized that in the present study, MSQ-A would have the same three-factor structure as its adult version, including Role Restrictive (items 1-7), Role Preventive (items 8-11) and Emotional Functioning (items 12-14) subscales. In the literature, where specific hypothesis about the factor structure of an instrument can be formulated based on theory and previous findings, confirmatory factor analysis (CFA) is used to examine the internal structure of the instrument (Brown, 2006; Nunnally & Bernstein, 1994).

A $\chi 2$-test statistic is usually used in the literature to assess the goodness-of-fit of a model in confirmatory factor analysis (Cole, 1987). Since the results from this statistical test are dependent on sample size (Marsh, Balla, & McDonald, 1988), several additional indices were also analyzed in this study to better assess adequacy of fit, including: the comparative fit index (CFI; Bentler, 1990), the Tucker–Lewis Index (TLI; McDonald and Marsh, 1990), and the root mean square error of approximation (RMSEA; Raykov, 1998). These indices were chosen based on their frequent use in the CFA literature, their suitability in model comparison, and the fact that they are relatively unaffected by sample size (Hooper, Coughlan & Mullen, 2008). For CFI and TLI, values greater than 0.95 are presently recognized as indicative of good fit (Hooper, Coughlan & Mullen, 2008; Hu & Bentler, 1999). RMSEA values of 0.05 or lower indicate good fit and values up to 0.08 represent reasonable errors of approximation in the population (Diamantopoulos & Siguaw, 2000; Hooper, Coughlan & Mullen, 2008; Hu & Bentler, 1999).

In the literature, CFA is usually used to examine the fit of the postulated factor structure of a measure while comparing it to the fit indexes of reasonable alternative models (Cole, Lin, & Rupnow, 2007; Holroyd et al., 1999; Jhingran et al. 1998). For the MSQ-A, the difference between fit indexes of a three-factor model and two alternative models, including a two-factor and single-factor models was tested. Since the Role Restrictive and Role Preventive subscales of the MSQ-A are both measuring functional disability due to migraines, and have been found in studies with adults to correlated highly with one another (Cole, Lin, & Rupnow, 2007; Jhingran et al., 1998A), it is possible that items on both subscales load on a single factor. Therefore a two-factor model including emotional functioning and a combined role restrictive and role-preventive factor was hypothesized as an alternative to the three-factor model. Finally, it was hypothesized that either: a) participants might struggle to distinguish between items that assess each of the three domains of migraine-related quality of life, or that b) all three types of impairment might occur together. In each of these cases, all items on MSQ-A would be expected to load on the same factor. Therefore, another alternative model for MSQ-A was a single-factor model. Overall, it was hypothesized that a three-factor model would be a better fit to the data than a two-factor and single-factor models.

Preliminary exploration of data available for factor analysis was performed to determine whether the number of participants available in this sample was adequate for confirmatory factor analysis of MSQ-A (see Appendix C for additional details). Data from this analysis suggested that a MSQ-A model with three factors is over-identified, and that its subject-to-variables ratio is good (*STV*=6.9). All item communalities were greater than .35, and eight were greater than .50 ($\bar{x}$ = .52). According to MacCallum et

al. (1999), when item communalities are in the range of .50, and factors are well-determined, a sample of 100 participants is sufficient to achieve good recovery of population factors. Similar recommendations have been made by Gorsuch (1983). Based on these studies, the current sample size of *N*=97 participants is marginally adequate for confirmatory factor analysis of MSQ-A to be performed.

Confirmatory factor analysis was performed using the MPlus 7 software package. A total of three confirmatory models were assessed, evaluating respectively the three, two and single factor structure of the MSQ-A. The assumption made by the authors of MSQ was that individual items on the instrument measure only a single factor of migraine-related impairment. The same assumption has been made in studies investigating the factor structure of the adult version of MSQ (Cole, Lin, & Rupnow, 2007; Jhingran et al., 1998B; Loftland et al., 1999; Martin et al., 2000). Consistent with the methodology of these studies, for all three models proposed for MSQ-A, all residual correlations between item errors were initially set to zero, all items of the same subscale were specified to load on the same factor, and the factors were allowed to correlate. However, as mentioned earlier, all of the studies exploring the factor structure of MSQ found high correlations between its three subscales. Additionally, one study (Cole, Lin, & Rupnow, 2007) found that the fit of the three-factor model for MSQ to data from their sample can be improved by adding several correlations between item errors. Thus, it is possible that in the current study, the proposed model with uncorrelated errors and zero cross-loading might be overly restrictive and unrealistic for a MSQ-A.

A summary of the fit indices for the 3 initial models is presented in Table 4. A CFA analysis of the model fit for a three factor model of MSQ-A yielded an overall

$\chi 2(74)$ value of 124.8 ($p<.05$), suggesting significant statistical difference between model and the data. However, the CFI, TLI and RMSEA indexes all suggested reasonable fit of the three factor model for MSQ-A, suggesting that small sample size may have influenced findings from chi-square analysis. Factor correlations for the three factor model are presented in Table 5. All three factors were highly correlated (r = .65 - .88).

CFA analysis of the model fit for a two factor model of MSQ-A yielded an overall $\chi 2$ (76) value of 140.1 ($p<.05$), suggesting significant statistical difference between model and the data. None of the other fit indexes suggested that a two-factor model is a good fit to the data. The two factors were correlated (r=.72, p<.001).

Finally, CFA analysis of the model fit for a single factor model of MSQ-A yielded an overall $\chi 2$ (77) value of 165.6 ($p<.05$), meaning that the null hypothesis of a good fit to the data can be rejected. None of the fit indexes suggested that such a model is a good fit to the data.

Overall, none of the three models had fit indexes that suggested good fit to the data. A $\chi 2$ comparison of the fit indexes of the three nested models indicated that Model 1 is a substantially better fit than Model 2 and Model 3 ($p<.05$) and that Model 2 is a substantially better fit than Model 3 ($p<.05$). However, in the literature, when lack of fit to the data is found for all models proposed for an instrument, it is recommended that a $\chi 2$ difference test to compare models is supplemented with comparison of the Akaike Information Criterion (AIC) for each model (Brown, 2006). The AIC provides information about the quality of a model relative to other models that seek to explain the same data, without providing information about how good a fit given model is to the data in the study. Smaller AIC values are indicative of better fit to the data. Examination of

the AIC of the three models proposed for MSQ-A also suggested that a 3 factor model of MSQ-A is better at explaining data from the current sample than the other two models (Table 4).

Although for all three models proposed for MSQ-A, discrepancy from data was significant, fit indexes were reasonable in magnitude for Model 1, suggesting modification indices could be examined to determine the effect of allowing several of the item errors to correlate. Due to the small sample size of this study, item errors were initially left uncorrelated during the CFA in order to not over-saturate the model. The assumption of uncorrelated item errors might be unrealistic considering how in the literature items on the same subscale of the same self-report measure are usually expected to have correlated errors due to similar item wording or content (Tomás & Oliver, 1999).

The assumption of no cross-loading was maintained by allowing only correlations of item errors within the same factor to correlate where modification indices indicated, starting with the pair of errors with highest modification index (Items 13 & 14; MI=16.59). The inclusion of correlated errors of items within the same factor of MSQ-A resulted in an updated model where the following item errors were correlated: 3&4, 3&5, 4&5, 4&6, 5&7, and 13&14 (Figure 1). Analysis of the modification indices of this updated model suggested that fit can be further improved by adding correlated errors of items from different factors (i.e. Items 1 & 12). However, these correlations were not added to maintain assumption that items on MSQ-A load on a single factor only.

Factor analysis of the updated three-factor model for MSQ-A yielded the following fit indexes: χ^2 (68) = 74.71, p =0.27; RMSEA = 0.03; TLI = 0.98; CFI = 0.99, suggesting good fit between model and the data. All 14 items had significant loadings

(>.5) on their specified factor. The factor loadings of individual items on MSQ-A for the updated three-factor model for MSQ-A are summarized in Table 7. The chi-square difference between the modified model and the original 3 factor model indicated significant improvement ($p < .001$) in model fit. All three subscales of the updated model were significantly correlated, with correlation between Role Restrictive and Role Preventive factors of MSQ-A being particularly high (r=.92, p>.01), suggesting poor discriminant validity of the three subscales (Table 6).

Factor Structure of HDI-A Headache Disability Inventory-Adolescent Form.

In previous studies, there has been no empirical support for the two-factor structure of HDI originally proposed by its authors, or for any alternative factor structure. In the literature, exploratory factor analysis (Child, 1990; Kim & Mueller, 1978) is the method of choice for examining the factor structure of an instrument when limited or no previous evidence exists to support its proposed factor structure. Therefore EFA was used to assess the factor structure of HDI-A without imposing any preconceived structure on the outcome. Maximum likelihood method was used to extract the initial set of factors. Evidence from the literature suggests that postulated HDI-A subscales are significantly correlated with one another (Jacobson et al., 1994). Therefore an oblique rotation was used to obtain a final solution of factors for HDI-A.

Preliminary exploration of data available for factor analysis was performed to determine whether the number of participants available in this sample was adequate for exploratory factor analysis of HDI-A (see Appendix C for additional details). The Kaiser-Meyer-Olkin Measure of Sampling Adequacy was .79, and a HDI-A model with two factors is over-identified, indicating that sampling was adequate to perform exploratory

factor analysis of HDI-A. However, subject-to-variables ratio was low with the current sample (*N*=97; *STV*=3.8). Item communalities were also low in magnitude, ranging from .08 to .50 ($\bar{x}$ = .25). Previous studies have suggested that when low subject-to-variables ratio and low item communalities are observed, samples of 150-300 are recommended to in order to achieve good recovery of population factors even when there is high overdetermination of factors (Clif & Penel, 1967; Velicer & Fava, 1998; MacCollum et al., 1999). Based on these findings, low sample size would likely either limit the interpretability of factor analysis of HDI-A, or prevent factor analysis from being performed.

Exploratory maximum likelihood factor analysis of HDI-A was attempted using SPSS 16 and identified eight factors with eigenvalues above 1. Together these 8 factors explained only 67.8% of the variance. Initial eigenvalues and percentage of variance explained by each component for exploratory factor analysis of HDI-A are summarized in Supplemental Table 3 (Appendix C) and visually represented on Supplemental Figure 1 (Appendix C). When attempting to extract these 8 factors, SPSS was unable to reach maximum likelihood factor solution 25 iterations, terminating the extraction and not allowing for the analysis to continue. The same message was repeated after 100 iterations. It is likely that with a sample size of *N*=97, and the fragmented factor structure of the instrument, exploratory maximum likelihood factor analysis of HDI-A through SPSS was not possible. Because no meaningful factors were identifiable in this sample for HDI-A, only the total score for HDI-A was used in the rest of the analyses. However, results from analyses using HDI-A total score should be interpreted with caution given

that exploratory factor analysis did not provide support for single-factor structure of the instrument.

Reliability of Migraine Specific Quality of Life-Adolescent and Headache Disability Inventory-Adolescent Forms

The Internal consistency of the three subscales of MSQ-A and the total score of the HDI-A at baseline and follow-up was examined. All scales and subscales demonstrated good-to-excellent internal consistency (Cronbach's $\alpha \geq .72$). The results of this analysis are summarized in Table 8.

Baseline and follow-up scores on MSQ-A and HDI-A were significantly correlated (Table 9), but all correlations were of moderate magnitude. As noted earlier, there was significant decrease in MSQ-A and HDI-A scores from baseline to follow-up, indicating improvement in quality of life, and this improvement was consistent with infrequent migraines of mild to moderate severity recorded by adolescents in the four-week period between the two assessments.

Within each of the three subscales identified by factor analysis of MSQ-A, items were evaluated to determine whether they satisfied the generally accepted criteria of combining items into a summated rating scale (Spector, 1992). Table 10 shows the Pearson item-dimension correlations for each item on MSQ-A, corrected for overlap by removing relevant item from its dimension for correlation. For all items, the item-to-intended dimension correlations were greater than 0.50. No items had statistically larger correlations with dimensions other than the ones they were written to assess providing evidence of item convergent validity. However, items 2, 6, 7, 9, 10 and 11 had correlations of similar magnitude with the Role Restrictive and Role Preventive subscales

on MSQ-A. Items 1 and 12 correlated equally with all three subscales on MSQ-A. These findings are consistent with the high inter-correlations among the three subscales of MSQ-A presented in Table 4 and Table 5 and provide no evidence of discriminant validity of individual items on MSQ-A.

All item-to-intended dimension correlations were equivalent in magnitude within each dimension, suggesting that items in the same dimension contain the same proportion of information about the dimension. Item-to-intended dimension correlations ranged from 0.51 to 0.71 for items in the Role Restrictive, 0.63 to 0.76 for items in the Role Preventive, and 0.57 to 0.67 for items in the Emotional Functioning dimension (Table 10). Standard deviations for items within each dimension were also equivalent in magnitude suggesting no need for standardization before summing items into a subscale.

Construct Validity of Migraine Specific Quality of Life-Adolescent and Headache Disability Inventory-Adolescent Forms

Three subscales of MSQ-A were confirmed by factor analysis, including Role Preventive, Role Restrictive and Emotional functioning subscales. These three subscales have been postulated to measure three domains of migraine-related impairment on quality of life, including direct and indirect functional impairment, and migraine-related affective distress. Items on the HDI-A were also written to assess the three dimensions of migraine-related impairment listed above. However, no subscale structure could be identified by factor analysis for HDI-A in the present study, and only the construct validity of the total score was examined. The construct validity of MSQ-A total and subscale scores and HDI-A total score was assessed by examining the Pearson correlation coefficients with other self-report measures of impaired functioning, internalizing

psychological symptoms, and with migraine activity data from the headache diary. Discriminant validity of MSQ-A and HDI-A was assessed by examining the difference in their relationships with internalizing and externalizing psychological symptoms reported by adolescents in this sample. Discriminant validity of the three subscales of MSQ-A was also assessed by examining their individual relationships with each criterion measure.

Hypothesis 1.

As predicted, all subscales and the total score on MSQ-A exhibited significant relationships of medium or higher magnitude ($r > .33$) with PedMIDAS (Table 11) and Migraine Disability Hours (Table 12). Significant positive correlations were also found between HDI-A total score at baseline with PedMIDAS ($r = .23$, $p < .05$), and between HDI-A total score at follow-up with Migraine Disability Hours ($r = .39$, $p < .01$).

Hypothesis 2.

All correlations between scores on MSQ-A and HDI-A at follow-up with migraine frequency and severity as recorded in the PalmOS electronic daily were in the predicted direction, indicating that greater number of migraine symptoms is associated with greater impairment in quality of life (Table 12). Also as predicted, all of these correlations were small to moderate in magnitude ($r = 0.15$ - 0.38), suggesting that MSQ-A and HDI-A assess factors that contribute to migraine-related impairment including, but not limited to, the effects of migraine characteristics.

Hypothesis 3.

As predicted, correlations between MSQ-A total and subscale scores with PedsQL subscales were small to moderate in magnitude ($r = -.12$ to $-.31$; Table 11). Correlations

between HDI-A total score and PedsQL Physical (r =-31, p< .01) and Psychosocial (r =-43, p< .01) subscales were also of moderate magnitude.

Hypothesis 4.

As predicted, moderate correlations were found between all subscales and total score on MSQ-A and HDI-A totals score with the Internalizing scale on the Youth Self Report (r = .29-.45; Table 11). Of the three MSQ-A subscales, Role Restriction and Role Prevention had correlations of larger magnitude with YSR Internalizing (r = .38-.40) than did MSQ-A Emotional Functioning (r =.29).

Hypothesis 5.

As predicted, all correlations between MSQ-A total and subscale scores with YSR Externalizing were small in magnitude ($r \leq .21$). All of these correlations were also smaller in magnitude than the corresponding correlations with YSR Internalizing, providing evidence for the discriminant validity of MSQ-A. HDI-A total score had significant positive correlations with both YSR Internalizing and Externalizing scales, and the magnitude of these correlations was similar, providing no evidence of discriminant validity of HDI-A (Table 11).

Discussion

Scale Structure

Migraine Specific Quality of Life Adolescent Form.

Results from the confirmatory factor analysis provide evidence in support of the hypothesis that items on MSQ-A can reasonably be conceptualized as assessing three dimensions of migraine-related impairment, including Role Preventive, Role Restrictive and Emotional Functioning, and that these dimensions correspond to the three theoretically postulated domains of migraine-related impact on adolescent quality of life, including direct and indirect impact due to migraines, and migraine-related affective distress. However, the utility of the three factor model for MSQ-A was compromised by high inter-correlations among the three subscales.

All three factors were significantly correlated (r=.63-.92) and the correlation was particularly high between the Role Restrictive and Role Preventive subscales (r=.92). Similar results have been reported in previous studies with adults, where high correlations between the Role Restrictive and Role Preventive subscales have been found (r=.81-.89; Cole, Lin, & Rupnow, 2007; Martin et al., 2000). High correlations between the Role Restrictive and Role Preventive scales found in this and other studies do not provide support for their usefulness as separate subscales of MSQ-A. These results could mean that a higher order factor is plausible and may need to be considered in future studies. It is also possible that high these correlations reflect the fact that direct and indirect functional impairment due to migraines tends to co-occur in this population, where adolescents experience impairment during a migraine episode, while also

selectively restricting their involvement in some activities when migraine free to reduce risk of a new migraine episode.

Modification indices for the three factor model of MSQ-A in the present study suggested that the fit of this model to the data can be improved by adding correlated errors for items within the same subscale as well as items on different subscales. This finding suggests that several MSQ items may be measuring more than one latent factor and is consistent with high intercorrelations between the three factors.

The high intercorrelations among factors and the need to include correlated errors for selected items on MSQ-A found in this study may be related to content overlap and similar phrasings across the instrument and particularly among items on the Role Restrictive and Role Preventive subscales. For example item 2 on the Role Restrictive subscale (In the past 4 weeks, how often have migraines interfered with fun activities (like hobbies, hanging out with friends, etc.)?), and item 11 on the Role Preventive subscale (In the past 4 weeks, how often were you not able to go to parties or out with friends because you had a migraine?) use similar wording to assess the two constructs. Future studies may benefit from identifying and re-writing similarly worded items on MSQ-A.

Headache Disability Inventory Adolescent Form.

Results from exploratory factor analysis of HDI-A in this sample revealed no readily interpretable factor structure. This finding could reflect sample size limitations, problems with item wording on HDI-A, or, most likely, a combination of both factors. The sample size available for factor analysis of HDI-A ($N = 97$) limited our ability to reliably identify the factor structure of the HDI-A. Several previous studies have

recommended sample size of 100 necessary for valid factor analysis for measures such as HDI-A, where there are small number of factors and large number of items, provided that the item communalities, or the proportion of variability for a given variable that is explained by the factors, are high (Gorsuch, 1983; Kline, 1979; MacCollum, et al., 1999). Unfortunately, in the current study, low communalities were observed for HDI-A. Samples of 150 - 300 participants have been recommended to assure good model fit when low subject-to-variable ratio and low communalities are observed even where the factors in a model are over-identified (Clif & Penel, 1967; Velicer & Fava, 1998; MacCallum et al., 1999). Thus, exploratory factor analysis in the present study may have provided only limited insight into the internal structure of HDI-A.

It should be noted that the absence of an interpretable factor structure for HDI-A is consistent with findings for the adult version of the instrument. In their original studies, the authors of the HDI hypothesized a two-factor structure for the HDI but provided no supporting evidence for this hypothesis (Jacobson et al., 1994; Jacobson et al., 1995). To this writer's knowledge, there has been only one other study that has examined the factor structure of the adult version of HDI, and results from that study did not provide support for this two factor structure (Holroyd et al., 1999).

An examination of the item content on HDI-A provides insight into item wording that might explain these findings. Both proposed Functional impairment and proposed Emotional distress items on HDI-A inquire about interviewee's feelings. For example, Item 2, which was intended to assess headache-related functional impairment, is worded as follows: "Because of my headaches I feel restricted in performing my daily routines" (Jacobson et al., 1994). Thus, items intended to assess direct or indirect functional

impairment due to migraines appear to be contaminated by emotional distress. While this would not necessarily compromise the validity or utility of the HDI total score, it could well undermine the proposed subscales, because items on both postulated subscales might assess the functional impact of headaches and headache-related affective distress. The use of postulated subscales of HDI cannot be recommended with adults or adolescents at this time. Further examination of the factor structure of HDI-A with a larger sample is necessary, particularly since a single-factor model was also not a good fit to data in the present study.

Reliability

Cronbach alpha coefficients were greater than 0.72 for all MSQ-A subscales and HDI-A total score at each study visit, suggesting acceptable internal consistency measures of reliability. Examination of item-to-subscale correlations suggested that multiple MSQ-A items correlated equally with the Role Restrictive and the Role Preventive subscales. Similar item-to-subscale correlations have been observed with the adult version of the instrument by Martin et al. (2000). These finding are also consistent with high correlation between Role Restrictive and Role Preventive dimensions observed in confirmatory factor analysis of the MSQ-A in this study and the MSQ in previous studies.

Comparison between MSQ-A and HDI-A mean scores at baseline and follow-up revealed significant reductions in migraine-related impairment reported by participants in this sample. This finding was consistent with expectations that adolescents reporting low frequency/ moderate severity of migraines and currently in treatment for their migraines would report reduced migraine-related impairment four weeks after the initial

assessment. However, there was no independent measure of change in migraine-related impairment over time used in the present study, and participants were not controlled for treatment they received. Thus, no test-retest reliability analysis could be performed and the possibility that the reduction in MSQ-A and HDI-A scores between baseline and follow-up was due to chance could not be ruled out.

Validity

The present study collected data specifically from adolescents with episodic migraines, who were receiving treatment. Participants generally experienced short and infrequent migraines accompanied by mild migraine-related impairment (Tables 1 and 2). This restricted range of impairment in our sample could have contributed to restricted range of Pearson correlations observed between experimental and criterion measures (Aron & Aron, 2003; Goodwin & Leech, 2006). Another limitation in the construct validity analysis in the present study was lack of ideal criterion measures. As discussed earlier, there are currently no valid measures of the three dimensions of migraine-related impairment in quality of life for adolescents that are the focus of this study, necessitating the need for the development of new instruments such as MSQ-A and HDI-A. Thus, the low to moderate magnitude correlations found between MSQ-A and HDI-A with available criterion measures could reflect problems with the validity of the two experimental measures, limitations of the criterion measures, sample characteristics such as the limited range of migraine severity and disability reported by participants, or some combination of these factors.

Migraine Specific Quality of Life Adolescent Form.

Despite the limitations described above, this study provides some evidence for the construct validity of MSQ-A. Correlations in the predicted direction and magnitude were found between MSQ-A total score and 8 of 9 criterion measures. Additionally, consistent with expectations, difference in the magnitude of the correlations between MSQ-A (total and subscale scores) and the Internalizing and Externalizing scales of the Youth Self Report (YSR) provides some support for the discriminant validity of MSQ-A. These findings suggest the MSQ-A total score may be a reasonable measure of overall migraine-related impairment and are consistent with previous findings in studies with adults and adolescents (Cole, Lin, & Rupnow, 2007; Martin et al., 2000; Tkachuk et al., 2003).

The hypothesis that correlations between MSQ-A (total and subscale scores) and headache-specific measures would be larger in magnitude than similar correlations with general quality of life measures such as the Pediatric Quality of Life questionnaire (PedsQL) was supported by results in this study. In studies with adults where both disease-specific and general quality of life instruments were available (Bagley et al., 2011; Cole, Lin, & Rupnow, 2007; Martin et al., 2000), correlations between total and subscale scores of the MSQ and other headache-specific measures have been larger in magnitude (r = .38 - .92) than similar correlations with general quality of life instruments (r = .26 - .38). These findings are consistent with the hypothesis that general quality of life questionnaires such as PedsQL provide limited information about disability experienced by adolescents with episodic pain conditions such as migraine. This possibility may be particularly salient for adolescents with low frequency and moderate

severity migraines, currently receiving treatment, who are functioning well overall, but experience impairment during a migraine episode, or selectively restrict their involvement in some activities even when migraine free to reduce risk of a migraine. The type of impairment experienced by such adolescents might not be accurately assessed by a quality of life measure inquiring only in general terms about overall functioning. Migraine-specific assessment tools may be necessary to accurately assess quality of life in this population and possibly other populations of adolescents with migraine.

The hypothesis that MSQ-A assesses primarily migraine-related impacts not captured by migraine characteristics alone was also consistent with results in this study. Migraine frequency and severity were positively related to impairment in health related quality of life as assessed my MSQ-A, but the magnitude of these correlations was small. The small magnitude of these correlations was also consistent with previously reported findings for the adult version of the instrument (r = .15 - .31; Bagley et al., 2011; Martin et al., 2000).

Problems with Construct Validity of Migraine Specific Quality of Life Adolescent Form.

Several important problems with the construct validity of the subscales of MSQ-A were identified and these problems are consistent with high inter-correlations between these two subscales, and with the finding that a number of items on MSQ-A exhibit correlations of a similar magnitude with both the Role Restrictive and Role Preventive subscales.

The magnitude of the correlations between the Role Restrictive and Role Preventive subscales on MSQ-A and criterion measures was similar across all validity

analyses, suggesting that while these two subscales have been postulated to assess two different constructs, there was no difference in the way these constructs related to other instruments in this study. These findings may be indicative of significant overlap between the direct and indirect functional impairment experienced by adolescents due to migraines, or of problems with the way these two constructs are measured by MSQ-A. Previous studies similarly revealed only limited evidence that the Role Restrictive and Role Preventive subscales of the adult MSQ differ in predictable ways in their correlations with criterion measures assessing different constructs (Bagley et al., 2011; Cole, Lin, & Rupnow, 2007; Martin et al., 2000). To the author's knowledge, no previous study has commented on this issue as a potential problem with either the adult or adolescent version of this instrument. However, findings from this and previous studies raise questions about the utility of the two functional impairment subscales of MSQ-A.

Another potential problem with the construct validity of MSQ-A was that the Emotional Functioning subscale on MSQ-A consistently exhibited correlations with criterion measures that were small in magnitude, including with measures of general emotional distress (i.e. PedsQL Psychosocial; the Internalizing Scale of the Youth Self-Report). It is possible that with the small sample in the present study, as the subscale with only three items, Emotional Functioning was least reliable subscale and thus exhibited correlations with criterion measures that were lower in magnitude than the other two MSQ-A subscales. Future studies may consider including additional items to the Emotional Functioning subscale of MSQ-A, and re-assessing its construct validity.

Overall, in this study, the Role Restrictive and Role Preventive subscales of MSQ-A were highly correlated, number of items correlated equally with both subscales,

and the correlations between these two MSQ-A subscales with criterion measures were of similar magnitude, suggesting no meaningful difference in the way they related to constructs associated with migraine-related impairment. These findings raise questions about the utility of the two subscales as separate constructs and further exploration of the psychometric properties of MSQ-A is necessary to support the use of its subscales. Until further evidence is available, it is recommended that only total score MSQ-A be used to assess direct and indirect functional impairment and affective distress due to migraines.

Headache Disability Inventory Adolescent Form.

Correlations between total HDI-A score with other measures used in this study were consistent with previously discussed hypothesis that individual items on HDI-A may assess both functional impairment due to migraines and migraine-related affective distress. HDI-A total score related significantly to measures of missed/interrupted activities and impaired performance due to the effects of migraines, and general measures of psychological distress. Correlations between HDI-A total score and all measures in the study were of a similar magnitude (r=.19-.42), including correlations of similar size with headache-specific impairment (Pediatric Migraine Disability Assessment Score, r=.23; and Migraine Disability Hours, r=.39) and impairment in general quality of life (the Pediatric Quality of Life Scale, r= -.31 to -.43). Additionally, HDI-A had correlations of similar size with both Internalizing (r=.45) and Externalizing (r=.36) symptoms reported on the Youth Self Report. While these findings suggest that HDI-A total score may be sensitive to disrupted functioning and general emotional distress experienced by adolescents with migraine, the present study does not provide evidence in support of the

hypothesis that HDI-A measures headache-specific impairment experienced by adolescents.

Overall, the present study provides limited evidence in support of the use of HDI-A total score as a measure of headache-related impairment in adolescents with migraine and no evidence in support any meaningful subscale structure for the instrument. It is possible that the various components of headache-related impairment assessed by HDI-A are not best conceptualized in terms of the three components of migraine-related impairment in quality of life that are the focus of this study (direct and indirect functional impairment and affective distress). The actual structure of HDI-A may reflect multiple minor components of Health-Related Quality of Life that are not conceptually useful, but do reflect disrupted functioning and emotional distress. Future studies with larger samples that include adolescents reporting wider range of migraine-related impairment are recommended to re-examine the psychometric properties of HDI-A and the utility of using HDI-A total score in the assessment of migraine-related impairment in quality of life.

Strengths and Limitations

The relatively small sample (N=97) is a significant limitation of this study and it likely limited confidence that can be placed in the analyses that were performed. A larger sample size would improve quality of the factor analysis for both instruments, but particularly for HDI-A where low subject-to-variable and small communalities likely rendered factor analysis for that instrument unreliable. However, it should be noted that this is the largest study to date to investigate the psychometric properties of MSQ-A, and the first study to investigate the psychometric properties of HDI-A.

Along with sample size, another potential limitation of this study was low level of migraine-related impairment reported by teens. It would be useful to continue studying MSQ-A and HDI-A using a sample of adolescents with chronic migraines, or teens with episodic migraines, who are not currently receiving treatment, or are in the early stages of treatment for their migraines, and are thus likely to experience greater migraine-related impairment.

This study did not control for treatment participants received in the 4 weeks between the two testing periods or for natural changes in symptomatology that often occur in the course of migraine even without treatment. Thus, true test-retest analysis could not be conducted. Using a sample of adolescents who are all receiving the same treatment for their migraines in future studies is recommended in order to allow for tests of stability of MSQ-A and HDI-A over time.

Finally, poor clarity of item content of MSQ-A and HDI-A might have been a limitation of the two instruments. With both MSQ-A and HDI-A, there was likelihood that high content overlap and similar phrasings influenced results of the analyses in this study. In the literature it has been recommended that a multi-trait multi-method (MTMM) analysis is conducted to account for limitations of an instrument related to item content (Campbell & Fiske, 1959; Brown, 2006). In the context of MTMM, the validity of a new measure is tested by examining the relationships of its subscales with the subscales of a previously validated measure that was designed to assess similar concepts, including the presence and absence of theoretically postulated relationships (convergent & discriminant validity). However, as mentioned earlier, the adolescent versions of MSQ and HDI were developed precisely because of current lack of valid measures of direct and indirect

functional impairment due to migraines and migraine-related affective distress for adolescents. In the absence of previously validated measures that assess direct and indirect functional impairment and affective distress due to migraines, no MTMM analysis could be conducted. Instead, the correlations between MSQ-A and HDI-A with available general and migraine-specific instruments were examined and provided some information about the construct validity of the two experimental measures. The limitations of available criterion measures likely limited conclusions that could be drawn about the construct validity with MSQ-A and HDI-A. In future studies, other types of measures of migraine-related impairment such as peer or parent ratings could be used in a MTMM analysis.

This study also had several important strengths. Where previous studies have tended to combine data from adolescents with data from younger children or pool data from participants with migraine and tension-type headache (Karwautz et al., 1999), the present study used data from a sample consisting only of adolescents with migraine. The latest diagnostic criteria from The International Headache Classification (ICHD-2, 2004) were used to diagnose participants in this sample, and participants were diagnosed by a pediatric neurologist specializing in headaches. A daily headache diary was used to collect data about participants' symptoms, which likely improved accuracy of collected information.

Although low frequency and moderate severity of migraines, and mild to moderate migraine-related impairment was reported on average by participants in this sample, this presentation likely provides a realistic perspective into the experience of adolescents with episodic migraines who are receiving treatment for their condition.

Other authors and anecdotal reports by clinicians have similarly suggested that mild to moderate severity and low frequency of episodes is common among adolescents receiving treatment for their migraines (Connelly & Rapoff, 2006; Cottrell et al. 2007; Kröner-Herwig, Heinrich & Vath, 2010).

Directions for Future Research

Several directions can be taken in future studies to further explore the psychometric properties of MSQ-A and HDI-A. It is recommended that future studies investigate the reliability and validity of MSQ-A and HDI-A with larger samples of adolescents, who report wider range of migraine symptoms and migraine-related impairment. For this purpose, adolescents with chronic daily migraine could be included in the analysis.

Results from this and other studies suggest that items on HDI-A might not be assessing what they were written to assess and that items on both scales may benefit from being re-written. It is recommended that additional focus groups be conducted with adolescents with migraine to assess whether items on MSQ-A and HDI-A are interpreted by teens as the intended constructs of direct and indirect functional impairment and affective distress, and to screen for item redundancy.

Findings from the present study also lead to several research directions in regards to the subscales of MSQ-A and HDI-A. It is possible that the addition of a higher order factor for the Role Restrictive and Role Preventive subscales on MSQ-A may improve fit of the three factor model for that instrument. Additionally, it may be useful to explore whether adding items to the Emotional Functioning subscale on MSQ-A could improve the quality of the measure. Finally, it would be useful to explore the factor structure of

HDI-A with a larger sample, and investigate the utility of using total score to assess migraine-related impairment.

Finally, it is recommended that future studies maintain the age and disease-specific approach taken by current study in order to ensure that their findings are directly applicable to adolescents with migraine. Overall, despite limitations mentioned earlier, this study does provide insight about a largely understudied population. It is the hope of this author that future research continues to advance age- and disease-specific assessment for adolescents with migraine.

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Table 1

ICHD-II Criteria for Pediatric Migraine

A. At least five attacks fulfilling criteria B–D

B. Headache attacks lasting 1–72 hours

C. Headache with at least two of the following features:

1. Unilateral or bilateral location,
2. Pulsating quality
3. Moderate to severe intensity
4. Aggravation by/or causing avoidance of routine physical activity

D. During the headache at least one of the following:

1. Nausea and/or vomiting
2. Photophobia (excessive sensitivity to light) and/or phonophobia (excessive sensitivity to sound)

E. Not attributable to another disorder

Note. ICHD-II (International Headache Classification – 2; Headache Classification Subcommittee of the International Headache Society, 2004)

Table 2

Descriptive statistics – Experimental Measures

Variable	Obtained Range	Mean	Standard Deviation	N
HDI-A Baseline				
HDI-A Total Score	14 – 94	54.2	19.2	96
HDI-A Follow-up				
HDI-A Total Score	12 – 92	47.4	20.4	84
MSQ-A Baseline				
MSQ-A Total Score	0-64	28.7	15.1	93
MSQ-A Role Restriction	0-74.3	32.6	15.7	97
MSQ-A Role Prevention	0-75	21.0	16.9	96
MSQ-A Emotional Function	0-86.7	28.6	20.9	97
MSQ-A Follow-up				
MSQ-A Total Score	0-64	23.5	15.6	82
MSQ-A Role Restriction	0-68.6	27.3	17.0	82
MSQ-A Role Prevention	0-75	17.7	17.2	82
MSQ-A Emotional Function	0-73.3	22.4	17.6	82

Note. MSQ-A (Migraine Specific Quality of Life Questionnaire Adolescent form); HDI-A (Headache Disability Inventory Adolescent form); Baseline and follow-up assessments were four weeks apart. For all scales, higher scores indicate greater disability.

Table 3

Descriptive statistics – Demographics and Criterion Measures

Variable	Obtained Range	Mean	Standard Deviation	N
Demographic Variables				
Age	11-17	14.3	1.6	96
Grade in School	6-12	9.0	1.8	97
Diary Data				
Migraines per 30 days	0-14	3.4	2.8	72
Average Migraine Severity	1-3	2.0	0.5	62
Associated Symptom Severity	0-7	2.5	1.8	62
Migraine Disability Hours	0-51.2	9.8	11.9	62
Impaired Functioning Due to Migraines				
PedMIDAS	0-120	24.8	19.6	93
General Health-Related Quality of Life				
PedsQL Physical	0-100	73.2	23.0	95
PedsQL Psychosocial	21-100	71.4	16.2	95
Psychological Symptoms				
YSR-I	38-79	55.0	9.3	97
YSR-E	29-69	48.0	9.0	97

Note. Migraines per 30 days (Number of migraine episodes per 30 days); Average Migraine Severity (Severity of migraines averaged across episodes); Associated Symptom Severity (Sum of average severity of Photophobia, Phonophobia and Nausea across migraine episodes); Migraine Disability Hours (Sum of hours disabled and .5 x hours impaired by migraine); PedsQL (Pediatric Quality of Life Scale); PedMIDAS (Pediatric Migraine Disability Assessment Score); YSR-I (Internalizing scale of the Youth Self Report); YSR-E (Externalizing scale of the Youth Self Report); For all scales except PedsQL, higher scores indicate greater disability; For PedsQL, lower scores indicate greater disability

Table 4

Fit Indices for the Three Models Proposed for MSQ-A

	CFI	TLI	RMSEA	$\chi 2$ (*df*)	AIC
Model 1 (3 factors)	0.91	0.89	0.08	124.8 (74)	3447.660
Model 2 (2 factors)	0.88	0.86	0.10	140.1 (76)	3459.342
Model 3 (single factor)	0.84	0.81	0.11	165.6 (77)	3489.783

Note. CFI (Comparative Fit Index); TLI (Tucker-Lewis Index); RMSEA (Root Mean Square of Approximation); AIC (Akaike Information Criterion); For CFI and TLI, higher values indicate better fit; for RMSEA, $\chi 2$, and AIC lower values indicate better fit.

Table 5

Factor Correlations for Model 1 of MSQ-A

	1	2
1. Role Restrictive	-	
2. Role Preventive	.88**	-
3. Emotional Functioning	.74**	.65**

Note. $^{**}p < .01$;

MSQ-A (Migraine Specific Quality of Life Questionnaire Adolescent form)

Table 6

Factor Correlations for Model 1 of MSQ-A with Correlated Errors

	1	2
1. Role Restrictive	-	
2. Role Preventive	.92**	-
3. Emotional Functioning	.80**	.63**

Note. $^{**}p < .01$;

MSQ-A (Migraine Specific Quality of Life Questionnaire Adolescent form)

Table 7

Factor loadings for Model 1 of MSQ-A with Correlated Errors

	Role Restrictive	Role Preventive	Emotional Functioning
MSQ1	0.65		
MSQ2	0.76		
MSQ3	0.60		
MSQ4	0.63		
MSQ5	0.67		
MSQ6	0.62		
MSQ7	0.70		
MSQ8		0.81	
MSQ9		0.70	
MSQ10		0.83	
MSQ11		0.77	
MSQ12			0.95
MSQ13			0.57
MSQ14			0.51

Note. MSQ-A (Migraine Specific Quality of Life Questionnaire Adolescent form)

Table 8

Reliability of MSQ-A Subscales and HDI-A Total Score

Scale	Number of Items	Cronbach's Alpha at Baseline	Cronbach's Alpha at Follow-up
MSQ-A Role Restrictive	7	0.86	0.92
MSQ-A Role Preventive	4	0.84	0.88
MSQ-A Emotional Functioning	3	0.78	0.72
MSQ-A Total Score	14	0.92	0.94
HDI-A Total Score	25	0.89	0.91

Note. MSQ-A (Migraine Specific Quality of Life Questionnaire Adolescent form);

HDI-A (Headache Disability Inventory Adolescent form);

Table 9

Correlations between Baseline and Follow-up MSQ-A and HDI-A

	1	2	3	4	5	6	7	8	9
1. MSQ- A Role Restrictive Baseline	___								
2. MSQ-A Role Restrictive Follow-up	.52**	___							
3. MSQ-A Role Preventive Baseline	.77**	.40**	___						
4. MSQ-A Role Preventive Follow-up	.47**	.78**	.53**	___					
5. MSQ-A Emotional Functioning Baseline	.56**	.42**	.50**	.35**	___				
6. MSQ-A Emotional Functioning Follow-up	.36**	.70**	.29**	.63**	.49**	___			
7. MSQ-A Total Score Baseline	.94**	.56**	.89**	.56**	.75**	.42**	___		
8. MSQ-A Total Score Follow-up	.52**	.96**	.46**	.89**	.46**	.82**	.58**	___	
9. HDI-A Total Score Baseline	.23*	.23*	.37**	.25*	.50**	.36**	.38**	.29**	___
10 HDI-A Total Score Follow-up	.17	.35**	.25*	.47**	.34**	.58**	.26*	.48**	.69**

Note. * $p < .05$; ** $p < .01$;

MSQ-A (Migraine Specific Quality of Life Questionnaire Adolescent form); HDI-A (Headache Disability Inventory Adolescent form); Baseline and follow-up assessments were four weeks apart.

Table 10

MSQ Item-Factor Correlation Matrix: Item Descriptive Statistics and Pearson Item-Dimension Correlations

Item		Mean	SD	Pearson Item-Dimension Correlations		
				MSQ-A RR	MSQ-A RP	MSQ-A EF
Name	Label					
Scale= Role Restrictive (RR)						
MSQ-A 1	Family	2.51	1.01	0.51†	0.50	0.51
MSQ-A 2	Leisure	2.57	1.01	0.66†	0.64	0.47
MSQ-A 3	Activity	2.67	1.04	**0.65**†	0.54	0.32
MSQ-A 4	School	2.63	1.02	**0.71**†	0.61	0.26
MSQ-A 5	Concentration	2.64	1.01	**0.70**†	0.60	0.42
MSQ-A 6	Tired	2.85	1.14	0.60†	0.53	0.43
MSQ-A 7	Energy	2.79	1.06	0.63†	0.61	0.48
Scale = Role Preventive (RP)						
MSQ-A 8	Activity	2.05	0.99	0.68	**0.76**†	0.38
MSQ-A 9	Help	1.93	0.93	0.57	0.63†	0.47
MSQ-A 10	Stop	2.30	1.02	0.68	0.74†	0.41
MSQ-A 11	Social	1.95	1.11	0.63	0.69†	0.42
Scale = Emotional Function (EF)						
MSQ-A 12	Frustration	2.98	1.30	0.64	0.55	0.57†
MSQ-A 13	Burden	2.23	1.25	0.37	0.37	**0.67**†
MSQ-A 14	Afraid	2.08	1.22	0.38	0.31	**0.62**†

Note. †Item-dimension correlation corrected for overlap (relevant item removed from its dimension for correlation). †Correlations hypothesized to be highest in same row. **Bolded** correlations are significantly larger (more than two standard errors) than the other correlations in the same row. MSQ-A RR (Role Restrictive Subscale); MSQ-A RP (Role Preventive Subscale); MSQ-A EF (Emotional Functioning Subscale);

Table 11

Correlations between Measures Administered at Baseline

	Pearson Correlation Coefficients (*r*)				
	MSQ-A RR	MSQ-A RP	MSQ-A EF	MSQ-A Total	HDI-A Total
Impaired Functioning due to Migraines					
PedMIDAS	.42**	.52**	.33**	.50**	.23*
	N=91	N=90	N=93	N=89	N=92
General Health-Related Quality of Life					
PedsQL Physical	-.21*	-.17	-.14	-.20*	-.31**
	N=93	N=92	N=95	N=91	N=94
PedsQL Psychosocial	-.30**	-.31**	-.12	-.29*	-.43**
	N=95	N=94	N=95	N=91	N=94
Psychological Symptoms					
YSR-Internalizing	.38**	.40**	.29**	.41**	.45**
	N=95	N=94	N=97	N=90	N=96
YSR-Externalizing	.16	.21*	.16	.20	.36**
	N=97	N=96	N=97	N=93	N=96

Note. * $p < .05$; ** $p < .01$;

MSQ-A (Migraine Specific Quality of Life Questionnaire Adolescent form); HDI-A (Headache Disability Inventory Adolescent form); MSQ-A RR (Role Restrictive Subscale); MSQ-A RP (Role Preventive Subscale); MSQ-A EF (Emotional Functioning Subscale); PedsQL (Pediatric Quality of Life Scale); PedMIDAS (Pediatric Migraine Disability Assessment Score); YSR-Internalizing (Internalizing scale of the Youth Self Report); YSR-Externalizing (Externalizing scale of the Youth Self Report); For all scales except for PedsQL, higher scores indicate greater disability; For PedsQL, lower scores indicate greater disability

Table 12

Correlations between MSQ-A and HDI-A at Follow-up with Daily Diary Data

	Pearson Correlation Coefficients (*r*)				
	MSQ-A RR	MSQ-A RP	MSQ-A EF	MSQ-A Total	HDI-A Total
Migraines per 30 days	.28* N=61	.30* N=61	.38** N=61	.34** N=61	.30* N=62
Average Migraine Severity	.30* N=62	.18 N=61	.15 N=61	.19 N=61	.38** N=62
Associated Symptom Severity	.30* N=63	.24† N=61	.34** N=61	.35** N=61	.19 N=62
Migraine Disability Hours	.42** N=61	.40** N=61	.43** N=61	.47** N=61	.39** N=61

Note. $p < .05$; **$p < .01$; †=relationship reaches significance ($p < .05$) if square root transformation of MSQ-A Role Preventive at follow-up is used in the analysis;

Only subjects reported to have had migraine attack in the previous 4 weeks were included in correlation analysis. All quality of life scores are from follow-up assessment.

MSQ-A (Migraine Specific Quality of Life Questionnaire Adolescent form); HDI-A (Headache Disability Inventory Adolescent form); MSQ-A RR (Role Restrictive Subscale); MSQ-A RP (Role Preventive Subscale); MSQ-A EF (Emotional Functioning Subscale); For MSQ-A and HDI-A, higher scores indicate greater disability; for migraine characteristics, higher scores indicate greater frequency and severity of migraines.

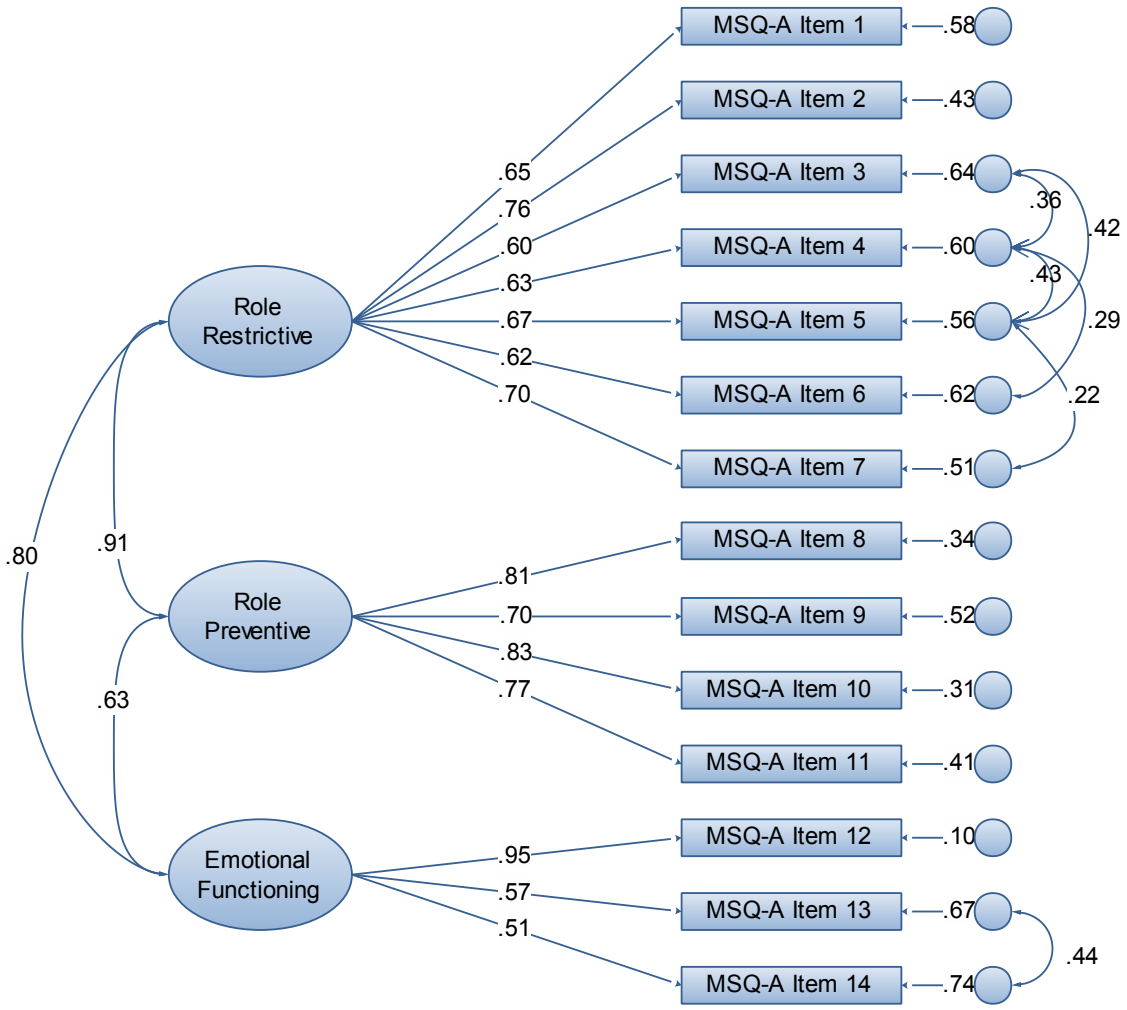


Figure 1: Three Factor Model of Migraine Specific Quality of Life questionnaire Adolescent form with Correlated Errors

Appendix A: Study Measures

Migraine Specific Quality of Life – Adolescent form (MSQ-A; Jhingran et al., 1998A; Jhingran et al., 1998B; Martin et al., 2000). MSQ-A consists of fourteen items, including seven items that are hypothesized to compose the Role Restrictive dimension (Items 1-7), four items for the Role Preventive dimension (Items 8-11), and three items for the Emotional Functioning dimension (Items 12-14). Items are answered based on how frequently given migraine-related behavior occurs on a five-point scale of "None of the time", "A little bit of the time", "Some of the time", "A good bit of the time", "Most of the time", and "All of the time". Consistent with scoring the adult version of MSQ-A, subscale scores were computed by summing up the items for each subscale and transforming the score to a 0 to 100 scale. A total quality of life score was computed from the sum of all items that was then transformed to a 0 to 100 scale. Higher total and subscale scores indicate greater migraine-related impairment. The transformation process was recommended by MSQ's authors (Martin et al., 2000) to allow each dimension score to reflect the percentage of the total possible score achieved (since 100 equals the highest score).

An initial investigation of the psychometric properties of MSQ-A was conducted by RTI Health Solutions (2007). Three focus groups with 25 adolescents were conducted in Atlanta, GA; Westerville, OH; and Memphis, TN. Teens were invited to read the MSQ-A instructions and answer the questions based on their recent migraine experiences. After completion of MSQ-A the moderators asked participants to comment on the clarity of the instructions for the instrument. Each MSQ-A item was then discussed to determine whether its content was relevant to the participants' experience. Finally, participants were

asked what, if any, migraine-specific impacts on their quality of life were omitted in the questionnaire.

Across all three groups, participants reported that the instructions for MSQ-A were easy to understand. Participants generally agreed that all items were relevant and addressed important domains of migraine impact. Participants agreed with the 3 domains of migraine-related quality of life measured by the MSQ-A (role-restrictive, role-preventive and emotional function) and no participant indicated that an area of impact was missing from the instrument. However, the participants also found it difficult to discriminate between "Some of the time" and "A good bit of the time" answer options on the MSQ-A. Some participants thought particular MSQ-A items were awkwardly worded and unclear, noting how the terms "fed up" (Item 12) and "felt full of energy" (Item 7) are not usually used in their peer groups.

Overall, the authors of the project concluded that the MSQ-A is appropriate for adolescents and suggested that recommendations from focus groups are taken into consideration and a second study be conducted to further refine the instrument and examine its construct validity (RTI Health Solutions, 2007). Although the scale structure of MSQ-A was never explored, the instrument has been used in several studies with adolescents (Cottrell et al. 2006; 2007; 2008; McDonald et al., 2011; Tkachuk et al., 2003). Cottrell et al. (2006) reported that MSQ-A has good internal consistency levels (.81 to .92) that were comparable to those reported for adult version of MSQ. The three subscales had moderate correlations with migraine frequency (r = .29-.56), while the Role Restrictive and Emotional Functioning were also moderately correlated with headache-related disability as recorded in the headache diary (r = .41-.56). Total MSQ-A

score has also been found to be sensitive to the effects of telephone-administered behavioral treatment and pharmacological management of adolescent migraines (Cottrell et al. 2007; McDonald et al., 2011).

Headache Disability Inventory Adolescent form (HDI-A; Jacobson et al., 1994; 1995). HDI-A was adapted from the adult version of the Headache Disability Inventory (Jacobson et al., 1994; 1995) for the present study. The adolescent form of the HDI consists of 25 items assessing difficulties in daily activities or emotional functioning that teens may be experiencing because of their headaches. Items on the HDI were re-written in age appropriate language based on informal feedback from adolescents undergoing migraine treatment through Nationwide Columbus Children's Hospital and input from members of the Ohio Headache Association. For example Item 13 "I am concerned that I am paying penalties at work or at home because of my headaches" became "I worry I lose out at work, school, or home due to headaches".

The HDI-A contains 25 items where the respondent is asked to rate the frequency of given migraine-related behavior or feeling on a three-point scale of "yes", "sometimes", or "no". For the adult version of the HDI, items are used to compute two subscales – Functional (the sum of items 2, 4, 7, 13, 15, 16, 17, 18, 19, 21, 24 and 25, transformed to a 0 to 100 scale) and Emotional (the sum of items 1, 3, 5, 6, 8, 9, 10, 11, 12, 14, 20, 22 and 23, transformed to a 0 to 100 scale). A total quality of life score is also computed from the sum of all 25 items (possible range of 0 to 100). Higher subscale and total scores on the HDI-A indicate greater headache-related impairment. However, because of lack of previous studies supporting the proposed factor structure of HDI, and

the fact that the adolescent version of the instrument has not been previously used, no hypothesis was made about its factor structure.

Pediatric Migraine Disability Assessment Score (PedMIDAS, Hershey et al., 2001). PedMIDAS was used to assess missed and/or interrupted activities and impaired performance due to migraines. The PedMIDAS is the most widely used and researched instrument for assessing disability related to migraines in adolescence and has consistently been shown to have good psychometric properties (Aykol et al., 2007; Hershey et al., 2004; Hershey, Kabbouche & Powers, 2010; Kröner-Herwig, Heinrich & Vath, 2010). It consists of 6 items that aim to assess the degree to which migraines are affecting day-to-day activity as indicated by days missed (i.e. "How many full days of school were missed in the last 3 months due to headaches?") or diminished functional status ("How many days in the last 3 months did you function at less than half your ability in school because of a headache") due to headaches. Higher score on PedMIDAS indicates greater migraine-related impairment. No subscales are obtained for the PedMIDAS. Adolescents with migraine have described PedMIDAS as clear and easy to use (Hershey et al., 2004). PedMIDAS scores have been found to be significantly correlated with migraine frequency ($r = 0.58$), duration ($r = 0.27$), and severity ($r = 0.23$) (Hershey et al., 2001). Similar results were found by Kröner-Herwig, Heinrich & Vath, (2010).

The Pediatric Quality of Life Inventory (PedsQL; Varni, Seid & Kurtin, 2001). PedsQL was used to assess general health-related quality of life. The PedsQL contains 23 items grouped into two subscales, including Physical (8 items) and Psychosocial (15 items). The Psychosocial Health subscale can be further broken down into 3 scales,

including Emotional, Social, and School Functioning. Lower scores on PedsQL indicate greater impairment. The PedsQL total score and its Physical and Psychosocial subscales have been validated for use for children and adolescents with migraine (Connelly & Rapoff, 2006). PedsQL total and subscale scores were found to have good internal consistency (Cronbach's α =.88-92) and were correlated with measures of migraine severity (r = -.38 to -.57) and missed activities due to migraines (r = -. 32 to -.49) (Connelly & Rapoff, 2006).

Youth Self Report (YSR; Achenbach, 1991; 2001). The YSR provides self-ratings of 20 competence items that measure the teen's participation in hobbies, games, sports, jobs, chores, friendship, and activities, and 112 items that are used to compute two subscales called Externalizing (assessing behavioral problems, inattention, aggression, etc) and Internalizing (assessing depression, anxiety and somatic complaints). Higher scores on the Internalizing and Externalizing scales indicate higher number of symptoms. For Externalizing Problems, and Internalizing Problems, T scores less than 60 are considered in the normal range, 60-63 represent borderline scores, and scores greater than 63 are in the clinical range (Achenbach, 1991).The YSR has a test-retest reliability ranging from 0.47 - 0.79 and a Cronbach alpha range of 0.71 - 0.95. It has been consistently found to have good construct validity (Achenbach, 1991; 2001; Ferdinand, 1995; Song, Singh & Singer, 1994).

Electronic Daily Diary (PalmOS; Holroyd & Chen, 2000). The PalmOS is a handheld computer capable of storing the daily entries of the participants and uploading them to centralized database. Entries include start and end time of headache, headache type, severity of headaches and of associated symptoms of migraine, and number of

hours where adolescents felt disabled by their migraines. Migraine frequency or number of migraines per 30 days (with the requirement that distinct episodes be separated by 24 hour pain free period), migraine severity (average severity of migraines; range 0-3) and associated symptom severity (the sum of the three average severity ratings provided for nausea, phonophobia and photophobia provided for each migraine; range 0-9) were computed using data from PalmOS. The PalmOS also assesses headache-related impairment by surveying number of hours teens felt "totally disabled" (unable to perform any school, work or social/recreational activities) and "partially disabled" (at least 50% impaired functioning in above activities). From this data, a total migraine-disability hours score (the sum of hours disabled and .5 x hours impaired) was computed.

MSQ -Adolescent

Date:_____ ID#:_____

Site:_____

Please check only one answer for each question. Be sure to answer all questions.

When answering, please think about *all migraines* you have had *in the past 4 weeks.*

1. **In the <u>past 4 weeks</u>, how often have migraines <u>affected</u> how well you dealt with people close to you? (Select <u>one</u> answer).**

   - ☐ **$_1$None of the time**
   - ☐ **$_2$A little bit of the time**
   - ☐ **$_3$Some of the time**
   - ☐ **$_4$Most of the time**
   - ☐ **$_5$All of the time**

2. **In the <u>past 4 weeks</u>, how often have migraines <u>interfered with</u> fun activities (like hobbies, hanging out with friends, etc.)? (Select <u>one</u> answer).**

   - ☐ **$_1$None of the time**
   - ☐ **$_2$A little bit of the time**
   - ☐ **$_3$Some of the time**
   - ☐ **$_4$Most of the time**
   - ☐ **$_5$All of the time**

3. **In the <u>past 4 weeks</u>, how often has it been hard doing school, work, or other tasks due to migraines? (Select <u>one</u> answer).**

   - ☐ **$_1$None of the time**
   - ☐ **$_2$A little bit of the time**
   - ☐ **$_3$Some of the time**
   - ☐ **$_4$Most of the time**

☐ $_5$**All of the time**

4. **In the <u>past 4 weeks</u>, how often did migraines <u>keep you</u> from getting as much done at school, work, or home as you would have liked? (Select <u>one</u> answer).**

   ☐ $_1$**None of the time**

   ☐ $_2$**A little bit of the time**

   ☐ $_3$**Some of the time**

   ☐ $_4$**Most of the time**

   ☐ $_5$**All of the time**

5. **In the <u>past 4 weeks</u>, how often did migraines <u>limit</u> your ability to concentrate on school, work, or other daily activities? (Select <u>one</u> answer).**

   ☐ $_1$**None of the time**

   ☐ $_2$**A little bit of the time**

   ☐ $_3$**Some of the time**

   ☐ $_4$**Most of the time**

   ☐ $_5$**All of the time**

6. **In the <u>past 4 weeks</u>, how often have migraines <u>left you too tired</u> to do school, work, or other tasks? (Select <u>one</u> answer).**

   ☐ $_1$**None of the time**

   ☐ $_2$**A little bit of the time**

   ☐ $_3$**Some of the time**

   ☐ $_4$**Most of the time**

   ☐ $_5$**All of the time**

7. **In the <u>past 4 weeks</u>, how often have migraines <u>limited</u> the number of days you have felt energetic? (Select <u>one</u> answer).**

   ☐ $_1$**None of the time**

   ☐ $_2$**A little bit of the time**

   ☐ $_3$**Some of the time**

☐ $_4$**Most of the time**

☐ $_5$**All of the time**

8. **In the <u>past 4 weeks</u>, how often have you had to <u>miss</u> school, work, or other activities because you had a migraine? (Select <u>one</u> answer).**

   ☐ $_1$**None of the time**

   ☐ $_2$**A little bit of the time**

   ☐ $_3$**Some of the time**

   ☐ $_4$**Most of the time**

   ☐ $_5$**All of the time**

9. **In the <u>past 4 weeks</u>, how often did you <u>need help</u> with everyday chores or other tasks when you had a headache? (Select <u>one</u> answer).**

   ☐ $_1$**None of the time**

   ☐ $_2$**A little bit of the time**

   ☐ $_3$**Some of the time**

   ☐ $_4$**Most of the time**

   ☐ $_5$**All of the time**

10. **In the <u>past 4 weeks</u>, how often did you have to <u>stop</u> schoolwork, your job, or other tasks to deal with a migraine? (Select <u>one</u> answer).**

    ☐ $_1$**None of the time**

    ☐ $_2$**A little bit of the time**

    ☐ $_3$**Some of the time**

    ☐ $_4$**Most of the time**

    ☐ $_5$**All of the time**

11. **In the <u>past 4 weeks</u>, how often were you not able to go to parties or out with friends because you had a migraine? (Select <u>one</u> answer).**

☐ $_1$**None of the time**

☐ $_2$**A little bit of the time**

☐ $_3$**Some of the time**

☐ $_4$**Most of the time**

☐ $_5$**All of the time**

12. In the <u>past 4 weeks</u>, how often have you <u>felt</u> frustrated because of your migraines? (Select <u>one</u> answer).

☐ $_1$**None of the time**

☐ $_2$**A little bit of the time**

☐ $_3$**Some of the time**

☐ $_4$**Most of the time**

☐ $_5$**All of the time**

13. In the <u>past 4 weeks</u>, how often have you <u>felt</u> you were a burden on others due to migraines? (Select <u>one</u> answer).

☐ $_1$**None of the time**

☐ $_2$**A little bit of the time**

☐ $_3$**Some of the time**

☐ $_4$**Most of the time**

☐ $_5$**All of the time**

14. In the <u>past 4 weeks</u>, how often have you been <u>afraid</u> of letting others down because of migraines? (Select <u>one</u> answer).

☐ $_1$**None of the time**

☐ $_2$**A little bit of the time**

☐ $_3$**Some of the time**

☐ $_4$**Most of the time**

☐ $_5$**All of the time**

HDI – Adolescent

Date_____

ID#_____

Site:_____

This scale asks about problems you may have due to headaches. Please circle "NO", "SOMETIMES", or "YES" for each item.

NO SOMETIMES YES 1. I feel disabled due to headaches.

NO SOMETIMES YES 2. I feel limited in my activities due to headaches.

NO SOMETIMES YES 3. No one knows the effect headaches have on me.

NO SOMETIMES YES 4. I limit my fun, like sports or hobbies, due to headaches.

NO SOMETIMES YES 5. My headaches make me mad.

NO SOMETIMES YES 6. At times I feel I will "lose it" due to headaches.

NO SOMETIMES YES 7. Due to headaches I spend less time with friends**.**

NO SOMETIMES YES 8. People do not know what I go through with my headaches.

NO SOMETIMES YES 9. My headaches are so bad I feel I may go crazy.

NO SOMETIMES YES 10. Headaches change my view of the world.

NO SOMETIMES YES 11. I am scared to go out when a headache starts.

NO SOMETIMES YES 12. I feel stressed due to headaches.

NO SOMETIMES YES 13. I worry I lose out at work, school, or home due to headaches.

NO SOMETIMES YES 14. My headaches put stress on my relationships.

NO SOMETIMES YES 15. I avoid people when I have a headache.

NO SOMETIMES YES 16. I get tense due to headaches.

NO SOMETIMES YES 17. I do not enjoy social events due to headaches.

NO SOMETIMES YES 18. I feel cranky due to headaches.

NO SOMETIMES YES 19. My headaches make it hard to get what I want in life.

NO SOMETIMES YES 20. I can not think clearly due to headaches.

NO SOMETIMES YES 21. I do not like to travel due to headaches.

NO SOMETIMES YES 22. My headaches make me feel confused.

NO SOMETIMES YES 23. My headaches make me frustrated.

NO SOMETIMES YES 24. I find it hard to read or study due to headaches.

NO SOMETIMES YES 25. It is hard to focus on things other than my headaches.

Appendix B: Study Informed Consent Forms

THE PERSON IN CHARGE OF THIS STUDY: Dr. Ann Pakalnis

Other Study Doctors: Dr. Connie Cottrell, R.N.

SUBJECT'S NAME: _____ DATE OF BIRTH: _____

We invite you to be in a research study at Children's Hospital. We want you to read and understand some things about being in this research study:

- **It's o.k. to say "no" if you don't want to be in the study.**
- **You are allowed to quit being in the study any time.**
- **We have to explain the study to you so you can understand it. You can ask questions.**

1. WHY ARE WE DOING THIS RESEARCH STUDY?

We are doing this study is make questionnaires that will tell us about headaches in adolescents like you. Scientists need to have ways to measure the things they are interested in. These measures must be tested to make sure they measure what they are supposed to. We are asking you to fill out these forms to test them. We also have to make sure the forms measure the same thing every time someone fills them out. That is why we are asking you to fill out the forms two times.

We are also doing this study is to find out what things may affect your headaches. That is, what things may make them better and what things may make them worse.

2. WHAT WILL HAPPEN DURING THE STUDY?

You will be asked to spend about 1 1/2 hours answering questions about your headaches on the first visit.

We will ask you to keep a diary of your headaches for the 4 weeks between the two visits. We will ask what time your headaches start and end. We will ask how much time your headaches keep you from doing the things you like to do. You will also be asked to tell us what medicines you take when you have headaches.

4. WHAT SHOULD I KNOW ABOUT THE MEDICINE?

You will continue to use the same medicine you use to treat your headaches now. You will not be asked to take any different medicine for this study.

5. WHAT ELSE DO I NEED TO KNOW?

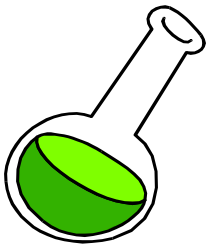
You will be asked to answer lots of questions. The questions will be about your health, your headaches and how headaches affect you. You will also be asked questions about how you think and feel. There are no right or wrong answers to any of the questions. You can skip any questions you do not want to answer. **If your answer to any question suggests that you may be thinking of hurting yourself or others we are required by law to do something to do to protect you or the person you are planning to hurt. This may include telling Dr. Pakalnis or Dr. Butz, the psychologist.**

There may be no benefit for you to be in the study.

Sometimes doctors write papers about research studies when they are done. If a paper is written about this research study, your name won't be used in it. We will keep your medical information private. People who work for the Clinical Study Center, Children's Research Institute, the study sponsor, and government agencies will be able to look at your medical information.

There is no cost to you or your parents to be in this study. You will be compensated for the amount of time you spend and any discomforts you may have while participating in this study. You will get $20 each time you fill out the forms. You will also get $10 for keeping a daily headache diary for 4 weeks.

I have read this form. I have had a chance to ask questions about things I don't understand. I want to be in this research study and understand what will happen to me.



_____ _____
Signature of the Subject Date

_____ _____
Signature of the Person Obtaining Assent Date

_____ _____
Signature of the Principal Investigator Date

Assent will be obtained by
a Study Doctor or Study Nurse

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

STUDY TITLE: Validation of Migraine Specific Assessment Measures for Adolescents

STUDY SPONSOR: Neurology Department at Children's Hospital and Ohio University

STUDY DOCTOR: Dr. Ann Pakalnis

CONTACT TELEPHONE NUMBER: 614-722-2000 (24 hours a day, 7 days a week)

SUBJECT'S NAME: _____ DATE OF BIRTH: _____

NOTE: The words "you" and "your" are used in this consent form. These words refer to the study volunteer whether a child or an adult.

1) INTRODUCTION

We invite you to be in this research study because your child has headaches. Please learn enough about this research study, its risks and benefits, to decide whether you should agree to participate. We must explain the study to you, and give you a chance to ask questions about anything you do not understand. This process is called "informed consent". It is up to you to choose if you want to be in this study. You may refuse to be in this study or quit this study at any time, and standard medical care will still be available here or at a doctor of your choice without a penalty or loss of benefits to you. It is important to understand that there may not be any benefit from being in this study, but we may learn something that could help others.

Before agreeing to participate, it is important to read and understand the study information in this consent form. By signing the consent form, you agree to be in this study. If this study involves a child between 9 and 18 years of age, he/she must also agree to be in the study by signing an Assent form or on the assent line of this form. You will be given a signed and dated copy of the consent and the assent form.

2) WHY ARE WE DOING THIS RESEARCH STUDY?

We are doing this study to develop questionnaires that can be used to assess headaches, their pain, and the difficulties that can occur with headaches in adolescents (for example, feeling sad, feeling mad, feeling misunderstood).

We are also doing this study is to find out what may affect a child's headaches. That is, what things may make headaches better and what things may make headaches worse. We do this to find out what we should focus our attention on to improve adolescents'

headaches. For example, if we find out that headaches are better when teens eats regular meals, then we can work with teenagers on ways to eat regularly.

3) WHERE WILL THE STUDY BE DONE AND HOW MANY SUBJECTS WILL TAKE PART?

This study will be done at Children's Hospital, the Dublin Close to Home. About 200 subjects will take part in this study here in Ohio. We hope to have about 150 subjects here at this hospital.

4) WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

This study will last 4 weeks and will require 2 visits to the doctor's office.

Visit 1 - Screening Visit

This visit will take about 1 1/2 hours. You will be asked to fill out forms about medical history, past and present diseases, allergies and medications. It is important to tell the Study Doctor all the information you can. You will answer questions about both you and your child's health and illnesses. You will spend about 30 minutes completing questionnaires. Some of the questionnaires will ask about you and some will ask about your child. These questions focus on physical symptoms as well as on thoughts and feelings of both you and your child. Your child is being asked to complete similar questionnaires, though they will have several more questionnaires to complete.

4-week Daily Headache Diary Recording

This will take your child 1-5 minutes daily over the next 4 weeks. The headache diary asks questions such as when headaches start and end, headache intensity, and whether or not there is any nausea or sensitivity to light or sound when your child has a headache. The diary also asks your child to record the number of hours headaches interfere with the things s/he likes to do. Your child will be asked to write down the medicine s/he takes for his/her headaches.

Visit 2 – Re-test Visit

This visit will take 30 to 60 minutes. You and your child will be asked to complete some of the same questionnaires you completed at the first visit.

This study does not involve any type of treatment or procedures.

5) WHAT BAD THINGS CAN POSSIBLY HAPPEN DURING THIS STUDY?

There are no foreseeable risks to this study. There may be some emotional discomfort when responding to questions of a personal nature on some questionnaires. This risk is very minimal.

There may be other risks of being in this research study which are not known at this time.

6) WHAT GOOD THINGS CAN POSSIBLY HAPPEN DURING THIS STUDY?
The benefits participants will receive are the satisfaction that they are contributing to the understanding of headache disorders and may be helping other headache sufferers. You may learn more about the pattern of your headaches by keeping the daily diary.

7) WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?
In the unlikely event that being in this study causes an injury, Children's Hospital will provide medical care. You may have to pay for the cost of this care. This does not mean that you give up any of your rights under state or federal laws to ask for this care to be paid by someone else.

8) OTHER IMPORTANT INFORMATION
You will not be told the results of this study at a later date.

The study doctor is not being paid for the time and knowledge needed to do this study.

Being in more than one research study at the same time may cause problems. Please tell the study doctor about being in any other research study so a decision can be made about being in more than one study at the same time

9) SPECIAL INFORMATION ABOUT PREGNANCY:
Not applicable to this study.

10) WHAT WILL HAPPEN IF NEW INFORMATION IS FOUND OUT ABOUT THE DRUG OR TREATMENT?

Not applicable to this study.

11) WHAT OTHER TREATMENTS OR OPTIONS ARE THERE?
Since this study does not involve any medicine or treatment, you will need to talk to your child’s doctor about treatment options available for your child’s headaches.

12) WHAT WILL HAPPEN IF I DO NOT FINISH THIS STUDY?
It is your choice to be in this study or to stop at any time. If you decide to stop being in this study, it is OK, but you must call the study doctor or the study coordinator. If you stop being in the study, there will not be a penalty or loss of benefits to which you are otherwise entitled. There are no medical issues regarding stopping.

If at any time the study doctor believes participating in this study is not the best choice of care, the study may be stopped. If the study instructions are not followed, participation in the study may also be stopped. If unexpected medical problems come up, the study doctor may decide to stop your participation in the study.

13) WILL THERE BE ANY COSTS TO ME?

It will not cost you anything to be in this study. Your only cost will be the cost of parking at each study visit. For your time and travel expenses, your child will be paid $20 per study visit. In addition, your child will receive an additional $10 for completing the daily diary. You will be paid $10 for the first time you complete the questionnaires and $15 for the second time. Thus, the total amount of compensation available upon completion of the study is $75 ($25 for parent/caregiver involvement and $50 for the child's involvement.)

14) HOW WILL MY STUDY INFORMATION BE KEPT PRIVATE?

Information collected for this study will be kept confidential to the extent allowed by law. Information used and/or disclosed (shared with someone outside of Children's Hospital) may include information that can identify you. This is called "protected health information" or PHI. By agreeing to be in this study, you are giving permission or authorizing Dr. Palkanis (Study Director) and her study staff to collect, use, and disclose your PHI for this research study. Information collected is the property of Dr. Palkanis and Ohio University. In the event of any publication regarding this study, your identity will not be revealed.

- People or Companies authorized to use, disclose, and receive PHI collected or created by this research study:

Dr. Ann Palkanis and the study staff
Ohio University Institutional Review Board
Children's Hospital Institutional Review Board
National Institutes of Health

Because of the need to give information to these people, absolute confidentiality cannot be guaranteed. Information given to these people may no longer be protected by federal privacy rules.

- PHI that may be used or disclosed:

Your and your child's name, age, race, and sex.
Your and your child's responses on the questionnaires

- Reason(s) why the use or disclosure is being made:

We need to know who you are so that we can compare the questionnaires you complete at the first visit to the ones you fill out at the second visit. We also need to compare your questionnaires with those your child completes. We need to know your and your child's age, sex, and race as these may be related to your child's headaches.

If your or your child's answer to any question suggests that you or he/she may be thinking of hurting yourself or others we are required by law to report that information to appropriate people. This may include telling Dr. Pakalnis or Dr. Butz, the psychologist.

- If you have a bad outcome or adverse event from being in this study, the Study Director and staff or other health care providers may need to look at your entire medical records.

The PHI collected or created under this research study will be used/disclosed as needed until the end of the study. The records of this study will be kept for an indefinite period of time.

You may decide not to authorize the use and disclosure of your PHI, however, if it is required for this study, you will not be able to be in this study. If you agree to be in this study and later decide to withdraw, you may also withdraw your authorization to use your PHI. This request must be made in writing to the Study Director. If you withdraw your authorization, no new PHI may be collected and the PHI already collected may not be used unless it has already been used or is needed to complete the study analysis and reports.

Dr. Pakalnis keeps a database of all subjects who participate in a research study. This database is used to contact people about future studies. Only Dr. Pakalnis and her staff have access to this database. The database will not be disclosed or sold to others outside Children's Hospital.

Please initial:

____ I want to be contacted about future research studies.

____ I do not want to be contacted about future research studies.

15) WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have questions about anything while on this study, you have 24-hour access to talk to your study doctor at (614) 722-2000. If you have questions about your child's diary, please call (614) 839-3254.

If you have questions or are worried about your rights as a research volunteer, please call (614) 722-2708, Children's Hospital, Institutional Review Board, (IRB, a committee that reviews all research in humans at Children's Hospital).

Subject's Name _____

Date of Birth_____

SUBJECT or SUBJECT'S LEGAL REPRESENTATIVE STATEMENT

I have been given a copy of the Children's Hospital Notice of Privacy Practices. I understand that my right to my patient information that is created or collected by Children's Hospital in the course of this research can be temporarily suspended for as long as the research is in progress. I also understand that my right to access will be reinstated upon completion of this research.

I agree to participate in this study. I will be given a copy of this consent form with all the signatures for my own records.

CONSENT SIGNATURES

_____ _____

SUBJECT or SUBJECT'S LEGAL REPRESENTATIVE DATE SIGNED

SUBJECT or SUBJECT'S LEGAL REPRESENTATIVE DATE SIGNED

PERSON OBTAINING CONSENT DATE SIGNED

I certify that I have explained the research, it's purposes, and the procedures to the subject or subject's legal representative before requesting their signature.

STUDY INVESTIGATOR DATE SIGNED

Appendix C: Supplemental Analyses

Univariate Outliers

Frequency analyses and Box Plot figures were used to screen for univariate outliers. One participant reported 14 migraine episodes during the 4 month period. Another participant reported 51.2 migraine disability hours. These two cases had z-scores greater than 3.3, which suggests these variables are outliers (Tabachnick & Fidell, 2001). Although rare in this sample, these reports are not unusual for adolescents with episodic migraine, and fit with study inclusion criteria (<15 migraine episodes per month). Therefore these cases were not removed from the analysis.

Multivariate Outliers

Mahalanobis Distance value was also computed to determine multivariate outliers. Nineteen variables were entered into the analysis, and a $\chi^2(13) = 34.5$, $p<.001$ was used as the cutoff. The variables were baseline and follow-up MSQ-A and HDI-A total scores, PedMIDAS, PedsQL, Internalizing and Externalizing scales on the YSR, migraines per 30 days, average migraine severity, average severity of associated symptoms of migraine, and migraine disability days. There were no multivariate outliers detected.

Sample Size Necessary for Factor Analysis of the Migraine Specific Quality of Life Questionnaire, Adolescent form and the Headache Disability Inventory, Adolescent Form

Research has demonstrated that the general rules of thumb regarding the minimum sample size necessary for factor analysis are not valid and useful (MacCallum et al., 1999). Instead, what has been recommended is that individual studies consider the

multiple criteria when determining sample size necessary for valid factor analysis of their particular instruments. The minimum sample size in factor analysis is generally thought to be dependent on the subjects-to-variables ratio, degree of overdetermination of the model, and communality of the variables (MacCallum et al., 1999). The subject to variables ratio (STV) is simply the number of participants per variable in the study. STV of 5 or higher has been recommended by multiple authors (Gorsuch, 1983; MacCallum et al., 1999). STV of 3 or higher has also been described as acceptable by some authors, but only in samples of 250 or larger (Arrindell & van der Ende, 1985).

The communality measures the percent of variance in a given variable explained by all the factors jointly and may be interpreted as the reliability of the indicator (MacCallum et al., 1999). It has been suggested that if communalities are high (.5 or higher), recovery of population factors in sample data is very good, even in small ($N<100$) samples.

Finally, a model is considered overidentified if there are more knowns than unknowns in the model. Preacher & MacCallum (2002) recommended that the factor-to-variable ratio be used as a measure of overdetermination of a model. At least 3 variables per factor and preferably 6-7 variables per factor have been recommended for a model to be overidentified, particularly when communalities are low (.4 or lower) (MacCallum et al., 1999).

Using the criteria described above, preliminary exploration of data available for factor analysis was performed to determine whether the number of participants available in this sample was adequate for factor analysis of the Migraine Specific Quality of Life Questionnaire, Adolescent form (MSQ-A) and the Headache Disability Inventory,

Adolescent form (HDI-A). Data from this analysis suggested that a MSQ-A model with three factors is over-identified, and that its subject-to-variables ratio is good (STV=6.9). The communalities of the 14 items on MSQ-A are listed in Supplemental Table 1. Communalities represent the proportion of variation in individual MSQ-A items explained by the three postulated factors, including Role Restrictive (items 1-7), Role Preventive (items 8-11) and Emotional Functioning (items 12-14). All item communalities were greater than .35, and eight were greater than .50 ($\bar{x}$ = .52). According to MacCallum et al. (1999), when item communalities are in the range of .50, and factors are well-determined, a sample of 100 participants is sufficient to achieve good recovery of population factors. Similar recommendations have been made by Gorsuch (1983). Based on these studies, the current sample size of 97 participants is marginally adequate for confirmatory factor analysis of MSQ-A to be performed.

The Kaiser-Meyer-Olkin Measure of Sampling Adequacy for HDI-A was .79, and a HDI-A model with two factors is over-identified, indicating that sampling was adequate to perform exploratory factor analysis of HDI-A. However, subject-to-variables ratio was low with the current sample (N=97; STV=3.8). The communalities of the 25 items on HDI-A are listed in Table Supplemental Table 2. All communalities were below .5 ($\bar{x}$ = .25) and four items had communalities lower than .10. Previous studies have suggested that when low subject-to-variables ratio and low item communalities are observed, samples of 150-300 are recommended to in order to achieve good recovery of population factors even when there is high overdetermination of factors (Clif & Penel, 1967; Velicer & Fava, 1998; MacCollum et al., 1999). Based on these findings, low sample size likely limits the interpretability of factor analysis of HDI-A.

Supplemental Table 1

Communalities for Individual Items on MSQ-A

Variable	Communality
MSQ-A Q1	.362
MSQ-A Q2	.536
MSQ-A Q3	.470
MSQ-A Q4	.541
MSQ-A Q5	.566
MSQ-A Q6	.421
MSQ-A Q7	.506
MSQ-A Q8	.684
MSQ-A Q9	.479
MSQ-A Q10	.679
MSQ-A Q11	.577
MSQ-A Q12	.763
MSQ-A Q13	.415
MSQ-A Q14	.354

Note: MSQ-A (Migraine Specific Quality of Life Questionnaire – Adolescent form)

Supplemental Table 2

Communalities for Individual Items on HDI-A

Variable	Communality
HDI-A Q1	.144
HDI-A Q2	.294
HDI-A Q3	.071
HDI-A Q4	.240
HDI-A Q5	.176
HDI-A Q6	.276
HDI-A Q7	.209
HDI-A Q8	.116
HDI-A Q9	.190
HDI-A Q10	.185
HDI-A Q11	.086
HDI-A Q12	.441
HDI-A Q13	.287
HDI-A Q14	.387
HDI-A Q15	.165
HDI-A Q16	.448
HDI-A Q17	.431
HDI-A Q18	.353
HDI-A Q19	.309
HDI-A Q20	.280
HDI-A Q21	.095
HDI-A Q22	.223
HDI-A Q23	.498
HDI-A Q24	.088
HDI-A Q25	.127

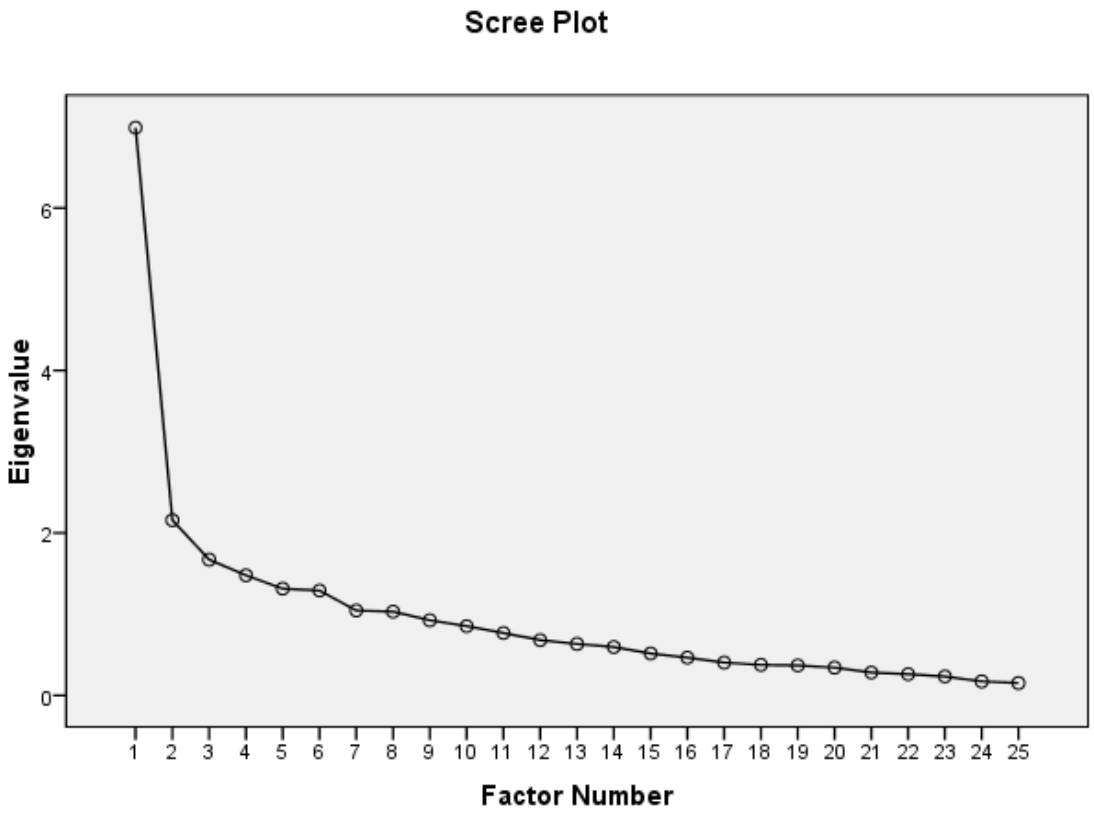
Note: HDI-A (Headache Disability Inventory – Adolescent form)

Supplemental Table 3

Initial Eigenvalues and Percentage of Variance Explained by Each Component for Exploratory Factor Analysis of HDI-A

	Initial Eigenvalues		
Component	Total	% of Variance	Cumulative %
1	6.988	27.953	27.953
2	2.158	8.630	36.584
3	1.671	6.686	43.269
4	1.478	5.912	49.181
5	1.313	5.252	54.434
6	1.290	5.161	59.594
7	1.046	4.183	63.777
8	1.031	4.123	67.900
9	.925	3.699	71.600
10	.852	3.408	75.008
11	.767	3.068	78.076
12	.680	2.721	80.798
13	.633	2.532	83.329
14	.596	2.382	85.712
15	.516	2.065	87.777
16	.465	1.859	89.636
17	.404	1.615	91.251
18	.376	1.504	92.755
19	.368	1.472	94.227
20	.342	1.369	95.595
21	.281	1.125	96.721
22	.261	1.044	97.765
23	.234	.935	98.700
24	.173	.690	99.390
25	.153	.610	100.000

Note. Extraction Method: Maximum Likelihood.



Supplemental Figure 1: *Scree Plot of the Eigenvalues Associated With the Eight Factors of HDI-A*

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