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## Transmission of risk from parents with chronic pain to offspring: an integrative conceptual model

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### Abstract

Offspring of parents with chronic pain are at increased risk for pain and adverse mental and physical health outcomes (Higgins et al, 2015). Although the association between chronic pain in parents and offspring has been established, few studies have addressed why or how this relation occurs. Identifying mechanisms for the transmission of risk that leads to the development of chronic pain in offspring is important for developing preventive interventions targeted to decrease risk for chronic pain and related outcomes (eg, disability and internalizing symptoms). This review presents a conceptual model for the intergenerational transmission of chronic pain from parents to offspring with the goal of setting an agenda for future research and the development of preventive interventions. Our proposed model highlights 5 potential mechanisms for the relation between parental chronic pain and pediatric chronic pain and related adverse outcomes: (1) genetics, (2) alterations in early neurobiological development, (3) pain-specific social learning, (4), general parenting and family health, and (5) exposure to stressful environment. In addition, the model presents 3 potential moderators for the relation between parent and child chronic pain: (1) the presence of chronic pain in a second parent, (2) timing, course, and location of parental chronic pain, and (3) offspring's characteristics (ie, sex, developmental stage, race or ethnicity, and temperament). Such a framework highlights chronic pain as inherently familial and intergenerational, opening up avenues for new models of intervention and prevention that can be family centered and include at-risk children.

### Keywords

Chronic pain; Parents; Offspring; Children

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#### Supplemental media

A supplemental video associated with this article can be found online at <http://links.lww.com/PAIN/A298>.

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Chronic pain poses a significant burden to affected individuals, their families, and society.<sup>66</sup> Estimates of chronic pain not associated with disease in the general adult population range from 10% to 40%,<sup>68</sup> whereas persistent, severe, and disabling chronic pain occurs in 3% to 8% of the population and incurs additional burden and cost<sup>9,150,154</sup> Similarly, in adolescents, moderate-to-severe chronic pain costs the United States approximately \$19.5 billion a year.<sup>52</sup> Although the societal cost of chronic pain in families has not been calculated, there is some evidence that it would be high as chronic pain symptoms tend to aggregate in families.<sup>59</sup>

A recent systematic review and meta-analysis identified increased risk for pain and adverse mental and physical health outcomes for offspring of parents with chronic pain.<sup>59</sup> Although there is increasing evidence for the relation between parent and child chronic pain, this systematic review identified gaps in the literature regarding how and why certain children with a parent with chronic pain may be at greater risk for poor outcomes than others. Identifying mechanisms for the transmission of risk for chronic pain in offspring is important for developing preventive interventions to decrease risk for chronic pain and common comorbidities (eg, functional disability, other somatic symptoms, and poor psychological functioning).

The current review aims to provide an integrative conceptual model for the transmission of risk for chronic pain from parents to offspring. The literature on the relation between parental chronic pain and outcomes in offspring contains substantial heterogeneity regarding study methodology, sample populations, and research questions.<sup>59</sup> Thus, our model serves to provide a hypothesized overarching framework to spur, guide, and organize future research in the field. We do not advocate that these proposed relationships are rigid, but instead fluid and plausible based on underlying theoretical frameworks and the existing literature.

Our goals for outlining a conceptual framework specific to the transmission of risk for chronic pain are to (1) set an agenda for future interdisciplinary research on risk and resiliency for chronic pain and related outcomes in children of parents with chronic pain and (2) lay a foundation for the development of preventive interventions. First, we provide a brief overview of the theoretical underpinnings, key terms, and components of our model. Next, we devote sections to describing research relevant to hypothesized mechanisms and moderators in the model. Finally, we draw conclusions regarding the current state of the research and future directions.

## 1. Overview of the model

Our model is adapted from (1) a model of the intergenerational transmission of maternal depression<sup>49</sup>; (2) models of family coping with maternal illness<sup>4,88</sup>; (3) an integrative model of parent and family factors in pediatric chronic pain<sup>103</sup>; and (4) a model of pain vulnerability mechanisms.<sup>33</sup> Our conceptual model proposes that having a parent with chronic pain heightens a child's risk for chronic pain through genetic, neurobiological, pain-specific social learning, general parenting and family health, and family stress pathways. We provide an overview of the existing literature supporting plausible mechanisms (eg, genetics, modeled pain, and disability) that contribute to vulnerabilities within the child (eg, pain-

related cognitions and pain sensitivity), ultimately leading to adverse outcomes (eg, chronic pain, pain-related disability, and poor psychological functioning). Although our model and review of the literature focus on chronic pain not related to disease, similar mechanisms may also operate in disease-related pain (eg, arthritis, sickle cell disease, inflammatory bowel disease, etc.) or in other contexts (eg, pain chronification after surgery or acute injury).

The model focuses on parental chronic pain as a specific risk factor that may increase the probability that offspring will develop chronic pain and related comorbidities (Fig. 1). There are likely many families where a parent may have chronic pain and offspring do not develop chronic pain or other adverse outcomes. Thus, our model focuses on outlining mechanisms, moderators, and vulnerabilities that may explain why some offspring of parents with chronic pain are at increased risk and develop adverse outcomes while others do not.

The *outcomes* addressed in our model correspond with the adverse outcomes identified in the meta-analysis on offspring of parents with chronic pain.<sup>59</sup> We focus on the development of pediatric chronic pain and associated disability as the primary outcome and also highlight poor psychological functioning (eg, internalizing or externalizing behavior problems, poor social competence, or low self-esteem) as an outcome that may occur in combination with or independent from children's pain outcomes. Many of the proposed mechanisms and vulnerabilities are associated with psychological outcomes in addition to pain outcomes.<sup>49</sup>

We posit that parental chronic pain influences the development of chronic pain in offspring through specific *mechanisms* or mediators (ie, *how or why* a specific effect occurs). Our proposed model highlights 5 potential mechanisms for the relation between parental chronic pain and children's outcomes: (1) genetics, (2) alterations in early neurobiological development, (3) pain-specific social learning, (4), general parenting and family health, and (5) exposure to stressful environment. Next, we focus on *moderators* or variables that might explain when, and under what circumstances, offspring are at greatest risk for developing chronic pain in the context of parental chronic pain. We discuss 3 possible moderators of this relation: (1) the presence of chronic pain in a second parent, (2) timing, course, and location of parental chronic pain, and (3) offspring's characteristics (ie, sex, developmental stage, race or ethnicity, and temperament).

In our model, *vulnerabilities* refer to factors that could be influenced by having a parent with chronic pain. These vulnerabilities could also be influenced by other biological, psychological, or contextual processes outside of parental chronic pain; thus, there is not a direct correspondence between mechanisms and vulnerabilities. Although we will not devote entire sections to these vulnerabilities, which are commonly proposed in models of pediatric chronic pain,<sup>5,152</sup> we highlight within our discussion of mechanisms and moderators 5 potential vulnerabilities that could characterize offspring at greatest risk for the development of chronic pain: (1) altered pain processing, (2) offspring's own pain-related cognitions and affect, (3) paincoping behaviors, (4) physical health factors, and (5) difficulty processing and regulating emotions.

The outlined mechanisms, moderators, and vulnerabilities likely interact over time to influence the development of chronic pain and related outcomes in offspring of parents with

chronic pain. The current state of the literature allows for few conclusive statements regarding timing of effects or specific interactions. We propose that the development of chronic pain in offspring is the result of multiple complex interactions among mechanisms, child vulnerabilities, and moderators.

## 2. Potential mechanisms for the transmission of risk

### 2.1. Mechanism 1: genetics

Offspring of a parent with chronic pain may be at increased genetic risk for heightened sensory and psychological components of pain which could contribute to the development of chronic pain. Heritability estimates for genetic influences on the development of chronic pain in children and adolescents vary depending on the type of pain and age.<sup>58,97,132,136</sup> These studies generally rely on twin designs and compute estimates for the amount of variability accounted for by genetic, shared environmental, and nonshared environmental factors. For example, a study of Danish twins computed heritability estimates for low back pain by age and found for young adolescents (age: 12–15 years), common environmental factors represented the strongest component.<sup>58</sup> However, for older adolescents (age: 16–18 years), genetic and nonshared environmental factors comprised the model with the best overall fit. Thus, for children and young adolescents, shared environmental factors (eg, family context) may have greater influence on chronic pain development than genetic factors in some pain phenotypes. The studies mentioned above represent the few that have examined genetic influences on the presentation of pediatric chronic pain.

Genetic research from studies on the development of chronic pain in adults may inform future research on genetic mechanisms that influence the development of pediatric chronic pain. Genetic factors contribute to roughly 50% of the risk for chronic pain in adults and influence both sensory and psychological factors that commonly co-occur with chronic pain.<sup>35</sup> Alterations in pain processing represents one vulnerability in our model which may have more genetic influence than others. Indeed, heightened pain sensitivity has been linked with genetic variants of the catecholamine-O-methyltransferase (COMT) gene.<sup>36</sup> There is some evidence that variants of the COMT gene interact with psychological factors (eg, perceived stress) to increase risk of chronic pain development.<sup>127</sup> For children, genetic components likely interact with the parent and child's life experiences, environment, and characteristics to influence the development of chronic pain.

Psychological components that often predict or co-occur with chronic pain are also influenced by genetic factors.<sup>35</sup> With regards to pain-specific psychological factors, a recent twin study<sup>139</sup> estimated genetic factors to account for 37% of the variance in pain catastrophizing. In further analyses, the genetic factors influencing pain catastrophizing were found to be unrelated to genetic factors influencing cold-pressor task outcomes. Thus, the genetic risk for some psychological components of the pain experience may be distinct from the genetic risk for sensory components of the pain experience (ie, laboratory pain sensitivity).<sup>44</sup> In a study of genetic risk for temporomandibular disorder (TMD) onset, prostaglandin-endoperoxide synthase 1 (PTGS1, rs3842803) was associated with global psychological symptoms, and amyloid- $\beta$  (A4) precursor protein (APP, rs466448) was associated with stress and negative affectivity,<sup>130</sup> indicating that more global psychological

factors predictive of chronic pain development are influenced by genetic factors. In addition to pain, offspring of parents with chronic pain are more likely to experience externalizing and internalizing problems.<sup>70</sup> Genetic contributions to these intermediate psychological phenotypes could help elucidate the transmission of risk for multiple outcomes in the context of parental chronic pain.

## 2.2. Mechanism 2: early neurobiological development

Having a parent with chronic pain has the potential to impact neurobiological features and function during critical periods early in development. These neurobiological changes, in turn, may increase vulnerability to chronic pain, particularly pain processing and ability to process and regulate emotions. Although we primarily address mothers in this section, parents of both sexes certainly contribute to their children's ongoing neurobiological functioning across development. First, we address 2 important factors through which maternal chronic pain may influence the neurobiological development of their offspring during the prenatal and perinatal periods: (1) maternal stress and (2) maternal health behaviors. Then, we discuss how neurobiological features may influence vulnerabilities for the development of chronic pain and related outcomes in offspring of mothers with chronic pain.

**2.2.1. Maternal stress during prenatal and perinatal periods**—Disruptions of fetal neurobiological development may be due to maternal chronic pain or comorbidities such as somatic and depressive symptoms altering maternal neuroendocrine or hypothalamic—pituitary—adrenal (HPA) axis function,<sup>137,163</sup> which in turn may alter fetal neuroendocrine systems and DNA methylation.<sup>13</sup> Similar mechanisms have been demonstrated in the case of maternal depression.<sup>13,89</sup> Maternal stress and cortisol levels during pregnancy impact the development of infant cardiac vagal tone,<sup>111</sup> which is strongly associated with children's later abilities to regulate emotions. Higher maternal cortisol levels during pregnancy were associated with infants' slower behavioral distress recovery and larger cortisol responses in response to a painful procedure at age 2.<sup>30</sup> There is also some evidence that early life pain responses (at age 5) are associated with somatic symptoms at age 12,<sup>115</sup> suggesting increased pain response vulnerability can lead to poor outcomes across development.

**2.2.2. Maternal health behaviors during prenatal and perinatal periods**—Early neurobiological development could be disrupted due to maternal health and health behaviors that co-occur with chronic pain. There is a growing body of the literature demonstrating that maternal physical activity, obesity, and high-fat diets affect offspring health and development.<sup>93</sup> These processes are important to consider as obesity is associated with chronic musculoskeletal pain and multisite pain in community and epidemiological samples of adolescents and adults.<sup>31,60,100</sup>

Classes of medications commonly prescribed for chronic pain management have the potential to negatively impact fetal development. Opioid pain medications disrupt endocrine system and HPA axis function.<sup>3,28,32</sup> Prenatal exposure to opioids is associated with negative behavioral and cognitive outcomes for offspring, in both human and animal studies,<sup>34,45,106</sup> and changes in analgesia in animals,<sup>138</sup> suggesting opioid exposure might

lead to changes in a child's pain processing system; note that the majority of human research in this area has focused on prenatal opioid exposure among offspring of mothers addicted to opioids.<sup>45</sup> Antiepileptic medications also carry increased risk of congenital abnormalities, preterm delivery, and low birth weight.<sup>6,46,147</sup> A meta-analysis showed that antidepressant use during pregnancy is related to increased risk for low birth weight and low Apgar scores<sup>116</sup> and is associated with increased anxiety in offspring at 3 years of age.<sup>14</sup> Thus, exposure to medications commonly used to treat chronic pain or comorbid conditions might lead to increases in a number of vulnerabilities for chronic pain development, including difficulty regulating emotions.

**2.2.3. Neurobiological features in offspring of parents with chronic pain during childhood and adolescence**—Minimal work has been done to examine neurobiological features or functioning of the offspring of parents with chronic pain. A recent review outlines brain networks that are likely candidates for increasing vulnerability for pain chronicity, including the descending pain modulatory system and the reward-motivation network.<sup>33</sup> Similar networks may be vulnerable in children with parents of chronic pain, and examining them early in life and across development will be key. Initial work in this area has shown that 11- to 15-year-old children of mothers with chronic pain show differences in brain activity during positive and negative emotion processing and differences during emotional inhibition tasks compared with controls.<sup>27</sup> One other study found that healthy children with stronger inhibitory control and working memory reported less stress and unpleasantness during painful stimuli,<sup>148</sup> suggesting that inhibition and attention networks may play a role in chronic pain development.

### 2.3. Mechanism 3: pain-specific social learning

Pain-specific social learning mechanisms that contribute to pain vulnerabilities in children are likely to be interdependent and mutually influence each other. Social learning theory<sup>7</sup> is a theoretical framework that can guide hypotheses regarding how children may learn responses to pain from parents. According to this theory, children learn behaviors through observations of models and reinforcement. Parents with chronic pain may model maladaptive pain behaviors and reinforce children's maladaptive pain behaviors through protective or solicitous responding to children's pain complaints. Both parental modeling of pain behaviors and parental reinforcement of children's pain behaviors may contribute to the development of children's pain beliefs and responses to pain which could increase risk for the development of chronic pain and related disability. Similarly, transmission of resilience, including pain acceptance, could occur through modeling and reinforcement.

Evidence for the hypothesis that parental modeling of pain behavior influences children's pain responses comes from one experimental study that manipulated parental responses to laboratory pain in the presence of their children.<sup>48</sup> The effect of modeling has also been inferred based on the identification of pain models.<sup>101</sup> Because evidence for the role of parental modeling of pain behaviors is limited, the goal of this section is to place parental pain behaviors in the broader context of parents' own cognitive and affective responses to pain to set an agenda for further research. When a parent with chronic pain holds strong beliefs that pain represents a significant threat, this could lead to increased vulnerability for

chronic pain and related disability in their children through parental modeling of maladaptive pain behaviors (eg, activity avoidance) and protective responses to children's pain.

Pain catastrophizing is a cognitive— affective factor that could influence parental pain behaviors and responses to children's pain behaviors and is associated with poor outcomes such as reduced quality of life, higher functional disability, and higher depressive symptoms in adults and adolescents.<sup>90,107</sup> Pain catastrophizing refers to the negative cognitive tendency to magnify the threatening value of pain sensations and functions to facilitate avoidance of pain and communicate distress to others.<sup>25</sup> Parents who catastrophize about their own pain or their children's pain likely communicate high threat information about pain to children through verbal and nonverbal means.<sup>81,99,107,159</sup> In turn, parental verbal and nonverbal pain behaviors are observed by children and may influence the development of children's pain-related beliefs. Parent catastrophizing about children's pain and children's own catastrophizing about pain have consistently been associated with higher levels of pain-related disability in youth,<sup>50,90,160</sup> and mothers and children have similar tendencies to catastrophize.<sup>90</sup> Pain treatment can reduce catastrophizing in both parents and children.<sup>156</sup>

Parents high in catastrophizing about their own pain or their children's pain behave differently toward their children in pain situations through restricting activities that might be painful.<sup>16,81</sup> Parental responses to children's pain and distress may be informed by their own pain experiences and beliefs. In a study comparing children of adult patients with chronic pain with children of adults without chronic pain, parents with chronic pain reported higher levels of catastrophizing about their children's pain and protective responses to children's pain.<sup>158</sup> Parental responses that are solicitous or protective (eg, letting their child stay home from school and giving their child special treats or gifts) are associated with higher levels of pain, disability, and catastrophizing in pediatric patients with chronic pain.<sup>124</sup> Children's own levels of pain catastrophizing and emotional distress are associated with parents' solicitous or protective responses to children's pain and may drive the relation between parents' responses to children's pain and children's symptoms and disability.<sup>19,54,151</sup> Laboratory studies have further corroborated the relation between parental attention or solicitousness and children's laboratory pain responses.<sup>18,153</sup>

In contrast, parents with chronic pain who are able to accept their own pain may respond to their children's pain with acceptance which could facilitate higher levels of emotional and physical functioning for both parents and children.<sup>92,126</sup> Parents' acceptance of children's pain has been associated with fewer attempts to engage in protective responses to children's pain and lower levels of functional disability in the child.<sup>129</sup> Acceptance of children's pain likely parallels parents' acceptance of their own pain, but to our knowledge, this has not been studied. Parents who are able to accept pain likely exhibit higher physical and emotional functioning than parents who struggle to accept both their own pain and their children's pain. In addition to acceptance, a number of other pain-specific psychological factors in parents may contribute to resilient child outcomes, including active coping, problem solving skills, and optimism.<sup>23,63,64,105</sup>

## 2.4. Mechanism 4: general parenting and health habits

**2.4.1. General parenting**—Parents with chronic pain may influence the development of chronic pain and other poor outcomes in their children through engaging in a number of general parenting behaviors often linked with adverse child outcomes (eg, permissive parenting, difficulties providing consistency and warmth, and difficulty responding effectively to child distress<sup>43,158</sup>). Parental warmth is consistently associated with psychological outcomes for children, including lower levels of warmth being related to increased internalizing problems.<sup>74,82</sup> Maternal responsiveness to distress is positively associated with a child's ability to regulate negative affect and emotions effectively.<sup>29,75</sup> Parents with chronic pain may be less able to respond to their child's distress,<sup>158</sup> which can impact children's ability to develop negative affect regulation.<sup>76</sup> Negative affect regulation has been tightly linked with pain in neuroanatomy<sup>40,121</sup> and is also associated with pain experiences on a day-to-day basis.<sup>22</sup> Poor negative affect regulation increases risk for the development of internalizing problems.<sup>38,39,125</sup> Parent—child communication and interaction styles investigated in the context of pediatric chronic pain have found associations between high conflict and low adolescent autonomy with increased depressive symptoms<sup>86</sup> and lower autonomy than expected for age in youth with pain.<sup>42</sup>

Attachment is also an important domain of parent—child relationships to consider,<sup>2,12</sup> as adult attachment style has been linked with parenting behaviors<sup>20</sup> and a number of pain outcomes, including pain self-efficacy.<sup>96</sup> Children with a parent with chronic pain may form insecure attachment styles, such as anxious attachment, that may increase their tendency to respond to a threat, such as pain, with passive coping strategies which may increase risk for the development of chronic pain.<sup>79,95</sup> Investigating the extent to which parental chronic pain affects overall parenting behaviors and responsiveness to their children is important for further understanding how parental chronic pain may contribute to the development of pediatric chronic pain and comorbid conditions. Many of these parenting and parent—child relationship mechanisms have the potential to be protective, and in that capacity might act as mechanisms for resilience, or as moderators that might attenuate the impact of other risk factors.

**2.4.2. Physical activity and general health habits**—One's family strongly influences the development of health and illness-related attitudes, beliefs, and behaviors,<sup>73</sup> and parents are salient models of health behaviors for their children.<sup>47,142</sup> Because of impairments in physical functioning, parents with chronic pain may model less physical activity and engage in less physical activity with their children. Parenting that includes logistical support for physical activity and modeling or joint physical activity participation is associated with lower child body mass index (BMI) and increased child activity levels.<sup>128</sup> Low levels of physical activity have a negative impact on physical fitness and function,<sup>65,164</sup> important factors in the development and persistence of pain.<sup>15</sup> In epidemiological samples, higher levels of sedentary activity are associated with increased pain in girls,<sup>60</sup> whereas higher activity is associated with reduced risk for chronic pain.<sup>80</sup> In addition, objectively measured activity levels have shown that lower physical activity is associated with greater pain and disability among youth with chronic pain and healthy youth.<sup>72,108,161</sup> Thus, engagement in physical activity may be particularly important for youth at risk for chronic pain.<sup>155</sup> Parents



who have chronic pain may be less involved in their children's activities and provide fewer opportunities for physical activity for their children.<sup>158</sup>

A number of other general health factors will be important to examine as potential mechanisms, including BMI, diet, and health care utilization. Higher BMI is a risk factor in and of itself for the persistence of chronic musculoskeletal<sup>8</sup> or headache pain<sup>57,112</sup> in children and adolescents and is associated with activity limitations in youth with pain.<sup>162</sup> In addition, dietary interventions have been shown to reduce pain in adults with irritable bowel syndrome,<sup>55</sup> and pain and psychological distress in adults with headache,<sup>110</sup> suggesting that diet and nutrition habits within a family might influence pain outcomes. Health care utilization may also play a role, as parental health status has been associated with pain-related medical visits in children,<sup>141</sup> and mother and child health care visit frequency are positively correlated in families in which the mother has irritable bowel syndrome.<sup>146</sup> Families who catastrophize about pain may be more likely to seek frequent medical care which, in turn, may further increase pain catastrophizing. Examination of these health factors as potential mechanisms might yield additional targets for preventive interventions.

#### **2.5. Mechanism 4: exposure to stressful environment**

The environmental context surrounding a family where a parent has chronic pain, particularly stressors, could contribute to the development of chronic pain in their children. Chronic pain is both influenced by stress and poses a significant chronic stressor for individuals suffering with chronic pain syndromes and their families.<sup>67</sup> Poor family functioning and family stress, such as low cohesion (ie, low positive emotional bonding) and high levels of marital conflict, chronic sources of stress, have consistently been shown to contribute to pain-related disability in youth.<sup>87</sup> Children raised in families with high conflict and low warmth are at high risk for mental and physical health disorders because of vulnerabilities for alterations in stress response systems, difficulties with emotion processing, and poor health behaviors.<sup>113</sup> Chronic stressors give the body little or no time to adapt or recover from the cognitive and physiological demands of the stressor and can produce a prolonged stress response associated with physiological dysregulation and stress-related diseases.<sup>69</sup> The extent to which an event, such as parental chronic pain or financial challenges associated with parental pain-related disability, represents a stressor and is associated with adverse consequences can be modulated by one's appraisal of the situation and attempts to cope with the situation.<sup>83</sup>

Children of parents with chronic pain likely experience unique stressors related to their parents' health.<sup>143</sup> Parents with chronic pain and pain-related disability may have difficulties completing household chores and everyday tasks that parents often complete to care for their families. Children of parents with chronic pain may feel pressure to help take care of their family and assume adult roles at an early age or try to assume responsibility for their parent's pain.<sup>144</sup> In addition, the financial burden of chronic pain due to health care utilization and lost productivity for adults could create additional stress for the family.<sup>66</sup> Thus, the unique challenges of children with parents with chronic pain represent significant chronic stressors.

### 3. Potential moderators of risk

#### 3.1. Moderator 1: pain status and the presence of second parent

The number of parents with chronic pain may influence the development of chronic pain in their children in a dose—response relation where having 1 parent with chronic pain increases risk for pediatric chronic pain, but having 2 parents with chronic pain poses greatest risk for pediatric chronic pain. The cumulative effect of having 2 parents with chronic pain has been reported in both clinical and community populations.<sup>61,123</sup> Having a healthy co-parent may buffer children from the negative effects of parental pain, as he or she may be able to provide support for the other parent or provide children with positive parenting that may be difficult for the parent with pain to provide at times (eg, physical activity parenting). In some families where a parent has chronic pain, a healthy co-parent may not be present or available (eg, single-parent homes). There is some evidence that pediatric patients with chronic pain are more likely to come from single-parent homes<sup>1,71</sup> and living in a single-parent home may be an important moderator when examining the association between parental chronic pain and the development of chronic pain in children.

#### 3.2. Moderator 2: timing, course, and location of parental chronic pain

The timing, course, and location of parental chronic pain may moderate the relation between parental chronic pain and the development of pediatric chronic pain, though to our knowledge, no studies have examined this association. Longer duration of exposure to parental chronic pain provides additional repeated opportunities for children to observe and adopt pain-related behaviors, fears, and responses. In addition, early life exposure to maternal distress is consistently associated with poor psychological and physical health outcomes in children,<sup>78,131</sup> and early life exposure to maternal pain may be similar. Timing of parental chronic pain with regards to children's developmental stages may be most relevant for determining when in childhood to target preventive interventions for both the parent and child.

Regarding the bodily location of parental chronic pain, some studies have found a stronger relation between parent and child chronic pain for congruent pain locations than incongruent locations,<sup>53,119</sup> whereas others have not.<sup>102</sup> Some studies test multiple pain locations and find a relation between parent and child chronic pain for a specific congruent body location (eg, head pain), but not for other congruent body locations.<sup>11,133</sup> Social Learning Theory would suggest that a child would be more likely to learn pain and pain behaviors from their parents when sharing the same pain location. Indeed, the literature examining illness behaviors has identified that childhood learning may be illness specific and may not generalize to other conditions.<sup>84,157</sup> Thus, stronger relations between pediatric chronic pain and parental chronic pain may occur when pain locations are the same.

However, chronic pain may represent a unitary disease state regardless of location, especially when pain is reported across multiple pain sites.<sup>165</sup> In some cases, the number of parental chronic pain sites may be related to children's chronic pain severity more than a specific body location.<sup>119,120</sup> The presence of multiple pain sites may be a marker of central sensitization which reflects alterations in the central nervous system with regards to pain

processing.<sup>134</sup> Therefore, parents with multiple chronic pain sites, reflecting possible central sensitization, may have children at greatest risk for developing widespread chronic pain because of underlying genetic bases and social learning that may be specific to multisite pain or comorbid pain conditions.

### 3.3. Moderator 3: children's characteristics

A number of child characteristics may moderate the relation between parental chronic pain and the development of pediatric chronic pain.

**3.3.1. Sex**—Girls seem to be more vulnerable to the influence of maternal pain and illness,<sup>77</sup> as well as to the influence of maternal responses to child pain.<sup>17,153</sup> Girls also have a greater risk of musculoskeletal pain persisting from preadolescence to adolescence compared with boys and seem to be more likely to develop persistent pain in the context of other risk factors (eg, depressive symptoms and hypermobility) than boys.<sup>41</sup> However, nonexperimental studies of the relation between parent and child chronic pain have not found differences between male and female offspring.<sup>61,123</sup> Because chronic pain is most common in females, many of these larger studies have unequal numbers of males and females reporting chronic pain and may have insufficient power to detect sex-specific effects.

**3.3.2. Race or ethnicity**—African Americans, compared with non-Hispanic whites, report higher chronic pain ratings and greater evoked pain responsiveness in adulthood.<sup>37,109,114</sup> In adolescence, African Americans have been shown to exhibit similar heightened evoked pain responsiveness compared with non-Hispanic whites.<sup>98</sup> Thus, a child's race or ethnicity may increase risk for heightened pain or the development of chronic pain in the context of parental pain. In addition, the extent to which certain mechanisms (eg, parental modeling or reinforcement) influence the intergenerational transmission of risk for chronic pain may differ by a child's ethnicity or culture.

**3.3.3. Developmental stage**—Children's developmental stage may influence both parental responses to children's pain and children's tendencies to express chronic pain complaints. The relation between parent and child pain may be strongest for children in early puberty stages vs those in later puberty stages.<sup>140</sup> As children become adolescents, they strive to achieve more autonomy from their parents and thus may direct more attention to peers than parents.<sup>94</sup> Thus, parental chronic pain may have greater influence on the development of children's pain than adolescents' pain. Similarly, the exposure to parental pain during critical early developmental periods may be more relevant for neurobiological mechanisms.

**3.3.4. Temperament**—Temperament is evident early in infancy and refers to individual differences in affective, attentional, and motor responses.<sup>117</sup> These individual differences have been categorized into 3 broad factors commonly studied in early and middle childhood: (1) positive affectivity, (2) negative affectivity, and (3) effortful control.<sup>117,118</sup> These factors could all moderate the extent to which offspring of parents with chronic pain are at risk for the development of pediatric chronic pain.

Children's positive affectivity may serve as a resilience resource in the context of chronic pain and may be one factor that could buffer the relation between parental chronic pain and risk for the development of pediatric chronic pain.<sup>24</sup> However, children characterized by high levels of negative affectivity, which is often linked with neuroticism, tend to experience higher levels of fear, anger, and sadness and have more difficulty engaging in coping efforts to modulate their own affect intensity in the face of challenges, such as pain.<sup>21</sup> Pediatric patients with chronic pain experience higher rates of lifetime anxiety and depressive disorders than pain-free individuals<sup>122</sup> suggesting higher levels of negative affectivity may confer greater risk for pediatric chronic pain, but whether these factors result from or contribute to the development of chronic pain in children is unknown.

Effortful control refers to the ability to modulate attention and inhibit automatic responses. Children with an attentional bias towards pain could be more susceptible to parental modeling and pain responses because of their attentional bias towards threatening pain information and difficulty shifting attention in the context of a threat such as pain.<sup>51</sup> This may be particularly true for children with low effortful control and a high tendency to catastrophize about pain.<sup>56</sup>

#### 4. Summary and future directions

The comprehensive intergenerational framework described here provides a starting point for examining potential mechanisms and moderators through which parental chronic pain might increase the risk for pain and related poor outcomes in children. Such a framework highlights chronic pain as inherently familial and intergenerational, opening up avenues for new models of intervention and prevention that can be family centered and include at-risk children. Parents suffering from chronic pain are not simply isolated patients who need effective treatment for themselves, but as parents may also hold the key to improving outcomes for their own children and for future generations. We have proposed a number of possible mechanistic pathways that might contribute to the development of chronic pain and related outcomes in the offspring of parents with chronic pain. This model has strong theoretical underpinnings from Social Learning Theory, as well as from existing models of intergenerational transmission of depression and physical illness. Although some portions of the model are supported by the existing literature, it has been inferred that many of these mechanisms exist based on high rates of pain in offspring. By elucidating specific pathways that can be tested, knowledge can be gained which will provide avenues and targets for prevention efforts, which have not traditionally been pursued in chronic pain. Additional research will help support or refute aspects of this conceptual model.

Many of these mechanisms and moderators have been studied in the context of other mental and physical health conditions (eg, depression and obesity), but the chronic pain literature lags behind. Drawing from these other knowledge bases and our review of the literature, we propose future directions in 3 key areas: (1) basic science, (2) prevention, and (3) intervention (Fig. 2). Finally, we will address current methodological issues that need to be addressed to move this area of research forward.

#### 4.1. Basic science

Although there is a growing body of work focused on biological factors contributing to the development of chronic pain, these factors have rarely been examined in the development of chronic pain in children. In adults, results from a large candidate gene study examining the development of TMD suggest that genetic polymorphisms may be associated with intermediate clinical, psychological, and sensory phenotypes predictive of TMD onset in the absence of direct associations with the onset of the disorder.<sup>130</sup> Similar methodologies could help discover genetic polymorphisms present in children of parents with chronic pain which confer greater risk for chronic pain development. In addition, research examining gene by environment interactions could elucidate when and under what circumstances each of these mechanisms increases risk for the development of chronic pain in children.

Work is also needed to better understand the potential impact of parental chronic pain on early neurobiological development and the potential long-term consequences of these early changes in childhood or adolescence. Examining brain networks proposed to contribute to pain chronicity (eg, descending pain modulatory system and reward-motivation network) early in development and over time among the offspring of parents with chronic pain may provide additional information about the ways in which parental chronic pain influences children's neurobiology. In addition to neuroimaging, assessment of HPA axis functioning, physiological responses, and laboratory pain responses might inform this area of study.

There is a great need for intergenerational and longitudinal studies. Although a few studies have examined samples of parents with chronic pain, eg,<sup>85</sup> the majority of this research has consisted of cross-sectional studies of group differences in the children of parents with a chronic pain condition compared with children of healthy control parents. Following high-risk children over time will allow for testing the proposed mechanisms and establishing targets for preventive interventions.

#### 4.2. Prevention

Although our framework has primarily focused on mechanisms which increase risk, many children of parents with chronic pain do not develop pediatric chronic pain or related outcomes. Understanding protective factors in both parents with chronic pain and their offspring will help identify targets for promoting resilience in parents with chronic pain and at-risk children and adolescents with the goal of pediatric chronic pain prevention. Prevention of the onset of chronic pain is a new frontier in pediatric pain. Existing treatments that are effective for youth with chronic pain might be adapted to serve as preventive interventions. Consideration should also be given to circumstances (eg, surgery and presentation in primary care with pain) and points in development that might provide good opportunities to deliver these preventive interventions to high-risk youth. Developing and testing preventive interventions through randomized controlled trials could also advance our understanding of timing effects and causal mechanisms in the intergenerational transmission of risk for chronic pain.

### 4.3. Intervention

Close to 50% of pediatric patients with chronic pain presenting to tertiary medical clinics have at least 1 parent with chronic pain.<sup>91</sup> We primarily discussed our model in the context of the development of chronic pain, but many of these mechanisms could also operate to maintain chronic pain and related comorbidities in children. For pediatric patients with chronic pain, it may be difficult to make lifestyle changes and maintain gains when parents hold strong beliefs regarding their own pain and engage in disability behaviors. Supplementing current interdisciplinary interventions for pediatric chronic pain with components that target parents' own chronic pain and disability may improve treatment efficacy. Researching and understanding barriers to treatment in families with chronic pain could provide targets for improving current treatments to address the needs of these families.

### 4.4. Methodological considerations

To conduct longitudinal studies on mechanisms for the intergenerational transmission of chronic pain from parents to offspring, greater attention is needed on how we measure and assess chronic pain in families. Although a number of epidemiological studies have examined the impact of the presence of chronic pain in mothers and fathers on offspring,<sup>62</sup> additional work is needed to assess the impact of other important dimensions of parental pain (eg, pain behaviors and pain-related disability) when considering chronic pain and other poor outcomes in offspring.<sup>104</sup> Additional information about heritability might also be gleaned by assessing the presence of chronic pain in first- and second-degree biological relatives. Interview methods have been used successfully to assess family history of alcoholism and yield continuous scores of family history density which are associated with offspring risk for substance use disorders.<sup>26,135</sup> Measuring the timing of parental chronic pain in relation to children's developmental stage, duration of parental chronic pain, and chronic pain location and severity will help further our knowledge of these moderators. In addition, it will be important to include both mothers and fathers in this research with careful attention to family compositions as a potential moderating variable. The development of additional measures is needed to test specific mechanisms (eg, social learning) in the model.

Currently, measures of parent responses to children's pain are limited and have typically been investigated with a single-parent self-report measure.<sup>145</sup> Observational tasks and measures that assess moment-to-moment interactions between parent—child dyads are needed to establish the behaviors that parents exhibit in response to children's pain, and behavioral or emotional responses that children may exhibit in response to parents' pain. A number of studies have examined parent—child dyads in the context of acute pain or laboratory tasks,<sup>10,149</sup> but this research has yet to be conducted in the context of parental chronic pain. In addition, using data collection and analytic techniques (eg, electronic momentary assessment and actigraphy) to capture daily variations in parental pain characteristics and stressors and child responses to parental pain might yield unique perspective on the synchrony of parent—child experiences and may provide insight into the implementation of prevention programs that could target symptoms and behaviors in daily life.

Finally, execution of many of these future research directions requires the creation of interdisciplinary teams to conduct complex studies examining interactions among mechanisms. These interdisciplinary research teams should be comprised a variety of disciplines, such as geneticists, neurobiologists, medical providers, psychologists, and physical therapists. Many of the pathways outlined interact, and thus researchers must interact to examine these specific interactive components between biology, psychology, and clinical presentation. These interdisciplinary teams will also be needed to execute effective family-based preventive interventions and interventions for children of parents with chronic pain. It is also important to note that this topic bridges both pediatric and adult chronic pain research. Teams comprised both pediatric and adult pain researchers could help bridge this gap to design studies that effectively capture mechanisms operating to maintain pain in both parents and their children. Forming diverse teams of researchers committed to carrying out this vision and addressing these current methodological issues and gaps is one of the first steps. It will take years of research to establish or refute each of these mechanisms, but the potential benefit of developing effective preventive interventions and interventions for children of parents with chronic pain is a worthwhile pursuit.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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### Conflict of interest statement

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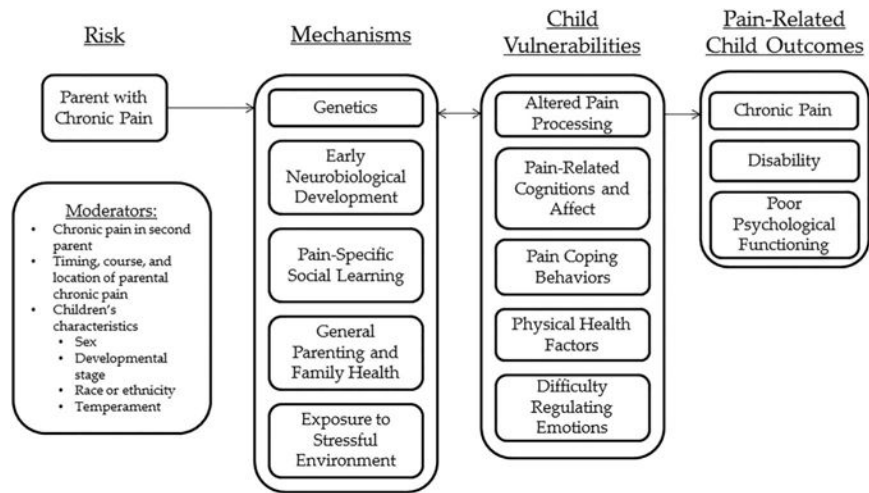
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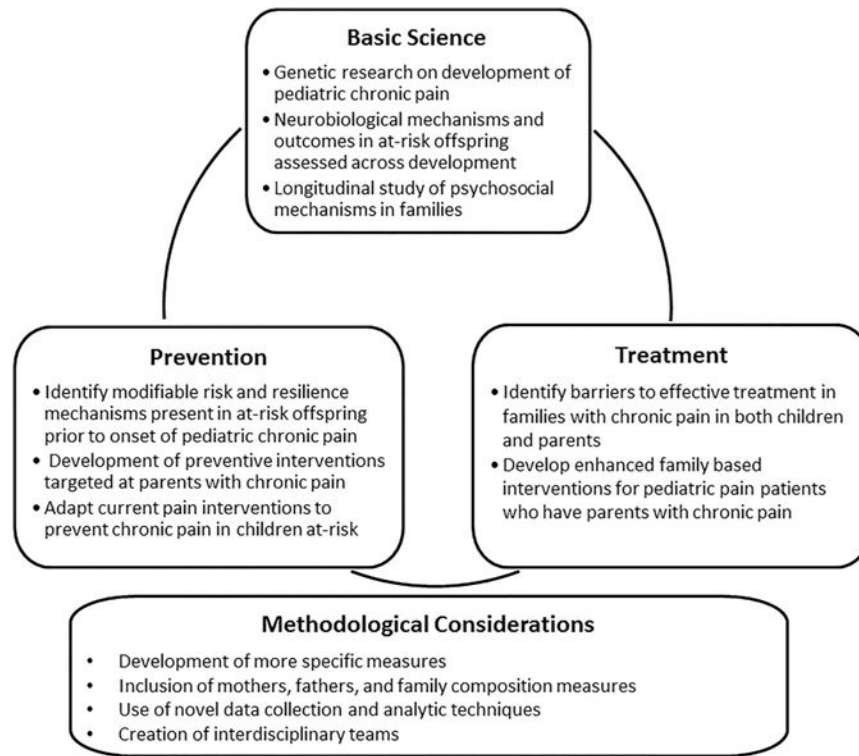
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**Figure 1.** Conceptual model of Intergenerational transmission of chronic pain risk.





**Figure 2.** Future directions for research on the intergenerational transmission of chronic pain risk.