Optimizing pain management and functional ability in the adolescent with chronic pain

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ABSTRACT

OPTIMIZING PAIN MANAGEMENT AND FUNCTIONAL ABILITY IN THE ADOLESCENT WITH CHRONIC PAIN

Background: Pain during childhood is a disruptive experience. Approximately 25% of children nationally experience chronic pain with 5-8% of them experiencing clinically disabling pain. These adolescents experience high levels of functional disability across physical, emotional and social domains of functioning. Current clinical recommendations include the prescription of exercise as part of a multi-modal treatment plan. Yet, limited research in support on the use of exercise in adolescent chronic pain populations exists.

Purpose: The purpose of this body of work was to determine the influence of yoga on pain and functional outcomes in the adolescent with chronic pain. To achieve this purpose, five specific aims were set: 1) synthesize clinical presentation, pathophysiology and current treatment recommendations in fibromyalgia; 2) quantify associations among pain characteristics, psychological factors, general health factors and functional disability in adolescents with chronic pain; 3) determine engagement in, perceived benefits and barriers to yoga participation in fibromyalgia; 4) explore the feasibility, acceptability, safety and efficacy of yoga as a therapeutic intervention in pediatric chronic pain populations; and 5) explore the feasibility and examine the effect of a yoga intervention on pain, functional disability and quality of life in the adolescent with chronic pain; 5a) to identify and characterize responders versus non-responders of the yoga intervention.

Methods: Information was synthesized on the clinical presentation, pathophysiology and current treatment recommendations in fibromyalgia. Two quantitative analyses were conducted

to quantify associations among pain characteristics, general heath factors and functional disability and to determine engagement in, perceived benefits and barriers to yoga participation in fibromyalgia. Next, information was synthesized current evidence on the feasibility, acceptability, safety and efficacy of yoga as a therapeutic intervention in a clinical population of adolescents with chronic pain. Lastly, a single arm interventional study exploring the feasibility, acceptability, safety and effect of a yoga intervention on pain, functional disability and quality of life in the adolescent with chronic pain was conducted.

Results: Specifically, this body of work found: 1) current management guidelines and treatment recommendations in adolescent chronic pain are aligned with those found in the adult literature; 2) after controlling for the known effects of pain characteristics and depressive symptoms, physical activity was the only variable that contributed significantly to functional disability; 3) engagement in yoga practice was associated most frequently with improved mobility, relaxation, pain reduction and improved sleep while fear of pain exacerbation was the most frequently cited barrier to yoga participation; 4) five studies were identified having tested yoga as an intervention in various pediatric pain populations with yoga practice being associated with a reduction in pain intensity and improved daily functioning; and 5) adolescents participating in the 8-week interventional study experienced a significant linear trend in pain reduction over the course of the study with the majority of adolescents and their parents reporting overall global improvement, none reported adverse events or worsening of symptoms during the intervention.

Conclusion: Taken as a whole, findings from this body of work present a solid foundation from which to build future clinical trials and support current clinical treatment guidelines on the use of exercise in pediatric chronic pain.

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CHAPTER 1: INTRODUCTION

The experience of pain during childhood is commonly considered to be benign and time-limited and just a part of being a "kid". Yet, this is not the case for all children. For some children, the pain persists into chronicity with disruptive and debilitating physical, social, and functional consequences (Haraldstad, Sorum, Eide, Natvig, & Helseth, 2011; Hoftun, Romundstad, Zwart, & Rygg, 2011; Simons, Sieberg, Carpino, Logan, & Berde, 2011). Current national estimates approximate that 25% of children (ages 1-18) live with chronic pain with 5-8% experiencing a clinical level of significantly disabling pain (Hoftun et al., 2011; Mathews, 2011; Perquin, Hazebroek-Kampschreur et al., 2000). The prevalence of chronic pain increases according to gender (affecting more females than males) and with age, peaking during the adolescent period (ages11-18) just prior to puberty (Huguet & Miró, 2008; Roth-Isegkeit, Thyen, Raspe, Stoven, & Schmucker, 2008). Notably, chronic pain that occurs during the adolescent period has been associated with the experience of chronic pain during adulthood (Holm, Ljungman, & Soderlund, 2012).

Chronic pain

By definition, chronic pain is pain occurring at least once per week for greater than a three-month period, irrespective of pain location (Perquin et al., 2000; Sherry & Malleson, 2002). The majority (83%) of adolescents with chronic pain report recurrent pain over a three-month period with 30.8% reporting pain that had been present for six months or greater (Roth-Isegkeit et al., 2008). Common presenting pain locations include the head, back and limbs with musculoskeletal pain accounting for the majority of all pain reported (Palermo, 2000; Perquin et al., 2000). Yet, the occurrence of single site chronic pain is relatively uncommon, with up to 77% of those with chronic pain reporting experiencing pain in more than one body location

(Carnes et al., 2007; Rathleff, Roos, Olesen, & Rasmussen, 2013). Widespread pain (in more than one body location and/or region) ranks as one of the top presenting reasons for specialty care and accounts for approximately 25% of all new adolescent pain patients (Bowyer & Roettcher, 1996). Yet, currently, there is no consistently applied criterion to define and diagnose the experience of multi-site pain during adolescence (Zernikow et al., 2012). For example, one subgroup of adolescents experience both widespread chronic pain and additional symptoms including (but not limited to) fatigue, sleep and emotional disturbances. Commonly known as juvenile primary fibromyalgia syndrome (JPFS), the lack of consistent definition operationalization describing this condition within the current literature (the use of "chronic widespread musculoskeletal pain" is commonly used interchangeably) complicates recognition and management. Further complicating, JPFS diagnostic criteria has yet to be scientifically established in an adolescent population (Zernikow et al., 2012; Kashikar-Zuck et al., 2014). Unlike in adult populations with burgeoning scientific advances, there is a paucity of evidence focused on JPFS. Despite an increase in scientific interest and emergence of more controlled studies examining clinical presentation and impact of JPFS on the adolescent in the past few years, JPFS remains under-recognized clinically and scientifically under-studied. For purposes of this dissertation, the terminology juvenile primary fibromyalgia syndrome (JPFS) will be used to describe the occurrence of widespread chronic pain with accompanying symptoms.

Juvenile primary fibromyalgia syndrome

Currently, there is ongoing debate among clinicians as to the legitimacy of FM and its occurrence in adolescence (McLeod, 2013). In fact, the diagnosis of JPFS is commonly rejected by clinicians due to an absence of scientifically based diagnostic guidelines (Sherry & Malleson, 2002). This may be, in part, related to the lack of objective confirmatory diagnostic tests (i.e. lab

findings), subjective pain reports and overlapping symptoms with other disorders (Arnold et al., 2008; Kashikar-Zuck & Ting, 2013; Kimura, 2000). In fact, clinical presentation (symptoms) is most often used to ascertain a diagnosis (Siegel, Janeway, & Baum, 1998). It has been almost 30 years since the first diagnostic criteria for JPFS was proposed by Yunus & Masi (1985) that included the presence of widespread chronic pain, painful tender points and concurrent symptoms (i.e. fatigue, sleep disturbances, and anxiety). However, ongoing debate continues regarding which criteria should be used in adolescent populations, the Yunus & Masi (1985) criteria versus American College of Rheumatology (ACR) classification criteria for fibromyalgia leading to inconsistent use of these diagnostic criteria both scientifically and clinically.

Consequently, the average duration of pain in JPFS is two years prior to multidisciplinary care referrals (and treatment initiation), whereas adolescents with other chronic pain disorders (e.g. juvenile rheumatoid arthritis) receive referrals quicker, often less than one year (Kashikar-Zuck, Vaught, Goldschneider, Graham, & Miller, 2002). Approximately 20% of adolescents seeking treatment for pain are told they would "grow out of it (Buskila et al., 1995; Mikkelson, 1999). About 25% percent of these adolescents report seeing more than six health-care providers before receiving an accurate diagnosis (Mease et al., 2009). Despite this delay, JPFS ranks third among new patient diagnosis in pediatric pain and rheumatology clinics across the United States (Siegel et al., 1998). Moreover, clinicians may be unaware of the extensive federally funded initiatives to better understand JPFS, or the three FDA approved medications for FM in adults.

Clinical characteristics

JPFS is typically characterized by diffuse musculoskeletal pain, multiple tender points at soft tissue sites (Alfven, 2012; Swain, Kashikar-Zuck, Brent Graham, & Prahalad, 2005), joint hypermobility (Gedalia, Press, Klein, & et al., 1993; Ting et al., 2012), fatigue (Gedalia, Garcia,

Molina, Bradford, & Espinoza, 2000; Kashikar-Zuck, Parkins et al., 2010), sleep disturbances (Roizenblatt et al., 1997; Tayag-Kier et al., 2000) and concurrent mood disorders (Kashikar-Zuck et al., 2002; Kashikar-Zuck et al., 2008b; Mikkelson, Sourander, Piha et al., 1997). JPFS accounts for approximately 25%-40% of all adolescents experiencing chronic pain, affecting the equivalent of approximately 6.2% of all adolescents nationwide (Anthony & Schanberg, 2001; Buskila, 2009).

Societal Impact

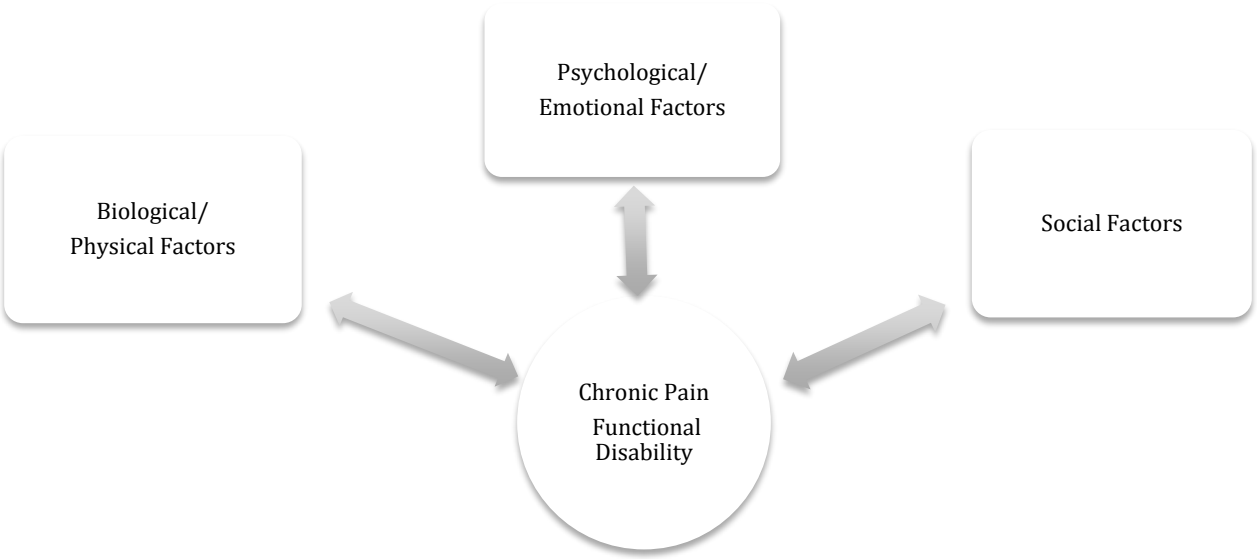
Economically, financial impact of JPFS is significant related to direct medical care costs resultant from frequent provider visits in addition to indirect costs such as parental lost work productivity and wages due to time off to care for the child (Ho et al., 2008; Perquin, Hazebrook-Kampschreur et al., 2000; Perquin et al., 2001). For example, the average adolescent with JPFS sees three or more primary care providers over a symptom duration period of two to three years prior to any rheumatologic evaluation and treatment initiation (Gedalia et al., 2000; Romano, 1991; Siegel et al., 1998). Furthermore, results from longitudinal and retrospective studies have indicated that pain experienced during childhood frequently persists into adulthood, impacting future social interactions, relationships and economic productivity (Brattberg, 2004; Jones, Silman, Power, & Macfarlane, 2007; Perquin et al., 2003). For instance, in a recent longitudinal study, 94 adolescents with JPFS originally seen at a rheumatology clinic with a mean onset age of 12.7 ± 2.6 years were followed up approximately 6 years post diagnosis into early adulthood (Kashikar-Zuck et al., 2014). Study findings indicated that greater than 80% continued to report FM symptoms including persistent pain and over half also met diagnostic criteria for adult FM. Moreover, the JPFS group reported significantly lower physical functioning, higher levels of

mood disorders, lower perceived health status and were less likely to attend college as compared to a healthy control group.

Pathophysiology

The underlying pathophysiology in JPFS is not well understood. Due to a scarcity of research in the area of JPFS and its pathophysiological underpinnings what is known is based on findings in the adult FM literature. Aligned with a biopsychosocial perspective, current literature suggests that both biological/pathophysiological aspects as well as psychosocial characteristics are associated with the development and maintenance of JPFS (**see Figure 1.1**) (Engel, 1977; Evans, Tsao, Sternlieb, & Zeltzer, 2009; Gatchel, Peng, Peters, Fuchs, & Turk, 2007). The biopsychosocial perspective purports that the experience of each adolescent is unique, with psychosocial and biological factors interacting in the modulation of JPFS symptoms and levels of functional disability.

Figure 1.1. The Biopsychosocial Model



Biological theories. A number of theories have emerged regarding the underlying pathophysiological basis of JPFS that include but are not limited to: (a) altered pain processing in the central nervous system (Desmeules et al., 2003; Staud, Vierck, Cannon, Mauderli, & Price, 2001), (b) neurobiochemical changes including increased level of excitatory (glutamate) and nociceptive (substance P) neurotransmitter leading to pain signal augmentation (Harris et al., 2009; Russell et al., 1994; Valdés et al., 2010), and decreased levels of serotonin an inhibitory neurotransmitter (Russell, Vaeroy, Javors, & Nyberg, 1992), (c) descending pain inhibitory pathway dysfunction (de Souza, Potvin, Goffaux, Charest, & Marchand, 2009), (d) autonomic dysregulation as evidenced by hyperactivity of the sympathetic nervous system and reduced parasympathetic activity (Cohen et al., 2000) and (e) disturbed sleep patterns (alpha wave intrusion in delta stage four non-rapid eye movement sleep) (Siegel et al., 1998). Further, potential neurobiochemical changes resulting in decreased levels of serotonin have been associated both in the pathophysiology of mood disorders, the pain process and FM (Wolfe, Russell, Vipraio, Ross, & Anderson, 1997).

Genetic predisposition. A possible genetic correlate has been extrapolated from the adult FM body of literature and is supported in the JPFS literature. First-degree relatives of those with FM experience an eight-fold risk of developing the illness (Arnold et al., 2004; Buskila, Neumann, Hazanov, & Carmi, 1996; Buskila & Neumann, 1997). In one genomic study of FM families, a 13.6 recurrence risk ratio for sibling recurrence was observed (Arnold et al., 2013). Similarly, in a study by Kashikar-Zuck et al. (2008a), a four-fold incidence of FM in mothers of JPFS adolescents as compared to mothers of healthy controls was observed. Taken together, these results seem to support both familial environmental and behavioral influences as well as a genetic component in development and maintenance of JPFS.

Psychosocial antecedents. Familial influences such as parental divorce, parental substance abuse, parental anxiety and depression are common psychosocial antecedents postulated in the development and maintenance of JPFS (Conte, Walco, & Kimura, 2003; Imbierowicz & Egle, 2003; Schanberg, Keefe, Lefebvre, Kredich, & Gil, 1998). Family environment factors including poor communication, increased conflict and disaffected relationships are also reported in JPFS as potential exacerbating factors (Kashikar-Zuck et al., 2008a). The presence of such psychosocial stressors may trigger pain onset or generalization of pain in adolescents with JPFS.

Functioning in JPFS

JPFS adversely impacts all aspects of quality of life including physical, social and emotional functioning creating significant functional disability (Hunfeld et al., 2001). Conceptually functional disability, while related to quality of life, is independently defined as a limitation, difficulty or restriction in completing activities across areas of daily life including physical, social and emotional functioning (Flowers & Kashikar-Zuck, 2011; Palermo et al., 2008). In fact, the JPFS adolescent was found to have the highest levels of functional disability as compared to other adolescent chronic pain conditions such as juvenile rheumatoid arthritis (Reid, Lang, & McGrath, 1997).

Physical function

Physical function in JPFS is severely compromised. Theoretically, physical function encompasses several areas of functioning including: (a) physical fitness, (b) subjective perception of ability to participate in day-to-day activities and (c) general physical activity (Wilson & Palermo, 2012). Difficulty participating in physical activities such as physical education in school, sports, and leisure or play (primary means of socialization adolescence) is

extensively reported by the JPFS adolescent (Kashikar-Zuck et al., 2010; Kashikar-Zuck, Flowers et al., 2010; Wilson & Palermo, 2012). To date, only a handful of studies have included objective measures of physical function, thus far, results have shown that the JPFS adolescent engages in lower physical activity levels as compared to healthy peer counterparts (Long, Palermo, & Manees, 2008; Wilson & Palermo, 2012). For example, through the use of actigraphy, objective measure of activity levels indicate that an adolescent with JPFS spends less time engaged in moderate or vigorous activity levels (Kashikar-Zuck et al., 2010; Stommen, Verbunt, Gorter, & Goossens, 2012) with only 23% meeting the rheumatology recommendations of 30 minutes of moderate physical activity daily and only one the national guidelines of 60 minutes daily (Kashikar-Zuck et al., 2010). Similarly, using actigraphy, Long and colleagues (2008) found that none of the chronic pain adolescents met physical activity recommendations. In fact, significant associations between the levels of physical activity the adolescent with JPFS engages in and the levels of pain intensity have been found (Kashikar-Zuck et al., 2010; Rabbitts, Lewandowski, Karlson & Palermo, 2014). Furthermore, in a recent study the majority of adolescents reported pain as the primary reason for avoiding engagement in physical activity (Roth-Isegkeit, 2005). Therefore, physical function is the primary dependent variable in this body of work. We expect to find that increasing engagement in physical activity through the practice of yoga (Manuscript V) will decrease functional disability consistent with other studies findings that functional disability was inversely associated with adolescent activity levels (Long et al., 2008; Rabbitts, Holley, Karlson, & Palermo, 2014).

Fear Avoidance in physical function. The fear-avoidance framework provides one proposed explanation for the relationship between pain, decreased physical activity and functioning. In adolescents, cognitively linking physical activity with pain leads to an avoidance

of participation in activities, due to fears of pain exacerbation (Asmundson, Norton, & Norton, 1999; Wilson, Lewandowski, & Palermo, 2011). Subsequently, the avoidance of physical activity leads to a spiral of physical deconditioning further aggravating pain and other symptoms (Gualano et al., 2010; Vlaeyen & Linton, 2000). In fact, pain-related fear has shown to be a predictor of limitations in physical activity (Wilson et al., 2011) and functional disability (Martin, McGrath, Brown, & Katz, 2007; Simons et al., 2011). In turn, fear of pain and pain-related anxiety may account for significant functional disability and higher pain ratings (Lynch, Kashikar-Zuck, Goldschneider, & Jones, 2006; Vervoort, Goubert, Eccleston, Bijttebier, & Crombez, 2006). Accordingly, further investigation into interventions aimed at decreasing fear-avoidance and increasing engagement in physical activity in the JPFS is needed.

Emotional function

Emotional function is generally considered to be a compilation of mood, emotion, and emotional regulation and relates closely to social function, particularly during the adolescent developmental period (Roeser, Eccles, & Sameroff, 1998; Yurgelun-Todd, 2007). Adolescents with JPFS are extremely vulnerable to emotional regulation difficulties with an estimated prevalence of concurrent mood disorders of 67.1% (Kashikar-Zuck et al., 2002; Kashikar-Zuck et al., 2008b; Mikkelson et al., 1997). JPFS adolescents experience higher levels of anxiety and depressive symptoms, as compared to healthy peer counterparts in community samples (Conte et al., 2003; Kashikar-Zuck, Goldschneider, Powers, Vaught, & Hershey, 2001; Kashikar-Zuck et al., 2008a). In fact, over half of adolescents with JPFS meet the criteria for anxiety disorder (Conte et al., 2003; Kashikar-Zuck et al., 2008b). The presence of anxiety and depressive symptoms has been linked to lower pain thresholds, augmented pain perception and decreased social interaction (Vlaeyen, Kole-Snijders, Boeren, & van Eek, 1995). In two separate studies,

Kashikar-Zuck and colleagues found strong associations between depressive symptoms and higher levels of functional disability (Kashikar-Zuck et al., 2002; Kashikar-Zuck et al., 2001).

JPFS adolescents also report feelings of ineffectiveness and difficulty dealing with their pain (Conte et al., 2003; Kashikar-Zuck et al., 2001). Current literature suggests that the adolescents' belief of self-control over their pain (pain self-efficacy) and emotional regulation is associated both with physical and emotional functional outcomes (Kashikar-Zuck, Sil et al., 2013; Libby & Glenwick, 2010; Turner, Holtzman, & Mancl, 2007). Furthermore, the adolescent's understanding of pain in addition to emotional regulation has been shown to strongly influence pain intensity and consequently functional disability (Arntz & Claassens, 2004).

Social function

JPFS also presents unique challenges in the social domain of function, as it coincides with Erickson's psychosocial developmental stage of identity development (Erikson, 1959). During this stage, the adolescent is attempting to establish autonomy with increasing dependence on peer relationships experiencing a strong desire to "fit it", gain social acceptance with fear of ridicule and social exclusion being the driving force of daily life (Kistner, David, & Repper, 2007; Rosenthal, Gurney, & Moore, 1981). For adolescents, the experience of pain and functional disability creates conflict with normal social development by means of limiting their opportunity for social interactions (Claar, Walker, & Smith, 1999; Eccleston, Wastell, Crombez, & Jordan, 2008).

JPFS adolescents have fewer friendships and are more socially isolated (Kashikar-Zuck et al., 2007) engaging less in social interaction (Forgeron et al., 2011). Further, social acceptance is compromised, with the majority of adolescents with chronic pain conditions

reporting social rejection (Forgeron et al., 2011; Merlijn et al., 2003). One theory is that social rejection results from the lack of observable disease processes in JPFS and the assumption that the pain behaviors are merely attention seeking (Kashikar-Zuck et al., 2007). As a result, the adolescent is more likely to withdraw from peer relationships and not discuss their diagnosis or pain experiences (Merlijn et al., 2003). For example, in a cross-sectional survey of 751 adolescents with chronic pain by Roth-Isigkeit and colleagues (2005), 46.7% reported avoiding meeting with friends due to their pain. Many find it difficult to explain JPFS to their peers (Kashikar-Zuck et al., 2007). A cycle of adolescent withdrawal and peer exclusion ensues that has been linked to elevated levels of depression and anxiety, further compromising functional outcomes (Hymel, Rubin, Rowden, & LeMare, 1990).

One primary context for social development during adolescence is school attendance (Logan, Simons, Stein, & Chastain, 2008). The adolescent with JPFS misses more school and is more likely to be homeschooled than their peers (Kashikar-Zuck, Johnston et al., 2010; Logan et al., 2008). In one study by Reid and colleagues (1997), it was determined that the JPFS adolescent missed 22.6 days of school per school year. In other cross-sectional studies, the average was 5 absences per month although some missed significantly more (Kashikar-Zuck et al., 2002; Logan et al., 2008). On anecdotal report, the majority of JPFS adolescents report missing school due to pain (Roth-Isegkeit, 2005). Taken together, the overall results seem to indicate the severity of the impact of pain on functioning (physical, emotional and social) and ensuing functional disability in adolescents with JPFS.

Management of JPFS

To date, there is an absence of standardized evidence-based treatment guidelines in JPFS. Multiple position statements call for the use of exercise and education as first-steps in treatment

of JPFS (Buskila, 2009; Cunningham & Kashikar-Zuck, 2013; De Blecourt, Preuper, Van der Schans, Groothoff, & Reneman, 2008). However, despite the clinical recommendations little evidence supporting their use exists. Although, limited educationally focused RCT's have proven education to be feasible in adolescent pain populations (Kashikar-Zuck et al., 2014; Kashikar-Zuck et al., 2012; Lommel, Bandyopadhyay, Martin, Kapoor, & Crofford, 2011), these results have also indicated that education alone does not improve physical function or pain (Cunningham & Kashikar-Zuck, 2013). Likewise, controlled studies of exercise are limited with mixed support for traditional aerobic exercise ability to relieve pain in general chronic pain adolescent populations (Singh-Grewal et al., 2007; Stephens et al., 2008; Takken et al., 2008). Only one study has examined the use of traditional aerobic exercise in a JPFS population (Stephens et al., 2008). In this study pain, symptom severity, emotional and functional outcomes were compared in 33 adolescents with JPFS randomized to either the aerobic intervention or Qigong movement therapy control group. The primary finding was that adolescents participating in the aerobic group exhibited improved physical function and decreased functional disability, while overall pain intensity and JPFS symptom severity were negative as compared to controls. The authors acknowledged sample size limitations and the comparison of two movement based groups on JPFS outcomes, calling for further controlled clinical studies to determine the effect of exercise training on adolescents with JPFS. Both intervention arms were found to be safe and free from adverse events. Despite limited scientific evidence supporting the use of exercise in JPFS, anecdotal clinical evidence suggests that adolescents participating in an exercise program have better clinical outcomes (pain, physical and psychosocial functioning) (Gedalia et al., 2000). Further investigation into exercise programs with a mind/body approach that may engage

adolescents in treatment and meet the physical challenges (such as deconditioning) of JPFS is needed (Kashikar-Zuck, Zafar et al., 2013).

Further complicating management is the poor response to conventional interventions by most JPFS adolescents. Although over 70% report taking one or more medications (most commonly selective serotonin reuptake inhibitors (SSRI's), non-steroidal anti-inflammatory drugs (NSAID's), and/or anti-convulsants) conventional pharmacotherapy treatments are limited in their ability to manage JPFS (Kashikar-Zuck et al., 2010). Current pharmacotherapy provides only modest and short-term symptom improvement in pain and physical function (Anthony & Schanberg, 2005; Gedalia et al., 2000). In one pediatric study, an association between the frequency of analgesic use and higher pain and functional disability levels was reported (Fichtel & Larsson, 2002). Frequently, undesirable medication side effects only potentiate the negative effects on adolescent functioning (Meldrum, Tsao, & Zeltzer, 2009). As with many medications used in pediatrics, there is a lack of controlled therapeutic clinical trials to support the efficacy and safety of FM pharmacotherapy in JPFS (Kashikar-Zuck, 2006). Examining management of JPFS from the biopsychosocial perspective, an integrative intervention addressing all three domains (biological/physical, emotional and social) is necessary for the adolescent with JPFS (Kashikar-Zuck, 2006).

Yoga as a therapeutic intervention

Yoga has produced promising results in the adult FM literature (e.g. Carson et al., 2010). Two recent meta-analysis of yoga for adults with FM demonstrated improvements in sleep and pain (Langhorst, Klose, Dobos, Bernardy, & Hauser, 2012; Mist, Firestone, & Jones, 2013). Moreover, meta-analyses of aerobic trials in adults consistently improve physical function with smaller improvements in pain, and no improvements in sleep (Hauser et al., 2010). An

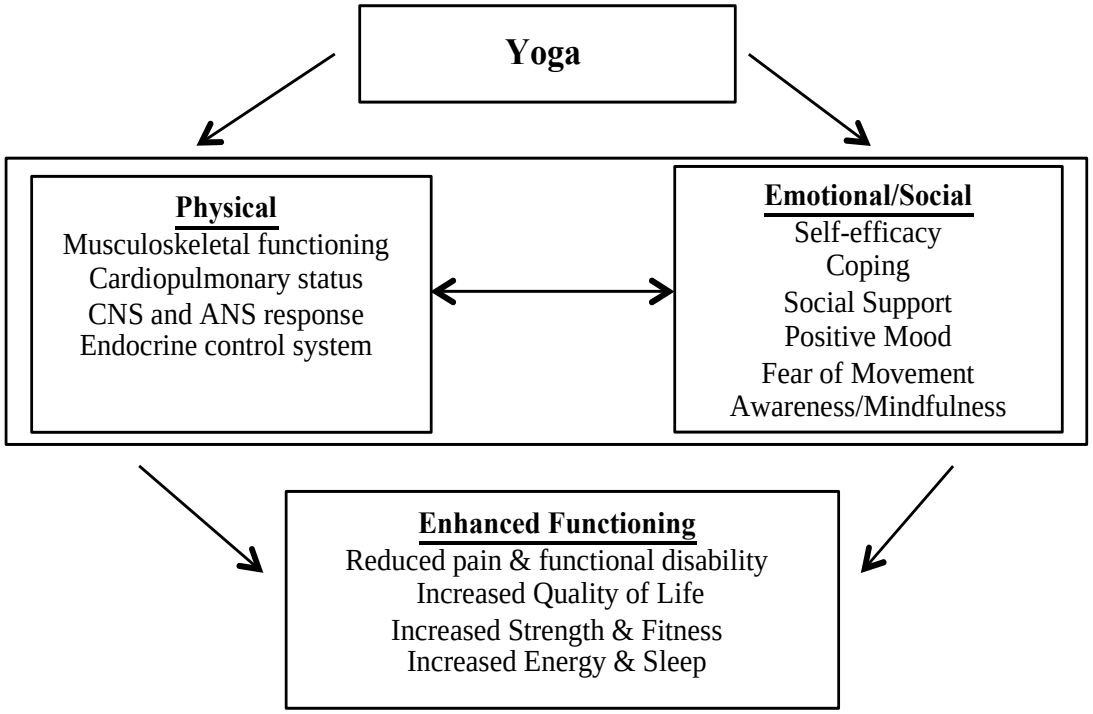
increasingly popular form of exercise, yoga includes a mind-body component (potentially combining both education and exercise effects) and is versatile and adaptable to both physical ability and developmental levels (Hartmann & Vlieger, 2012).

Yoga, as physical exercise, has become popularized in Western society in recent years and encompasses a variety of methods and approaches. However, central to the yoga tradition, mindfulness strategies are incorporated to increase awareness of negative self-talk, automatic judgment of sensations, and other unhelpful emotional patterns. Yoga practice promotes awareness of oneself, ones illness and limitations (McCracken, Carson, Eccleston, & Keefe, 2004). Mindfulness is being open and receptive to the present, being willing to learn from their experiences, minimizing negative self-thoughts and living through the pain (Biegel, Brown, Shapiro, & Schubert, 2009; Carson et al., 2010; Evans et al., 2009; Gatchel et al., 2007). These mindful strategies have been linked to lower stress, improved mood, and decreases in functional disability (Degotardi et al., 2006; Kashikar-Zuck, Swain, Jones, & Graham, 2005; Kashikar-Zuck et al., 2012; Merlijn et al., 2005; Wetherell et al., 2011). Further, mindfulness is an accepted component of many mainstream psychological interventions such as cognitive behavioral therapy (CBT) and acceptance and commitment therapy (ACT), both of which have produced beneficial effects on mood and functioning in JPFS (Degotardi et al., 2006; Kashikar-Zuck et al., 2005; Kashikar-Zuck et al., 2013; Kashikar-Zuck et al., 2012). As mindfulness is an inherent component to yoga practice (mind/body union) for purposes of this body of work mindfulness will not be considered an independent concept.

Conceptually, considered from the biopsychosocial perspective, yoga shows potential to impact body, mind and social environment leading to improvement in pain, functional disability and quality of life outcomes (Evans et al., 2009). Therefore, the model of the biopsychosocial

benefits of yoga (**Figure 1.2**) developed by Evans and colleagues (2009a), derived from the biopsychosocial model and modified for JPFS guides the conceptual understanding of how yoga may impact functioning in JPFS in this body of work.

Figure 1.2. Conceptual Model of the Biopsychosocial Benefits of Yoga modified for JPFS adapted from Evans et al., 2009



Effect on physical function

Several explanations on how yoga benefits the juvenile FM patient have been explored. Comprised of physical movement and a focus on breathing and relaxation techniques, yoga has shown results in all domains of functioning. In the structural/physiological domain, yoga movement promotes strength and flexibility (Evans, Subramanian, & Sternlieb, 2008; Raub, 2002) and produces a relaxation response by increasing parasympathetic activity (Sarang &

Telles, 2006) resulting in vascular and muscular relaxation. This relaxation response is beneficial in JPFS, as symptom etiology has been linked to autonomic dysregulation (Petzke & Clauw, 2000). Moreover, a recent systematic review indicated yoga's' ability to improve physical health and fitness, decreasing functional disability in generalized clinical pediatric populations (Birdee et al., 2009).

Effect on emotional function

Mood enhancing effects (Streeter et al., 2007; Woolery, Myers, Sternlieb, & Zeltzer, 2004), increased social functioning and peer interaction (derived from group participation) (Birdee et al., 2009; Evans, Tsao, & Zeltzer, 2009; Kaley-Isley, Peterson, Fischer, & Peterson, 2010; Woolery et al., 2004) are all positive psychosocial benefits found to be associated with yoga practice. In two separate RCT's, significantly reduced levels of adolescent depression and anxiety following yoga practice (Kuttner et al., 2006; Woolery et al., 2004). Moreover, anecdotal reports from the Khalsa et al. (2012) RCT revealed the adolescents felt more "calm", "relaxed" and that yoga gave them tools to "handle day-to day life". One premise behind the significant impact on depression and anxiety found in these studies is yoga's focus on breath awareness and control. The slow, expansive and focused breath balances the sympathetic and parasympathetic nervous systems slowing the rapid, shallow breathing commonly found associated with anxiety or breath holding often found in those experiencing pain (Hennard, 2011). Of note, in one study, it was found that yoga practice reduced breathing rates and anxiety more than traditional forms of physical activity during the same treatment period (Telles & Naveen, 1997).

Effect on social function

Group practice, and being in a like group of peers, has also been associated with positive social benefits, promoting enhanced social functioning and quality of life (Moadel et al., 2007; Weinberger, Tierney, Booher, & Hiner, 1990). Furthermore, the feelings of mastery of yoga poses that comes with practice has shown to improve feelings of effectiveness and increased perception of ability to deal with pain (Carson et al., 2010; Steuck & Gloeckner, 2005; Woolery et al., 2004).

Yoga for adolescent chronic pain populations

Unfortunately, to date, there is limited evidence on the use of yoga for adolescent chronic pain with no studies on the use of yoga for the JPFS adolescent. Yet, the evidence from five separate studies in other pain populations (irritable bowel, juvenile rheumatoid arthritis, headaches and primary dysmenorrhea) shows the potential of yoga practice to reduce functional disability and pain (Brands, Purperhart, & Deckers-Kocken, 2011; Evans et al., 2010; Hainsworth et al., 2013; Kuttner et al., 2006; Rakhshaee, 2011). All but two studies showed significant reduction in pain intensity (Evans et al., 2010; Kuttner et al., 2006; Rakhshaee, 2011) while the remaining two indicated improvement trends (Brands et al., 2011; Hainsworth et al., 2013). Four of the studies reported a decrease in functional disability and improvement in physical functioning and two of the four studies reported global improvement in quality of life (Evans et al., 2010; Kuttner et al., 2006). In contrast, one study reported no significant pre-post differences of daily functioning scores and quality of life, although improvement trends were noted (Hainsworth et al., 2013). Across studies, there were no reported adverse events. Additionally, the adolescents participating in these studies reported enjoying practicing yoga, producing positive emotional and social effects (Brands et al., 2011; Evans et al., 2010; Kuttner

et al., 2006) and in a separate study reported willingness to participate in yoga practice (Tsao, Meldrum, Kim, Jacob, & Zeltzer, 2007). Taken as a whole, the extant data indicate the safety, feasibility and acceptability of yoga, used a therapeutic intervention.

Purpose and Specific Aims

The purpose of this body of work is to determine the influence of the use of yoga on functional outcomes in adolescents with JPFS. The first specific aim is to synthesize clinical presentation, pathophysiology and current treatment recommendation in fibromyalgia (**Table 1.1**). To address this aim, a clinical review of fibromyalgia and its treatment was performed. Currently, due to the limited evidence in JPFS in comparison to the significant scientific advances found in the adult literature, this review was done presenting findings using an adult FM population and is assumed to mirror key components of JPFS. Current evidence suggests that JPFS clinical characteristics and management recommendations are in alignment with those found in adult FM (Kashikar-Zuck et al., 2014).

Accordingly, it is this lack of a clinical description and understanding of what contributes to functional disability in adolescent chronic pain populations that leads to the next aim in this body of work. The second aim is to quantify associations among pain characteristics, psychological factors, general health factors and functional disability in adolescents with idiopathic chronic pain (**Table 1.1**). In this analysis, the relationship between functional disability, pain characteristics (worst pain, typical pain, pain frequency and widespread pain), psychological factors (depressive symptoms and pain self-efficacy), sleep, BMI, and physical activity (general health factors) will be explored. We hypothesize that pain characteristics, psychological factors; sleep problems, BMI, and physical activity will be significant constructs of functional disability. We also hypothesize, that general health factors will contribute

significantly to functional disability after controlling for the influence of pain characteristics, psychological factors and sleep problems. This analysis will be based on data gathered on 314 adolescents from an academic health centers pediatric pain management clinic in the Pacific Northwest.

The third aim is to determine engagement in, perceived benefits and barriers to yoga participation in FM (**Table 1.1**). To address this aim a 16-item cross-sectional survey study was conducted on-line accessing participants from a database maintained by two fibromyalgia support and advocacy non-profit organizations. In this analysis a convenience sample of adults with FM was used.

The fourth aim is to synthesize current evidence on the feasibility, acceptability, safety and efficacy of yoga as a therapeutic intervention for pain and functional disability in a clinical population of adolescents with chronic pain (**Table 1.1**). To address this aim, a systematic review of literature on the use of yoga in adolescents was conducted. To date, only 5 studies have been done in adolescent pain populations. Despite the small number of studies, this evidence supports the case for further study on the use of yoga in JPFS.

Building on aim four, aim five is to explore the feasibility and examine the effects of a yoga intervention on functional disability, pain, and quality of life in adolescents with chronic pain. A sub-aim is to identify and characterize responders versus non-responders of the yoga intervention (**Table 1.1**). This aim will be tested using an open label, single group 8-week interventional study. It is hypothesized that adolescents participating in yoga will demonstrate improvement in functional disability, pain and quality of life.

Table 1.1. Specific Aims and How Addressed	
Specific Aim	**Title of Paper for How Aim Will be Addressed**
1) Synthesize clinical presentation, pathophysiology and current treatment recommendations in fibromyalgia	**Chapter II:** Optimizing fibromyalgia management
2) To quantify associations among pain characteristics, psychological factors, general health factors and functional disability in adolescents with idiopathic chronic pain *Hypothesis 1:* Pain characteristics (worst pain, typical pain, pain frequency and widespread pain), psychological factors (depressive symptoms, pain self-efficacy and optimism) sleep problems and general health factors (sleep disturbances, BMI, and physical activity) will be significant constructs of functional disability. *Hypothesis 2:* General health factors will contribute significantly to functional disability after controlling for the influence of pain characteristics, psychological factors and sleep problems.	**Chapter III:** Predictors of functional disability in adolescent idiopathic chronic pain
3) Determine engagement in, perceived benefits and barriers to yoga participation in fibromyalgia *Hypothesis:* Perceived benefits of yoga will include improvement of symptoms while fear of yoga difficulty will be most commonly reported perceived barrier.	**Chapter IV:** Interest in yoga among fibromyalgia patients: An international internet survey

4) Explore current evidence regarding the feasibility, acceptability, safety, and efficacy of yoga as a therapeutic intervention in pediatric chronic pain populations. *Hypothesis:* Yoga practice will be associated with better functional outcomes (decreased pain and functional disability).	**Chapter V:** Yoga for pediatric chronic pain populations: A review
5) Explore the feasibility and examine the effect of a yoga intervention on pain, functional disability and quality of life in the adolescent with chronic pain. *Hypothesis:* Adolescents participating in yoga will demonstrate greater improvement in functional disability, pain and quality of life. 5a) Identify and characterize responders versus non-responders of the yoga intervention	**Chapter VI:** Yoga for the adolescent with chronic pain: A pilot study

Summary

This body of work will be the first to explore the efficacy of yoga as a therapeutic intervention in JPFS**,** filling a critical gap in knowledge. Results from the analysis will add to the knowledge the effects of yoga on pain, functional disability and all aspects of the adolescent quality of life and could be applied to a broader clinical population of adolescents with chronic regional pain and contribute to the development of treatment recommendations/guidelines for JPFS.

CHAPTER II: OPTIMIZING FIBROMYALGIA MANAGEMENT

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Abstract

Fibromyalgia (FM) is a persistent pain state that is commonly diagnosed and managed by nurse practitioners. FM affects approximately 10 million people in the U.S, with women accounting for 80-90% of the cases (Lawerence, Felson, Helmick, & et al., 2008; Weir et al., 2006). This article summarizes current tenants regarding the etiology, pathophysiology, clinical presentation, diagnostic standards, pharmacological and non-pharmacological treatments that are needed for the successful management of FM. Nurse practitioners are ideally suited to coordinate a collaborative, multidisciplinary treatment approach. These may include medications, exercise, cognitive strategies, and selected complementary/alternative treatments. Also critical is for the nurse practitioner to provide hope and gently redirect patients away from dangerous treatments or therapies that have clearly tested negatively.

Optimizing Fibromyalgia Management

Fibromyalgia (FM), a chronic widespread pain disorder, is common, costly and can be highly debilitating affecting approximately 10 million people in the U.S, with women accounting for 80-90% of the cases (Lawerence et al., 2008; Weir et al., 2006). Fibromyalgia most commonly presents in the 3rd and 4th decade with a prevalence peaking at 7% of females in the 6th decade (Jones, Bennett, Ward, & Deodar, 2011). Provider misconceptions of the illness being psychosomatic in nature as well as few visible signs often lead to under diagnosis or misdiagnosis leading to delayed or inappropriate treatment. The average FM patient sees 5 different health care providers over an 8 year period before receiving a FM diagnosis, with over 27% feeling that their health care provider did not view FM as a "very legitimate" disorder (Bennett, Jones, Turk, & et al., 2007). FM is a debilitating disorder affecting the patients' quality of life, socially and economically impairing their ability to work and maintain relationships with family and friends (Arnold et al., 2008). The nurse practitioner is a vital component of the treatment team, who can diagnose FM, identify of co-morbidities, and treat associated symptoms (Paiva & Jones, 2012). This article summarizes current tenants regarding the etiology, pathophysiology, clinical presentation, diagnostic standards, pharmacological and non-pharmacological treatments that are needed for the successful management of FM.

Etiology

Pre-disposing factors long associated with the increased incidence of FM are two-fold: environmental stimuli and genetics. Environmental triggers may include viral infections (parvovirus, hepatitis, HIV and possibly Lyme), adverse life events such as past history of painful conditions related to injury or trauma (motor vehicle trauma, regional pain syndromes, post-traumatic stress disorder) or traumas such as abuse, but not natural disasters (Bennett et al.,

2007; Buskila, Atzeni, & Sarzi-Puttini, 2008; Hauser, Kosseva, Uceyler, Klose, & Sommer, 2011).

Additionally, research has shown a genetic correlate in the development of the disorder with first degree relatives showing an eight times greater risk of developing the illness (Arnold et al., 2004). Providers should be aware of family history of chronic pain and advise patients to minimize risk of environmental triggers. Many suggest more aggressive pharmacologic and non-pharmacologic treatment for these patients at the onset of symptoms (Kindler, Jones, Perrin, & Bennett, 2010; Williams & Clauw, 2009).

Pathophysiology

People with FM have objective, reproducible findings of enhanced sensory processing. These findings are proposed to be the biological basis for most symptoms of FM and include: altered pain processing in the central nervous system or "central sensitization" that is characterized by hyperexcitable nociceptors leading to an increased pain response to non-painful stimuli (allodynia), the experience of pain at lower levels of stimulation than a healthy individual (hyperalgesia), and the expansion of receptive fields outside the initial pain locus (Paiva & Jones, 2012). Further supporting the theory of central sensitization is that FM patients exhibit abnormal windup or temporal summation in which ongoing nociceptive input results in dorsal horn neurons exhibiting increased excitability and spontaneous activity resulting in worsening pain with the repetition of pressure (Staud et al., 2001). Contributing to altered pain sensitivity in FM patients is increased levels of glutamate (excitatory neurotransmitter) and substance P (nociceptive neurotransmitter) at 2-3 times the level of an healthy individual (Harris et al., 2008). Increased levels of these neurotransmitters result in increased duration, amplification and augmentation of the pain signal (Desmeules et al., 2003). In addition to central sensitization, FM

patients have shown dysfunction in descending inhibitory pathways with absent or attenuated analgesic response in "pain inhibits pain" testing (de Souza et al., 2009). Low levels of serotonin, norepinephrine and dopamine in the cerebrospinal fluid of FM patients also support the idea of descending inhibitory pathway dysfunction. These biomarkers are commonly analyzed in research settings but are not useful in clinical practice as they do not alter treatment decisions.

Clinical Presentation

The FM patient may appear healthy with no outward signs of illness, yet will report multiple symptoms with varying degrees of physical dysfunction. The most common chief complaint being widespread body pain described as originating from muscles and joints (Bennett, 2009). Other common presenting complaints including fatigue, sleep disturbances, cognitive dysfunction, stiffness (morning stiffness being reported as having the most impact on ADL's), tenderness and fitness considerably lower than age-expected norms (Bennett, 2009). People with FM often report perceived symptom exacerbating factors from changes in weather, sleep deprivation, increase in activities or strenuous activity and stress (Bennett et al., 2007).

The clinical presentation of FM includes symptoms that may be related to alterations in central processing. Fatigue and sleep disturbances, in the form of non-restorative sleep or insomnia, are cited as a significant factor for morbidity (Arnold, 2010). Cognitive symptoms include the presentation of "Fibro Fog" a phenomena of patient difficulty multi-tasking under distraction, forgetfulness, short-term memory loss, decreased mental alertness and concentration difficulties (Arnold, 2010). Approximately 45-69% of FM patients have concurrent mood disorders most commonly anxiety disorder and depression (Arnold, 2010). Many FM patients also experience difficulty with other common comorbidities such as restless leg syndrome,

irritable bowel/bladder syndrome, chronic headaches, and temporomandibular disorder (TMD) (Arnold, 2010).

Diagnostic Criteria

Formal recognition of FM began in 1990 with the American College of Rheumatology (ACR) classification criteria. The combination of widespread pain and mild or greater tenderness in greater than or equal to 11 of 18 tender point sites yields a sensitivity of 88.4% and a specificity of 81.1%. Arguments for adopting the preliminary 2010 criteria include the perception that the tender point exam is often either performed incorrectly or skipped entirely. For these reasons some think that fibromyalgia has become a symptom-based diagnosis (Staud, Price, & Robinson, 2010). Others are concerned that the proposed 2010 criteria may misdiagnose highly symptomatic persons with regional pain as fibromyalgia. **Table 2.1** outlines both the 1990 and the 2010 ACR criteria (Wolfe et al., 1990; Wolfe et al., 2010).

Table 2.1. 1990 vs. 2010 ACR FM Diagnostic Criteria

1990 ACR Criteria	Preliminary 2010 ACR Criteria
Widespread pain (bilateral pain above & below waist; axial skeletal pain involving cervical thoracic, lumbar spine & anterior chest) present for 3 months or greater, with no known disorder as explanation for pain	FM diagnosis is made when either of the two criteria below is met: 1) Widespread pain index ≥ 7 and a symptom severity scale score of ≥ 5. 2) A widespread pain index 3-6 and a symptom severity scale ≥ 9.
	Widespread Pain Index (WPI) 0- 7 possible points (areas of pain in past week) Areas: Left/Right for each: Shoulder girdle, upper/lower arm, hip/buttock/trochanter, upper/lower leg, jaw, chest, abdomen, upper/lower back, neck.
Pain in 11 of 18 tender points upon digital palpitation with 4kg of pressure: • occiput at the sub occipital muscle insertions • low cervical at the anterior aspects of the intertransverse spaces at C5-C7, • trapezius at the midpoint of the upper border, • the supraspinatus at the origins near the medial border, at the second rib, • upper lateral to the second costochondral junction, • lateral epicondyle, 2 cm distal to the epicondyles, • gluteal, in the upper, outer quadrants of the buttocks in the anterior fold of the muscle, • the greater trochanter, posterior to the trochanteric prominence, • knee, at the medial fat pad, proximal to the joint line	Symptom Severity (SS) Scale Score between 0-12 possible points SS scale score=sum of the 3 symptoms + extent of somatic symptoms SS scale includes: Fatigue, waking unrefreshed, cognitive symptoms for each symptom patient rates severity of problem as: 0=none, 1= slight, mild or intermittent, 2= moderate, considerable, 3=severe, life disturbing Somatic Symptoms (muscle pain, irritable bowel, fatigue/tiredness, thinking/remembering problems, muscle weakness, headache, pain/cramps in abdomen, numbness/tingling, dizziness, insomnia, depression, constipation, nausea/vomiting/diarrhea, blurred vision, dry mouth, loss of appetite, and more) rated as: 0=no symptoms, 1=few symptoms, 2=moderate number of symptoms, 3=great deal of symptoms
	Symptoms present for 3 months or greater
	No known disorder as explanation for pain

Differential Diagnosis

Few disorders present at midlife with longstanding widespread pain. Nonetheless, the NP must be certain that patients not only meet diagnostic criteria for FM, but also have no other illness that mimics FM or its common co-morbidities. Specialized rheumatic/autoimmune labs (e.g., ANA, RA titer, Anti-dsDNA, anti-Sm, anti-phospholipid) are more sensitive and specific when ordered after a positive history or physical exam, and thus are not recommended for screening. Other diagnostic tests may be indicated based on specific positive history or physical exam findings. **Table 2.2** outlines differential diagnoses, history, physical exam pearls and tests to consider.

Table 2.2. Differential Diagnosis for FM

Symptom	Differential Diagnosis	Laboratory test/pertinent history/PE
Widespread pain	Metastatic disease, hyperthyroidism, inflammatory / autoimmune disorder (rheumatoid arthritis, SLE etc.), Hepatitis C, vitamin D deficiency	pain > 6 months, physical exam normal except musculoskeletal exam, lack of weight change, TSH, RA titer, CBC, sedimentation rate, Chemistry panel with liver enzymes, hepatitis titers, urinalysis for protein, vitamin D (OH)-25
Fatigue	Anemia, Sleep Apnea, narcolepsy, hypothyroidism, HIV	Weight change, falling asleep in dangerous situations (e.g. driving), metorrhagia, CBC, TSH, polysomnogram with or without multiple sleep latency test, HIV serum antibody
Depression	Major depressive disorder, Bipolar disorder, hypothyroidism	DSM criteria for subtype of major depressive disorder and bipolar disorder, TSH
Anxiety	Generalized Anxiety Disorder, PTSD, hyperthyroidism	DSM criteria for anxiety subtype or PTSD, TSH
Abdominal pain/ diarrhea/constipation	Celiac disease, inflammatory bowel disease versus irritable bowel syndrome	Weight loss, synovitis, eye involvement, bloody diarrhea, CBC, tissue transglutaminase antibody followed by small bowel biopsy to rule out celiac, sedimentation rate +/- CRP for inflammatory bowel
Numbness/tingling in legs	Restless leg syndrome(RLS), vitamin B 12 deficiency, large or small fiber neuropathy, heavy metals (unlikely)	RLS- uncomfortable feelings in legs (or less commonly arms) that are exacerbated by rest and relieved by movement; commonly responds to challenge with dopamine agonist. Large fiber neuropathy-EMG test. Small fiber neuropathy, biopsy, but may not be covered by insurance or alter treatments, serum vitamin B +/- serum methylmalonic acid and homocysteine levels, serum tests for heavy metals
Muscle pain/weakness	Degenerative neurologic disorder, metabolic muscle disease, polymyalgia rheumatica, polymyositis, statin-induced myopathy	History of acute onset of muscle pain and stiffness in hip and shoulder girdles in someone older than 65- check an ESR. serum CK, inquire about statin medication use
Back pain	Compression fracture due to osteoporosis, neurologic origin of back pain such as stenosis, autoimmune origin of back pain such as ankylosing spondylitis, pyelonephritis	History especially spine pain that wakes patient up at night, numbness, bowel/bladder changes, pain exacerbated by bending, twisting or walking down stairs, physical exam with point tenderness over spinal processes, kyphosis, positive neurologic signs including muscle weakness, loss of sensation, negative straight leg raise. New York or Rome criteria and serum HLA-B27 for ankylosing spondylitis, urinalysis for infection

Key: ANA (anti nuclear antibody), RA titer (rheumatoid arthritis titer), CRP (C-reactive protein), SLE (systemic lupus erythmatosus), TSH (thyroid stimulating hormone), CBC (complete blood count), HIV (human immunodeficiency virus), DSM (The Diagnostic and Statistical Manual of mental Disorders), EMG (electromyography), ESR (erythrocyte sedimentation rate), CK (creatine kinase), *HLA-B27 (Human leukocyte antigen, B 27 subtypes)*

Management of Fibromyalgia

The management of the FM patient is patient-centered and highly individualized including both pharmacological and non-pharmacological treatment modalities aimed at achieving optimal functional health status. Treatment is complex and it often takes trial and error to find a combination of modalities to optimally alleviate symptoms.

Pharmacological Management of FM. Pharmacological management of FM is influenced by the severity, functional disabilities and presence of co-morbidities and will require frequent follow up and modifications dependent on patient response. The pharmacological agents which have shown the strongest evidence of efficacy in the management of FM symptoms include tramadol, duloxetine, milnacipran, and pregabalin (Arnold, Lu et al., 2004; Bennett, Kamin, Karin, & Rosenthal, 2003; Vitton, Gendreau, M., & Kranzler, J., Rao, S.G., 2004). Other medications with less conclusive research data in current use include TCA's such as amitriptyline and cyclobenzaprine (Arnold, Keck, & Welge, 2000). Sodium oxybate, a sleep and pain medication, has shown statistically significant improvement in multi-site phase III clinical trials, but as of yet has failed to attain an FDA indication for FM, perhaps due to concerns about diversion (Russell et al., 2011). This agent may not be easily reimbursed by third party payers without extensive prior authorization unless the patient also has narcolepsy (marked by excessive daytime sleepiness). Notably absent from the list of recommended agents are steroids, non-steroidal anti-inflammatory agents. These have not shown therapeutic benefit in FM. Unless the provider is using NSAIDs or steroids for an acute injury or concurrent inflammatory condition, one treatment pearl is to consider removing these from the medication regimen. Rationale polypharmacy may include pairing drugs with activity in ascending pathways such as anticonvulsants with agents that target descending pathways such as SNRI's (Russell, 2008).

Analgesics. Tramadol, a centrally acting analgesic, alone or when combined with acetaminophen, was found to significantly improve pain and functionality (Bennett et al., 2003). Tramadol is not recommended in patients with seizure disorder as it may lower the seizure threshold. It should be used cautiously in patients on SSRIs, SNRIs or other agents that activate serotonin pathways.

Antidepressants. Antidepressants are used in FM to treat pain as well as to address the common co-morbidities of depression and anxiety disorders. The use of serotonin and norepinephrine reuptake inhibitors (SRNI's) such as Duloxetine and Milnacipran, has been shown to enhance transmission in the descending inhibitory pain pathways resulting in the reduction of pain severity, stiffness and improvement in function (Arnold et al., 2004; Vitton et al., 2004). SRNI's lack the side effect profile, drug interactions and efficacy issues of the tricyclic antidepressants (TCA's) making them a more desirable treatment option. Older medications such as amitriptyline and cyclobenzaprine have shown only moderate benefit for FM symptoms and are used mainly at nighttime due to their effect on sleep quality (Arnold et al., 2000). SSRIs, while commonly prescribed in FM for mood, have not tested positively in clinical trials for FM pain. One treatment pearl is to consider SNRIs over SSRIs for people with FM.

***Anticonvulsants*.** Anticonvulsants have long been used in the treatment of neuropathic pain and in recent studies have been shown to be effective in the management of FM. Pregabalin, approved in 2007 for the treatment of FM, inhibits the release of substance P and glutamate in the CNS and has shown significant improvement in pain severity, fatigue, sleep and functionality (Arnold, Russell et al., 2008; Mease et al., 2008). **Table 2.3** outlines pharmacologic agents commonly employed in FM (Arnold et al., 2004; Arnold et al., 2008;

Bennett et al., 2003; Goldenberg, Burckhardt, & Crofford, 2004; Mease et al., 2008; Russell et al., 2000; Vitton et al., 2004).

Table 2.3. Pharmacologic Agents Commonly Employed in FM

Pharmacologic Agent	Starting Dose	Maximum Dose Studied in FM	Adverse Effects
Tramadol*	50-100mg TID - QID	300mg/ day	Headache, dizziness, somnolence, nausea, vomiting, constipation, diarrhea, dyspepsia, CNS stimulation
Duloxetine	30mg/ day	60 mg BID (FDA indicated at 60mg qd)	Nausea, dry mouth, constipation, diarrhea, fatigue, decreased appetite, dizziness, somnolence, insomnia, headache, LFT elevation
Milnacipran	12.5mg/ day	50 mg BID (FDA indicated at 50-100mg bid)	Headache, GI complaints, orthostatic dizziness, lethargy, palpitations, sweating, hot flashes
Pregabalin	50mg TID	600 mg/day (FDA indicated at 300mg bid)	Dizziness, somnolence, dry mouth, asthenia, peripheral edema
Amitriptyline**	10-25mg/ day	50 mg/ day	Dry mouth, constipation, blurred vision, urinary retention, drowsiness, insomnia, anxiety, cardiac arrhythmias
Cyclobenzaprine**	10mg/ day	40mg/ day divided doses	Drowsiness, dry mouth, dizziness, fatigue, dyspepsia, nausea, constipation, unpleasant taste, headache, nervousness, confusion, blurred vision

*= not indicated by FDA specifically for fibromyalgia. Tramadol is indicated for moderate to moderately severe pain based in part on two multi-site randomized controlled trials in fibromyalgia

**Amitriptyline and/or cyclobenzaprine were generic before any drugs were FDA indicated for fibromyalgia. Position statements recommend these drugs for fibromyalgia based on multiple studies. Third party payers in certain states require failure of these agents (side effects or inadequate pain relief) before FDA indicated drugs are covered by payers.

Non-Pharmacological Management of FM. The cornerstones of non-pharmacologic management in FM are exercise and cognitive behavioral strategies. These are supported by the most extant literature with over 100 studies in exercise and 60 in cognitive behavioral therapy. Patients are increasingly choosing other non-pharmacologic modalities such as complementary and alternative therapies as well as requesting dietary counseling. Therefore, emerging evidence for these therapies is presented. Long-term management of chronic illnesses like fibromyalgia often use a multidisciplinary approach including NPs (primary management), physicians (evaluate and manage recalcitrant comorbidities), psychologists (counseling, cognitive behavioral strategies), physical therapists (individualize exercise prescription and provide specific rehabilitation plans), occupational therapists (modify work and home environment), speech therapists (employ cognitive therapy for fibro-fog) and exercise specialists (carry out exercise classes long-term) (Casanueva-Fernandez, Llorca, Rubio, Rodero-Fernandez, & Gonzalez-Gay, 2012; Jones et al., 2011).

Exercise. Promoting structured exercise that targets aerobic, strength, flexibility and balance training are critical in FM. When supervised multimodal exercise sessions can be successfully performed without triggering an exercise induced flare, efforts to increase physical activity can be added. Multiple physiologic deficits in central and peripheral pain processing, autonomic dysfunction, neuroendocrine and inflammatory processes are known to hinder exercise success in FM (Elvin, Siosteen, Nilsson, & Kosek, 2006; Jones, Deodhar, Lorentzen, Bennett, & Deodhar, 2007; Staud, Robinson, & Price, 2005). Modifying the exercise prescription to accommodate these deficits will increase the likelihood that a patient can tolerate exercise which will eventually improve most all FM symptoms and regain physical function (Jones & Liptan, 2009; Paiva & Jones, 2012). Both land-based and water-based (balneotherapy)

programs are recommended providing that the programs are modified for FM. Ten evidence-based strategies an exercise instructor can employ include: 1) keep movement near the body's midline and limit time spent with arms overhead to decrease muscle microtrauma and delayed onset muscle soreness; 2) gradually increase standing time to maximize use of the large muscles of the hips and thighs, though chair exercises are usually employed initially; 3) allow muscles to return to baseline resting state by alternating limbs, rather than working one side for 8 counts, for example; 4) reverse pain posture with the following movements: chin back, shoulders down, crown of head lift, deep breathing, anterior chest stretches and back strengthening exercises; 5) modify poses for joint hypermobility which is common in FM; 6) limit fast or pivot turns and use a cane, wall or chair to reduce fall risk- eventually retrain balance with foam balance trainers and one-legged standing activities; 7) find an instructor who is willing to modify the exercise routine as outlined above and who uses kind self-talk as part of the class, rather than body-shape oriented verbiage; and 8) find an FM exercise friendly environment, namely one that minimizes bright light, loud noise, cold temperatures, has close proximity to restrooms and does not allow strong smells such as cigarette smoke or perfume; and, lastly, 9) start-low, go slow, but eventually get there, meaning keep working toward a full-scope exercise program. **Table 2.4** outlines additional strategies to decrease pain and fatigue in activities of daily living.

Table 2.4. Strategies to Decrease Pain and Fatigue in Activities of Daily Living

- Take shorter steps when walking downhill
- Avoid carrying a heavy shoulder bag
- Always use handrails and canes if needed
- Break often when reaching overhead repeatedly
- Use a grabber for reaching objects on high shelves
- Rearrange kitchen by placing frequently used items near waist level
- Change positions frequently
- Sit in the middle of an auditorium to keep from twisting
- Use a telephone headset and other ergonomic aids
- Use a wheeled shopping cart rather than a hand basket
- Balance rest with exercise

Cognitive Behavioral Therapy (CBT). Formal testing of cognitive behavioral strategies in FM is often positive for improving mood, reducing distress, pain-related behavior, coping and sometimes for enhancing physical function (Bernardy, Fuber, Kollner, & Hauser, 2010). These studies generally added CBT to standard care such as medications. In clinical practice, patients sometimes have access to therapists like those in the studies, but more often use strategies employed in CBT at home, in a small group or with a therapist with less expertise in FM. Nonetheless, some of the helpful CBT strategies include: reframing problems to decrease catastrophic thinking, time-based rather than task-based pacing (energy conservation), and scheduling pleasurable activities. It is notable that CBT is not a replacement for accurate diagnosis and treatment for Axis I or II disorders.

CAM. Patients with FM frequently seek alternative medicine as a treatment option with many inquiring about acupuncture. National surveys indicate that 15% of FM patients have sought acupuncture treatment (Bennett et al., 2007). The evidence is mixed on how effective acupuncture treatments are for the treatment of FM (Mayhew & Ernst, 2007). However, all of the reviews agree that true needle placement acupuncture is a successful adjunct treatment, at

least in the short term (Duncan, White, & Rahman, 2007). Acupuncture may be a useful treatment option in patients who do not respond to biomedical approaches, such as those sensitive to side effects of medications. As with other referrals, one should base their referrals on professional credentials and personal knowledge. Acupuncturists are generally licensed by a state credentialing board - in many cases the same medical board that licenses nurses and doctors.

There is less research available on the treatment of fibromyalgia with herbal or nutraceutical treatments in spite of many patients seeking these treatments. Research has found that 43% of women with fibromyalgia were taking at least one herb or supplement compared to 23% of healthy women (Shaver, Wilbur, Lee, Robinson, & Wang, 2009). Herb-drug interactions are a serious concern of which most acupuncturists are very aware. One should inform patients about possible interactions and communicate with any practitioner that might be offering such treatments to ensure the safety of the patient.

The most promising bodywork data to date supports the use of a massage technique called myofascial release. Studies indicate that this type of massage reduces anxiety, and improves sleep, pain quality of life. Those exercise therapies that naturally incorporate mindfulness such as certain yoga therapies and Tai chi have been demonstrated to improve many symptoms in FM including pain (Wang et al., 2010).

Diet. Although many FM patients report that they seek dietary guidance for helping to manage their symptoms, dietary manipulation in FM is still in its infancy. A few studies have examined the effect of a raw food vegan diet in FM subjects (Bennett et al., 2007; Donaldson, Speight, & Loomis, 2001; Hanninen et al., 2000; Kaartinen et al., 2000). These studies were able to demonstrate symptom improvement; however, no subjects were able to continue the diets

post-study due to their highly restrictive nature. It is possible that the restrictive diets may have caused improvement by inadvertently removing food additives from the diet. A study examining the effects of a class of food additives including monosodium glutamate (MSG) and aspartame, recently demonstrated that those who experienced >30% remission of symptoms on a 4 week additive-free diet, had a significant return of symptoms when challenged with MSG as compared to challenge with placebo. Published case series also support the idea that food additives like MSG and aspartame could be contributing to symptoms in FM (Ciappuccini, Ansemant, Maillefert, Tavernier, & Ornetti, 2010; Smith, Terpening, Schmidt, & Gums, 2001).

Various studies have also suggested that FM patients may be low in certain nutrients important to neurologic function including: iron, magnesium, zinc, vitamin B12, and antioxidants (Altindag & Celik, 2006; Ortancil, Sanil, Eryuksel, Basaran, & Ankarali, 2010; Regland et al., 1997; Sendur, Tastaban, Turan, & Ulman, 2008). A nutritious, whole food diet which is also low in food additives, could optimize nutrient intake, has no risk of harm, and could help prevent other diet-related comorbidities as well. Referral to a registered dietician should be considered to aid patients in optimizing their diets and to help screen for reactions to certain foods/additives.

Implications for Practice

In conclusion, nurse practitioners are ideally suited to diagnose and manage people with FM. It often requires a collaborative multidisciplinary approach including medications, exercise, cognitive strategies, and an open mind when evaluating the efficacy of newer CAM-related treatments as they emerge in the literature. Also critical is for the nurse practitioner to provide hope and gently redirect patients away from dangerous treatments or therapies that have clearly tested negatively.

CHAPTER III: PREDICTORS OF FUNCTIONAL DISABILITY IN ADOLESCENT IDIOPATHIC CHRONIC PAIN

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Abstract

Pain intensity and psychological function has been shown to be important in understanding pain related functional disability in adolescents with chronic pain. However, less is known about the contribution of general health factors (sleep disturbances, BMI and physical activity) to functional disability. Therefore, the purpose of this study is to quantify associations among pain characteristics, psychological factors, general health factors and functional disability in adolescents with idiopathic chronic pain. Data were collected from a consecutive series of 314 new pediatric pain patients in an academic pain clinic. Variables included demographics, pain intensity, location, history, frequency, pain self-efficacy, depression, and engagement in physical activity and the Children's Activity Limitations Interview (CALI), the independent variable. Findings included that pain characteristics, psychological function, sleep disturbances, and physical activity measures were strongly correlated with functional disability. A hierarchical regression analysis revealed that, pain characteristics, contributed significantly to the model and accounted for 22.7% of variance in functional disability (stage 1). Psychological function, explained an additional 12.2% of variation in functional disability (stage 2). Sleep problems, accounted for an additional 3.0% of variance (stage 3). Physical activity, explained an additional 2.4% of the variance in functional disability (stage 4). Significant predictors of functional disability included pain frequency, worst pain intensity, depressive symptoms, and physical activity. Together, all independent variables accounted for 37.7% of the variance in functional disability. Understanding a more comprehensive set of variables that contribute to adolescents' functional disability is an important step in designing effective interventions in adolescents with chronic pain.

Predictors of functional disability in adolescent idiopathic chronic pain

It is estimated that approximately 25% of children live with recurrent or chronic pain in the United States (Hoftun, Romundstad, Zwart, & Rygg, 2011). The prevalence of chronic pain increases with age, peaking during the adolescent period (ages 11-18), and occurs more commonly in girls than boys (Coffelt, Bauer, & Carroll, 2013; King et al., 2011). While adolescent chronic pain is most commonly classified by an occurrence of at least once a week and a duration of at least three months (Perquin et al., 2000), approximately 48% of adolescents with chronic pain report experiencing the pain for at least 12 months (Holm, Ljungman, & Soderlund, 2012). Likewise, the majority of adolescents report experiencing pain on a daily basis (Zernikow et al., 2012). Common presenting locations include the head, back and limbs with musculoskeletal pain accounting for the majority of all pain reported (Hoftun et al., 2011). The occurrence of single site pain is relatively uncommon (King et al., 2011), with 58-77% of those with chronic pain reporting multi-site pain, or pain in greater than one body location (Holm et al., 2012). For over half of these youth this pain is idiopathic with no identifiable cause or underlying pathology to explain the pain (Hoftun et al., 2011). This is in contrast to pain conditions associated with autoimmune disorders and hematological or cancer pain.

In these youth, this pain experience is disruptive to their daily functioning resulting in the development of functional disabilities (Haraldstad, Sorum, Eide, Natvig, & Helseth, 2011). In the adolescent, functional disability is manifested as a limitation, difficulty or restriction in completing age-appropriate activities across all domains of functioning (e.g. academic, social, emotional and physical) (Flowers & Kashikar-Zuck, 2011; Palermo et al., 2008). Aligned with a biopsychosocial perspective, biological and physical aspects as well as psychosocial factors have all been suggested as antecedents to the development of functional disability in the adolescent

with chronic pain. Relatively little is known regarding the interplay of these factors and how they contribute to the development of functional disability.

Pain and Psychological Factors

Research with adolescent chronic pain supports the presence of a relationship between pain characteristics and functional disability (Gauntlett-Gilbert & Eccleston, 2007; Hunfeld et al., 2001). However, other contextual factors may also play a role in the development of functional disability. For example, an association between depressive symptoms and functional disability in adolescents with chronic pain has been established in multiple studies (Kashikar-Zuck, Vaught, Goldschneider, Graham, & Miller, 2002; Kashikar-Zuck, Goldschneider, Powers, Vaught, & Hershey, 2001). Adolescents with chronic pain experience higher levels of depressive symptoms than their healthy peer counter parts in community samples with an estimated prevalence of concurrent mood disorders of 67% (Kashikar-Zuck et al., 2008). Furthermore, depressive symptoms have been linked to lowered pain thresholds and augmented pain perception exhibiting a bidirectional relationship between pain and depression (Vlaeyen, Kole-Snijders, Boeren, & van Eek, 1995). Other psychological factors may also be associated with the development of functional disability in these youth. Adolescent pain self-efficacy or the belief of confidence in one's own ability to tolerate, cope, and deal with pain and perform daily activities despite the pain (Asghari & Nicholas, 2001; Bandura, O'Leary, Taylor, & .et al., 1987) and adolescent optimism has been shown to exert influence on physical and psychological health outcomes (Miro, Huguet, & Jensen, 2014; Vervoort, Eccleston, Goubert, Buysse, & Crombez, 2010).

Sleep and Physical Factors

In addition to pain and psychological factors, emerging evidence promotes a range of other factors that may also affect disability. Sleep problems (difficulty initiating or maintaining sleep) are common in the adolescent chronic pain population with as many as 50% reporting sleep difficulties (Kanstrup, Holmstrom, Ringstrom, & Wicksell, 2014). Moreover, emerging evidence suggests a salient association between sleep quality, pain and deleterious effects on overall functioning (Palermo, Fonareva, & Janosy, 2008; Siu, Chan, Wong, & Wong, 2012).

Physical factors such as engagement in physical activity and body mass index (BMI) also hold potential to affect overall functional disability. The adolescent with chronic pain exhibits lower levels of engagement in physical activity as compared to their healthy peer counterparts spending more time in sedentary activities as compared to moderate or vigorous physical activity (Wilson & Palermo, 2012). Furthermore, decreased engagement in physical activity is related to higher levels of self-reported physical activity limitations, and increased risk for functional disability (Long, Palermo, & Manees, 2008). Likewise, adolescent weight status (either overweight or obese) exacerbates pain intensity and negatively impacts physical functioning further increasing the risk for functional disability (Hainsworth, Davies, Khan, & Weisman, 2009). Moreover, higher BMI scores exhibit a bidirectional relationship with decreases in peak physical activity levels (Wilson, Samuelson, & Palermo, 2010).

Overall, there is strong evidence that pain characteristics and psychological factors such as depressive symptoms contribute significantly to functional disability. However, less is known about the contribution of general health factors (such as sleep disturbances, BMI and physical activity) to functional disability. Furthermore, given our limited understanding of the relationship between general health factors and the development of functional disability,

independent of the relationship between pain characteristics and psychological factors, establishing this connection would be influential in the development of targeted future interventional research aimed at the development of interventions tailored to ameliorate the effects of pain and disability and restore functioning. Therefore, the purpose of this study is to quantify associations among pain characteristics, psychological factors, general health factors (independent variables) and subjective reports of functional disability (dependent variable) in adolescents with chronic pain. We have two hypotheses for this study:

Hypothesis 1: Pain characteristics (worst pain, typical pain, pain frequency and widespread pain), psychological factors (depressive symptoms, pain self-efficacy and optimism) sleep problems and general health factors (sleep disturbances, BMI, and physical activity) will be significantly correlated with functional disability.

Hypothesis 2: Physical activity and BMI will contribute significantly to functional disability after controlling for the influence of pain characteristics, psychological factors and sleep problems.

Design and Methods

Participants

Data was collected from a consecutive series of 314 new pediatric pain patients referred to a pediatric pain management clinic in the Pacific Northwest over a four-year period (2009-2013). The final sample of 314 was the number of pediatric patients seen in the time window for data collection. Patient medical records were accessed for demographic and clinical information. Patients and a parent or guardian completed self-report measures as part of an initial pain clinic visit assessment, which was part of the medical record. For

purposes of this study, only the adolescent reported data was included. This chart review research protocol was approved by the IRB at the academic medical center.

Participants were eligible for study inclusion if they were (1) between the ages of 11-18 years of age; (2) reported the experience of pain in duration of 3 months or greater regardless of location prior to their initial visit; (3) no other known causes of pain (must be idiopathic); (4) presented for care during the study time period; (4) completed the initial pain clinic assessment forms.

Measures

Participants completed self-report questionnaires assessing demographics, pain, activity limitations (functional disability), sleep interference, depressive symptoms, physical activity participation, and pain self-efficacy.

Pain. Pain intensity was assessed using an 11-point (0-10) numerical rating scale (NRS). Response options range from 0 or "no pain" to 10 or "worst pain". The adolescents were asked to rate their "typical level" of pain and their "worst pain" level experienced. Further, frequency of pain episodes over the past month was assessed. The numeric rating scale has been well established for use in pediatric clinical populations for the self-reported measurement of pain (Miro, Castarlenas, & Huguet, 2009; Ruskin et al., 2014). Number and location of pain sites was assessed by self-report using a standardized body map of nine potential pain locations (face, head, shoulders, chest, arms, abdomen, spine, lower back, legs) with the participants selecting which locations they experienced pain (Lester, Lefebvre, & Keefe, 1994). Participants endorsing 2 or more pain locations on the body map were considered to have multi-site pain.

Functional Disability. Functional disability was assessed by the Children's Activity Limitations Interview (CALI-21), designed to assess pain-related activity limitations in children

and adolescents (ages 8-18) by parent- and child-written report. The measure asks participants to report on pain-related limitations within the past month on 21 activities in a variety of domains, rating the difficulty in completing each activity on a 5-point rating scale, ranging from "not difficult" to "extremely difficult". A score is calculated by summing ratings for all 21 items (possible range from 0 to 84), with higher scores indicating greater functional disability. Studies of the psychometric properties of CALI-21 have demonstrated its reliability and validity (Hainsworth, Davies, Khan, & Weisman, 2007). The CALI-21 has demonstrated a high internal consistency, with Cronbach $\alpha = 0.95$ (Palermo, Witherspoon, Valenzuela, & Drotar, 2004).

Psychological Symptoms. Psychological function was assessed using the 10-item major depressive disorder (MDD) subscale of the Revised Child Anxiety and Depression Scale (RCADS). This scale was used to assess the frequency of depressive symptoms in children. Items are rated on a 4-point Likert-sale from "never" to 3 always with higher scores indicating higher frequency. Corresponding T-scores were calculated. T-scores of 65 or higher are indicative of borderline clinical threshold for depression. This measure has demonstrated good internal consistency (alpha = 0.77 for the MDD scale) and adequate one-week test-retest reliability (Chorpita, Moffitt, & Gray, 2005).

Body Mass Index. Height and weights as measured at clinic were used to calculate BMI's. BMI was calculated using the standard formula of weight (in pounds) divided by height (in inches squared) multiplied by 703. The use of BMI for weight status is consistent with other pediatric studies of physical activity and chronic pain (Wilson et al., 2010).

Sleep. Sleep disturbance was assessed by asking participants to answer "yes" or "no" to the questions "Does pain make it difficult to fall asleep" and "Does pain wake you after you fall asleep?" Further, participants reported the frequency of sleep disturbances (how often they had

difficulty falling asleep and staying asleep in a typical week) using a 4-point rating scale. General ratings of sleep quality have been used previously in other pain pediatric studies (Rabbitts, Holley, Karlson, & Palermo, 2014). Participants reporting difficulties in both falling asleep and waking due to pain were considered to have sleep problems.

Physical Activity. The adolescents' level of engagement in physical activity for a total of at least 60 minutes within the past week and over a typical week was evaluated with two single-item measures using an 8-point numeric rating scale. The two scores were then averaged to form a physical activity composite measure (Prochaska, Sallis, & Long, 2001). Weekly summative physical activity self-reports when evaluated against physical activity measures of direct observation and motion detection, have shown to have a correlation coefficient of R = 0.51 (Sirard & Pate, 2001).

Pain Self-Efficacy. The adolescents perceived ability to deal with their pain was assessed using an 11-point numeric rating scale in response to the question "How able do you feel you are able to cope or deal with your pain?" with anchors of "not able to cope at all" and "confident in my ability to cope". Another item assessing optimism, "How optimistic are you about getting better had anchors of "not optimistic at all" to "very optimistic".

Analytic Strategy

Analyses were conducted using SPSS version 23. Missing data was handled using multiple imputations. Summary statistics were used to describe the characteristics of the sample. Means and standard deviations were used for continuous data, and categorical items were described using frequency statistics. Composite variables for multi-site pain (presence of 2 or more pain locations) and sleep problems (if pain made falling and staying asleep difficult) were computed. Correlational analyses (Pearson product-moment correlation coefficients) were used

to examine the relationship between functional disability (CALI-21) and potential predictor variables. Hierarchical multiple regression analysis was performed to investigate the contribution of independent variables to functional disability after controlling for pain characteristics such as typical and worst pain intensity, known contributors to functional disability in step one.

Results

Mean scores, standard deviations and percentages for all measures are presented in **Table 3.1**. The current mean age of the sample was 15.95 (SD =3.16), predominately female (64%), and Caucasian (78.7%). Overall, adolescents reported high levels of pain with a typical pain intensity of M = 5.82 (SD =1.98) and worst pain intensity of M = 8.95 (SD =1.33). In regards to frequency, 78.5% of participants reported experiencing pain at least daily within the last month and 54.1% reported an increase in overall pain within the past month. The majority of adolescents (65.5%) reported the presence of multi-site pain. The head (31.9%), abdomen (23.4%), legs (13.6%), lower back/spine (18%), upper extremities (7%) were the most commonly reported most problematic pain locations. High levels of sleep disturbances were reported, with 67.2% of adolescents experiencing difficulty-initiating sleep due to pain and/or pain wakes them during sleep. 26.8% reported sleep disturbances occurring $\geq$ 4 nights/week.

Adolescent mean pain self-efficacy was 4.86 (SD =2.29) and mean optimism was 4.74 (SD =2.82). The RCADS depression T-score mean was 61.99 (SD =15.29). Activity limitations were evident with a CALI-21 sum mean score of 43.86 (SD =17.89). The adolescents reported a mean of 3.46 (SD = 2.34) days per week of physical activity.

Table 3.1. Adolescent Characteristics		
Age *M* (SD)		15.95 (3.16)
Gender *n* (%)	Female	201 (64.0)
	Male	113 (36.0)
Ethnicity *n* (%)	Caucasian	247 (78.7)
Parental Marital Status *n* (%)	Single	25 (8.2)
	Married	219 (72.0)
	Separated/Divorced	45 (14.8)
Familial history of chronic pain issues *n* (%)		197 (62.7)
Familial history of depression *n* (%)		164 (52.2)
BMI *M* (SD)		23.14 (6.12)
Total Number of Pain Locations *n* (%)	1	103 (34.6)
	2	69 (23.2)
	3 or greater	126 (42.3)
Pain Intensity *M* (SD)	Typical	5.82 (1.98)
	Worst	8.95 (1.33)
Pain Frequency *n* (%)	1-3x/month	8 (2.8)
	1x/week	7 (2.4)
	2-3x/week	16 (5.6)
	4-6x/week	29 (10.1)
	Daily	226 (78.5)
Pain Intensity Increase (within past month) *n* (%)		170 (54.1)
CALI Sum Score *M* (SD)		43.86 (17.89)
Sleep Problems *n* (%)		211 (67.2)
Sleep Problems Frequency *n* (%)	0-1x/week	60 (19.1)
	2-3x/week	85 (27.1)
	4-6x/week	54 (17.2)
	Nightly	30 (9.6)
Pain Self-efficacy *M* (SD)		4.86 (2.29)
Physical Activity *M* (SD)		3.46 (2.34)
RCADS T-Score *M* (SD)		61.99 (15.29)
Adolescent Optimism		4.74 (2.83)

Pain characteristics were shown to be significantly associated with functional disability (**Table 3.2**). Significant positive correlations were also found between worst pain intensity, typical pain intensity, pain frequency and functional disability. No correlation between multi-site pain and functional disability was noted. Individual traits such age was positively correlated with functional disability, yet no correlation with BMI and gender was found. Physical activity was negatively correlated with functional disability. Positive correlations between depressive symptoms and sleep problems with functional disability were also found. A significant negative correlation between functional disability and pain self-efficacy exists, yet no correlation with adolescent optimism was evident. Other demographic factors thought to influence the development of functional disability, such as familial history of chronic pain showed no relationship to physical function. Overall, positive correlations with functional disability were found between age, pain characteristics, depressive symptoms and sleep problems. Comparably, negative correlations were found among engagement in physical activity, pain self-efficacy and functional disability.

Table 3.2. Bivariate Correlations among Measure of Physical Function and Potential Predictor Variables

Subscale	1	2	3	4	5	6	7	8	9	10	11	12	13
1. CALI sum	1	.098	.186*	.115	.313**	.336**	.342**	.142	.520**	-.277**	.259**	-.260**	-.109
2. Gender[1]			.194*	..148	.154	.180*	.132	.121	.115	-.027	.218**	.153	-.098
3. Age				.440**	.019	.131	.155	-.085	.177*	-.152	.047	.028	-.222**
4. BMI					.059	.085	.035	.105	.110	-.115	.099	-.026	-.249**
5. Worst pain						.518**	.128	.108	.170*	-.045	.338**	-.156	.025
6. Typical pain							.229**	.064	.328**	-.184*	.318**	-.098	-.017
7. Pain frequency								.132	.359**	-.006	.176*	.010	-.162*
8. Multi-site pain[2]									.172*	-.024	.083	-.042	.018
9. RCADS										-.262**	.255**	-.290**	-.227**
10. Physical activity											.008	.157	.069
11. Sleep problems[3]												-.168*	-.038
12. Pain self-efficacy													.185*
13. Optimism													1

[1] Coded male = 0 female = 1
[2]Multi-site pain = >2 locations
* p < .05 **p < .01

A four step hierarchical multiple regression was conducted with the functional disability (CALI-21) as the dependent variable. Pain characteristics (worst pain intensity, typical pain intensity, pain frequency, and multi-site pain) were entered at stage one of the regression to control for the known influence of pain on functional disability. Further controlling for known influencing factors, measures of psychological function (depressive symptoms and pain self-efficacy) were entered at stage two, sleep problems were then entered in stage three, and physical activity at stage four. Regression statistics are reported in **Table 3.3**.

Table 3.3. Hierarchical Multiple Regression for Variables Predicting Functional Disability

Predictor Variable		R^2	ΔR^2	β at entry	β at final step
Step 1: Pain Characteristics		.227	.227**		
	Worst Pain			.227	.217*
	Typical Pain			.150	.023
	Pain Frequency			.296	.216*
Step 2: Psychological Function		.349	.122**		
	Depressive Symptoms			.300	.253*
	Pain Self-Efficacy			-.173	-.153
Step 3: Sleep Problems		.352	.003		
	Sleep Problems			.061	.072
Step 4: Physical Variables		.377	.024*		
	Physical Activity				-.164*

* p < .05 **p < .01 ***p<.001

The hierarchical regression analysis revealed that at stage one, pain characteristics contributed significantly to the model and accounted for 22.7% of variance [*F* (3, 106) = 10.366, p<. 001] in functional disability. Stage two, psychological function, explained an additional 12.2% of the variance [*F* (2, 104) =11.16, p<. 001]. Adding sleep problems to the regression model in stage three accounted for an additional 3.0% of the variance in functional disability [*F* (1, 103) =9.34, p<. 001]. Finally, the addition of physical activity to the model in stage four explained an additional 2.4% of the variance in functional disability [*F* (1, 102) = 8.81, p<. 001]. When all potential predictor variables were included in the final stage of the model significant predictors of functional disability include pain frequency, worst pain intensity, depressive symptoms, and physical activity. Typical pain intensity, and sleep problems were not significant predictors of functional disability. Pain self-efficacy trended towards significance. Together, all independent predictor variables accounted for 37.7% of the variance in functional disability.

Discussion

The results indicate that the adolescents in this study report substantial impairments in multiple domains of functioning that contribute to overall functional disability. In fact, levels of functional disability in this sample of adolescents were higher than the levels of functional disability found in other adolescent chronic pain studies (Lewandowski, Palermo, Kirchner, & Drotar, 2009; Palermo, Wilson, Peters, Lewandowski, & Somhegyi, 2009). Likewise, the comorbidity of sleep and pain problems in our sample was 67% of the adolescents, higher than reported in previous studies (at approximately 50%) (Long, Kirshnamurthy, & Palermo, 2008; Palermo, Wilson, Lewandowski, Toliver-Sokol, & Murray, 2011). Of note, one potential factor influencing our high functional disability findings is that our sample of adolescents reported considerably higher level of pain intensity (M=5.82) and depressive symptoms (RCADS T Score M=61.99) than other comparable studies. For example, in the (Lewandowski et al. 2009) study, pain intensity (M=4.57) and depressive symptoms (RCADS T score M=49.89) were significantly lower.

Our results indicate that pain characteristics, sleep problems and depressive symptoms are strongly associated with functional disability comparable to previous study findings (Kashikar-Zuck et al., 2001; Lewandowski et al., 2009; Palermo et al., 2008) supporting the postulation of a bidirectional relationship between these covariates. As expected, levels of worst pain intensity, frequency of pain and depressive symptoms were found to be most predictive of functional disability in our models. However, after controlling for the effects of these pain characteristics and depressive symptoms our findings suggest that physical activity was the only variable that contributed significantly to functional disability. Unexpectedly, sleep problems were not found to be predictive of functional disability. Our findings contrast those of Palermo

et al. (2012), which found sleep problems over a one-year period to be predictive of functional limitations in a sample of 61 pediatric pain patients. One interpretation of the differences we found in sleep problems, as compared to previous study findings, could be the influence of the adolescents' current pain and/or health status at the time of data collection on sleep patterns. Additionally, to have a sleep problem in our study, sleep had to be interfered with by pain.

The mean levels of depression found in our study were higher than findings from other studies conducted in generalized chronic pain populations (e.g. Lewandowski et al., 2009; Palermo et al., 2009) evidencing a high level of disruption in psychological functioning among our participants. Our findings contribute to the growing evidence that the emotional distress of depressive symptomatology influences the relationship between pain and functioning increasing the adolescents' susceptibility to disability. Likewise, a strong relationship between adolescent pain self-efficacy and functional disability was found, corresponding with reports from adult studies (Ferreira-Valente, Pais-Ribeiro, & Jensen, 2014; Skidmore et al., 2015). Yet, pain self-efficacy's strength was reduced when entered into our model alongside the other covariates and was not a significant predictor of disability. These findings suggest that as the adolescent builds confidence in their own ability to deal with pain the adolescent may be less likely to report experiencing higher levels of functional disability. However, further investigation into the relationship between adolescent pain self-efficacy and functional disability is needed to confirm this theory.

As hypothesized, our findings indicate a strong association between physical activity and disability, contrasting findings from other chronic pain studies (Kashikar-Zuck et al., 2010; Stommen, Verbunt, Gorter, & Goossens, 2012). In fact, our findings were more in line with the findings of Long et al. (2008) who reported that physical activity and disability (CALI) were

inversely related (r= -.40, p =. 01, n=20). Meaning, the more physically active the adolescent is, the lower the level of functional disability reported. This finding is similar to other recent studies that found the adolescents that report higher levels of physical activity were also more likely to report lower levels of pain and functional disability (Kashikar-Zuck et al., 2010). Further examination of our results found similarity to other adolescent chronic pain studies in that our sample was less physically active than healthy peer counterparts with a higher likelihood of being overweight and/or obese (Lelieveld et al., 2008; Wilson et al., 2010). Interestingly, BMI was not significantly correlated with measures of functional disability, and therefore not included in our hierarchical model. These findings contrast those in other studies, which has found BMI to be a significant contributor to physical activity limitations and disability (Wilson et al., 2010). Taken together, these findings indicate a need for future studies evaluating the use of physical activity as a potential treatment modality for adolescents experiencing chronic pain.

Limitations

Several limitations of this study should be noted. As our design was cross sectional, no causal relationships can be inferred. Also, our sample lacks in ethnic diversity further limiting generalizations of our findings to non-Caucasians. Our sample consists of adolescents seeking specialty treatment for their chronic pain and therefore may experience higher levels of pain and disability than those seen in general pediatric clinics. Finally, the use of self-report may differ from laboratory measurement of sleep, psychological functioning and physical activity.

Conclusion

In conclusion, adolescents with chronic pain chronic pain experience high levels of widespread pain and functional disability. Our model explained 37.7% of the variability in functional disability with, physical activity making significant contributions while controlling for

pain characteristics and psychological functioning. Although our sample reported high levels of sleep problems, it did not significantly contribute to functional disability. While the exact relationship between these variables and functional disability remains unknown, clearly these factors are significant for understanding and intervening in the development of functional disability in the adolescent with chronic pain. Future research in this area should include information about how to tailor interventions to include a physical activity component and what physical activity interventions are most effective in addressing the unique needs of this highly debilitated population.

How might this information affect nursing practice?

Overall, our findings have important clinical implications. Adolescents presenting to clinics should receive a comprehensive assessment that includes evaluation for the presence of concurrent mood disorders, engagement in physical activity, sleep hygiene, and levels of functional disability above and beyond the usual screening for pain characteristics. Increased awareness and education regarding early recognition and interventions among health care personnel is needed. Additionally, interventions that are multidisciplinary and tailored to promote psychological health and engagement in physical activity in these adolescents should be implemented and recommended. Primary care nurses are ideally located to accomplish these screening and treatment goals and recommendations.

CHAPTER IV: INTEREST IN YOGA AMONG FIBROMYALGIA PATIENTS: AN INTERNATIONAL INTERNET SURVEY

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Abstract

Studies in circumscribed clinical settings have reported the adoption of yoga by many fibromyalgia (FM) patients. However, it is unclear from existing studies which types of yoga practices FM patients are typically engaging in, and the extent to which they experience yoga as helpful or not. The purpose of this study was to survey FM patients in many different regions to inquire about their engagement in various yoga practices, perceived benefits, and obstacles to further practice. A 16-question internet survey of persons self-identified as FM patients was conducted among subscribers to two electronic newsletters on the topic of FM. Respondents (n=2543) replied from all 50 U.S. states and also Canada, Australia and the United Kingdom. On average respondents were 57 years of age, 96% female, with an average time since diagnosis was 13 years. Of these, 79.8% had considered trying yoga and 57.8% had attended ≥1 yoga class. Their classes typically focused almost exclusively on yoga poses, with minimal training in meditation, breathing techniques or other practices. The most commonly cited benefits were reduced stiffness, relaxation, and better balance. The most frequently cited obstacles were concerns about the poses being too physically demanding, and fear that the poses would cause too much pain. These findings confirm strong interest in yoga across geographically diverse range of FM patients. However, concerns about yoga-induced pain, and yoga poses being too difficult, are common reasons that FM patients do not engage in yoga exercises. This study supports the need for yoga programs tailored for FM that include modification of poses to minimize aggravating movements, and substantive training in meditation and other yoga-based coping methods to minimize pain-related fear.

Interest in yoga among fibromyalgia patients: An international internet survey

Fibromyalgia (FM) is one of the most common chronic pain syndromes, affecting approximately 6% to 11% of adults in the United States (Weir et al., 2006). Fibromyalgia proportionately affects more women than men. It commonly presents in the third or fourth decade of life with a prevalence reaching 7% of women in their fifties (White & Harth, 2001). Characterized by widespread musculoskeletal pain and muscle-tendon junction tender points, FM is highly debilitating (Fitzcharles, Rampakakis, Ste-Marie, Sampalis, & Shir, 2014). In addition to chronic widespread musculoskeletal pain, those with FM experience sleep disruptions, affective distress, fatigue, diminished cognitive function, and poor physical functioning, all of which have a significant negative impact on their overall well-being and quality of life (Jacobson et al., 2014). Moreover, FM brings an alteration in lifestyle and a decrease in physical activities that leads to physical deconditioning (Aparicio et al., 2014). As a result of all these factors, FM patients use health care services extensively, with direct-care costs exceeding $20 billion per year in the U.S. (Thompson et al., 2011).

Current drug therapies are only effective for significant symptom relief in only approximately 30-50% of patients, and effective at improving physical functioning in only about one-fifth of patients. Moreover, these drugs produce significant side effects and are too expensive for many patients (Crofford et al., 2005; Hauser, Petzke, & Sommer, 2010; Mease & Choy, 2009; Mease et al., 2009; Russell et al., 2008).

Multiple position statements recommend exercise as a supplement to pharmacological therapies for FM (Carville et al., 2008; Jones, Adams, Winters-Stone, & Burckhardt, 2006). A 2007 national survey on the use of complementary and alternative medicine, identified yoga as one of the therapies most commonly used by U.S. adults, and current estimates suggest that 5-

7.5% of the U.S. adult population engages in yoga practice (Barnes, Bloom, & Nahin, 2008). Furthermore, 12.2% of surveyed internal medicine patients indicated that they had used yoga for their primary medical problem, with FM being one of the most commonly reported conditions targeted by yoga (Cramer et al., 2013).

Although yoga's popularity is on the rise, to our knowledge there are only four controlled studies of yoga in FM populations (Mist, Firestone, & Jones, 2013). These studies have shown yoga to improve physical function, fatigue, sleep, pain and to relieve emotional distress (Carson et al., 2010; Curtis, Osadchuk, & Katz, 2011; Hennard, 2011). However, beyond this preliminary evidence related to its effectiveness, very little is known about interest in, experiences with, and barriers to yoga participation among individuals with FM. Moreover, given that yoga styles vary in the methods they emphasize, it is unclear from existing studies which types of practices FM patients have typically engaged in, and the extent to which they experience yoga as helpful or not. Therefore, the purpose of this study was to survey a range of fibromyalgia patients in their home setting in a variety of geographical regions. The main objective was to elucidate the extent of the respondents' engagement in yoga practice, and the obstacles to continued yoga practice.

Methods

A 13-item cross-sectional survey study was conducted on-line, using participants from a database maintained by two fibromyalgia support and advocacy non-profit organizations (Fibromyalgia Network eNews Alert, and Fibromyalgia Information Foundation). The questionnaire (see **Appendix B**) included a comment field whose content was analyzed by identifying recurrent themes and novel commentary. We employed and IRB-exempt anonymous survey protocol during which no protected health information was captured. All potential

participants over 18 years of age with self-report of a medical provider diagnosis of fibromyalgia, regardless of prior yoga experience. Potential participants responded to a link embedded in an email from the non-profits organizations. The email described the study purpose, contained the informed consent, and led interested individuals to a confidential Survey Monkey link that coded Internet provider addresses so that only one survey per computer was accepted. Data were collected between October 6, 2010 and July 24, 2011. Data were analyzed using STATA 11.2 (College Station, TX). Data analysis characterized variables using descriptive statistics.

Results

Respondent Characteristics

Of the 6710 total subscribers sent the invitational email, 4658 (69%) of the subscribers initially opened the invitational email, and 2543 completed the survey, representing a 38% total response rate and a 55% response rate for those subscribers who opened the invitational email. Responses were received from all fifty US states and more than two dozen foreign countries, with the majority of international responses coming from Canada, Australia, and the United Kingdom. Other nationalities included in the survey were: Brazil, Colombia, Costa Rica, France, Greece, India, Ireland, Israel, Italy, Malta, Mexico, New Zealand, Panama, Puerto Rico, Oman, Portugal, Saudi Arabia, Singapore, South Africa, Spain, Switzerland, and United Arab Emirates. The term "respondents" will be used here-after to refer to subscribers who completed the survey. The mean age of respondents was 57 years of age (range 21-90 years) and most (96.3%) were female. The average time reported since fibromyalgia diagnosis was 13.4 years (range 1-41) (**Table 4.1**).

Table 4.1. Respondent Demographics (n=2543)

Characteristic	N	%
Age (M)[a]	57	
Gender (female)	2449	96.3
Gender (male)	94	3.7
Years diagnosed (M)	13.4	
Previous yoga class attendance		
Yes	1181	57.8
No	864	42.2
Considered attending a yoga class		
Yes	2029	79.8
No	514	20.2

[a] Range 21-90 years

Interest in and Previous Practice of Yoga

Among the respondents, 79.8% had considered engaging in yoga practice, and 57.8% reported that they had attended at least one yoga class since their FM diagnosis (**Table 4.1**). About a third of the 1181 respondents who had tried yoga reported attending 1-4 yoga classes (32.8%), and 39.4% said they had attended more than 12 yoga classes. Most of the reported yoga classes lasted 45-60 minutes (54.4%), but nearly a quarter lasted 60-90 minutes (24.7%). Respondents most commonly endorsed "Beginner's" "Level 1," or "Gentle" as the types of classes they attended (multiple choices were allowed), but several also ticked "Restorative" (12.7%) or "Therapeutic" (15.7%) (**Table 4.2**). Respondents described these yoga classes as focused on yoga poses (asanas) with little time spent in seated meditation, breathing exercises (pranayama) or other yoga practices (**Table 4.3**). Among respondents who had attended at least one yoga class, the majority (65.9%) reported that they were able to participate fully (**Table 4.2**).

Table 4.2. Yoga Class Demographics (n=1181)		
	N	%
Number of yoga classes attended		
1-2		21.1
3-4		11.7
4-8		16.8
8-12		10.9
>12		39.4
Class duration		
30-45 min		19.2
45-60 min		54.4
60-90 min		24.7
90-120 min		1.7
Types of classes		
Beginner	551	46.7
Level 1	247	20.9
Gentle	383	32.4
Therapeutic	150	12.7
Restorative	185	15.7
Able to fully participate		
Yes		65.9
No		34.1

Reported Benefits of Yoga Practice

The survey assessed the respondent's perceived physiological benefits of participation in yoga practice (**Table 4.4**). Of those who attended yoga class (n=1181), 49.4% reported reduced stiffness and improved mobility, 47.5% reported feelings of relaxation, 38.5% endorsed improved balance, and 36.7% said movement was generally easier. They also reported improvements in strength (31%), reduced pain and soreness (30.4%), easier breathing (23.1%), and better sleep (21.1%). Reported changes in psychological factors included improved outlook on life (32.1%), less stress (36%), feeling peaceful (36.8%), and being glad to join in a community (25.7%).

Table 4.3. Reported Yoga Practice Distribution (n=1181)

	Most of class (%)	Some of class (%)	Short while (%)	Minimal or none (%)
Yoga poses, holding each pose for a short while	44.7	38.2	14	3.2
Yoga movements, in a flowing sequence	19.1	42.2	19.2	19.5
Reclining relaxation (shavasana)	10.7	34.2	41.2	14
Breathing exercises (pranayama)	18.1	36.2	31.2	14.6
Seated meditation with focused attention	6.4	20.7	33.7	39.3

Reported Difficulties with Initial and Continued Yoga Class Attendance

Almost half of all respondents (49.2%) who reported no yoga class attendance indicated that concerns regarding the physical demands of yoga poses prevented them from initially attending a class (**Table 4.5**). Apprehension about pain, both after (45.5%) and during (35.8%) class, kept many respondents from trying yoga. Such class characteristics as inconvenient time (32.9%), inconvenient location (30.1%), and price (28.5%) were also cited as obstacles to initial yoga class attendance.

Respondents also experienced obstacles to continued class attendance (Table 4). Among those who had attended at least one yoga class, 26.1% reported that the postures were too physically demanding. Many respondents reported that the postures caused too much pain during (21.3%) or after (20.7%) class. A minority of respondents cited teacher characteristics as a reason for their decision to stop attending classes: in some cases, the teacher did not modify postures for pain-related difficulties (15.3%) and in other cases, the teacher did not ask about the

respondent's pain related difficulties (13.9%). Only 11.9% reported concerns about the ability to do specific poses correctly as an obstacle to continued class attendance (**Table 4.4).**

Table 4.4. Reported benefits of yoga practice (those reporting class attendance) (n=1181)

	%
Reduced stiffness and improved mobility	49.4
Felt relaxed	47.5
Improved balance	38.5
Felt peaceful	36.8
Easier movement	36.7
Less stress	36
Improved life outlook	32.1
Increased strength	31
Reduced pain and soreness	30.4
More energy	30.4
Glad to join a community	25.7
Easier to breathe	23.1
Better sleep	21.1

Table 4.5. Reported difficulties to initial (n=864) and continued (n=1181) yoga class attendance

	Initial Attendance		Continued Attendance	
	n	%	n	%
Inconvenient location	260	30.1	34	2.9
Inconvenient time	284	32.9	47	4.0
Too costly	246	28.5	54	4.6
Concerns about ability to do postures	340	39.4	141	11.9
Age group/fitness level too different from self	239	27.7	112	9.5
Postures too physically demanding	425	49.2	3089	26.1
Postures causing too much pain during class	309	35.8	251	21.3
Postures causing too much pain after class	393	45.5	245	20.7
Inability to sit on the floor	253	29.3	109	9.2
Hard time following instructions	99	11.5	91	7.7
Classroom atmosphere not suitable (e.g. incense, religious icons, or chanting)	108	12.5	41	3.5
Teacher did not ask about difficulties (e.g. back pain, neck pain, etc.)			164	13.9
Pose modifications for difficulties not offered			181	15.3
Felt singled out related to difficulties			50	4.2

Discussion

Among people with FM, 79.8% of survey respondents reported having at least considered attending a yoga class in their own community, and 57.8% said they attended at least one yoga class. Of those who had attended at least one yoga class, 65.9% reported being able to participate fully in class. Respondents most often associated yoga practice with improvements in stiffness and mobility, relaxation, balance, movement, and peacefulness and reduction in stress. Anecdotal reports from those attending at least one yoga class also suggested that yoga practice was helpful in managing their FM symptoms. For example, one respondent commented that "it helps significantly with my FM symptoms by keeping me moving and flexible, making other kinds of exercise easier, as well as providing deep relaxation." However, fear of pain and the physical demands of the postures were the most commonly identified reasons for refraining from attending, or ceasing to attend yoga classes.

To our knowledge, this is the first study to assess yoga interest, participation, perceived benefits, and barriers to practice in a FM population. Although research on the application of yoga for FM remains limited, our findings are consistent with a growing number of yoga studies reporting positive effects of yoga practice on FM symptomatology (Langhorst, Klose, Dobos, Bernardy, & Hauser, 2012; Mist, Firestone, & Jones, 2013). The high rates of yoga interest and attendance we found in this study are also reflective of the good completion and adherence rates reported by several yoga trials in FM, suggesting high levels of acceptability in the FM population (Carson et al., 2010; Curtis, Osadchuk, & Katz, 2011; Da Silva, Lorenzi-Filho, & Lage, 2007; Hennard, 2011; Rudrud, 2012). The prevalence of yoga use we found in this sample is far higher than the 12.19% reported by a general internal medicine population (Cramer et al., 2013) and the 8% to 12% reported in two recent surveys of the general population in Australia

(Sibbritt, Adams, & van der Riet, 2011; Xue, Zhang, Lin, da Costa, & Story, 2007). Moreover, the 2007 National Health Interview Survey estimated prevalence of yoga use in the United States at 6.1%, significantly lower than our findings (Barnes, Bloom, & Nahin, 2008). Although the differences between these diverse populations limit the comparability of results, the findings seem to indicate that FM patients are more likely to consider yoga and attend yoga classes than the general population. Female gender has been associated with higher prevalence of yoga use (Birdee et al., 2008; Penman, Cohen, Stevens, & Jackson, 2012; Saper, Eisenberg, Davis, Culpepper, & Phillips, 2004; Tindle, Davis, Phillips, & Eisenberg, 2005). The great majority of respondents to our survey were female, and this may contribute to the increased prevalence relative to the general population.

Our survey findings of overall positive perceived benefits of yoga practice are consistent with previous yoga surveys, the majority of whose respondents reported that yoga had been helpful in improving their health (Cramer et al., 2013; Penman, Cohen, Stevens, & Jackson, 2012). Also consistent with our findings, stress management, increased relaxation, and improvement in musculoskeletal stiffness and mobility issues were the most commonly perceived health benefits in a previous general population yoga study (Penman, Cohen, Stevens, & Jackson, 2012).

There are no published data on the perceived barriers to yoga practice in either a general population or other specific medical population. We found that fear of pain and fear of yoga practice being too physically demanding were the most common reasons cited for not attending yoga classes. Previous studies have reported that the fear of pain with physical activity experienced by persons with FM often hinders their adoption of an exercise program (Clark, 1994; Jones, Clark, & Bennett, 2002; Jones & Hoffman, 2006). Interestingly, however, from the

yoga studies conducted thus far in FM populations have reported no adverse events. In a general population survey 78.7% of those who had practiced yoga reported no injuries, not even minor muscle strains (Penman, Cohen, Stevens, & Jackson, 2012). However, any comparisons between a FM population and the general population of yoga users is of limited value, due to the unique central and peripheral pathophysiology associated with the diagnosis of FM. The results of our study support the need for yoga programs tailored for those with FM, including the modification of poses to minimize challenging and pain-aggravating movements (Carson et al., 2010). Moreover, substantive training in meditation, breathing techniques, and other yoga-based coping methods (e.g., mindful attention to sensations and accompanying thoughts and feelings) has been proposed as a way to address the fear of pain and render asana practice more tolerable, meaningful, and sustainable for FM patients (Carson et al., 2012).

There are several notable limitations to this study. The cross-sectional survey design does not lend itself to causal interpretations. There is a significant risk of selection bias, given that all respondents were recruited from two FM advocacy groups and volunteers to participate in this survey. Moreover, all subjects self-reported their physician-diagnosed FM, and this study did not attempt to confirm their diagnosis by a physician. Finally, the web-based survey may have excluded that without internet access.

In conclusion, the findings of this preliminary survey study suggest a) that many individuals with FM are already practicing yoga and finding it beneficial and b) that yoga holds strong potential for becoming more widely accepted and therapeutic for people with FM, once important obstacles to yoga practice are overcome. Additionally research into the therapeutic application of yoga to individuals with FM is warranted.

CHAPTER V: YOGA FOR PEDIATRIC CHRONIC PAIN: A REVIEW

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Abstract

Chronic pain is a debilitating condition affecting approximately 15-25% of adolescents in the United States. The experience of chronic pain during adolescence has been associated with; fatigue, sleep disturbances, poor academic performance, social limitations and changes in physical function and physical activity. Adolescents experiencing chronic pain engage in less moderate to vigorous physical activity than their healthy counterparts and spend more daytime hours in sedentary activity further exacerbating the symptom cycle. Multiple position statements recommend exercise as an adjunct to pharmaceutical therapy for adolescent chronic pain. Although recommended, there is little evidence to support the use of exercise as an adjunct therapy with few studies focusing on the effectiveness of exercise as a treatment in adolescent chronic pain. Therefore, the purpose of this review was to explore the feasibility, acceptability, safety, and efficacy of yoga as a therapeutic intervention in pediatric chronic pain populations.

An electronic database search was conducted using five MESH terms on Medline/PubMed, CINAHL, SCOPUS, and the Cochrane Library through January 2015. Of the 91 records evaluated, five original data papers enrolling 198 patients met inclusion criteria for this review.

The yoga interventions were delivered in groups or individuals (home with video). Mean duration was 8 (range 4-12) weeks, with a mean dose of 90 minutes a week. The evidence from five separate studies in pediatric pain populations shows the potential of yoga practice to reduce pain and functional disability, though this effect was highly variable. Across the studies reduction in pain intensity was noted by an average change of 1.18 points (range = .18 – 2.0) in pre-post differences in VAS scores. Improvement in daily functioning scores and in functional disability was also noted. High adherence (mean = 80.6%, range = 75-100%) and low attrition

(mean = 14.6%, range = 11-23%) rates were reported in all five studies. No serious adverse events were reported across all studies identified. Methodologic quality was limited by design (1 RCT, 2 randomized wait-listed trials and 2 open labeled trials).

Taken as a whole, the evidence from fair methodologically conducted trials indicate the feasibility, acceptability and safety of yoga in a pediatric pain population. Further data are needed to confirm a consistent effect on physical function, pain and related symptoms. Optimal dose of yoga interventions remain unknown.

Yoga for Pediatric Chronic Pain: A Review

Pain that is chronic, persistent or recurring in children is common with approximately 15-25% of children nationally presenting for care each year with complaints of chronic pain (Mathews, 2011; Perquin et al., 2000). Of these children experiencing chronic pain, most (83%) have experienced pain at least weekly in duration of 3 months or greater, with 30.8% reporting pain for greater than six months (Roth-Isegkeit, Thyen, Raspe, Stoven, & Schmucker, 2008). Adversely impacting all aspects of quality of life, pediatric chronic pain creates significant functional deficits across physical, social and emotional domains (Hunfeld et al., 2001). These children report difficulty participating physical activity such as leisure, play, and sports (Kashikar-Zuck et al., 2010; Wilson & Palermo, 2012) with the majority engaging in significantly lower physical activity levels than healthy peer counterparts (Long, Palermo, & Manees, 2008). Socially, they are more likely to withdraw from their peers and experience social isolation (Forgeron et al., 2011; Kashikar-Zuck et al., 2007). Likewise, they are more vulnerable to emotional difficulties and experience higher levels of depressive symptoms with a prevalence of concurrent mood disorders of approximately 67% (Kashikar-Zuck et al., 2008b; Kashikar-Zuck et al., 2008a).

Traditional treatments for chronic pain (largely focused on the management of pain through medication) exhibit poor response rates and/or side effects outweigh symptom benefit, leaving the child to live with unresolved pain. Pharmacotherapy provides only modest symptom improvement in both pain and physical function (Anthony & Schanberg, 2005; Gedalia, Garcia, Molina, Bradford, & Espinoza, 2000). Furthermore, there is a lack of controlled therapeutic clinical trials to support the efficacy, safety and use of pharmacotherapy in pediatric chronic pain populations (Kashikar-Zuck, 2006).

Multi-disciplinary treatment (including education and exercise) is considered a cornerstone of comprehensive pediatric pain treatment. As such a meta-analytic review of 25 cognitive behavioral therapy (CBT) studies involving a total of 1,247 participants report an improvement in pain and small non-significant effects on functional disability (Palermo, Eccleston, Lewandowski, de C Williams, & Morley, 2010). Yet, most expert reviews and non-exercise RCTs call for movement related studies in this population. Likewise, clinical treatment recommendations aimed at the restoration of functioning incorporate the use of mild to moderate exercise (Buskila, 2009; Gedalia et al., 2000; Kimura, 2000). However, to our knowledge, only one controlled trial to date has been conducted examining the use of traditional aerobic exercise in a pediatric chronic pain population, with mixed support for the effectiveness of traditional exercise participation to relieve pain and increase functioning (Stephens et al., 2008). Yet, anecdotal clinical evidence indicates that children participating in an exercise program have better outcomes clinically (Gedalia et al., 2000).

One type of exercise that has become increasingly recommended and popular in pediatric populations is yoga. According to the 2012 National Health Statistics Report, the incidence of children using yoga as a therapeutic modality had increased by approximately 400,000 from the 2007 survey results (Black, Clarke, & Barnes, 2015). Further evidence of the increasing interest in yoga is evidenced by its use as the most commonly employed movement modality in a pediatric outpatient pain clinic setting (Barnes, Bloom, & Nahin, 2008; Birdee et al., 2008; Tsao et al., 2005). Conceptually, when viewed from a biopsychosocial perspective, yoga has the potential to impact all areas of functioning (physical, emotional and social; **Figure 5.1**) (Evans, Tsao, Sternlieb, & Zeltzer, 2009).

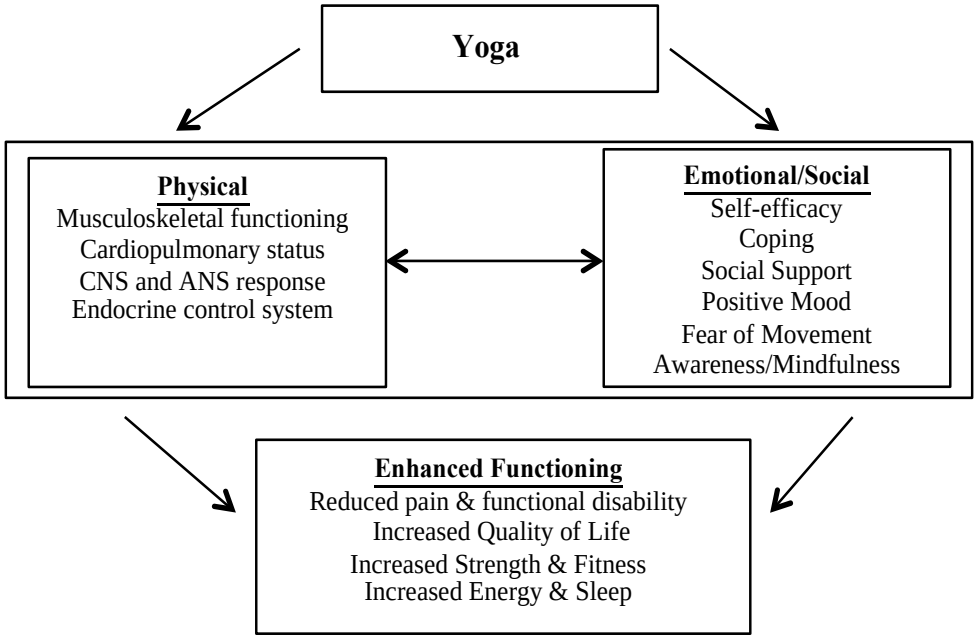

Figure 5.1. Conceptual Model of the Biopsychosocial Benefits of Yoga modified for the child with chronic pain, adapted from Evans et al., 2009

Despite the potential promising results of yoga for the child with chronic pain, the majority of literature addressing the use of yoga as a movement modality during childhood has focused on general physical fitness, emotional, mental and behavioral outcomes. Yet, thus far, yoga has produced positive results in the adult chronic pain literature (Carson et al., 2010) with two recent meta-analyses of yoga for adults with chronic pain demonstrating overall improvements in pain (Langhorst, Klose, Dobos, Bernardy, & Hauser, 2012; Mist, Firestone, & Jones, 2013). Moreover, yoga is currently mainstreamed in treatment recommendations of the adult with chronic pain. To our knowledge, there have been no reviews of research focused on the use of yoga as a therapeutic movement modality to reduce pain and functional disability in children experiencing chronic pain. Therefore, the purpose of this review is to explore the feasibility, acceptability, safety, and efficacy of yoga as a therapeutic intervention in pediatric chronic pain populations.

Methods

The following databases were searched through January 2016: MEDLINE/PubMed, Scopus, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Cochrane Library. The key medical subject heading (MeSH) terms used for initial inclusion included: "yoga" combined with "pain" or "chronic pain" and "child", "adolescent" or "pediatric". To maximize search results, no additional search limitations of language, year or study design were implemented.

Studies were considered eligible for inclusion if met the following criteria: (1) enrollment of participants from adolescence to young adult (11-21), (2) met the criteria of chronic pain (experiencing pain greater than 3 months), (3) study intervention of yoga and (4) measurement of pain as a study outcome. All methodological designs were considered for inclusion. The decision to include studies aimed at the young adult (up to age 21) was based on growth and developmental considerations as the young adult is in a transitional period between adolescence and adulthood and exhibits many of the same special health care needs evidenced in adolescent populations (NAPNAP, 2008).

Among the studies that met inclusion criteria, data on design, disease/condition, treatment duration, frequency and dose, yoga tradition, adherence to treatment, attrition rates, adverse events, and outcome results were extracted.

Results

Literature search

Our initial search strategy yielded 91 records (**Figure 5.2**). After exclusion of duplicates (8 records), we screened and excluded articles that were not yoga interventional studies (68 records), were in adult-only populations with a mean age >21 years (6 records), were in

malignant pain conditions (1 record), or did not measure pain as an outcome (3 records). We identified 5 studies that met our inclusion criteria, which are detailed in **Table 5.1**.

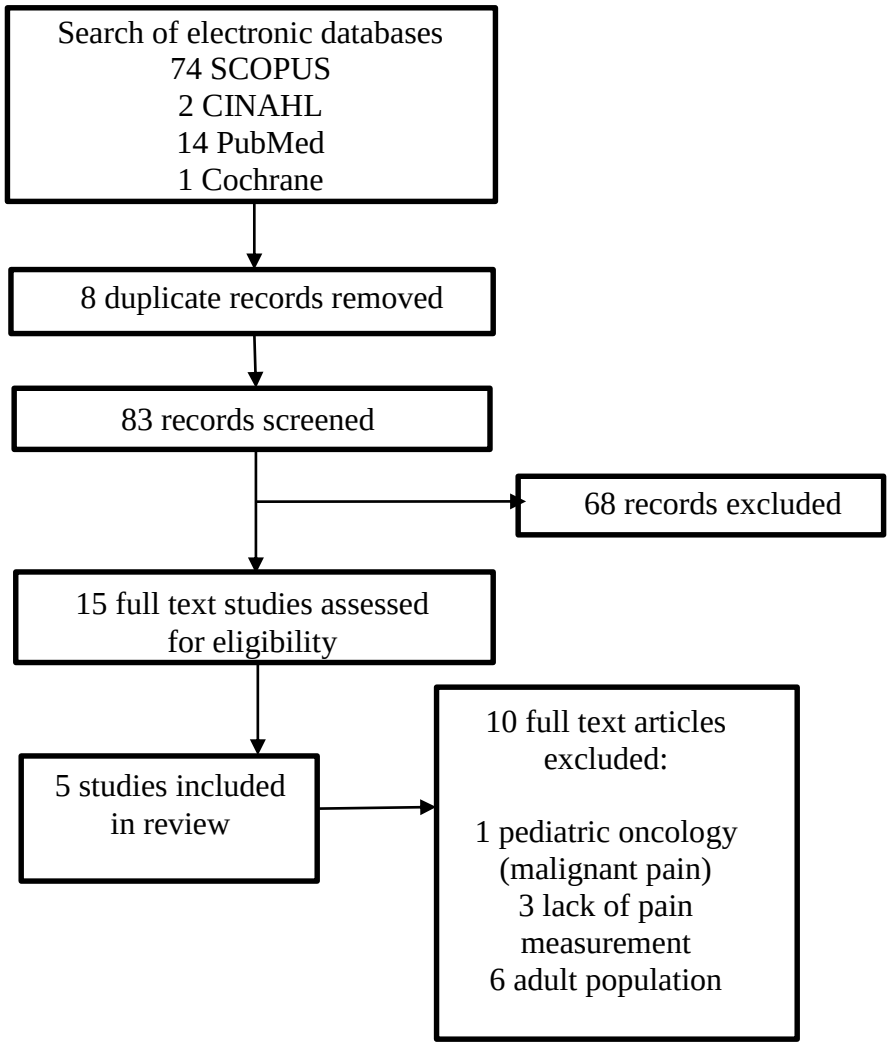

Figure 5.2. Search strategy results

Table 5.1. Summary of Pediatric Yoga Studies Included in Review

Author (s), Study Design & Population	Acceptance Rates, Attrition & Adverse Events	Intervention, Dose & Adherence	Sample Size & Age
Brands, Purperhart, & Deckers-Kocken (2011) Single arm study Functional abdominal pain & Irritable bowel syndrome	Attrition = 15% Reasons for attrition= loss of motivation, unexpected pregnancy Adverse events = No information provided	Hatha yoga Intervention = 90 min sessions weekly for 12 weeks Adherence = No information provided	n= 20 Mean age = 11.95 years (range = 8-18 years)
Evans, Lung, Seidman, Sternlieb, Zeltzer, & Tsao (2014) Wait-list control with randomization Rheumatoid arthritis	Acceptance rate = 73.8% Reasons for declining participation= Busy/time conflict, distance, unknown Attrition at Baseline = 24% Reasons for attrition = medical reason, distance too far Adverse events = one non-serious event	Iyengar yoga Intervention = 90 minute sessions biweekly for 6 weeks Adherence = Yoga group = 77.5%	n= 51 Mean age = 19 years (range = 11-26)
Hainsworth, Salamon, Khan, Mascarenhas, Davies, & Weisman (2013) Single-arm study Chronic Headaches	Acceptance rate = 33.3% Reasons for declining participation= Distance too far, too busy, time conflicts Attrition= 63% prior to first yoga class Reasons for attrition= Inconvenience Adverse events = None	Iyengar yoga Intervention = 75 minutes sessions weekly for 8 weeks Adherence = 75%	n= 7 Mean age = 13.4 years
Kuttner, Chambers, Hardial, Israel, Jacobsen, & Evans (2008) Wait-list control Irritable Bowel Syndrome	Acceptance rate = No information provided Attrition = 11% Reasons for attrition= No information provided Adverse events= No information provided	Non-specified yoga Intervention = Initial 1 hour instructional session and then yoga video for home practice thereafter for 4 weeks Adherence = No information reported	n= 28 Mean age = 14.15 years
Rakhshaee (2011) RCT Primary Dysmenorrhea	Acceptance rate = 26.7% Reasons for declining participation= No information provided Attrition= 23% Reasons for attrition= Irregular menstruation Adverse events = No information provided	Use of three yoga poses = cobra, cat and fish Intervention= Practice of three poses daily for 20-minutes for 14 days during luteal cycle over 3 months Adherence= No information provided	n= 92 Mean age= 20.7 years

Participant and setting characteristics

The five studies included a total of 198 participants. Pediatric chronic pain populations represented included: irritable bowel syndrome (Brands, Purperhart, & Deckers-Kocken, 2011; Kuttner et al., 2006), rheumatoid arthritis (Evans et al., 2014), primary dysmenorrhea (Rakhshaee, 2011), and chronic headaches (Hainsworth et al., 2013). Sample sizes ranged from 7 to 92 with a median of 28 participants and a mean age of 16.5 years (range 12 to 20 years). Across studies, the percent of female participants varied from 43% to 100% with a mean of 58.2%. Overall, participants were predominately Caucasian (median = 72%), however, two of the five studies did not report ethnicity.

Study design, characteristics, and safety

Of the five studies identified, only one (in primary dysmenorrhea) used a randomized controlled design evaluating the effectiveness of yoga to reduce pain as compared to usual care (Rakhshaee, 2011). Two studies were single arm interventional trials (IBS and headaches), and two were wait-list control trials with randomization (IBS and rheumatoid arthritis). In both wait-list control trials, the control group received usual care during the wait or "control" time period.

Yoga styles varied across the studies. Yoga styles ranged from a non-specified selection of various poses (Kuttner et al., 2006; Rakhshaee, 2011), to Iyengar (Evans et al., 2014; Hainsworth et al., 2013), and Hatha yoga (Brands et al., 2011). Specific description and discussion of poses used during the intervention was provided in three of the five studies (Evans et al., 2014; Kuttner et al., 2006; Rakhshaee, 2011). All studies reported the use of yoga poses/postures (asanas) as well as the modification of these poses for specific use within their target population. The use of yogic breathing practices (pranayama) was reported in two of the five studies (Brands et al., 2011; Kuttner et al., 2006) and one study incorporated mindfulness

techniques (Brands et al., 2011).

The mode of intervention delivery varied across the studies. In three studies, the yoga was provided as formal group practice (n=78 participants) (Brands et al., 2011; Evans et al., 2014; Hainsworth et al., 2013) and held in a designated room within an outpatient clinic. No yoga classes were conducted in community based and publicly accessible yoga studios. The remaining two studies delivered the yoga intervention via home practice (n=120 participants) through the use of either a yoga video (Kuttner et al., 2006) or a yoga instructional booklet with pose illustrations (Rakhshaee, 2011). Yoga intervention duration ranged from four to twelve weeks, with a mean duration of 8 weeks and a mean dose of 90 minutes a week. Across all studies, one study reported a non-serious musculoskeletal strain, which occurred in the group practice setting under the supervision of a yoga instructor and did not hinder the study progression of the participant involved (Evans et al., 2014). No serious adverse events were reported.

Acceptability and Feasibility

Recruitment across studies primarily focused on identifying participants accessing care from specialty pediatric gastroenterology, rheumatology and headache clinics. Only one study recruited participants from a general university student population (Rakhshaee, 2011). Reported recruitment numbers with initial study acceptance rates ranged from 26.7% to 73.79% and an overall mean acceptance rate of 44.6% in three of the five studies (Evans et al., 2014; Hainsworth et al., 2013; Rakhshaee, 2011). The remaining two studies did not report recruitment statistics (Brands et al., 2011; Kuttner et al., 2006). Of those participants declining participation, the top reasons provided included (1) being too busy, (2) the distance to class was too far to travel, and (3) scheduling conflicts and difficulties. None of the studies reported that participants

had declined participation due to a lack of interest in or dislike of yoga.

Attrition rates across the studies ranged from 11% to 23% with a mean of 14.6%. Top reasons that participants dropped from the studies included (1) transportation issues, (2) time limitations, and (3) changes in health status (i.e. participant pregnancy). Only one study reported a participant (n=1) that dropped out of the study due to lack of motivation to participate in yoga practice (Brands et al., 2011). The mean adherence rate was 80.6% in the two studies that reported adherence data (Evans et al., 2014; Hainsworth et al., 2013) and in one study, almost half (44%) of the participants completed 100% of the yoga intervention (Evans et al., 2014). Among the three studies not reporting adherence rates, two used home practice interventions that tracked adherence by daily practice journaling. In one, the intervention group received instructions to complete the yoga pose sequence daily with the adolescents reporting practicing yoga on a "fairly frequent" basis (mean 6.81± 2.52 out of 10) (Kuttner et al., 2006). In this same study, the experience of pain itself was identified as the key barrier to yoga practice with the reasoning that some of the yoga poses were difficult to achieve when already in pain which consequently decreased their motivation to practice. Overall, (1) scheduling, (2) time constraints, and (3) transportation were the most commonly identified barriers to either initiation of or maintaining yoga practice in children.

Pain outcomes

Yoga was associated with a reduction in pain intensity in four of the five studies reviewed. In the Evans (2014) study, ratings of "worst pain" were significantly reduced overtime (mean =-1.27 reduction; p=0.04) with improvement trends noted at the beginning of study week four (total study duration = 6 weeks). This improvement was sustained at the two-month follow up data collection point. Likewise, in the Rakhashaee (2011) study, pain intensity and duration

were significantly decreased (mean = -1.25 reduction, p=0.00) and continued to improve with each subsequent month of yoga practice. One study (Brands et al., 2011) reported pain scores that changed one point or greater as rated on the numerically rated pain scale representing a meaningful change in pain from a clinical perspective (Hirschfeld, Wager, Schmidt, & Zernikow, 2014). In this study, after a twelve-week outpatient yoga intervention in children with irritable bowel syndrome, overall pain intensity decreased on the visual analog scale (VAS) from a mean of 9.0 at baseline to a 7.0 post-intervention, the results did not reach statistical significance. In the Hainsworth (2013) study, despite no pre- post- differences found for pain intensity, the majority of participants average pain intensity ratings decreased across time. Finally, in the one study that did not report changes in pain intensity, pain as an outcome was omitted from analysis after study initiation due to significant differences between the intervention and control groups at baseline measures (Kuttner et al., 2006). However, at the end of the study 76.5% of the adolescents reported on a post study researcher developed questionnaire, that they had experienced a decrease in their pain over the course.

Functional outcomes

Three of the five selected studies included formal measures of pain related disability or functional disability in the study protocols (Evans et al., 2014; Hainsworth et al., 2013; Kuttner et al., 2006). In the Kuttner et al. (2006) study, participants reported lower levels of functional disability trending toward significance as compared to the wait list control (F[1,23]=3.52, p=0.07). These youth also reported that yoga provided enough pain control that even though it didn't completely eliminate their pain, they could continue to participate in daily life activities. Likewise, in another study of young adults with rheumatoid arthritis, participants reported a significant decrease in functional disability as compared to controls (F[1,19]=5.06, p=0.04)

(Evans et al., 2014). In the remaining reporting study, a non-significant improvement trend in daily functioning was noted (z=-1.83, p= .068) (Hainsworth et al., 2013). Additionally, adolescent study participants reported using learned yoga poses when they felt pain developing in order to limit its intensity and duration so that they could continue to participate in daily activities (Kuttner et al., 2006).

Discussion

The evidence presented in this review contributes to the body of knowledge a better understanding of the use of yoga as an intervention in pediatric populations experiencing pain. The use of therapeutic yoga appears to be safe, feasible, acceptable, and adaptable to a range of pediatric pain conditions. Interpretation of efficacy is limited by only one study having a parallel, designed RCT. However, the majority of studies consistently reported improvements in pain and functional ability. In the research identified, thus far, yoga demonstrated promising results in the reduction of pain. Findings from this review also indicate that yoga practice shows the potential to produce positive and sustaining results even when administered in small doses (with the average dose in this review being 90 minutes weekly). Furthermore, high adherence (>80%) and low attrition rates (<15%) suggest yoga is an intervention that is feasible and well accepted by children. Overall, yoga practice has shown potential to decrease pain related disability in children, consequently improving their functional capacity.

One of the challenges seen across studies is difficulty in the recruitment of participants. The recruitment findings found in this review are similar to other pediatric interventional studies citing time, transportation and convenience as barriers to participation (Bavdekar, 2013; Nguyen et al., 2014). All of which are representative of the child's busy school and parental work schedules. Recruitment for pediatric studies presents a unique challenge in that "buy in" is

needed from both the child and the parent, as the parent is most likely responsible for transportation to the study location. Alternatively, three of the five trials were located in academic settings, rather than in community yoga studios, potentially adding burden related to distance and parking. Overall, the difficulty appears to be in getting participants to begin the study; not keeping them in the study once the study begins.

While the literature to date highlights the potential of yoga as a pediatric intervention, results are far from conclusive due to the studies variable methodological quality. Review results indicate the need for improved methodology in the study of interventional yoga in children. Common limitations found in the current literature include: (a) lack of a control group (n=2), (b) relatively small sample sizes and (c) gender and ethnicity based homogenous samples. Furthermore, few studies adequately describe the intervention protocol in relation to yoga style and poses used. More rigorous and systematic study is needed to confirm the safety and clinical efficacy of interventional yoga in children. Methodologically, parallel RCTs enrolling more sample diversity in terms of gender and ethnicity are needed in order to enhance the generalizability of study findings. In addition, larger sample sizes are desirable to increase statistical power and the ability to measure changes in multiple variables of interest. Future RCTs need formal follow-up metrics to determine the duration of effects of yoga practice in children. Lastly, studies should use standardized measures in line with the PedIMMPACT recommendations (McGrath et al., 2008) that are validated for use in children to allow for comparison and statistical interpretation of results between studies.

In addition to addressing the methodological limitations found in the current literature, exploration in future pediatric research should address yoga specific intervention components (e.g. the examination of whether specific yoga techniques or poses are more effective than

others) is needed. Investigation into the relationship between intervention dose and emergence of a beneficial response would be decisive in the determination of future chronic pain clinical recommendations related to practice frequency.

In conclusion, although findings from this review are promising and preliminary evidence suggests that yoga holds the potential to reduce pain and functional disability, larger more rigorous trials are needed to support these current findings.

Chapter VI: YOGA FOR THE ADOLESCENT WITH CHRONIC PAIN: A PILOT STUDY

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Abstract

Approximately 25% of adolescents in the United States experience chronic pain negatively impacting psychological, social and physical functioning. Current treatment recommendations include the use of exercise. One increasingly popular form of exercise is yoga. Yoga is versatile and adaptable to both physical ability and developmental levels, with promising results thus far in the adult chronic pain literature. Currently, a limited number of studies has been conducted in specific disease populations (e.g. irritable bowel, headaches, primary dysmenorrhea) but none in a generalized adolescent chronic pain population. Therefore, the purpose of this pilot study was to explore the feasibility of a yoga intervention in adolescents with chronic pain. Additionally, we aimed to examine the effect of a yoga intervention on pain, functional disability and quality of life (QOL) as well as identify and characterize responders versus non-responders of the yoga intervention.

Eighteen adolescents between the ages of 13-18 with chronic pain participated in a 90-minute weekly, 8-week single-arm interventional yoga study. Pain, functional disability, and QOL were measured a baseline, 4-weeks and 8-weeks.

A 53.49% recruitment rate, 78.26% retention rate, and 93.75% adherence rate was noted in this study. There were no reported adverse events. Pain was significantly reduced (p=.046), with no statistically significant changes noted in functional disability or QOL. A total of 72.2% (n=13) of the participants were treatment responders, exhibiting a clinically important difference in functional disability or pain. Of these responders, 77% (n=10) showed a clinically important difference in pain and 23% (n=3) showed a clinically important difference in functional disability.

Yoga appears to be a feasible and safe intervention with the potential to reduce pain and functional disability in the adolescent chronic pain population. Future randomized studies with larger sample size are warranted.

Yoga for the adolescent with chronic pain: a pilot study

Chronic pain in the adolescent is associated with significant functional consequences. Affecting approximately 25% of the children (ages 1-18), chronic pain negatively impacts physical, psychological and social functioning. Difficulty participating in physical activities at school, leisure and at play is common (Kashikar-Zuck et al., 2010; Wilson & Palermo, 2012) and prevalence of concurrent mood disorders in these youth is high as compared to healthy peer counterparts in community samples (Conte, Walco, & Kimura, 2003; Kashikar-Zuck et al., 2008; Kashikar-Zuck, Goldschneider, Powers, Vaught, & Hershey, 2001). Likewise, these youth have fewer friendships and experience more social isolation (Forgeron et al., 2011; Kashikar-Zuck et al., 2007) reporting feelings of social rejection by their peers (Merlijn et al., 2003).

Treatment for these youth is often delayed with approximately 20% of adolescents who seek treatment being told they will simply "grow out of it" (Buskila et al., 1995; Mikkelson, 1999). To date, there is a lack of standardized evidence-based treatment guidelines in adolescent chronic pain. However, multiple position statements call for the use of education and exercise as a first round treatment in adolescent chronic pain (Cunningham & Kashikar-Zuck, 2013; Tesher, 2015). Yoga is one form of exercise that has shown promising results in the adult chronic pain literature (Carson et al., 2010; Mist, Firestone, & Jones, 2013). To date, a limited number of studies examine the use of yoga in a variety of adolescent pain populations (irritable bowel, juvenile rheumatoid arthritis, headaches, and primary dysmenorrhea) (Brands, Purperhart, & Deckers-Kocken, 2011; Evans et al., 2014; Evans et al., 2010; Hainsworth et al., 2013; Kuttner et al., 2006; Rakhshaee, 2011). However, no studies have been completed examining the use of yoga in a generalized adolescent chronic pain population. Therefore, the purpose of this study was to:

1. Explore the feasibility of yoga in adolescents with generalized chronic pain
2. Examine the effect of a yoga intervention on pain, functional disability and quality of life in the adolescent with chronic pain.
3. Identify and characterize responders versus non-responders of the intervention.

Methods

Design and participants

Eighteen adolescents with chronic pain were recruited from pediatric pain management, rheumatology and other pediatric specialty clinics in an academic health center in the Pacific Northwest via provider referral and targeted mailings. Potential participants were contacted by the study investigators and were screened for eligibility. Once potential study eligibility was confirmed, participants and their family were invited to a 2-hour onsite program orientation meeting to learn about the class structure and to discuss study expectations with the research team as described elsewhere (Jones & Reiner, 2010). Following the orientation meeting, those adolescents electing to participate in the study made individual appointments for consent and baseline testing.

Participants were eligible if (1) they were between 13-18 years of age; (2) pain in duration of 3 months or greater regardless of location; (3) no other known causes for pain such as neurologic and/or genetic disorders, cancer, arthritis or recent surgical procedures; (4) no planned elective surgeries in the next 4 months; (5) not practiced yoga for more than once per week in the last 3 months; (6) not been in treatment for drug, alcohol and/or chemical abuse in the prior 6 months; or (7) not pregnant or planning on becoming pregnant during the study time period. The Institutional Review Board approved this study. Parental consent and adolescent assent was obtained from all participants at study enrollment prior to baseline measures.

Intervention

Classes met weekly in groups of 6-10 over the 8-week study period. All classes were held in a specifically designed studio within the academic health center, and led by two certified yoga instructors with experience working with adolescent mindfulness and chronic pain populations. The yoga treatment protocol was based on recently published RCT's of yoga in adult chronic pain populations and other adolescent chronic pain conditions (Carson et al., 2010; Evans, Tsao, & Zeltzer, 2009). Each 90-minute class session consisted of yoga (gentle stretching, balance poses, relaxation, and breathing techniques) and mindfulness (e.g. being in the present moment, noticing thoughts without judgment, managing negative self-talk, emotional self-care, and finding balance). A heavier emphasis on mindfulness was placed in the earlier classes as the yoga practice progressed in intensity and duration (including greater time in standing poses) throughout the intervention. Each class began with a pose introduction, demonstration and "optional assist" from the teachers. Other yoga movements/poses were then introduced throughout the session ending with a resting pose to promote deep relaxation of the body. Instructors monitored for any difficulties and provided participants modification of poses using props (e.g. chairs, blocks, straps) to accommodate for common chronic pain-related movement concerns, hypermobility, deconditioning and other limitations as needed.

Measures

Data were collected at a median of two weeks prior to program initiation (baseline), at the end of week four (mid-study), and at the end of the week eight (post-test). Questionnaire data were completed by the subjects via an internet link to the questionnaires. Standard demographics were collected at baseline. The instruments described below (with the exception of global impression of change and pain location inventory) were collected at all time points and

in accordance with the Pediatric Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (PedIMMPACT) (McGrath et al., 2008).

Feasibility. Feasibility was assessed using the following criteria (1) recruitment rate; (2) retention rate; (3) class adherence rates; and (4) safety as measured by reporting of adverse events.

Functional Disability Inventory. Adolescent levels of functional disability due to pain related health status was assessed using the Functional Disability Inventory (FDI) 15-item measure (Claar & Walker, 2006; Walker & Greene, 1991). The FDI was designed to measure limitations in performance in activity of daily living across home, school, recreation and social domains in adolescents with chronic pain. Participants were asked to rate their level of difficulty completing a variety of tasks such as "doing chores at home", "walking the length of a football field", "doing something with a friend", and "being at school all day" within the past two weeks. Items are rated on a 5-point scale where 0 = no trouble, 1 = a little trouble, 2 = some trouble, 3 = a lot of trouble, and 4 = impossible with higher scores indicating greater functional disability (range 0 to 60). Scores >12 are more clinically concerning (Kashikar-Zuck et al., 2011). The FDI has shown high internal consistency ($\alpha = 0.85$ to 0.92) and high test-retest reliability correlations ($r = 0.80$, $p < 0.001$) in this population (Claar & Walker, 2006; Walker & Greene, 1991).

Pain characteristics. A standard 28-site pain location inventory was used to determine pain locations. Participant report of pain intensity (both current and usual) was assessed using an 11-point (0-10) numeric rating scale (NRS). Responses range from 0 or "no pain" to 10 being "worst pain". Participants were asked to rate their pain level within the past week (current pain) and how much pain they usually have (usual pain) using this likert scale. Further, pain frequency

within the past month was assessed using a 7-point likert type scale (1 = not at all, 2 = less than 1 time per month, 3 = more than 1 time per month and less than 1 time per week, 4 = 1 time per week, 5 = 2-3 times per week, 6 = 4-6 times per week, 7 = daily). Categorical scales are commonly used in the assessment of pain frequency in pediatric pain studies (Perquin et al., 2000; Wilson & Fales, 2015). To better capture the multidimensional aspects of chronic pain, a pain index score was computed using the adolescents' pain intensity and multiplying it by pain frequency, with a range of 0 to 70. Use of a pain index composite variables is common in other pediatric pain clinical studies (Huguet & Miró, 2008; Wilson & Fales, 2015).

Pain duration was assessed by asking participants "how long do your aches or pain usually last" with responses options including: <1 hour per day, 1-4 hours per day, 5-8 hours per day and >8 hours per day.

Quality of Life. Adolescent quality of life was assessed using the 23-item Pediatric Quality of Life Inventory 4.0 (PedsQL) measure with four subscales (physical, emotional, social, and school functioning). Participants were asked to rate the extent to which they have had problems in each subscale over the past month using 5-point Likert scale (ranging 0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = almost always). Items are reversed scored and linearly transformed with higher scores indicate higher perceived quality of life (0-100). The PedsQL has been used across a variety of pediatric chronic health conditions and has demonstrated good internal consistency ($\alpha = 0.88$) (Varni, Seid, & Kurtin, 2001).

Symptom Impact Questionnaire (SIQR). A modified version of the revised Fibromyalgia Impact Questionnaire (FIQR), the SIQ symptom subscale was used to measure symptoms known to be associated with the experience of chronic pain syndromes. The SIQR is identical to the FIQR symptom domain, with no reference to fibromyalgia (Bennett et al., 2009).

Using a numerical rating scale (0-10), participants are asked to rate the level to which they had experienced symptoms (pain, energy, stiffness, sleep, depression, memory problems, anxiety, tenderness to touch, balance problems, sensitivity to loud noises, bright lights or odors) within the past 7 days. The symptom scores are summed and then divided by 2 to determine the overall symptom score (upper limit = 50).

Global Improvement. In an attempt to quantify the effect of the intervention over time, global improvement was evaluated on the 7-point Patient Global Impression of Change (PGIC) scale at post-test (Kamper, Maher, & Mackay, 2009). Participants were asked "Compared to the way you felt before you began this study, how would you describe the change (if any) in activity, limitations, symptoms, emotions and overall quality of life related to your painful condition?" The parent or guardian of the participant was asked the same questions worded to reflect the change in their child. Response options ranged from (1) = "no change" to (7) = "substantially improved". Global improvement is noted for participants indicating moderate to substantial improvement. Global rating of change scales are widely used in clinical practice and research, and have shown to be sensitive to change in previous studies (Fischer et al., 1999; Lauridsen, Hartvigsen, Korsholm, Grunnet-Nilsson, & Manniche, 2007). Additionally, an open field code was included allowing participants to respond to the question "is there any additional information you feel the researchers should be aware of".

Statistical Methods

Data analyses were conducted using SPSS version 23. Descriptive statistics were used to profile the sample. Within subjects repeated measures analysis of variance (ANOVA) were used to test the effect of the yoga intervention on pain, functional disability and quality of life over time. Mauchly's test of sphericity was used to test the assumption of compound symmetry. No

violations were noted across measures (pain index χ^2 (2) = .906, p = .636, the FDI χ^2 (2) = 3.029, p = .220, and PedsQL χ^2 (2)= 3.89, p = .143). Significance was set at 0.05, and significant trends were noted at 0.10.

Exploratory analyses were used to identify and characterize study responders and non-responders to the yoga intervention. Group and individual mean scores were evaluated at baseline and at the end of 8 weeks for a clinically important difference (change in score to which the participant perceives benefit from the intervention) signaling a treatment response to the intervention. Responders were defined by a clinically important difference as noted on either the FDI or pain intensity on the NRS. Using established clinical reference points (0-12=no/minimal disability, 13-29=moderate disability, and 30-60=severe disability) (Kashikar-Zuck et al., 2011) participants with a FDI disability level category change (e.g. from moderate to no/minimal disability) were considered to exhibit treatment response (Sil et al., 2014). Likewise, a decrease in pain intensity of >1 point (10%) on the 0 to 10 NRS scale was used to indicate pain treatment response (Hirschfeld, Wager, Schmidt, & Zernikow, 2014; Powell, Kelly, & Williams, 2001). Next, independent samples t-tests and χ^2 test of independence (for categorical variables) were conducted to compare group (responders versus non-responders) differences at baseline.

Results

Demographics

The majority of the sample was female (83.3%), Caucasian (72.2%) and with a mean age of 15.24 (SD=1.41 years) (**Table 6.1**). Most participants were enrolled in school (83.3%) with 72.2% attending full time, in person. The adolescents reported current pain levels at baseline of 5.11 (SD=1.28) and typical mean pain level of 5.06 (SD=1.79). 66.7% reported daily pain within the past month with half (50%) reporting average pain duration of 5 hours per day or

greater. The majority (77.78%) reported multi-site pain (in 2 or more locations). Primary pain locations included the head and neck (50%), abdomen (27.8%) and lower extremity musculoskeletal pain (22.3%). The mean symptom domain (SIQR) score was 19.98 (SD=6.2). Group mean functional disability (FDI) was 17.78 (SD=9.28) and overall quality of life (PedsQL) was 61.12 (SD=14.44).

Table 6.1. Demographic and clinical characteristics at baseline		
	N	**%**
Age M (SD)	15.24 (1.41)	
Gender		
Female	15	83.3
Racial Background		
Caucasian	13	72.2
Asian	1	5.6
Native Hawaiian/Pacific Islander	1	5.6
Mixed	1	5.6
Other	2	11.1
Enrolled in School		
Yes	15	83.3
Enrollment Type		
FT, in person	13	72.2
PT, in person	1	5.6
FT, online	2	11.1
Other	2	11.1
Current Pain Level M (SD)	5.11(1.28)	
Pain Frequency		
1x/week	1	5.6
2-3x/week	2	11.1
4-6x/week	3	16.7
Daily	12	66.7
Pain Duration		
<1 hr/day	2	11.1
1-4 hrs/day	7	38.9
5-8 hrs/day	3	16.7
>8 hrs/day	6	33.3
FDI Score M (SD)	17.78 (9.28)	
PedsQL M (SD)	61.12 (14.44)	
Primary Pain Locations		
Head/Neck/Shoulders		50
Trunk (Back/Abdomen/Pelvis)		27.8
Lower Extremities		22.3
Widespread Pain	14	77.78

Recruitment, retention and adherence

Of a total of 132 provider referrals, 43 adolescents met eligibility requirements of which 23 were enrolled in the current study (rate of recruitment = 53.49%). Two dropped out prior to the first yoga class citing pain exacerbation or time constraints related to multiple ongoing

medical visits. An additional three persons dropped out prior to the mid-point data collection due to inadequate time to devote to study (rate of retention = 78.26%). The study flow diagram is shown in **Figure 6.1**. A total of 18 adolescents participated in a range of 5 to 8 classes with an average dose of 7.5 yoga classes (adherence rates = 93.75%). The primary reasons for not attending class was family time conflict. There were no reported adverse events.

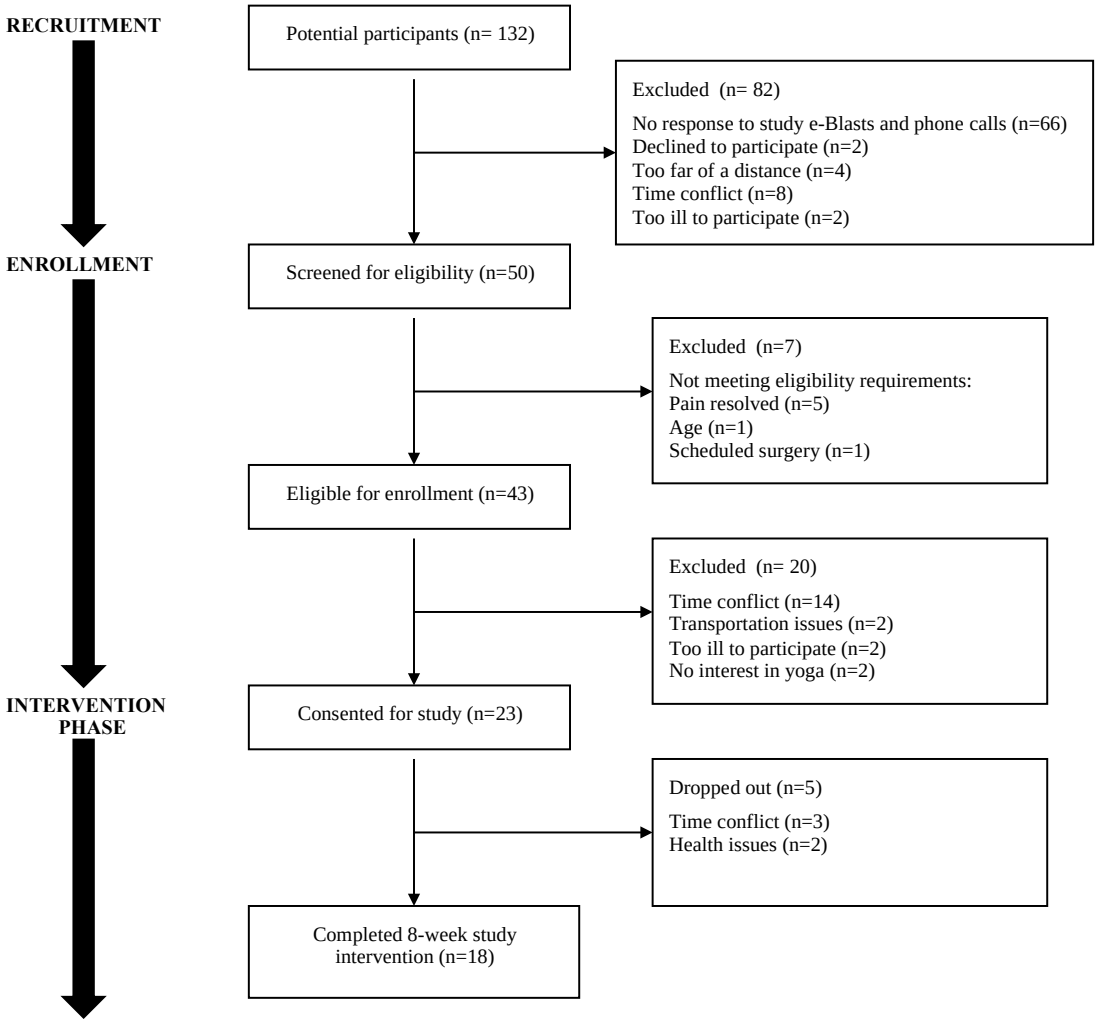

Figure 6.1. Study flow diagram

Pain and functional outcomes

Mean scores across time for both primary and secondary outcome variables were computed (**Table 6.2**). The analysis revealed an improvement trend in pain at the study end F (2, 16) = 2.98, p = 0.06, *d* = .53. Orthogonal polynomial contrasts were applied to describe the change in pain across time. A significant linear trend described the change in pain across time, with a reduction in pain from baseline to 4-weeks (mid-study) that then continued from 4-weeks to 8-weeks (end of study) F (1, 17) = 4.85, p = .04, *d* = .55. No significant improvement in functional disability F (2, 16) = .02, p = .98, *d* = .03 or quality of life was found F (2, 17) = .47, p = 0.63, *d* = .53. Effect sizes noted were in the small to medium range.

Table 6.2. Study means and ANOVA's for primary and secondary outcome variables

	Baseline	Mid-study	Post-Study	F Score	P value	Cohen's *d*
Pain Index	33.06 (9.89)	30.61 (12.44)	27.33 (12.27)	4.85	.04**	.53
FDI	17.78 (9.28)	17.83 (8.49)	18.0 (8.37)	.02	.98	.03
PedsQL	67.29 (13.51)	63.28 (11.95)	60.82 (9.04)	.47	.63	.53

*trended towards significance at p<.10
**significant at p<.05

Patient global improvement

A total of 52.2% (n=13) reported global improvement, 27.8% (n=5) reported no change. Analysis of parental report of global improvement indicated a total of 83.3% (n= 15) reported child improvement while 16.7% (n=3) reported no change. No child or parent reported worsening compared to the beginning of the intervention.

Responders versus non-responders

A total of 72.2% (n=13) of the participants were identified as treatment responders, given that they exhibited a clinically important difference in functional disability or pain. Of these

responders, 23% (n=3) showed a clinically important difference in functional disability and 77% (n=10) showed a clinically important difference in pain. There were no participants that showed a clinically important difference on both outcomes.

Independent sample t-tests and χ^2 test of independence were used to compare group differences at baseline (**Table 6.3**). No significant differences in age t(16)= -.52, p=.61, number of pain locations t(16)= -1.08, p=.31, baseline pain index scores t(16) = -1.90, p=.08 and symptoms (SIQR) scores t(16) = -.43, p=.68 between responders versus non-responders were noted. Additionally, there were no statistical differences noted in functional disability t(16)= -1.52, p=.15 and QOL t(16)= .615, p=.55 at baseline between the two groups. No significant gender difference χ^2 = 1.27, p =.26 was noted between groups.

Table 6.3. Baseline means and t-tests for responders versus non-responders

	Responders (n=13)	**Non-Responders (n=5)**	**t score**	**d*f***	**P value**
Age	15.4 (1.39)	15.0 (1.41)	-.52	16	.62
Sum of locations	7.23 (3.61)	5.4 (3.05)	-1.08	16	.31
Pain Index	35.62 (9.86)	26.4 (6.88)	-2.24	16	.08*
SIQR	19.89 (7.23)	18.4 (4.25)	-.54	16	.60
FDI	19.8 (9.58)	12.6 (6.69)	-1.79	16	.10*
PedsQL	59.8 (15.64)	64.5 (11.48)	.71	16	.50

*trended towards significance at p<.10
**significant at p<.05

Discussion

Findings of this study indicate yoga to be a feasible, acceptable and safe intervention in adolescents with chronic pain. Our recruitment rate of 53.49% was higher than the average recruitment rate of 44.6% across other pediatric yoga studies (Firestone, Wilson & Jones, under review). Similar to other pediatric interventional studies, the primary reason declining participation was time conflicts and constraints. Our finding indicate that the yoga intervention

was acceptable, with participant adherence at 93.75% and average attendance at 7.5 of 8 classes offered as compared to a 80.64% mean adherence rate in previous pediatric yoga studies (Firestone, Wilson & Jones, under review). In line with previous research, our attrition rate was at 21.7%, which is within the range of attrition reported (11-23%) yet higher than the mean attrition rate of 14.6% across studies (Firestone, Wilson & Jones, under review). Comparable to reasons for declining participation, time conflicts and constraints was the primary reason reporting for not completing the study. In regards to safety, no adverse events were recorded during the study, which is consistent with the previous pediatric yoga research reporting no adverse events during the study period (Brands et al., 2011; Hainsworth et al., 2013). Currently, only one study (Evans et al., 2014) reported a non-serious musculoskeletal strain that did not prevent the participant from completing the intervention. Our high adherence rates, low attrition rates and lack of adverse events supports that yoga, as an intervention is acceptable, feasible and safe in this population.

Despite the small sample size, a significant yoga treatment effect on pain was noted. Over the course of the study, a significant linear improvement in the composite pain score (pain intensity x pain frequency) was noted with a medium effect size. Extending findings from other pediatric chronic pain yoga studies, our findings support yoga as an effective intervention for pain (Evans et al., 2014; Evans et al., 2010; Rakhshaee, 2011). Our findings are similar to the Evans et al. (2014) yoga study in adolescents and young adults with rheumatoid arthritis where ratings of "worst pain" were significantly reduced. Likewise, a significant reduction in pain intensity and duration was noted in 92 females with primary dysmenorrhea over the 3-month study (Rakhshaee, 2011). In contrast to previous yoga studies, quality of life remained statistically unchanged over the course of our study (Brands et al., 2011; Evans et al., 2010;

Hainsworth et al., 2013). Of note, caution should be taken in the interpretation of our study findings secondary to our small sample size.

Our analysis examining functional disability differences indicated no statistical change with scores remaining relatively stable. Baseline functional disability levels in our study were in line with other pediatric yoga populations, yet, our findings contrasted those found in other pediatric yoga studies (Evans et al., 2014; Hainsworth et al., 2013; Kuttner et al., 2006). For example, in the Kuttner et al. (2006) study, 28 adolescents with IBS reported lower levels of functional disability and increased interaction with activities of daily living after a 4-week yoga intervention. Despite not finding an improvement in functional disability, anecdotal reports from the adolescent participant parents indicate that they felt participating in the yoga intervention had helped them in their daily functioning reporting "I have witnessed her using techniques learned in class to work through her pain and manage her daily tasks". There may be a number of explanations for the lack of functional disability improvement found in our study including a potential for higher levels of physical deconditioning in our sample of adolescents. As our sample was recruited from a specialty pain clinic, these adolescents may have been experiencing pain and associated symptoms for a longer duration than other pain populations seen in general clinics increasing the risk of lower engagement in physical activity and increased levels of physical deconditioning. In general, adolescents with chronic pain are less physically active than their healthy peer counterparts (Lelieveld et al., 2008; Wilson & Palermo, 2012) increasing their risk for physical deconditioning. Physical deconditioning is well documented in adult chronic pain populations (Jones, Clark, & Bennett, 2002) influencing factor in engagement in physical activity and may initially delay treatment response (Clark, Jones, Burckhardt, & Bennett, 2001). Involvement in exercise may temporarily increase perceived functional limitations, but in the

long-term improve overall functioning (Simons, Logan, Chastain, & Cerullo, 2010). Additionally, our limited sample size may have prevented detection of change in functional disability, had we had more participants we might have seen more movement on this measure. Future studies with larger sample sizes to detect change and longer exposure to the yoga intervention are warranted to be able to determine the effect of a yoga intervention on functional disability.

Clinically important differences were noted in our study. While statistically significant results indicate the mean group effect of an intervention, the determination of clinically important outcomes is central to the evaluation of individual treatment effectiveness. Currently, the evaluation of clinically important changes in research has been used in adult chronic pain populations (Mease et al., 2011) but has been minimally applied to pediatric populations (Sil et al., 2014). Of the total 18 completing participants, 10 (77%) adolescents exhibited clinically important difference in their pain. Yet, only three completing participants (16.7%) exhibited a clinically important difference in their functional disability from baseline to post-test. Treatment responders (those that exhibited a clinically important difference in pain or functional disability) tended to report higher pain intensity, higher functional disability and a slightly lower quality of life at baseline. However, no significant statistical difference between groups at baseline was found.

Anecdotally, parental comments indicated that participating in the study and making connections with others "like them" giving an outlet to talk about their struggles was beneficial and encouraging to their child in their daily life. One parent reported "I think it is helpful for them to see that they have some control and they are not alone". The group setting of this study was designed to provide a safe space where the adolescents are with peers who can relate to their

experiences with chronic pain. The group setting also decreases the sense of isolation reported by the adolescent living with chronic pain. The goal is to foster a feeling of connection and support within the group that may be unavailable to the students in their daily life (Gallant, 2003). This was also evident in adolescent reports of feeling "less abnormal" and "loving the friendships" they made. Overall, participants reported a sense of "belonging" and finally being able to "relax and be themselves". The majority of the adolescents ask to continue with the study even at study end.

Limitations

The main limitation of this study is the small sample size and lack of randomization. Therefore, study results reported should be interpreted with caution. As this study recruited from an academic health center pediatric pain clinic there is a risk of our participants experiencing more pain than those in primary care and may not represent nor generalize to all kids with chronic pain. Although both genders are represented, the majority of participants were Caucasian, which limits generalizability to broader populations. Moreover, due to the nature of the study, the lack of control group limits the overall interpretability and applicability of study results.

Conclusion

The current study adds to the building body of literature on the therapeutic use of yoga in adolescent chronic pain populations. The findings of our 8-week pilot study indicate yoga to be a feasible and safe intervention in the adolescent chronic pain population. Our preliminary findings indicate that yoga is effective for reducing pain. Despite the non-significant functional disability and quality of life findings, the information from this study is beneficial to the development of future research studies.

Recruitment into pediatric interventional studies continues to be a challenge. Similar to other pediatric interventional studies, the primary reason for declining participation in our study was family time conflicts (Brands et al., 2011; Kuttner et al., 2006; Stephens et al., 2008). Designing future studies considering parental and adolescent work and school schedules is necessary to obtaining sufficient sample sizes. Finally, as we did not see movement in functional disability or quality of life scores, further investigation into the relationship between dose and response is needed to establish clinical recommendation guidelines.

CHAPTER VII: SUMMARY AND CONCLUSIONS

The experience of chronic pain during the adolescent period is an important clinical problem affecting a significant number of adolescents. Affecting all aspects of daily life, these youth experience significant disruption across all domains of functioning. Physical function in the adolescent with chronic pain is compromised, as these youth are less physically active than their healthy peer counterparts (Long, Palermo, & Manees, 2008; Wilson & Palermo, 2012). Further, these youth commonly exhibit symptoms of overall physical deconditioning. Emotional functioning is also affected, with high prevalence rates of concurrent mood disorders (anxiety and depressive symptoms) reported (Kashikar-Zuck et al., 2008) as compared to other pediatric chronic illness populations. Further exacerbating the experience and consequences of chronic pain, the presence of these mood disorders have been linked to increased pain perception (Vlaeyen, Kole-Snijders, Boeren, & van Eek, 1995) and higher levels of functional disability (Kashikar-Zuck, Vaught, Goldschneider, Graham, & Miller, 2002). Socially, these youth tend to have fewer peer relationships and report feeling socially rejected by their peers (Forgeron et al., 2011; Kashikar-Zuck et al., 2007) due to the difficulty of explaining their pain related limitations. Moreover, these social complications further feed into the ongoing cycle of chronic pain, depression, and functional disability

The management of adolescent chronic pain is complex and challenging. Currently, there is limited evidence to guide clinical practice guidelines in the adolescent with chronic pain and a lack of standardized criteria to define the experience of chronic widespread pain during adolescence (Zernikow et al., 2012). An array of overlapping symptoms and clinical presentation in addition to the interchangeable use of terminology (i.e. chronic pain, chronic widespread pain, juvenile primary fibromyalgia syndrome, diffuse idiopathic pain syndrome)

used to describe these symptoms, within the scientific literature, further complicates overall recognition and establishment of clinical guidelines (Sen & Christie, 2006). For purposes of this body of work, the use of the terminology juvenile primary fibromyalgia syndrome (JPFS) was used to refer to the adolescent experiencing chronic widespread pain. Yet, we recognize the overlapping symptomatology across non-disease specific pain conditions and a subsequent overlap in goal for management. These treatment goals are aimed at the reduction of pain and the restoration of age appropriate functioning (Clinch, 2009; Sherry & Malleson, 2002). Exercise is considered to be one therapy of benefit in these youth, yet there is limited scientific evidence in support of the use of exercise in adolescent chronic pain populations. Yoga, an increasingly popular form of exercise, had produced promising results for reducing pain and functional disability in the adult literature (Hauser et al., 2010; Mist, Firestone, & Jones, 2013). To date, there is limited evidence on the use of yoga for adolescent chronic pain populations.

Therefore, the overarching purpose of this body of work was to determine the influence of the use of yoga on pain and functional outcomes in the adolescent with JPFS. Specific aims were to 1) synthesize clinical presentation, pathophysiology and current treatment recommendations in fibromyalgia, 2) quantify associations among pain characteristics, psychological factors, general health factors and functional disability in adolescents with chronic pain, 3) determine engagement in, perceived benefits and barriers to yoga participation in fibromyalgia, 4) explore the feasibility, acceptability, safety, and efficacy of yoga as a therapeutic intervention in pediatric chronic pain populations, and 5) to explore the feasibility and examine the effect of a yoga intervention on pain, functional disability and quality of life in the adolescent with generalized chronic pain and to identify and characterize responders versus non-responders to the yoga intervention. This final chapter begins with a summary of the overall

principle findings for each of the specific aims and associated manuscripts concluding with a discussion findings identified across all studies and recommendations for future research and applications to clinical practice.

Summary of Principle Findings

Optimizing fibromyalgia management

To address the first aim of this body of work, a clinical review of the current information on etiology, pathophysiology, clinical presentation, diagnostic standard, and current treatments (pharmacologic and non-pharmacologic) were presented. Currently, there is a paucity of evidence in JPFS as compared to the adult FM literature, therefore this review presented findings found in the adult literature in line with current clinical thought that clinical characteristics and management guidelines in JPFS are aligned with those found in adult FM (Kashikar-Zuck et al., 2014). Regarding the clinical review of current evidence in FM there were three principle findings (**Table 7.1**). First, clinical presentation of the adult with FM mirrors what is seen in JPFS. The most common chief complaint is the presence of widespread body pain with varying degrees of functional disability. Concomitant symptomatology includes reports of fatigue, sleep disturbances, stiffness, tenderness, and fitness levels lower than healthy peer counterparts. We found an approximated 45-69% of adults with FM report concurrent mood disorders such as anxiety and depression (Arnold, 2010) reflecting those found in JPFS (Kashikar-Zuck et al., 2008). A majority of FM patients also report difficulty with other co-morbidities including chronic headaches and irritable bowel symptoms.

Secondly, formal diagnostic criteria for the adult with FM was established in 1990 by the American College of Rheumatology (ACR) and has undergone several revisions over the past 26 years, with the most current revision being the 2010 ACR criteria. The 1990 ACR diagnostic

criteria of FM focuses on the presence of widespread pain present for 3 months or greater, with no known disorder as explanation for pain, the presence of tender points (11 of 18) upon digital palpitation (Wolfe et al., 1990). Whereas the 2010 ACR diagnostic criteria are primarily symptom based and focuses on the presence of widespread pain and severity of concurrent symptomatology (Wolfe et al., 2010). Notably, we found an inconsistent application of diagnostic criteria using various versions interchangeably across the evidence evaluated for this clinical review.

Finally, our review found that current treatment recommendations in adult FM is multi modal and includes both pharmacological and non-pharmacological recommendations. Current recommended drug therapies are effective for symptom relief in only about one-half of patients (Hauser, Petzke, & Sommer, 2010; Mease et al., 2009). Current evidence suggests that in light of these findings, patients are increasingly requesting and choosing to implement non-pharmacologic therapies to complement current pharmacotherapy. Most commonly, exercise and cognitive behavioral strategies are the non-pharmacological interventions of choice. Exercise used within the FM population, must take into consideration and be adaptable to common pain related limitations.

Table 7.1. Principle Findings for Specific Aim 1

Specific Aim 1: Synthesize clinical presentation, pathophysiology and current treatment recommendations in fibromyalgia	
Study	**Principle Findings**
Optimizing fibromyalgia management	Clinical presentation includes multiple symptomatology (e.g. fatigue, stiffness, sleep problems, mood disorders, chronic headaches, irritable bowel symptoms) and varying degrees of pain and physical dysfunction Current diagnosis recommendations are based of the 1990 and/or the 2010 ACR diagnostic criteria Management requires a multidisciplinary approach including exercises that are adaptable to pain related limitations

Predictors of functional disability in adolescent chronic pain

The second specific aim of this body of work was to quantify associations among pain characteristics (worst pain, typical pain, pain frequency and widespread pain), psychological factors (depressive symptoms, pain self-efficacy and optimism), general health factors (sleep disturbances, BMI, and physical activity) and functional disability in adolescents with chronic pain. To address this aim, cross-sectional data was collected from a consecutive series of 314 new pediatric pain management clinic patients. Correlational analyses were used to examine relationships between the predictor variables (pain characteristics, psychological factors, and general health factors) and functional disability. Hierarchical multiple regression analysis was performed to investigate the contribution of significantly correlated predictor variables to functional disability after controlling for the known effects of pain characteristics in step one. We proposed that physical activity and BMI would contribute significantly to functional

disability after controlling for the influence of pain characteristics, psychological factors and sleep problems.

The principle findings from this study (**Table 7.2**) indicate that adolescents presenting for care exhibit widespread pain and high levels of functional disability. Pain characteristics, sleep problems and depressive symptoms were found to be strongly associated with functional disability. Notably, we found a strong negative association between physical activity and functional disability. This can be interpreted as the more physical active the adolescent with chronic pain is, the lower the levels of functional disability reported. Our hierarchical model explained 37.7% of the variance in functional disability and indicated that after controlling for the influence of known contributors to the development of functional disability (pain characteristics and depressive symptoms) the adolescents' engagement in physical activity was the only variable to contribute significantly to functional disability. BMI was not a significant predictor of functional disability.

Table 7.2. Principle Findings for Specific Aim 2

Specific Aim 2: To quantify associations among pain characteristics, psychological factors, general health factors and functional disability in adolescents with chronic pain.	
Study	**Principle Findings**
Predictors of functional disability in adolescent chronic pain	Adolescents with chronic pain experience high levels of widespread pain (65.5%) and functional disability (mean CALI score = 43.86, SD=17.89) Positive correlations with functional disability were found between age (*r*=.19, p=<.01), pain characteristics: worst pain (*r*=.31, p<.01), typical pain (*r*=.34, p=<.01), depressive symptoms (*r*=.52, p=<.01), and sleep problems (*r*=.26, p=<.05). Negative correlations with functional disability were found between physical activity (*r*=-.28, p=<.01), and pain self-efficacy (*r*= -.26, p=<.01) Significant predictors of functional disability include pain frequency (p=<.05), worst pain intensity (p=<.05), depressive symptoms (p=<.05), and physical activity (p=<.05). All independent predictor variables accounted for 37.7% of the variance in functional disability.

Interest in yoga among fibromyalgia patients: An international internet survey

The third specific aim of this body of work was to determine engagement in, perceived benefits of and barriers to yoga participation in FM. To address this aim, a cross-sectional survey of 2,543 self-identified fibromyalgia patients was conducted online. Data was analyzed by characterizing variables using descriptive statistics. Responses were received from all 50 US states and more than two-dozen foreign countries. Principle findings of this study (**Table 7.3**)

indicated that a majority of respondents had either considered attendance or had attended a community style yoga class. Respondents most frequently associated yoga practice with improved mobility, relaxation, reduced pain and soreness, and improved sleep. Fear of exacerbating current pain levels and the physical demands of yoga practice were the most commonly cited barriers to beginning or continuing with yoga practice. The results of our study support the acceptability of yoga to a FM population and the need for yoga programs tailored to address their specific physiological limitations.

Table 7.3. Principle Findings for Specific Aim 3

Specific Aim 3: Determine engagement in, perceived benefits and barriers to yoga participation in fibromyalgia	
Study	**Principle Findings**
Interest in yoga among fibromyalgia patients: An international internet survey	57.8% had previously attended a yoga class and 79.8% had considered attending a yoga class Physical benefits reported included: Improved mobility (49.4%), relaxation (47.5%), reduced pain and soreness (30.4%), and improved sleep (21.1%) Psychological benefits reported included: Less stress (36%), improved outlook on life (32.1%), glad to join a community (25.7%) Barriers to initial yoga practice: Pain apprehension during practice (35.8%) and after practice (45.5%), inconvenient time (32.9%), inconvenient location (30.1%), and price (28.5%) Barriers to continued yoga practice: Physical demands (26.1%), pain during class (21.3%), pain after class (20.7%)

Yoga for pediatric chronic pain populations: A review

The fourth specific aim of this body of work was to synthesize current evidence on the feasibility, acceptability, safety, and efficacy of yoga as a therapeutic intervention for pain and functional disability in a clinical population of adolescents with chronic pain. To address this aim, an integrative review of the current literature was conducted extracting data on study design, disease/condition, yoga intervention frequency, dose and duration, study adherence, attrition rates, adverse events and pain and functional disability outcomes. A total of five studies were identified as meeting inclusion criteria and conducted in various pain conditions: irritable bowel syndrome, rheumatoid arthritis, primary dysmenorrhea, and chronic headaches. There were four principle findings from our review (**Table 7.4**). First, yoga as a therapeutic intervention appears to be feasible in pediatric populations. We found moderate study acceptance rates; with the primary reason reported for declining study participation was time related conflicts. Study adherence rates were high and attrition rates were low. Similar to reasons for initial study declination, time related conflicts were the most common reason for study attrition.

Secondly, our findings suggest that yoga is safe intervention in pediatric pain populations. No serious adverse events were reported across the identified studies. Only one study reported a non-serious musculoskeletal strain, which did not prevent the participant from further participation. Third, our findings indicate that yoga holds promise in decreasing pain and improve functioning. Yoga practice was associated with a reduction in pain intensity ratings in four of the five studies reviewed. Likewise, three of the five studies included formal measures of functional disability all of which reported a decrease in functional disability. Last, our findings

indicate that yoga shows the potential to produce these positive results when administered in small doses.

Table 7.4. Principle Findings for Specific Aim 4

Specific Aim 4: Explore the feasibility, acceptability, safety, and efficacy of yoga as a therapeutic intervention for pain and functional disability in pediatric chronic pain populations	
Study	**Principle Findings**
Yoga for pediatric chronic pain populations: A review	Yoga appears to be feasible in pediatric populations, with high mean adherence rates (>80%) and low mean attrition rates (<15%) and moderate mean study acceptance rates (44.6%) No serious adverse events were reported Pain reductions noted in four of the five studies reviewed Functional disability was improved with adolescents reporting increased ability to participate in activities of daily living Improvement was noted administered in relatively small doses (average dose = 90 minutes weekly over an 8-week period)

Yoga for the adolescent with chronic pain: A pilot study

Building on aim four, the fifth aim of this body of work was to explore the feasibility and to examine the effect of a yoga intervention on pain, functional disability and quality of life in adolescents with generalized chronic pain. Aim six, also addressed by this manuscript, was to identify and characterize responders versus non-responders of the yoga intervention. To address

both aims, an 8-week single-arm yoga interventional pilot study with 18 adolescents with chronic pain was conducted.

Primary findings of this study indicate the yoga intervention to be safe, feasible and acceptable to the adolescent with generalized chronic pain (**Table 7.5**). In regards to feasibility, the recruitment rate in our study was found to be higher than the average recruitment rate in other similar pediatric interventional studies. Additionally, high patient adherence and weekly attendance rates in combination with low study attrition rates suggest that the intervention was acceptable. Importantly, there were no adverse events reported during the study period. Examining pain and functional outcomes, our findings indicate significantly reduced pain intensity at study end. However, no change in functional disability or pediatric quality of life was noted with individual scores remaining relatively stable over the course of the study.

Table 7.5. Principle Findings: Specific Aim 5

Specific Aim 5: To explore the feasibility and examine the effect of a yoga intervention on pain, functional disability and quality of life in the adolescent with generalized chronic pain and to identify and characterize responders versus non-responders to the yoga intervention.

Study	Summary of Principle Findings
Yoga for the adolescent with chronic pain: A pilot study	Study recruitment rate = 53.49%, retention rate = 78.26%, adherence rate = 93.75%, no adverse events reported Pain was significantly reduced at end of study (p=.04) No improvement was noted in functional disability (p=.98) or quality of life (p=.63) A total of 72.2% (n=13) of the participants were identified as treatment responders (exhibited clinically important differences) Of the responders, 23% (n=3) showed clinically important differences in functional disability and 77% (n=10) showed clinically important differences in pain

Addressing the sub-aim of specific aim 5 (**Table 7.6**), a majority of participants were identified as treatment responders (72.2%), meeting the guidelines for clinically important differences on either pain or functional disability. Of these responders most were pain responders (77%) while only 23% exhibited a clinically important difference in functional disability. No significant difference at baseline was found between responders versus non-responders in age, gender, sum of pain location, pain, symptoms, functional disability or quality of life.

Table 7.6. Principle Findings: Specific Aim 5a

Specific Aim 6: Identify and characterize responders versus non-responders of the yoga intervention	
Study	**Summary of Principle Findings**
Yoga for the adolescent with chronic pain: A pilot study	A total of 72.2% (n=13) of the participants were identified as treatment responders (exhibited clinically important differences) Of the responders, 23% (n=3) showed clinically important differences in functional disability and 77% (n=10) showed clinically important differences in pain

Discussion of Selected Themes

Current knowledge of chronic pain during childhood is based in the adult literature

It is commonly accepted that the biological underpinnings of chronic pain mimic that of the adult population with current pediatric diagnostic and treatment recommendations extrapolated from the adult literature. To date, although emerging, there are limited scientific studies investigating the underlying pathophysiology of pediatric chronic pain with the majority of research focusing on chronic pain conditions with identifiable underlying disease related etiology (e.g. juvenile rheumatoid arthritis). Therefore, the first manuscript in this body of work (Chapter II) a synthesis of the clinical presentation, pathophysiology and current treatment recommendations in fibromyalgia and our manuscript of perceived benefits and barriers to yoga (Chapter IV) is based in the adult literature. However, caution should be taken when applying and/or interpreting results inferred from the adult literature as one cannot guarantee that the adolescent is identical to the adult. When done so, the application of evidence from the adult literature should be done so through a developmental lens. The onset of chronic pain typically occurs around the onset of puberty, during the adolescent developmental period. It is during this

developmental stage, emotionally and socially the adolescent is striving to develop their personal identity with a primary focus on social outlets and peer acceptance (Erikson, 1959). The experience of chronic pain during this stage disrupts development resulting in increased dysfunction particularly within the social and emotional domains that may be even more troubling to the adolescent than actual physiological manifestations of pain itself. A cycle ensues of social and emotional distress that has been associated with pain exacerbation that causes the adolescent to further withdraw socially (Jones, Silman, & Macfarlane, 2003). Consequently, clinical presentation and adolescent treatment priorities may differ from the adult. All treatment recommendations should be developmentally appropriate addressing their unique developmental challenges, not simply adapted from the adult world. Simply, what may work for the adult may not necessarily be developmentally appropriate for the adolescent.

Lack of current clinical guidelines in JPFS

A recurrent theme found in this body of work, is a lack of consistently applied definition of JPFS. Further complicating the matter is the controversial nature of a JPFS diagnosis among many pediatric providers (Kashikar-Zuck & Ting, 2014). This debate is in part due to a lack of observable, tangible diagnostic findings in JPFS as a diagnosis remains primarily symptom based, ruling out underlying pathology. Consequently, initiation of treatment in these youth is commonly delayed, in some up to 4 years as they visit multiple providers before diagnosis. During this delayed time period, commonly these youth receive minimal interventions for their symptomatology negatively impacting their overall functional ability. In light of these findings, there is a call for treatment recommendations in pediatric chronic pain that are symptom and functionally based, highlighting the utility of classifying children with an absence of underlying disease into categorical groups as potentially problematic at the individual level. Yet, there is a

need for some criterion that helps guide clinicians in early recognition and initiation of interventions to diminish the functional consequence of the chronic pain experience.

Currently, the only pediatric-based criterion was developed in 1985 by Yunus & Masi (Yunus & Masi, 1985). Yunus & Masi's suggested criteria for identifying JPFS include the presence of diffuse (3 or more sites) pain ≥ 3 months, absence of underlying disease, five or more tender points, and 3 of the following 10 associated symptoms: 1) anxiety, 2) fatigue, 3) poor sleep, 4) headaches, 5) irritable bowel syndrome, 6) subjective soft tissue swelling, 7) numbness, 8) pain modulation by physical activities, 9) pain modulation by weather factors, and 10) pain modulation by stress/anxiety. Additionally, four tender points were considered to meet criteria given 5 of the 10 associated symptoms were present. In contrast, the 1990 ACR criteria for adult fibromyalgia includes the presence of widespread pain (bilateral pain, pain above and below the waist and axial pain), and pain in 11 of 18 tender points on digital palpitation (F. Wolfe et al., 1990). Many providers and researchers alike apply both adult criterions interchangeably in children. However, a lower occurrence of tender points in children have been noted suggesting that the 1985 Yunus and Masi and 1990 ACR criteria may not be interchangeable, not to mention that the adult criterion have never been validated in pediatric populations. Some children might or might not have the typical pain trigger points as seen in adults. Moreover, it has been suggested that in the early stages of JPFS development, symptoms are not as prevalent (Kashikar-Zuck & Ting, 2014) leading to the potential of delaying recognition and intervention when attempting to apply the adult criterion in a pediatric population. This lack of consistency creates difficulty as well in case determination for adequate research sampling and for comparison of findings across pediatric chronic pain studies.

Identification of modifiable factors in JPFS

This body of work supports previous findings of high levels of debilitation in the adolescent with chronic pain. The youth in our samples exhibited high levels of functional disability across domains (physical, social, emotional) and presence of co-morbid symptoms such as sleep problems. One aim was to examine the clinical presentation of the adolescent with chronic pain to determine what potentially modifiable health factors contribute significantly to functional disability (Chapter III). Our findings indicate that after controlling for other known significant influencing factors (theoretically non-modifiable) such as pain intensity and levels of depressive symptoms, the lack of engagement in physical activity was the only noteworthy modifiable factor to contribute to functional disability. Previous research findings indicate that the adolescent with chronic pain engage in lower levels of physical activity than healthy peer counterpart's (Long et al., 2008). Getting these youth active may be foundational to a successful multi-modal treatment plan aimed at the amelioration of symptoms and restoration of daily functioning (from a development perspective).

Need for continued development of exercise interventions

Multiple position statements call for the use of exercise in adolescent chronic pain management (American Pain Society, 2005), despite the scant evidence on the use of exercise and what forms of exercise would be most effective. Moreover, in light of this body of works findings that lack of physical activity increases the risk for functional disability (Chapter III) in conjunction with the high levels of functional disability noted in our sample (Chapter VI), the need for exercise or activity based interventions is underscored. To date, few movement modalities have been tested in adolescents with chronic pain, yet exercise is considered a cornerstone of multi-disciplinary treatment.

Little is known about movement modalities in terms of adolescent preferences

Epidemiological studies of treatment preferences results indicate interest in complementary alternative medicine (CAM) is growing. In one study over 60% of respondents indicated they would prefer to use CAM therapies for pain (Tsao, Meldrum, Kim, Jacob, & Zeltzer, 2007) with yoga being a top choice for movement modalities. Additionally, youth reporting greater pain and associated functional disability were more likely to consider a CAM therapy. Yet, the estimated CAM therapy usage by children was only at 1.8% in a population based study (Davis & Darden, 2003). It has been suggested that these numbers underestimate the prevalence of CAM therapy due to sampling methods targeting only children having consulted a CAM practitioner, and not including those self-prescribing easily accessible therapies such as yoga (Rosen, 2004). What continues to remain unclear is what factors might attract or preclude a patient from participating in yoga. This body of work aimed to determine patients perceived benefits and barriers to yoga practice (Chapter IV). Understanding what might draw a patient to yoga practice (e.g. pain relief, increased functioning, and relaxation) in light of potential barriers (e.g. fear of pain, availability and scheduling) is key to developing future clinical trials and clinical practice recommendations.

Recruitment in clinical trials with adolescents: Practical issues

The recruitment of study participants is widely accepted as one of the most challenging parts of conducting a clinical trial. In fact, it has been reported that approximately ¼ of trials fail to recruit a single participant (Blanton et al., 2006). Recruitment challenge in pediatric populations is even greater, as it requires acceptance of the intervention by both the parent and youth and continues to plague pediatric research (Baiardi et al., 2011). Complicating the issue, the current lack of diagnostic criterion and consistently applied definition of JPFS limits the number of

potential participants to recruit from. When the pool of potential participants is already diminished, expectations of recruiting youth at rates to power randomized clinical trials should be adjusted and alternative methodological strategies considered (e.g. waitlist controls, multi-site trials). Likewise, alternate recruitment strategies may need to be employed to recruit sufficient numbers of participants to include online resources, print media (including public bulletin boards), online support groups (parent and/or youth) for targeted pediatric conditions, and provider office referrals.

Reasons for enrollment refusal must also be considered and addressed within the study design. Consistent with the findings from our clinical trial (Chapter VI), the reasons most commonly reported for enrollment refusal include being too busy (time conflicts) and distance to intervention (transportation issues) (Karlson & Rapoff, 2009). Interventions should be offered at times that do not conflict with parental work and youth school schedules, including options for weekend attendance. In light of findings from this body of work (Chapter VI) and reports from other clinical trials, it appears that once the barriers to recruitment are addressed and the youth begins a yoga intervention, acceptability is high and attrition rates are relatively low.

Future Directions

Given the impact of chronic pain on the adolescent, there is a paucity of scientific evidence supporting current clinical practice recommendations. Future work focused on identifying the underlying mechanisms and course of chronic pain during childhood from a developmental perspective is needed to advance understanding of the unique needs of adolescent chronic pain populations. There is a need for empirically derived classification systems to enhance the reliability and relevance of pediatric chronic pain clinical research and to guide clinical practice. Currently, studies using exercise (either aerobics or yoga) are limited. As it is

highly unlikely that there is only one form of exercise that is effective for all adolescent chronic pain patients, further studies exploring the best type of exercise training should be completed. Furthermore, including a determination of what an optimal dose is needed to produce and sustain improvement in pain and subsequent functioning would be helpful in the development of future clinical trials and the development of clinical practice recommendations.

Given the previously discussed recruitment challenges and the methodological limitations identified across this body of work, future work should include the improvement of clinical trial quality. There is a distinct need for more pediatric trials with larger samples sizes to fully evaluate the effectiveness of a yoga intervention. As recruitment challenges in pediatric clinical trials have previously been discussed, the use multi-site trials to acquire larger sample sizes may be the answer to some localized recruitment challenges.

Conclusion

Despite the limited scientific evidence supporting the use of yoga in adolescent chronic pain populations, the evidence presented in this body of work is promising. Confirming what has been reported previously we found support for the high levels of functional disability experienced by the adolescent with chronic pain. We added to the current literature an examination of the strength of association of factors known to be related to the development of functional disability (e.g. pain characteristics, depressive symptoms, physical activity, sleep). Our findings indicate, that above and beyond controlling for the known influences of pain and depressive symptoms, engagement in physical activity (a modifiable factor) was the only significant predictor of functional disability development.

Findings from this body of work also presented new and encouraging evidence of the feasibility and safety of yoga when used as a therapeutic intervention for adolescent chronic

pain. Supported by our critical review of the current pediatric yoga literature and in the findings presented in our own clinical trial, yoga has exhibited preliminary effectiveness in reducing pain However, in contrast to other studies we found no change in functional disability over the course of the study. Taken as a whole, findings from this body of work present a solid foundation from which to build future clinical trials and support current clinical treatment guidelines on the use of exercise in pediatric chronic pain.

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Appendix A: Copy Right Permissions

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Wolters Kluwer

Title: Optimizing fibromyalgia management

Author: Kari Firestone, Kathleen Holton, Scott Mist, et al

Publication: Nurse Practioner

Publisher: Wolters Kluwer Health, Inc.

Date: Jan 1, 2012

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Comments? We would like to hear from you. E-mail us at customercare@copyright.com

From: **Laura Schmalzl** laura@iayt.org
Subject: Re: Copyright Permissions
Date: February 3, 2016 at 6:15 PM
To: Kari Firestone fireston@ohsu.edu

LS

Dear Kari,

Many thanks for your e-mail.

Yes it is ok to include the published article into your dissertation.

All the best,

Laura

Laura Schmalzl, PhD
Managing Editor
International Journal of Yoga Therapy (IJYT)
laura@iayt.org
http://www.iayt.org/?page=AboutIJYT

On Jan 31, 2016, at 6:48 PM, Kari Firestone <fireston@ohsu.edu> wrote:

> Dear Editor,
>
> My name is Kari Firestone and I am currently a PhD candidate at Oregon Health & Science University in Portland, OR. I am writing in regards to the article I first authored:
>
> *Firestone, K.A., Carson, J.W., Mist, S.D., Carson, K.M., Jones, K.D. (2014). Interest in yoga among fibromyalgia patients: an international internet survey, 24, 117-124.*
>
> I am requesting your permission to include it in my thesis/dissertation in its entirety with no modification and providing full publisher acknowledgement.
>
> I appreciate you consideration to this matter,
>
> Kari Firestone
> PhD Candidate
> Jonas Nurse Leader Scholar 2014-2016
> Oregon Health & Science University

Appendix B: Internet Survey

Yoga survey questions for persons with fibromyalgia. Note that (1) the online structure and format of the questions cannot be fully replicated herein and (2) that because differing responses to items 1, 2, and 7 led to different follow-up questions, the total number of questions was 13, rather than 10, as may appear from the numerical labeling of the questions.

1. Since the onset of your fibromyalgia symptoms, have you ever considered attending a yoga class in your community?
   - ❑ No
   - ❑ Yes

(if answered No to question #1)

2. What concerns did you have about attending yoga classes that kept you from considering it? Check all that apply:
   - ❑ Classes not available at a convenient location for you
   - ❑ Classes not available at a convenient time for you
   - ❑ Concerned that you wouldn't be able to do the postures right
   - ❑ The age group or fitness level of the classes would be so different from you
   - ❑ The postures would be too physically demanding
   - ❑ The postures would cause too much pain during the class
   - ❑ The postures would cause too much pain after the class
   - ❑ You couldn't sit on the floor
   - ❑ You would have a hard time following instructions
   - ❑ Classroom atmosphere would not suit you (for example, incense, religious icons, or chanting)

   (survey ends here for this response set)

(if answered Yes to #1)

2. Did you attend yoga classes in your community?
   - ❑ No
   - ❑ Yes

(if answered No to #2)

3. What concerns did you have about yoga classes that kept you from attending? Check all that apply:
   - ❑ Classes not available at a convenient location for you
   - ❑ Classes not available at a convenient time for you
   - ❑ Concerned that you wouldn't be able to do the postures right
   - ❑ The age group or fitness level of the classes would be so different from you
   - ❑ The postures would be too physically demanding
   - ❑ The postures would cause too much pain during the class
   - ❑ The postures would cause too much pain after the class

- ❑ You couldn't sit on the floor
- ❑ You would have a hard time following instructions
- ❑ Classroom atmosphere would not suit you (for example, incense, religious icons, or chanting)

(survey ends here for this response set)

(if answered Yes to #2)

3. How were the classes described? Check all that apply:
   - ❑ Beginner's class
   - ❑ Level 1
   - ❑ Gentle
   - ❑ Therapeutic
   - ❑ Restorative
   - ❑ Other (please describe)

4. What has been the typical length of the yoga classes you have attended?
   - ❑ 30–45 minutes
   - ❑ 45 minutes–1 hour
   - ❑ 1 hour–1 1/2 hours
   - ❑ 90 minutes–2 hours

5. Rank in order the amount of time you usually spent during the classes doing the following practices:
   - ❑ Yoga poses
   - ❑ Supine relaxation (shavasana)
   - ❑ Breathing exercise (pranayama)
   - ❑ Seated meditation with focused attention
   - ❑ Group discussions about yoga practice

6. How many classes did you continue to attend? Please choose one of the following:
   - ❑ 1–2
   - ❑ 3–4
   - ❑ 4–8
   - ❑ 8–12
   - ❑ More than 12

7. Were you generally able to fully participate in these classes?
   - ❑ No
   - ❑ Yes

(if answered No to #7)

8. What about the classes made it too difficult or poorly suited? Check all that apply:

- ❑ Classes not available at a convenient location for you
- ❑ Classes not available at a convenient time for you
- ❑ Concerned that you wouldn't be able to do the postures right
- ❑ The age group or fitness level of the classes would be so different from you
- ❑ The postures were too physically demanding
- ❑ The postures caused too much pain during the class
- ❑ The postures caused too much pain after the class
- ❑ You couldn't sit on the floor
- ❑ You had a hard time following instructions
- ❑ Classroom atmosphere did not suit you (for example, incense, religious icons, or chanting)

(if answered Yes to #7)

8. What helped make it possible for you to participate fully in the classes and kept you coming back? Check all that apply:
   - ❑ Classes were available at a convenient location for you
   - ❑ Classes were available at a convenient time for you
   - ❑ Felt relaxed
   - ❑ More energy
   - ❑ Reduced pain and soreness
   - ❑ Slept better
   - ❑ Felt less stress
   - ❑ Able to breathe easier
   - ❑ Felt peaceful
   - ❑ Improved my outlook on life
   - ❑ Glad to join in a community

9. Please provide some information about yourself:

   Age _____

   Gender _____

   Years since onset of fibromyalgia symptoms _____

   If you live in the United States, in which state do you live? _____

   If you live outside the United States, in what country do you live? _____

10. If you have additional comments to add about your experience with yoga classes, please provide those here. Please do not ask us questions that require a response in the survey comments sections because we will not be able to identify you (everyone is anonymous).

Appendix C: Yoga Pilot Study IRB approval

OREGON HEALTH & SCIENCE UNIVERSITY

Research Integrity Office (L106-R)
3181 SW Sam Jackson Park Road
Portland, OR 97239-3098
(503) 494-7887

Memo

Date: October 24, 2014

To: Kim Jones, PHD, MSN

From: Kathryn Schuff, MD, MCR, Chair, Institutional Review Board
Elizabeth Haney, MD, Vice-Chair, Institutional Review Board
Lynn Marshall, ScD, Vice-Chair, Institutional Review Board
Penny Hogarth, MD, Vice-Chair, Institutional Review Board
Kara Manning Drolet, PhD, Associate Director, OHSU Research Integrity Office
Andrea Johnson, JD, CIP, Assistant Research Integrity Officer, Institutional Review Board
David Holmgren, MS, IRB Manager, Institutional Review Board
William Hoffman, PhD, MD, VA IRB Co-Chair

Subject: IRB00011153, Yoga For Youth

Initial Study Approval

The above submission was reviewed and approved for one year effective 10/24/2014.

Review category: Expedited Category # 7.

Copies of all approved documents are available in the study's Official Documents list in the eIRB. Any additional documents that require an IRB signature (e.g. IIAs, IAAs, DUAs) will be posted when signed. If this applies to your study, you will receive a notification when these additional signed documents are available.

Ongoing IRB submission requirements:

- Six to ten weeks before the expiration date, you are to submit a continuing review to request continuing approval.
- Any changes to the project must be submitted for IRB approval prior to implementation.
- Unanticipated problems and protocol deviations must be submitted per OHSU policy.
- You are required to submit a termination request when your research is completed.

Guidelines for Study Conduct

In conducting this study, you are required to follow the guidelines in the document entitled, "Roles and Responsibilities in the Conduct of Research and Administration of Sponsored Projects," as well as all other applicable OHSU IRB Policies and Procedures.

Requirements under HIPAA

If your study involves the collection, use, or disclosure of Protected Health Information (PHI), you must comply with all applicable requirements under HIPAA. See the HIPAA and Research website and the Information Privacy and Security website for more information.

Appendix D: Yoga Pilot Study Recruitment Letter

IRB# 11153

Pediatric Pain Management Clinic

Doernbecher Children's Hospital

[Date]

Dear [Parent Names]:

Your child, [patient name], was recently seen in [management specialty] clinic here at Doernbecher Children's Hospital. We are inviting 12-18 year old patients with chronic pain and their parents to participate in a research study examining the impact of a 8-week yoga course on pain and functioning. Participating youth would be randomly assigned to complete the course beginning in January or in March. All youth and parents would complete questionnaires at different time points during the study. If you are interested in participating, you will need to review and sign the enclosed consent and assent forms, complete questionnaires [enclosed or online: link], and return all paperwork in the enclosed postage paid envelope. Participants will receive gift cards for their time spent completing questionnaires.

We hope that the information we gain from this study will enable us to better help children and teens with chronic pain in the future. Please do not hesitate to contact me if you have additional questions.

Sincerely,

Anna Wilson, PhD
Pediatric Pain Management Clinic
(503) 418-5188

Kim Jones PhD
School of Nursing
(503) 890-0589

APPROVED: SEP 25, 2015

Appendix E: Yoga Pilot Study Telephone Recruitment and Screening Script

eIRB #00011153

Study Title: **Yoga for Youth**

Telephone Recruitment and Screening Script

Hello, my name is _____. I'm calling from Oregon Health & Science University about a research study. Am I speaking to the parent or guardian of _____ (name of recruit)?

If "no," wait for recruit to pick up, arrange to leave a message, or ask for a time to call back.

If "yes":

I got your phone number from the OHSU _____ clinic. Is this a good time to talk? I expect this phone call will take about 5 minutes.

Arrange to call at another time, if appropriate.

I'm calling about a research study of youth with chronic musculoskeletal pain called Yoga for Youth. The purpose of this research study is to learn more about the effects of participating in a yoga exercise class on the daily functioning and pain in youth with chronic musculoskeletal pain. We know that yoga can be helpful in adults experiencing chronic pain and want to find out if it can help adolescents with chronic pain.

I'm calling to see if you are interested and if you might be eligible to participate. If you agree, I will ask you some questions to see if you can be in the study. If it looks like you might be eligible, we will invite you to come to a town hall meeting, where we will discuss the study with you in more detail, and you can decide if you and your child want to participate.

Before we go on to the questions, let me tell you a little bit about your rights as a research subject.

The main risk of answering my questions today is loss of confidentiality. However, we will do our best to keep your information confidential by keeping it coded and on a password-protected computer.

You don't have to answer these questions, and you can choose to stop at any time without penalty. If you have questions about the study, you can call us at (503) 890-0589. If you have questions about your rights as a research subject or research-related injuries, you can call the OHSU Research Integrity Office at 503-494-7887.

May I go ahead with the eligibility questions?

If no, thank the individual and end the call.

If yes:

Appendix F: Yoga Pilot Study Recruitment Flyer

Yoga-for-Youth

We are seeking Youth who have chronic pain

What is the purpose of this research?

The purpose of this research study is to learn more about the effects of practicing yoga on pain and physical functioning in youth with chronic pain

What will participants do?

Youth participating will attend an 8-week yoga program and answer questions about their pain, and how attending yoga may effect pain.

What does it cost to be in this study?

There are no costs to participate in this study. Youth can receive up to $40 and parents can receive up to $20 compensation for their time and assistance.

Who can participate in the study?

- Youth between the ages of 12 and 18 with chronic pain

Youth and parents who can speak and read English

APPROVED: SEP. 25, 2015

If interested or to learn more about the study:

CALL: 503-807-3291

OREGON HEALTH & SCIENCE UNIVERSITY

OHSU

Study Title: Yoga-4-Youth Principle Investigator: Kim D. Jones, Ph.D. IRB#00011153

Appendix G: Yoga Pilot Study Research Consent Form

OREGON HEALTH & SCIENCE UNIVERSITY

IRB#: 11153

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

Clinical Research Consent Summary

TITLE: *Yoga for Youth*

PRINCIPAL INVESTIGATOR: Kim D. Jones, Ph.D. (503) 890-0589

You are being asked to join a research study. You do not have to join the study. Even if you decide to join now, you can change your mind later.

1. The purpose of this study is to learn more about yoga practice and youth with chronic pain.
2. Yoga has been used with individuals experiencing pain and has been shown to be helpful for adults with chronic pain. It has not, however, been designed for or previously delivered to youth with chronic pain.
3. If you join the study, you will participate in weekly, 90-minute yoga sessions for 8 weeks.
4. You will have a maximum of 10 visits to OHSU.
5. There are minimal risks involved in participating in the study.

CO1450

OREGON HEALTH & SCIENCE UNIVERSITY

IRB#: 11153

MED. REC. NO. ____
NAME ____
BIRTHDATE ____

Clinical Research Consent and Authorization Form

TITLE: Yoga for Youth

PRINCIPAL INVESTIGATOR: Kim D. Jones, Ph.D. (503) 890-0589

CO-INVESTIGATORS: Anna C. Wilson, Ph.D. (503) 494-0333
Kari A. Firestone, M.S. (909) 224-9153

FUNDED BY: American Nurses Foundation/Society of Pediatric Nurses

PURPOSE:

You have been invited to be in this research study because you are between 12-18 years old and have pain that is interfering with some part of your life. "You" means you or your child in this consent form. This study includes only subjects who choose to take part. Please take your time to make your decision. You do not have to join the study and even if you decide to join now, you can change your mind later.

The purpose of this study is to see if yoga practice will help your child's pain. Yoga has been used with individuals experiencing pain and has been shown to be helpful for adults with chronic pain. It has not, however, been designed for or previously delivered to youth with chronic pain. This study requires weekly yoga sessions and will take 8 weeks to complete.

A total of 48 youth will take part in this research study at Oregon Health & Science University (OHSU) in Portland, OR.

PROCEDURES:

CO1450

During the first study visit you will be given an orientation to the study. If you decide to participate, you will be asked to attend one 90-minute yoga class per week conducted at the OHSU School of Nursing for the first 8-weeks of the research study. All yoga equipment (mats etc.) will be provided for you. During weeks 9-16 you will not participate in yoga classes, but will continue with your usual medical care. During the entire study, you are encouraged to continue with any medical recommendations made by your physician.

Over the course of the study, you will complete four assessments over 4 months:

- Time 1 assessment will happen after enrollment and before you begin yoga classes.
- Time 2 assessment will happen during week 4 of the research study
- Time 3 assessment will happen during week 12 of the research study
- Time 4 assessment will happened during week 16 of the research study.

During each of the study assessments, you will complete several questionnaires online or on paper, whichever you prefer. The questionnaires will ask about demographics, your pain, your ability to participate in activities, and how much pain interferes with your daily activities. You may refuse to answer any of the questions in the questionnaires. The questionnaires should take approximately 15 minutes to complete.

During Time 1 and 3 assessments you will also be asked to complete a series of physical tests described as follows:

1. You will be asked to stand and reach over your shoulder and down your back with one arm while your other arm reaches up your back from the other side.
2. You will be asked to rise and sit from a chair as many times as you can in a 30 second period.
3. You will be asked to stand on 1 foot with your eyes closed for up to 60 seconds.
4. You will be asked to stand with both feet together and arms outstretched, 90 degrees from shoulder and reach as far forward as possible without losing balance or taking a step
5. You will be asked to sit and squat against a wall with one foot raised for as long as you can.

All of the physical tests together will take approximately 15 minutes to complete.

PARENTS:

You will complete one questionnaire online or on paper, whichever you prefer. The questionnaire will ask about your impression of the intervention your child received. You will complete this questionnaire in Week 8 of the study. The questionnaire should take approximately 2-3 minutes to complete.

While another parent is welcome to review the questionnaire, the parent who provides consent must be the parent who completes the questionnaire.

You can stop participating at any time. If you have questions, concerns, or complaints regarding this study now or in the future, contact Dr. Kim Jones at (503) 890-0589.

RISKS AND DISCOMFORTS:

As with any form of exercise training, the risk of injury is increased. We have taken precautions to make the exercises as safe as possible. A certified yoga instructor that has experience working with youth will lead all yoga classes. You should talk to the investigator about any side effects that you have while taking part in the study.

One risk to taking part in this study is that participation in yoga may not provide you with any health-related benefits. This means you may spend time in the study without experiencing any health-related benefits.

Some of the questions asked on the surveys may seem very personal or embarrassing. They may upset you. You may refuse to answer any of the questions you do not wish to answer. If the questions make you very upset, we will help find a counselor.

BENEFITS:
You may or may not personally benefit from being in this study. However, by serving as a subject, you may help us learn how to benefit patients in the future.

ALTERNATIVES:

You may choose not to be in this study. Your participation or non-participation will not affect your health care.

CONFIDENTIALITY

We will take steps to keep your personal information confidential, but we cannot guarantee total privacy.

We will create and collect health information about you as described in the Purpose and Procedures sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The Office for Human Research Protections, a federal agency that oversees research involving humans

Those listed above may also be permitted to review and copy your records, including your medical records.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

Under Oregon law, suspected child abuse must be reported to appropriate authorities.

When we send information outside of OHSU, they may no longer be protected under federal or Oregon law. In this case, your specimens or information could be used and re-released without your permission.

Data from this study may be shared with other investigators for future research studies. A code number will be assigned to you, as well as to information about you. Only the investigators and people involved in the conduct of the study will be authorized to link the code number to you. Other investigators who may receive samples of your information for research will be given only the code number, which will not identify you.

We may continue to use and disclose your information as described above indefinitely.

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

COMMERCIAL DEVELOPMENT:
Samples and information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

COSTS:

There will be no cost to you or your insurance company to participate in this study. In the form of gift cards, you will receive $10 for the completion of each of the 4 assessment times, for a maximum of $40.

We may request your social security number in order to process any payments for participation.

LIABILITY:

If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact Kim Jones, Ph.D. (503) 890-0589.

If you are injured or harmed by the study procedures, you will be treated. OHSU and the American Nurses Foundation/Society of Pediatric Nurses does not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you

or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.

If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

PARTICIPATION:

This research is being overseen by an Institutional Review Board ("IRB"). You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study.

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Kim Jones, Ph.D.
3455 SW US Veterans Road
SN-ORD
Portland, OR 97239
joneskim@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

If you decide you no longer want to participate in this research, we will remove your name and any other identifiers from your information, but the information will not be destroyed and we will continue to use it for research.

You may be removed from the study if the investigator stops the study, decides it is in your best interest, or if you don't follow study instructions.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

OREGON HEALTH & SCIENCE UNIVERSITY
INSTITUTIONAL REVIEW BOARD
PHONE NUMBER (503) 494-7887
CONSENT/AUTHORIZATION FORM APPROVAL DATE

SEP 25, 2015

Do not sign this form after the expiration date of:
09-24-2016

Subject Printed Name	Subject Signature (if aged 15 or older)	Date
Parent/Legal Guardian Printed Name	Parent/Legal Guardian Signature	Date
Description of Relationship to Subject		
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Appendix H: Yoga Pilot Study Child Assent Form

OREGON HEALTH & SCIENCE UNIVERSITY

Child Assent Form

IRB# 11153

Protocol Approval Date: 09-25-2015

TITLE: Yoga for Youth

PRINCIPAL INVESTIGATOR: Kim D. Jones, Ph.D. (503) 890-0589

CO-INVESTIGATORS: Anna Wilson, Ph.D.
Kari Firestone, M.S.

A member of the research team has explained this research study to me. I know that participating may or may not help me. I also know that this study will help doctors learn more about the effect of yoga on chronic pain.

1. To explain what I will do and what will happen in this study.
2. If I have any questions or want to know anything else about this study or chronic pain.
3. To explain some of the good and bad things that might happen to me if I enter this study.

I have thought about being a part of this study. I have had a chance to ask questions about the study and received answers to my questions. I know that I can call the study phone number if I have questions in the future.

I agree to be in this study. I know that I don't have to agree to be in the study. Even though I agree to be in it now, I know I may feel differently later on and can ask to stop being in the study.

I know that I may talk with my parents and/or investigator about not being in this study at any time. I know that participating in this study will not affect my health care.

Name/Signature:_____ Date:_____