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## Long-Term Outcomes in Juvenile Fibromyalgia (JFM) Patients with Early Reports of Potentially Traumatic Events (PTEs)

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Long-Term Outcomes in Juvenile Fibromyalgia (JFM) Patients with Early Reports of Potentially  
Traumatic Events (PTEs)

A Thesis Presented in  
Partial Fulfillment of the  
Requirements for the Degree of Master of Arts

By

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Date: February 19, 2019

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### **Biography**

The author was born in Birmingham, United Kingdom, December 18, 1991. She graduated from Lakota East High School in Liberty Township, Ohio. She received her Bachelor of Arts degree from Miami University in 2014.

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### **Abstract**

Juvenile Fibromyalgia (JFM) is a pediatric chronic pain condition characterized by widespread musculoskeletal pain and multiple tender points. JFM impacts individuals both physically and mentally with symptoms including frequent headaches, chronic fatigue, decreased physical activity, anxiety, and depression. The impact of potentially traumatic events (PTEs) on the JFM population is poorly understood in the literature. However, it is well understood that exposure to PTEs are commonly associated with increased psychopathology and somatic symptoms. It is important to understand whether individuals with a combination of PTEs and JFM are placed at greater risk for negative long-term outcomes. This study sets out to gain an understanding of the types of PTEs that are experienced by a sample of youth diagnosed with JFM. Additionally, utilizing data over an eight-year time period, long-term outcomes in youth with JFM and PTEs were explored through a dose-response model. Results found that more than half of the sample endorsed exposure to a PTE. A dose-response relationship was observed with PTEs and JFM symptom severity. Conversely, PTEs did not predict depression, average level of pain, pain locations, physical function or role limitations due to physical problems. Similarly, PTEs did not predict health care utilization (outpatient visits, radiological scans, and emergency department visits). Results suggest that PTEs are complex and require additional research to understand the extent to which PTEs impact youth with chronic pain. Preliminary findings show a significant relationship between PTEs and JFM symptom severity, however, the mechanisms that influence this relationship is not well understood. Thus, future work should focus on identifying the mechanisms that influence this relationship in order to better understand this complex subgroup.

## **Introduction**

Juvenile Fibromyalgia (JFM) is a common pediatric pain condition characterized by widespread musculoskeletal pain. Patients with JFM experience fatigue, headaches, psychomotor retardation, anxiety, depression, and many other symptoms afflicting youth both mentally and physically. Limited literature exists examining patients with JFM and a history of trauma or potentially traumatic events (PTEs). Exposure to PTEs places both children and adults at risk for increased psychopathology and psychosomatic symptoms therefore it is important to gain a richer understanding of how PTEs in combination with a chronic pain condition can impact an individual over time. This current study sets out to explore the clinical profiles of patients with JFM and early reports of PTEs. Utilizing data from a longitudinal study stemming over an eight-year time period (initial assessment to final follow-up), the long-term physical and psychological outcomes of individuals with JFM and PTEs will be examined.

### **Juvenile Fibromyalgia**

JFM is a common rheumatologic pain condition characterized by chronic widespread musculoskeletal pain and associated symptoms such as chronic fatigue, multiple tender points, and headaches (Yunus & Masi, 1985). The diagnostic criteria for JFM as proposed by Yunus and Masi (1985) include: widespread pain at 3 or more different locations for 3 or more months with an absence of an underlying condition, at least five distinct tender points observed upon manual palpations, and at least 3 additional symptoms such as headaches, irritable bowel syndrome, numbness or tingling in the extremities, or sleep disturbance. It is estimated to affect 2-7% of school-aged youth, specifically adolescent girls (Mikkelsen, Salminen, & Kautiainen, 1997). Although the etiology of JFM is unknown, some of the common symptoms include: fatigue, chronic headaches, anxiety, pain modulated by physical activity, and multiple tender points (Anthony & Schanberg, 2001). It is not so much the pain intensity alone that negatively

impacts functioning but rather the constellation of symptoms that impacts quality of life. This population is commonly afflicted with chronic fatigue. Specifically, a co-morbid diagnosis of JFM occurred in 29.6% of children who had a prior diagnosis of chronic fatigue syndrome (Bell, Bell, & Cheney, 1994). A likely contributing factor to chronic fatigue is an inconsistent sleep pattern which is commonly observed in patients with JFM; 43% of patients in Brazil reported being unable to achieve restorative sleep (Liphaus, Campos, Silva, & Kiss, 2001). Similarly, in a study examining the efficacy of a cognitive behavioral intervention (CBT), data from the initial evaluation showed 90% of youth with JFM reported sleep difficulty on the Pittsburgh Sleep Quality Index.

The JFM population is generally more vulnerable to emotional distress with 71.2% of patients meeting criteria for a lifetime psychiatric diagnosis (Kashikar-Zuck, Parkins, et al., 2008). In a study conducted across four different children's hospitals, 57.5% of patients with JFM had an anxiety disorder diagnosis (Kashikar-Zuck, Parkins, et al., 2008). In addition to anxiety, depressive symptoms are common in JFM patients. In a study assessing the prevalence of JFM in an urban population, youth with JFM had significantly more depressive symptoms endorsed on the Children's Depression Inventory (CDI) compared to those without JFM (Durmaz et al., 2013). Though youth with chronic migraines had slightly higher levels of pain intensity compared to patients with JFM (5.48 versus 5.36 respectively), those with JFM had poorer school, social, physical and emotional functioning (Kashikar-Zuck et al., 2013). In addition to increased psychopathology, pain, fatigue, and decreased quality of life, patients with JFM experience school difficulties. Many adolescents with JFM are subject to missing school thus impeding developmental expectations. In a study conducted by Kashikar-Zuck and colleagues (2010) examining adolescents with juvenile primary fibromyalgia syndrome (JPFS), over 12% of school-aged children were homeschooled (Kashikar-Zuck, Johnston, et al., 2010).

Those who were enrolled in conventional schooling were missing, on average, 2.9 days per month (Kashikar-Zuck, Johnston, et al., 2010).

### **PTEs**

Potentially traumatic events (PTEs) are experiences such as those defined by Criterion A.1 for Post-Traumatic Stress Disorder (PTSD) the DSM-IV which includes exposure to (Association, 1994) a traumatic event in which the person experienced, witnessed, or was confronted with an event(s) that involved actual or threatened death or serious injury, or threat to physical integrity of self or others. Updated Criterion A for PTSD in the DSM 5 (American Psychiatric Association, 2013) includes exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways: 1) directly experiencing the traumatic event(s), 2) witnessing, in person, the event(s) as it occurred to others, 3) learning that the traumatic event(s) occurred to a close family member or close friend (in cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental), or 4) experiencing repeated or extreme exposure to aversive details of the traumatic event(s). For the purpose of this study, DSM-IV PTSD criteria will be used as the corresponding measure, the Kiddie Schedule for Affective Disorders, is based on DSM-IV criteria.

Not all adverse events have a detrimental impact on an individual. There are many factors that influence whether or not such events develop into a trauma. However, this inclusive definition allows researchers to understand the impact of a broader list of events and gain an understanding of how these events can potentially negatively impact an individual. An estimated 33% of youth in middle childhood and adolescence have experienced at least one PTE in their lifetime (Costello, Erkanli, Fairbank, & Angold, 2002). While limited literature exists examining early childhood exposure, Briggs-Gowan (2010) estimate by 24-48 months 26.3% of young children have been exposed to at least one PTE (Briggs-Gowan, Ford, Fraleigh,

McCarthy, & Carter, 2010). Exposure to potentially traumatic events (PTEs) in late adolescence and young adulthood have been strongly associated with increased psychopathology (Briggs-Gowan et al., 2010; Copeland, Keeler, Angold, & Costello, 2007) with exposure most closely linked to anxiety and depression (Copeland et al., 2007).

Several factors such as demographics, age, environment, gender, parenting style, and peer deviance can influence how an individual processes a PTE and whether or not they are greater risk for subsequent PTE exposure (Breslau, 2002; Kaysen, Rosen, Bowman, & Resick, 2010; Overstreet, Berenz, Kendler, Dick, & Amstadter, 2017; Rubens, Vernberg, Felix, & Canino, 2013; Yeates et al., 2001). Factors such as demographic characteristics and early environmental factors impact how an individual might not only react to a PTE but also whether or not they are at risk of being exposed to a PTE (Overstreet et al., 2017). In a study conducted by Breslau (2002) examining gender differences in trauma and PTSD, females who had experienced a traumatic event were two times more likely to be at risk for PTSD compared to males (Breslau, 2002). Age also impacts an individual's risk of a PTE exposure and development of PTSD where individuals in late adolescence and early adulthood are at greatest risk (Breslau, Davis, Andreski, Federman, & Anthony, 1998). Early environmental factors, such as authoritarian parenting style, can place individuals at an increased risk for poorer outcomes following PTE exposure (Yeates et al., 2001). Moreover, peer deviance (i.e., delinquent peer behavior) is linked to increased risk for PTE exposure (Rubens et al., 2013). In addition to demographic characteristics and environmental factors, the number of PTEs an individual is exposed to over their lifetime (PTE load) leads to greater possibility for psychopathology development (Kaysen et al., 2010).

Exposure to PTEs are commonly associated with mental health sequelae and physical health comorbidities. Past literature has examined trauma exposure and poor physical health

mediated by PTSD (Qureshi, Pyne, Magruder, Schulz, & Kunik, 2009; Scott et al., 2011). However, the mediating role of PTSD is not easily understood as emerging literature supports the independent association of PTEs and physical health comorbidities (Cloitre, Cohen, Edelman, & Han, 2001; Norman et al., 2006; Sledjeski, Speisman, & Dierker, 2008). In an examination of lifetime traumatic stress exposure, independent of PTSD, traumatic event exposure was associated with 9 out of 11 physical health conditions examined (i.e., arthritis, back and neck pain, headaches, and heart disease) (Scott et al., 2013). Relatedly, Atwoli and colleagues (2016) examined the associations of PTEs and chronic physical health conditions in South Africa. Individuals who reported PTE exposure had an increased odds of a physical health condition (i.e., arthritis, cardiovascular, chronic pain) compared to those who reported no PTE exposure (Atwoli et al., 2016).

One of the main criticisms surrounding much of the trauma literature is that it relies largely on retrospective reporting. Retrospective reporting is defined as recounting memories from the past (Hardt & Rutter, 2004). Many researchers approach retrospective reporting with caution as the validity of adults retrospectively reporting PTEs has raised concerns. Adults are generally able to accurately respond to whether or not an incident early in life occurred, but the details of the event are less reliable (Chess, Thomas, & Birch, 1966). Young adults are more able to recall episodic (times, places, associated emotions) details compared to older adults (St. Jacques & Levine, 2007). Recall also depends on the timing of the event. Early in life infantile amnesia is likely to occur wherein there is no recollection of what took place in the first two to three years of life (Pillemer & White, 1989).

Furthermore, bias exists with retrospective reports because many people have a fixed, rehearsed memory that they have repeated to others that limit their cognitive ability to recall details beyond that fixed description (Hardt & Rutter, 2004). Repression and disassociation are

mental processes commonly employed after a traumatic event that impede the recollection of memory (Rothschild, 2000). For example, the impact of child sexual abuse on an individual might be so traumatic that the details of the event are inaccessible due to psychological defenses such as repression and disassociation (Goodman et al., 2003). Lalande and Bonanno (2011) examined the frequency of PTEs of college students over a 4-year period utilizing weekly web-surveys and upon the completion of the study participants were asked to recall the events they originally endorsed (Lalande & Bonanno, 2011). Results revealed 23.2% of individuals overestimated the number of PTEs they had endorsed and 66.7% underestimated. Events that result in emotional distress were more accurately recalled compared to events that did not cause emotional distress. Not all PTEs result in psychological impact or emotional distress which might explain the large number of participants that underestimated the number of PTEs (Lalande & Bonanno, 2011). Results suggest there are inaccuracies in recall of events. Thus, since recall of details of PTEs rely on judgement or interpretation, retrospective report should be approached with caution. Therefore, obtaining early reports of PTEs closer to the time which they occurred could provide a more valid assessment of the experience relying less on recall bias and uncertainty surrounding recalling from long-term memory.

### **PTEs and Pain**

Limited literature exists examining the intersection of chronic pain disorders and PTEs in youth, however research has more broadly focused on general stress and chronic medical conditions. In a sample of adults with Fibromyalgia (FM), patients reported exposure to an average of 3.29 potentially traumatic events (Conversano et al., 2018). In a study examining PTEs more broadly in a general population of 4351 African adults who endorsed PTEs, the most commonly reported chronic medical condition was chronic pain (46.6%) followed by cardiovascular disease (19.5%; Atwoli et al., 2016). Individuals with a presence of PTEs had an

increased odds of endorsing chronic pain (OR=1.74, CI=1.37-2.2) compared to respondents reporting no PTE exposure after controlling for age, sex, race/ethnicity, education, employment, marital status, race/ethnicity, mood, anxiety, substance use disorder and PTSD (Atwoli et al., 2016). Findings from this study also revealed a dose-response relationship between the number of PTEs and risk for a chronic physical condition (Atwoli et al., 2016). A dose-response relationship between increasing PTE exposure and chronic medical condition risk is well-supported the literature (Conversano et al., 2018; Husarewycz, El-Gabalawy, Logsetty, & Sareen, 2014; Keyes et al., 2013; Scott et al., 2013). In a nationally representative sample of United States adults, a dose-response relationship was observed between the number of traumatic events and physical conditions, where experiencing an increasing number of traumatic events increased the odds of a comorbid physical health condition (Husarewycz et al., 2014).

Children who have a history of stressful life events can potentially be at an increased risk for a chronic pain condition such as a functional gastrointestinal disorder (Rasquin-Weber et al., 1999). It is possible that a child who experiences a stressful life event may develop a psychological disorder as a result of the event, such as anxiety, and experience accompanying somatic symptoms such as pain (Rasquin-Weber et al., 1999). Childhood abuse, in particular, might be related to the development of chronic pain in adulthood (Davis, Luecken, & Zautra, 2005). Individuals who have a report of being abused or neglected in childhood report greater pain symptoms than those without a history of abuse or neglect (Davis et al., 2005). Individuals with chronic pain are more likely to report childhood adversities or experience abuse or neglect than healthy controls (Davis et al., 2005) or patients with medically explained pain (Imbierowicz & Egle, 2003). Specifically, traumatic experiences (physical and sexual abuse as well as neglect) in childhood are reported more often by patients with FM compared to individuals with another medical illness or healthy controls (Davis et al., 2005; Imbierowicz & Egle, 2003).



Similarly, those with JFM are more likely to have a report of sexual abuse compared to healthy controls (Cunningham et al., 2015).

Although there are preliminary links in the literature suggesting that there is an increased likelihood for youth with chronic pain to report trauma, an understanding of this relationship needs to be explored in more detail. Given that many of these studies rely on retrospective reporting, it is unclear whether PTEs lead to the exacerbation of the pain and associated symptoms or JFM places youth at an increased risk to report traumatic events. However, regardless of which preceded the other, the co-occurrence of JFM and PTEs is likely to increase negative outcomes for this population.

### **Potential Outcomes of a History of PTEs and Pain**

#### **Pain**

Pain is inherent in JFM as it is commonly regarded as a pain amplification syndrome (Conte, Walco, & Kimura, 2003). Patients with JFM report increased levels of pain compared to healthy controls (Yunus & Masi, 1985). In a 2017 study conducted by King and colleagues examining females with and without JFM significant differences in pain were found between JFM patients and healthy controls where JFM patients reported significantly greater current, average, and worst pain levels compared to their healthy counterparts (King et al., 2017).

While a clear connection between JFM and PTEs has yet to be established, the literature has demonstrated a link between PTEs and pain or, more generally, trauma and pain. In a meta-analytic review, nine different studies examined whether a report of childhood abuse or neglect increased an individual's risk of a pain condition (Davis et al., 2005). Although the nature of the samples differed widely, individuals with report of abuse or neglect are more likely to show more pain symptoms compared to those without a history of abuse or neglect (Davis et al., 2005). Chronic widespread pain, a common symptom associated with juvenile fibromyalgia, has

shown to be related to early life adversity (Jones, Power, & Macfarlane, 2009). Children who experienced a myriad of social and physical early life adversity (e.g., maternal death, familial financial hardship and hospitalization following a traffic accident) were at significant increased risk for chronic widespread pain forty years later (Jones et al., 2009). Despite having experienced these events much earlier on in life, these individuals were placed at significantly greater risk for negative health outcomes decades later. Headaches are a pain symptom commonly associated with JFM and exposure to PTEs (Stensland, Dyb, Thoresen, Wentzel-Larsen, & Zwart, 2013; Yunus & Masi, 1985). Fifty-four percent of patients with JFM report chronic headaches (Yunus & Masi, 1985); and in a study examining potentially traumatic interpersonal events (PTIEs, i.e., family adversity, domestic violence, physical abuse, neglect, and bullying), results showed a dose-response relationship between exposure to PTIEs and recurrent headache disorders (Stensland et al., 2013). As the exposure to PTIEs increased, a greater incidence of recurrent headache disorders was observed (Stensland et al., 2013).

The literature has yet to address a clear link between patients with both PTEs and JFM and whether or not they are placed at an increased risk for increased pain frequency and pain intensity. However, the literature clearly delineates that by nature, JFM is a chronic pain condition and individuals who have experienced PTEs have reported experiencing symptoms of pain (Atwoli et al., 2016; Husarewycz et al., 2014) and headaches (Stensland et al., 2013). Therefore, it is likely that because both populations are afflicted by pain, the combination of PTEs and JFM will increase the intensity and frequency of the pain experienced.

### **Physical Functioning**

Youth with JFM are significantly more disabled and less physically active compared to healthy controls (Reid, Lang, & McGrath, 1997). Prior to enrolling in CBT, individuals with JFM reported moderate levels of functional disability (Kashikar-Zuck et al., 2012). In a study

assessing physical activity in adolescents with JFM, only 23% of youth met rheumatology recommendations for 30 minutes of moderate to vigorous daily physical activity (Kashikar-Zuck, Flowers, et al., 2010). It is likely that the combination of the physical, social, and emotional impairment contributes to the increased functional disability of this population.

Congruent with the JFM population, individuals with PTEs are more disabled than their healthy counterparts. In a study examining health status of women with a history of child abuse and neglect, compared to women who did not meet criteria for childhood maltreatment, women with reports of abuse and neglect indicated significantly greater levels of functional disability (Walker et al., 1999). Similarly Monnat and Chandler (2015) evaluated the associations between adverse childhood events and adult physical health from 52,250 US adults and found that experiencing adversity in childhood is linked to poor adult physical health (Monnat & Chandler, 2015).

Individuals with JFM and those who have experienced PTEs are both at increased risk for poor physical functioning because both these populations are influenced by physical, psychological, and emotional factors that interact and ultimately negatively influence functioning. It is probable that because youth with JFM have increased levels of disability and individuals with a history of early life adversity are linked to poor physical health outcomes, the combination of JFM and PTEs will further compromise physical functioning.

### **Depression**

Previous literature has elucidated the link between JFM and depression where patients with JFM have demonstrated increased levels of depression compared to their healthy counterparts (Kashikar-Zuck et al., 2014). Additionally, there are many overlapping characteristics of depression and JFM such as fatigue, decreased interest in activities, diminished exercise, and psychomotor delay are amongst symptoms characteristic of JFM and depression.

The many overlapping symptoms of JFM and depression illuminate the complexity of this chronic pain condition and highlight a need for a deeper understanding of these clinical profiles. An increased incidence of depression has been observed in patients with a history of trauma (Heim, Newport, Mletzko, Miller, & Nemeroff, 2008) as well as patients with chronic pain (Weiss et al., 2013).

Similar to depression and JFM, individuals with a history of PTEs are at an increased risk for depression (Gupta & Bonanno, 2010; Vrana & Lauterbach, 1994). Past research has evidenced a strong dose-response relationship between PTEs and symptoms of depression (Mollica, McInnes, Pham, et al., 1998; Mollica, McInnes, Pool, & Tor, 1998; Overstreet et al., 2016). College undergraduates with a history of PTEs had greater levels of anxiety and depression compared to undergraduates without a history of PTEs (Vrana & Lauterbach, 1994). A lifespan perspective on PTEs revealed exposure to PTEs significantly impacted depression in childhood, adolescence, young adulthood, and middle age (Dulin & Passmore, 2010). Notably, PTEs experienced in young adulthood and middle age were more predictive of depression compared to exposure in childhood or adolescence. Cumulative exposure to PTEs is associated with a strong dose-response relationship in both men and women where an increasing number of PTEs was significantly associated with a greater number of psychiatric symptoms (Overstreet et al., 2016).

Though limited literature exists understanding the relationship between pain, depression, and PTEs, a recent study conducted by Sachs-Ericsson and colleagues (2017) examined the role of mood and anxiety as mediating and moderating variables in the relationship between adverse childhood experiences (ACEs), such as stressful or traumatic events including abuse and neglect (Felitti et al., 1998), and pain. Results showed the adverse impact of ACEs across mental and physical fields (Sachs-Ericsson, Sheffler, Stanley, Piazza, & Preacher, 2017). Through

mediation analyses, results demonstrated that ACEs were associated with an increase in anxiety and mood disorders which resulted in a greater number of painful medical conditions (Sachs-Ericsson et al., 2017). Moderation analyses revealed the deleterious impact of ACEs on increasing painful medical conditions at low and high levels of anxiety and mood disorders (Sachs-Ericsson et al., 2017). Participants with 4 to 7 ACEs had high rates of depression (41.18%) and on average 1.3 pain conditions (Sachs-Ericsson et al., 2017).

It is possible, that individuals who are exposed to a PTE are at an increased risk of being diagnosed with depression which could consequently increase their risk of chronic pain; or it may be that those with PTEs and JFM are overall more physically disabled thus at risk for increased psychopathology, such as depression. The combination of JFM *and* PTEs early in life places this group at greater risk for psychopathology.

### **Health Care Utilization**

Individuals with chronic pain are not only more likely to seek out health care resources but also utilize these resources frequently (Blyth, March, Brnabic, & Cousins, 2004; Ho et al., 2008). Often times when an individual presents to a multidisciplinary pain clinic, they are directed to physical therapy, radiology, behavioral services, and other specialty care (Ho et al., 2008). Moreover, those who seek out specialty care, such as a pain clinic visit, tend to be individuals of a higher socioeconomic status thus they have the means to pursue additional health care resources (Kuhlthau, Nyman, Ferris, Beal, & Perrin, 2004). In contrast, use of specialty care is significantly lower for minorities, children of parents of lower education status (less than some college, an Associate's, or Bachelor's degree), and families at or slightly above the poverty level (Kuhlthau et al., 2004). The combination of JFM *and* PTEs adds an additional layer of complexity which could potentially lead to the pursuit of added health care resources. ACEs can lead to poor adult health and high health care utilization (Atwoli et al., 2016; Scott et al., 2013).

Gawronski and colleagues (2014) examined health care utilization in participants exposed to PTE. A dose-response relationship was observed between PTEs and number of doctor visits where a greater number of potentially traumatic events was associated with an increase in the frequency of doctor visits (Gawronski, Kim, & Miller, 2014). A similar relationship was observed with number of nights spent at the hospital. Each addition of a PTE was associated with an 18% increase in nights spent in the hospital (Gawronski et al., 2014).

The specific types of services being utilized is an important delineation to make because different services achieve different results. For example, emergency department visits are not structured to create consistent medical care whereas non-emergency related visits might encourage the use of consistent check-ups which might be necessary for a patient's care (Reese & Smith, 1997). A primary reason for emergency department visits over non-emergency department visits is related to access and insurance type. Emergency department visits are highly sought out by the medically underserved population where individuals who are uninsured or underinsured are not able to readily access consistent medical care and present to the emergency department with more severe complications or illnesses (Tang, Stein, Hsia, Maselli, & Gonzales, 2010). Given the sociodemographic profile of JFM youth, this population likely utilizes more non-emergency related visits. The additional layer of PTEs increases the complex profile of this group and requires a necessary increase in services in order to meet their medical needs. A greater number of health care services leads to increased medical costs which could result in financial burden on the family.

### **Biopsychosocial Model: PTEs and Pain**

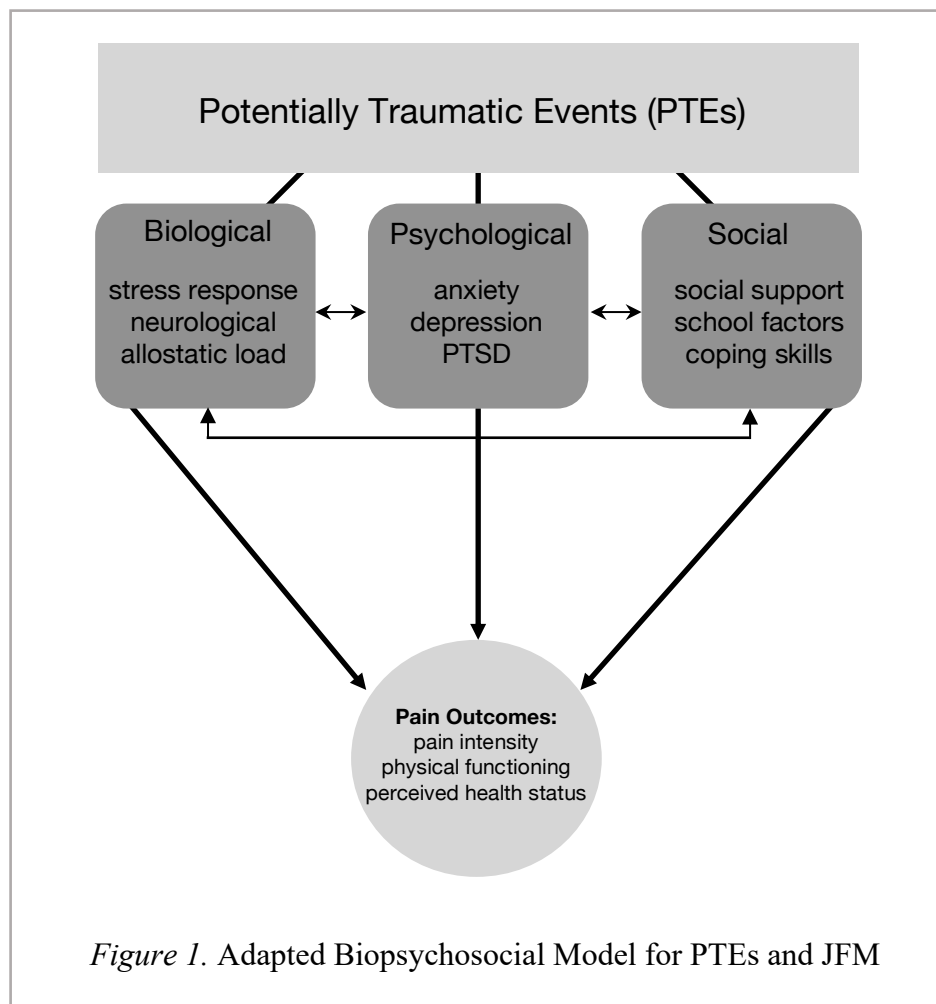
The biopsychosocial model elucidates how biological, psychological, and social factors all interact to ultimately impact health (Engel, 1977). The model takes into account a holistic approach to health by recognizing the mind-body connection. Pain is not sufficiently explained

via biological factors because biology alone does not explain severity and chronicity of pain. By including two additional determinants, psychological and social factors, the pain experience is better understood (Nelson, Cunningham, & Kashikar-Zuck, 2017). JFM literature has been examined through the lens of a biopsychosocial model. For example, Kashikar-Zuck and colleagues (2008) examined how various psychological variables (i.e., depression, behavioral and emotional problems), social acceptance, and fibromyalgia symptoms all interact to ultimately impact how youth cope with JFM (Kashikar-Zuck, Parkins, et al., 2008). An individual experiences pain in a very unique manner so by understanding the interaction of these constructs (biological, psychological, social factors) modulate a patient's symptomatology, highlights the importance of multidisciplinary care in providing the best course of treatment for a patient.

While JFM serves as an outcome of biological, psychological, and social factors interacting with one another, PTEs lead to the development of biopsychosocial events. For example, PTE exposure places toddlers at risk for psychological (emotion dysregulation) and biological impact (poor stress modulation; Mongillo, Briggs-Gowan, Ford, & Carter, 2009). Further, early stress and child maltreatment has been linked to reduced corpus callosum size and decreased development of the left neocortex, amygdala, and hippocampus (Teicher et al., 2003). Reduction in size of the corpus callosum has been associated with reduced communication of the left and right hemisphere (Yazgan, Wexler, Kinsbourne, Peterson, & Leckman, 1995) and potential impact on memory recall (Schiffer, Teicher, & Papanicolaou, 1995).

The biological, psychological, and social impact of JFM have been examined through the framework of the biopsychosocial model, though the unique contribution of PTEs has yet to be examined within the context of this model. Recently, Nelson and colleagues (2017) proposed an adapted biopsychosocial model (see Figure 1 adapted from (Nelson, Cunningham, & Kashikar-

Zuck, 2017)) to represent the influence of ACEs in the development of chronic pain (Nelson, Cunningham, & Kashikar-Zuck, 2017). Given many of the overlapping constructs that impact individuals with chronic pain the ACEs, the adapted model delineates the biological, psychological and social risk factors of ACEs and the impact on chronic pain. The model includes ACEs broadly and the interplay of factors such as HPA activation, emotional difficulties, and the family environment and its impact on chronic pain. The authors also suggest a bidirectional relationship where chronic pain leads to negative outcomes (i.e., decreased school functioning) and negative outcomes can exacerbate pain.





As a chronic pain condition, JFM also shares many commonalities with PTEs that may ultimately lead to increased psychopathology, decreased quality of life, compromised stress response, decreased physical functioning, and increased health risks. Figure 1 proposes exposure to PTEs leading to the development of biological, psychological, and social consequences which ultimately influence JFM. The literature lacks a clear understanding of how PTEs uniquely impact biopsychosocial processes that influence JFM across the lifespan. Therefore, the current study begins to explore how exposure to PTEs early in life impact important pain outcomes.

#### Aims

The first aim of the study is to identify PTEs experienced by a sample of youth diagnosed with JFM using the PTSD portion of the Kiddie-Sads-Present and Lifetime Version (K-SADS-PL). The frequencies of responses and the clinical characteristics of participants will be examined to obtain a greater understanding of the frequency, nature, and type of PTEs experienced by youth with JFM.

The second aim of this study is to examine the long-term outcomes (i.e. depression, health care utilization, pain intensity, physical functioning) in youth with JFM and PTEs through a dose-response model. In order to understand if this dose-response relationship is present, analyses will examine whether JFM patients with an increasing number of PTEs experience poorer long-term outcomes.

#### Hypotheses

With regard to Aim 1, it is hypothesized that the majority of individuals with JFM will have an early report of at least one PTE.

With regard to Aim 2, it is hypothesized that JFM patients with a greater number of PTEs will have poorer long-term outcomes.

*Hypothesis I.* Greater number of PTEs will predict increased pain intensity, pain locations, and symptom severity in patients with JFM compared to JFM patients with fewer or no history of PTEs.

*Hypothesis II.* JFM patients with a greater number of PTEs will have decreased physical functioning and perceived health status compared to JFM patients with fewer or no history of PTEs.

*Hypothesis III.* JFM patients with a greater number of PTEs will have increased rates of depression compared to JFM patients with fewer or no history of PTEs.

*Hypothesis IV.* JFM patients with a greater number of PTEs will have increased health care utilization compared to JFM patients with fewer or no history of PTEs.

## **Methods**

### **Participants**

Forty-two adolescents who completed the Kiddie Schedule of Affective Disorders and Schizophrenia (K-SADS) as part of a large randomized controlled trial for youth with JFM were included in this study (Kashikar-Zuck et al., 2012). Participants at the initial timepoint were between the ages of 11-18 years of age. Inclusion criteria included the following: 1) a diagnosis of JFM according to Yunus and Masi criteria (Yunus & Masi, 1985); 2) self-reported average pain severity of  $\geq 4$  on a 0-10 cm visual analog scale as indicated on a seven day pain diary; 3) eight weeks of stable medication and willingness to continue to receive medication for the remainder of the study; and 4) a score of  $>7$  on the Functional Disability Inventory (Walker & Greene, 1991). Exclusion criteria included: 1) other rheumatologic conditions; 2) developmental delay; 3) current diagnosis of panic disorder or major depression or history of psychosis or bipolar disorder; and 4) opioid use. A subset of youth from this trial matriculated into an 8-year longitudinal study (Kashikar-Zuck et al., 2014). Participants in the longitudinal study were

assessed on psychological and physical outcomes at 4 different time points over a 8-year period ( $M_{ages} = 15, 19, 21.6, \text{ and } 23.4$  years; Nelson, Cunningham, Peugh, et al., 2017).

For the purpose of this study, data were examined from two time points – the initial time point (T1) and the last follow-up point approximately eight years later (referred to as T2 for this study). In summary, participants were eligible if they completed the K-SADS at T1 and the outcome measures at T2.

## **Procedure**

### **Initial Assessment (T1)**

As part of a multisite trial, study rheumatologists from four different sites identified potential participants and informed them about the study. In addition, they obtained verbal consent for a research assistant to follow-up with the families. Research assistants contacted the families by phone or during a clinic visit where they were informed about the study and requested participation. Informed consent was obtained from the caregiver of the patient and signed/verbal assent was obtained from the children and adolescents. The K-SADS-PL was administered to the parent and child together with the exception of the post-traumatic stress disorder (PTSD) section which was administered to the child on their own so they could answer freely and honestly. In the event the child disclosed a reportable event or safety concern, the appropriate procedure was followed. After the evaluation was complete, participants were compensated for their participation. The study protocol received approval from the institutional review boards at all four participating sites (Kashikar-Zuck, Parkins, et al., 2008).

### **Follow-up Assessment (T2)**

Participants were re-contacted by phone and provided with information about the follow-up study. Verbal consent was obtained over the phone, and a signed consent was obtained via mail. After the signed consent form was obtained, participants were provided with an individual

login name/password for access to a secure, online portal to complete study questionnaires. The online study questionnaires consisted of demographic information, and questions regarding social/emotional functioning, and fibromyalgia symptoms. After completing the questionnaires, an in-person visit was scheduled with trained study staff (postdoctoral fellow) who was supervised by a clinical psychologist and psychiatrist. Participants were also compensated for their participation.

### **Measures from Initial Assessment (T1)**

#### **Background Information**

Demographic information including age, sex, race, and ethnicity were obtained.

#### **Potentially Traumatic Events**

The K-SADS-PL (Present and Lifetime Version) was adapted from the K-SADS-P (Present Episode Version). The objective of the assessment is to obtain severity ratings of current and lifetime psychopathology. The K-SADS-PL is a semi-structured diagnostic interview for children and adolescents based off criteria in the DSM-III-R and DSM-IV criteria. Present and lifetime DSM-IV diagnoses were recorded. The interview is a multi-informant interview administered by interviewing the parent(s), child, and summary ratings which include information from the parent, child, school medical chart, or other sources. For the purpose of this study, endorsement of the PTSD portion of the interview was utilized to determine PTEs. The K-SADS-PL has high interrater agreement and test-retest reliability  $k$  coefficients were in the good range for PTSD (.63 to .67) (Kaufman et al., 1997).

### **Measures from Follow-up Assessment (T2)**

#### **Background Information**

Demographic information including age, sex, race, and ethnicity were recorded.

### **Pain Intensity, Pain Locations, Symptom Severity**

Patients were asked to report their pain in the past week using an 11-point numeric rating scale based on the Brief Pain Inventory (Cleeland & Ryan, 1994). Average pain ratings ranged from 0 = “no pain” to 10 = “pain as bad as you can imagine”. The Widespread Pain Index (WPI) and the symptom severity scale (SS; Wolfe et al., 2010) were utilized to gather information regarding participants’ symptoms of fibromyalgia. The WPI and the SS were both adapted from the 2010 American College of Rheumatology diagnostic criteria for Fibromyalgia (Wolfe et al., 2010) and delivered as self-report measures in order to gain insight about specific fibromyalgia symptoms.

On the WPI, participants reported up to 19 areas of their body where they experienced pain over the past week (scores ranged from 0-19). The SS asked participants questions regarding 3 cardinal symptoms in the past week (fatigue, waking unrefreshed, cognitive symptoms) with response options on a 4-point Likert scale ranging from 0 (no problem) to 3 (severe: pervasive, continuous, life disturbing problems). Also, participants were asked to indicate other somatic symptoms based on a list of 41 symptoms (muscle pain, nausea, headaches etc.). Based on the number of somatic symptoms reported, a rating was assigned 0 = no symptoms, 1 = few symptoms, 2 = moderate symptoms, 3 = great deal of symptoms. The final SS score is derived from combining the somatic symptom rating score and the scores from the 3 cardinal symptoms (final score range: 0 to 12 with higher scores indicating greater symptomatology).

### **Depression**

The Beck Depression Inventory – II (BDI-II) is a 21-item self-report measure to assess symptoms corresponding to criteria in the DSM-IV for depression for adolescents ( $\geq 13$  years-old) and adults (Beck, Steer, & Brown, 1996). The BDI-II contains four options for each item

ranging from not present (0) to severe (3). Item content includes sadness, pessimism, loss of pleasure, suicidal thoughts or wishes, worthlessness, and other topics related to diagnostic criteria for depression. Unlike the original BDI which assessed symptoms of the past week, the BDI-II assesses ratings over the past two weeks. A total score is derived with higher scores indicating greater depressive symptoms. The BDI-II demonstrates moderately high correlation with the Hamilton Psychiatric Rating Scale for Depression-Revised ( $r=.71$ ; Beck et al., 1996). The internal consistency for the BDI-II is around 0.9 with the retest reliability ranging from 0.73 to 0.96 (Wang & Gorenstein, 2013).

### **Physical Functioning and Perceived Health Status**

The 36-item Short Form Health Survey version 2 was developed in order to assess physical and mental health in adolescents ( $\geq 14$  years-old) and adults. The current study examined two of the eight subscales: physical health (physical functioning) and role limitations due to physical problems (role physical). The physical functioning subscale asks 10 questions pertaining to activities encountered during a typical day (climbing stairs, walking, bathing, etc.) with 3-point response options ranging from (1) “yes, limited a lot” to (3) “no, not limited at all”. The role physical subscale is comprised of 4 questions related to physical limitations (e.g., “were limited in the kind of work or other activities”) with 5-point response options ranging from (1) “all of the time” to (5) “none of the time.” Lower scores indicated poorer functioning where scores were transformed on each subscale utilizing norm-based scoring (mean  $\pm$  SD  $t$  score:  $50 \pm 10$ ).

### **Healthcare Utilization**

Participants reported whether or not they utilized health care in the past three months (yes/no). Additional items included questions about outpatient visits (primary care, mental health services, specialty care, physical therapy, etc.), as well as number of inpatient visits and

trips to the emergency room. Information was also obtained regarding the number of healthcare trips and amount of time spent at each visit (in hours).

### **Analytic Plan**

Analyses were conducted using SPSS v. 21 (Corp., 2012). Sample characteristics on demographics such as age, sex, and race were analyzed for the whole sample.

*Aim 1.* It was hypothesized that the majority of individuals with JFM would have an early report of at least one PTEs. In order to determine the frequency of PTEs experienced by youth with JFM, and the PTEs commonly reported in this population, the frequencies of PTEs reported on the PTSD portion of the K-SADS-PL were examined.

*Aim 2.* It was hypothesized that patients with a greater number of PTEs would have worse outcomes. In order to understand if a graded relationship was present between JFM patients and several, continuous long-term outcome variables, linear regression analyses were conducted.

Hypothesis I. JFM patients with a greater number of PTEs in adolescence (T1) have increased pain intensity, pain locations, and greater symptom severity in young adulthood (T2) compared to JFM patients with fewer or no history of PTEs. For Hypothesis I, a series of linear regressions were conducted to examine whether or not a dose-response relationship exists between number of PTEs and level of pain intensity, number of pain locations, and symptom severity. The number of PTEs reported by JFM patients was the independent variable and pain intensity, number of locations, and symptom severity were the dependent variables.

Hypothesis II. JFM patients with a greater number of PTEs in adolescence (T1) have decreased physical functioning and perceived health status in young adulthood (T2) compared to JFM patients with fewer or no history of PTEs. For Hypothesis II, two linear regressions were conducted to examine whether or not a dose-response relationship exists between the number of PTEs and physical functioning and perceived health status subscale scores. The number of PTEs

reported by JFM patients was the independent variable and physical functioning and perceived health status subscale scores were the dependent variables.

Hypothesis III. JFM patients with a greater number of PTEs in adolescence (T1) have increased rates of depression in young adulthood (T2) compared to JFM patients with fewer or no history of PTEs. For Hypothesis III, a linear regression was conducted to examine whether or not a dose-response relationship exists between the number of PTEs and BDI total score. The number of PTEs reported by JFM patients was the independent variable and the BDI II total score was the dependent variable.

Hypothesis IV. JFM patients with a greater number of PTEs in adolescence (T1) have increased health care utilization in young adulthood (T2) compared to JFM patients with fewer or no history of PTEs. For Hypothesis IV, a linear regression was conducted to examine whether or not a dose-response relationship exists between the number of PTEs and use of health care services. The number of PTEs reported by JFM patients was the independent variable and outpatient services, imaging scans, and emergency department services were the dependent variables.

## **Results**

### **Participant Characteristics at Time 2**

The original sample at T1 was comprised of 118 individuals with JFM, of which 76 patients did not complete the follow-up assessment measures, therefore, the final sample in the current study consisted of 42 participants. The sample was largely female (95%) and Caucasian (78.6) ranging from age 19 – 25 ( $M = 21.7$   $SD = 1.4$ ) (Table 1). The most frequently reported pain locations in the JFM sample was lower back (62.8%), right shoulder (55.8%) and upper back (53.5%).



Table 1.

*Participant Characteristics (N=42)*

	<i>m</i>	<i>sd</i>	n	%
Age (19-25 years)	21.7	1.4		
Sex				
Female			40	95.2
Male			2	4.7
Race				
White			33	78.6
African-American			4	9.5
Asian			1	2.4
American Indian/Alaskan Native			2	4.8
Other			2	4.8

In review of the dependent variables (Table 2), on average participants reported 7 pain locations (range = 0-19). JFM participants indicated an average symptom severity score of 6.54 out of a maximum possible score of 12. According to preestablished cutoffs, 16.67% of the sample indicated moderate depression (moderate depression range = 20-28) and 9.52% of the sample endorsed severe depression (severe depression range = 29-63) (Beck et al., 1996). Participants endorsed physical functioning almost one standard deviation below the mean with lower scores indicating poorer functioning (norm-based t-score  $50 \pm 10$ ) (Table 2). Correlations between outcome variables are noted in Table 3.

Table 2.

*Mean and standard deviations of outcome variables (N=42)*

Variable	Range	M	SD
Symptom Severity	1-11	6.54	2.59
Widespread Pain Index	1-14	7.17	3.69
Average Pain	0-8	3.38	2.51
Depression	0-44	14.50	10.42
Physical Functioning*	17-57	42.88	10.05
Role Physical*	20-57	41.06	9.69

\*The mean norm-based t score was  $50 \pm 10$ .

Table 3.

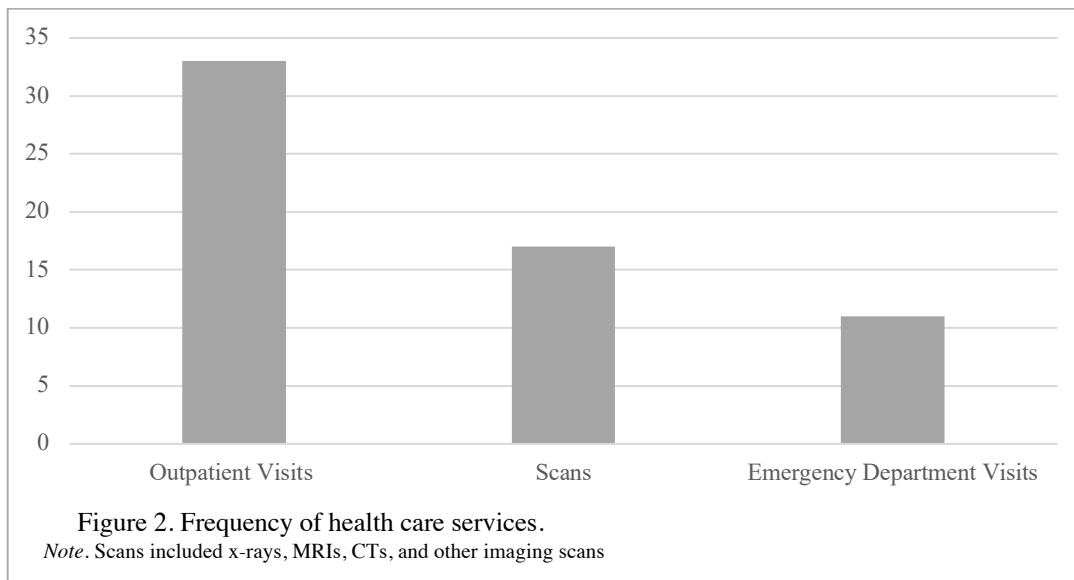
*Correlations among outcome variables*

Variables	1	2	3	4	5	6
1. Symptom Severity	-					
2. Widespread Pain Index	.672**	-				
3. Average Pain	.434**	.349*	-			
4. Depression	.667**	.550**	.373*	-		
5. Physical Functioning	-.364*	-.428*	-.490**	-.452**	-	
6. Role Physical	-.522**	-.407**	-.426**	-.532**	.646**	-

\* $p < .05$ . \*\* $p < .01$ .

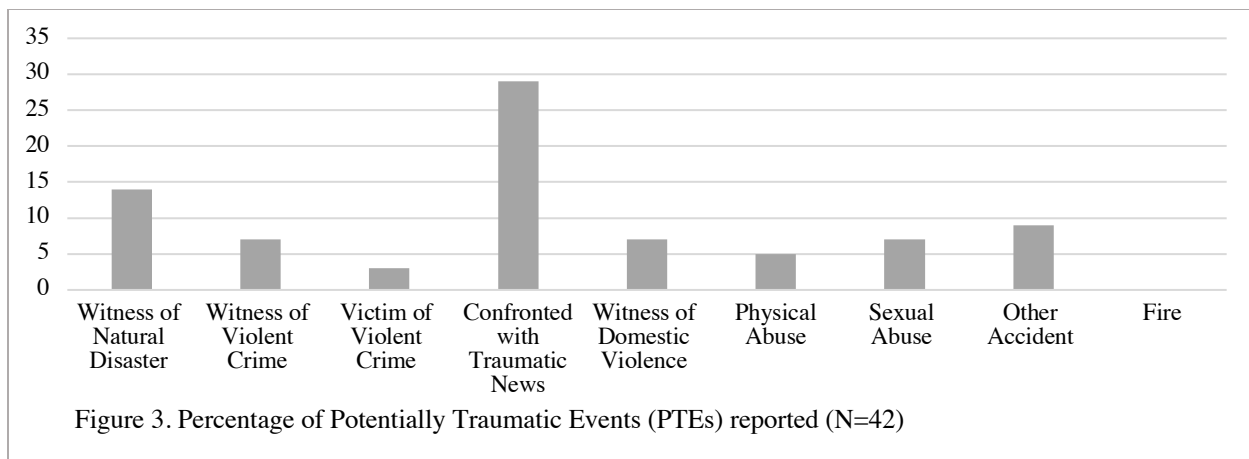
Health care utilization variables were analyzed by summing the total number of outpatient visits (i.e., primary care, specialty care, physical therapy). The total number of emergency room visits were summed to obtain the emergency department visits. Magnetic resonance imaging (MRI), x-rays, computed tomography (CT), and other imaging scans were

combined into a composite variable, scans. Analysis of health care utilization revealed the most commonly utilized services were outpatient services followed by imaging scans and emergency department services (Figure 2).



### PTE Prevalence

In reference to aim 1 of our study, this supports our hypothesis where the majority of participants endorsed PTEs. Of the 42 participants included in the analyses, 32 participants reported PTEs ranging from 1 to 7 PTEs. The most commonly reported potentially traumatic events were confronted with traumatic news (29%), witness of natural disaster (14%), and other accident (9%) (Figure 3). PTEs of individuals who did not follow-up (N=76) were compared to those who did follow-up (N= 42). The frequency of PTEs amongst both groups was consistent with the exception of *witness of domestic violence* where 25.3% of the sample that did not follow-up reported *witnessing domestic violence* compared to 7% of the sample that did follow-up ( $z = -2.46, p = .018; \chi^2(1, 41) = 0.46, p = .830$ ). Given that only one event differed significantly amongst both groups, it is likely that the final sample is representative of the larger JFM sample.



### Linear Regression Results

Simple linear regression analyses were used to understand if the number of PTEs reported by JFM patients significantly predicted symptom severity. The results of the regressions partially supported our hypothesis and revealed PTEs significantly predicted symptom severity ( $R^2=.106$ ,  $F(1,33)=3.93$ ,  $p<.05$ ; Table 4). A simple linear regression analysis used to test if PTEs significantly predicted number of pain locations. The results revealed that the PTEs did not significantly predict number of pain locations ( $R^2=0.048$ ,  $F(1, 33)=1.65$ ,  $p=.208$ ; Table 4). Similarly, a simple linear regression analysis revealed PTEs did not significantly predict average level of pain intensity ( $R^2=0.043$ ,  $F(1,37)=1.68$ ,  $p=.203$ ; Table 4). PTEs did not significantly predict physical functioning ( $R^2=0.005$ ,  $F(1, 38)=.206$ ,  $p=.652$ ; Table 4) or role limitations due to physical problems ( $R^2=0.009$ ,  $F(1, 38)=.358$ ,  $p=.553$ ; Table 4). A simple linear regression demonstrated PTEs did not predict depression ( $R^2=0.001$ ,  $F(1,38)=.005$ ,  $p=.815$ ; Table 4). Further, examination of health care utilization variables revealed PTEs did not significantly predict outpatient visits ( $R^2=0.008$ ,  $F(1, 30)=.255$ ,  $p=.618$ ), radiological scans ( $R^2=0.039$ ,  $F(1, 39)=1.58$ ,  $p=.217$ ), and emergency department visits ( $R^2=0.010$ ,  $F(1, 8)=.084$ ,  $p=.780$ ; Table 4).

Table 4.

*Simple Linear Regressions of number of PTEs on outcome variables*

Dependent Variables	n	B(SE)	p	R <sup>2</sup>
Symptom Severity	34	-.326(.271)	<.05	.106
Widespread Pain Index	34	-.218(.398)	.208	.048
Average Pain	38	.209(.260)	.203	.043
Physical Functioning	39	-.023(.936)	.886	.005
Role Physical	39	.074(.899)	.652	.009
Depression	39	-.038(.970)	.815	.001
Outpatient Visits	31	.092(.833)	.618	.008
Radiological Scans	40	.197(.195)	.217	.039
Emergency Dept. Visits	9	.102(.393)	.780	.102

### Discussion

The present study is one of the first to examine PTEs and a pediatric chronic pain condition, thus providing a preliminary overview of the potential impact of PTEs on pain-related outcomes. The study explored the impact PTEs have on a Juvenile Fibromyalgia sample and whether or not PTEs place this population at an increased risk for poorer outcomes. We aimed to identify PTEs experienced by a sample of youth diagnosed with JFM and to examine the long-term outcomes in youth with JFM and PTEs through a dose-response model. Linear regression analyses helped us determine whether a greater number of PTEs were predictive of poorer outcomes in youth with JFM compared to those with fewer or no history of PTEs. Results from this study revealed the majority of the JFM sample has been exposed to at least one PTE and the combination of PTEs and JFM are associated with increased symptom severity.

Our findings supported our first hypothesis demonstrating 76% of youth with JFM reported the presence of one or more PTEs. The most commonly reported PTEs were: confronted with traumatic news, witness of a natural disaster, and other accident. Previous literature in a non-clinical sample of children reported 26-33% have been exposed to at least one PTE (Briggs-Gowan et al., 2010; Costello et al., 2002), substantially less than that of the current JFM sample. This disparity highlights the magnitude of PTEs in a chronic pain population and the importance of understanding key risk factors that place this sample an increased likelihood of exposure to PTEs. The current study does not have access to specific demographic characteristics to parse out potential risk factors, but past literature has identified specific risk factors such as demographics, age, gender, parenting style, and the number of PTEs (Breslau, 2002; Kaysen et al., 2010; Overstreet et al., 2017; Rubens et al., 2013; Yeates et al., 2001). Specifically, females who endorsed exposure to a PTE were twice as likely to be at risk for the development of PTSD (Breslau, 2002). Pediatric pain samples are largely comprised of females and given the increased likelihood for psychopathology in females with PTEs, it underscores the importance of closely monitoring this group (Campo et al., 2004; Goulart, Pessoa, & Lombardi, 2016; Kashikar-Zuck, Parkins, et al., 2008; Lynch-Jordan, Sil, Bromberg, Ting, & Kashikar-Zuck, 2015). Individuals in late adolescence and early adulthood with PTE exposure are at greatest risk for PTSD development (Breslau et al., 1998). Given PTE exposure was assessed as participants were approaching late adolescence (M = 15-years-old), it is possible participants were exposed to a PTE around an at-risk age which could help in explaining the prevalence of PTEs in the sample. Further, lack of parental involvement is also a risk factor associated with increased PTEs. Past literature on family factors in a JFM sample suggest parental pain history is associated with greater functional impairment and family conflict (Kashikar-Zuck, Lynch, et al., 2008; Schanberg, Keefe, Lefebvre, Kredich, & Gil, 1998). Therefore, disentangling the

impact of various family factors can be helpful in better understanding what specifically can place youth with JFM at a greater risk for PTEs. Additionally, the number of PTEs (PTE load) exposed over an individual's lifetime can lead to greater possibility for psychopathology, thus providing support for analyzing the data through a dose-response model in order to examine an increasing number of PTEs.

The current literature as well as emerging literature on PTEs demonstrate a detrimental impact of PTE exposure on overall health (Atwoli et al., 2016; Cloitre et al., 2001; Norman et al., 2006; Qureshi et al., 2009; Scott et al., 2011; Sledjeski et al., 2008), and in fact, more PTEs significantly predicted symptom severity suggesting that an increasing number of PTEs is linked to a greater number of physical symptoms. The significant association between increasing PTEs and symptom severity might be explained by a repeated activation of the allostatic systems (McEwen & Wingfield, 2003). Repeated stress or trauma leads to dysregulation of the HPA axis leading to sustained activation of allostatic systems creating an allostatic overload (McEwen, 2001). Increased allostatic load has adverse physiological consequences thus compromising physical health (McEwen & Wingfield, 2003) and placing this portion of the population at greater risk for adverse health outcomes. It is likely that PTE exposure leads to greater symptom severity because of the increased activation of allostatic systems consequently causing negative physiological impact.

Treating youth who present with a complex profile of JFM and PTEs requires a more multifaceted level of care in order to treat both the somatic and psychological profile. Understanding the mechanisms that impact youth with JFM and PTEs through measuring allostatic load can help to discern this complex profile. Current research on allostatic load has attempted to identify a group of biomarkers to create an allostatic load algorithm. Findings have provided preliminary support for an allostatic load algorithm to understand the impact of chronic

stress on health (Geronimus, Hicken, Keene, & Bound, 2006; Seeman, McEwen, Rowe, & Singer, 2001). Some variability exists between the 10 biomarkers included in the algorithm. Many researchers have adopted the same algorithm as Merkin and colleagues (2009) who used the following biomarkers: waist circumference, hypertension, asthma, c-reactive protein concentration (mg/dL), triglyceride concentrations (mg/dL), glycosylated hemoglobin level (%), fasting glucose concentration (mg/dL), low density lipoprotein cholesterol concentration (mg/dL), high density lipoprotein cholesterol concentration (mg/dL), insulin resistance (Merkin et al., 2009). In fact, there is some research on pediatrics demonstrating links between ACEs and overweight and obesity where children who endorsed  $\geq 4$  ACEs are at a greater likelihood for overweight or obesity (Burke, Hellman, Scott, Weems, & Carrion, 2011). Similar findings were observed in the current study where the JFM patients with an increasing number of PTEs endorsed a greater number of physical symptoms. While research understanding how to best measure allostatic load is still developing, examination of these biomarkers can help to inform how we examine these symptoms in pediatric youth with PTE exposure.

Previous literature provides support for the association between JFM and increased symptom severity as well as identifies the link between PTEs and adverse health outcomes. The current study has bridged these findings by demonstrating the combination of JFM and an increasing number of PTEs is predictive of greater symptom severity. However, it remains unclear if there is a specific clinical profile unique to this group because the symptom severity scale is comprised of an all-encompassing list of symptoms (i.e., frequent urination, dry mouth, dizziness etc.). In order to better understand the relationship between JFM and PTEs and whether or not there is a unique constellation of symptoms for this subset of the population, future work should focus on specifically assessing JFM patients that present with greater symptom severity and better understand the nature of the symptom presentation.



PTEs were not significantly predictive of pain locations, physical functioning, role limitations due to physical problems, depression, or health care utilization. In considering the nature of JFM as a chronic condition, it is important to understand the detrimental impact JFM has on overall functioning. Because physical functioning is already so low in individuals with JFM, it might be harder to detect the unique effect of PTEs on functioning. By examining this construct in an already impaired population, significant findings would reflect a great deal of impact on a portion of this sample. For all outcome variables, the null findings could also be attributed to the longitudinal research design which could limit an understanding of the mechanisms that predict these outcomes in youth with PTEs and JFM. Because participants filled the outcome measures eight years after they endorsed PTE(s), a significant amount of time has elapsed that if the findings were significant it is difficult to assume it is exclusively because of exposure to PTEs. It is very likely that there are a number of intervening variables or life events that occurred over this period of time that could influence outcomes. For example, those who were exposed to a PTE might have developed coping techniques over the eight-year period to deal with somatic or psychological consequences stemming from PTE exposure. It is possible that this subset of the JFM sample sought services (e.g., psychotherapy) or have a strong social support network that mitigated the impact of PTE exposure. Also, not all PTEs are detrimental or lead to the development of psychopathology and because we do not have information on the nature, frequency, or severity of the event this sample may not have suffered negative consequences captured by the outcomes measured. Conversely, it is possible that participants exposed to PTEs experienced adverse outcomes that are not identified from the outcome measures used in this study.

Further analyses were conducted for the following purposes: 1) to address outliers in reporting PTEs, and 2) to better understand the impact of PTEs on youth with JFM. Upon

examination of the range of PTEs reported, there was one outlier reporting 7 PTEs.

Winsorization was used to address this outlier. Following winsorization, natural log transformation was applied to PTEs and the skewness observably decreased from 1.01 to .209.

Regression analyses with the log transformed values were conducted to understand the contribution of the outlying PTE; however, analyses yielded no additional significant findings.

To understand whether the presence of any PTEs impacted youth with JFM, independent sample t-tests compared JFM participants with and without PTEs, however, results were not significant.

Comparing those with and without PTEs created disproportionate groups as the JFM+PTE (n=32) group was much larger than the JFM without PTEs group (n=10). Also, it is difficult to compare the two groups because there is a lot of variability in the JFM+PTE group amongst the different types of PTEs.

69% of the sample endorsed “confronted with traumatic news” (e.g., death of a pet or grandparent) and 29% of the sample endorsed physical or sexual abuse. While we do not have information on the severity of the event(s), it is possible that the events have a varying level of impact which makes the JFM+PTE group more difficult to analyze as one distinct group.

Further, it is challenging to examine the JFM+PTE as one group because the JFM+PTE group had PTEs ranging from one event to seven events. While the dose response, model assumes that more PTEs has greater impact than fewer PTEs, it is possible that one event might have a greater impact on an individual compared to an individual who has experienced four PTEs.

Without knowing the varying level of impact each PTE has on the participants with JFM, it limits our ability to divide these groups based on the presence or absence of PTEs. A dose-response model would not detect the greater impact of one PTE versus four PTEs, however, given the robust body of literature supporting this model in examining trauma it provides the best framework to examine PTEs.

## Limitations

The study was not without several limitations. The sample size was small ( $n=42$ ) which limited the sophistication of statistical analysis that could be performed. In order to detect significance ( $p<0.05$ ), a projected sample size of  $N\geq 74$  would have been required to have sufficient power (95%; Cohen, 1988). And while the sample was consistent with other pediatric pain populations (predominately Caucasian and female), the sample was demographically homogenous thus lacking generalizability to the general population. Additionally, the longitudinal nature of the research design makes the findings difficult to interpret. Because information about PTEs was collected at the first time point and several years elapsed ( $M= 8$  years) until time 2 data was collected, it is difficult to assume data from the outcome measures are linked to PTEs from 8 years prior. While it is very possible that a PTE experienced in childhood impacts overall functioning in adulthood (Steel, Silove, Phan, & Bauman, 2002), we have little information regarding the timing, frequency, and severity of the event(s) therefore it is challenging to draw conclusions about early reports of PTEs and long-term outcomes. Moreover, utilization of the PTSD portion of the K-SADS might not best capture PTEs. In this study, the method to determine PTEs derives from an instrument designed to determine psychopathology in children. The PTSD portion of the K-SADS is helpful in determining if a child meets diagnostic criteria for PTSD. While PTEs and PTSD have many similarities, PTEs are more broadly defined and exposure can potentially develop into PTSD but does not always. A measure that more broadly captures stressful life events might have been better at determining PTEs. For example, Traumatic Event Screening Inventory for Children (TESI-C) is a 24-item, publicly available measure that assesses for the presence of a broad range of PTEs.

In addition to using a different measure to assess PTEs, health care utilization could have been assessed differently. There is literature to suggest certain symptoms play a role in whether

or not individuals seek out care (Cameron, Leventhal, & Leventhal, 1993). Greater perceived symptom severity is associated with increased care-seeking behavior (Janz & Becker, 1984). Therefore, given the link between symptom severity and care-seeking behavior, it is possible that health care utilization could have been best captured differently to better understand care-seeking behavior. Further, there is extensive literature on the psychological impact of trauma, however, there was only one outcome variable (BDI-II) capturing a psychological construct. It is likely that PTEs impact pediatric youth beyond depression. It would have been useful to have additional measures that capture psychological risk beyond depression to better understand the complex nature of PTEs. Copeland and colleagues (2007) identified psychiatric disorders in children exposed to multiple traumatic events. In addition to depression, anxiety was common in this population and served as outcome for additional trauma exposure.

Finally, the lack of a comparison group limits our understanding as to whether these findings are unique to the JFM population or not. It would have been helpful to have time 1 and time 2 data on individuals without JFM with PTEs in order to determine if youth with JFM and PTEs are at greater risk for poorer outcomes compared to those without chronic pain.

### **Future Directions**

Findings from this study revealed a large majority of JFM youth experience PTEs which provide support for the use of a well-validated trauma measure to understand the extent to which trauma impacts pain. JFM and trauma are both complex and the combination of the two increase the complexity of the clinical profile with regard to JFM symptom severity. A similar co-occurrence occurs across pediatric conditions where pediatric youth with chronic liver disease, diabetes, and chronic heart disease all had co-occurring post-traumatic stress symptoms (Shemesh et al., 2005). Therefore, pediatric youth generally might benefit from the use of a trauma measure to help providers better understand the diagnostic presentation. Further, it is

likely that different PTEs yield different outcomes consequently, research in this area should parse out the specific types of events to understand how each event uniquely impacts youth with chronic pain. Our findings showed a significant relationship between PTEs and symptom severity where PTEs significantly predicted symptom severity. While it is unclear the mechanisms that impact symptom severity, it is possible that increased allostatic load is contributing to symptom severity. Therefore, future work should focus on measuring allostatic load to better understand if it is a mechanism influencing the relationship between PTEs and symptom severity.

### **Conclusion**

This is one of the first studies to examine PTEs within the context of a pediatric pain population. While many of the hypotheses regarding long-term outcomes of PTEs and JFM were not supported, the current study suggests youth with JFM may experience greater PTE exposure which may increase their risk for poor outcomes. Greater exposure to PTEs in youth with JFM is predictive of increased symptom severity. The results highlight the need for long-term monitoring and tailored care for this subset of the population. Additionally, future research on individuals with JFM should focus on understanding the mechanisms that drive these poor outcomes. A better understanding of these mechanisms will help to provide a clearer picture of the clinical profiles of this population.

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