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various influences refers to trajectories (Henly et al., 2011). Therefore, the terms “onset” and “trajectory” were both adopted to inform the focus of this review. These terms ascertain the influencing factors present at baseline, or early, modifiable variables relevant to primary healthcare practice with children at risk of, or presenting with, chronic pain.

Childhood Chronic Pain: Formulation of the Practice Problem

Chronic pain is multifactorial, personal and complex (Hinton & Kirk, 2016). In the following sections, chronic pain in children is defined. An argument is presented as to why childhood chronic pain should be a healthcare priority. The evaluation of pain through the biopsychosocial model is introduced, then childhood developmental theories are presented and applied to pain learning and pain construction. Family, especially parents, are presented as central mediators of their child’s pain. Finally, service provision for childhood chronic pain in primary healthcare in New Zealand is explained.

The International Association for the Study of Pain (IASP) recently updated the definition of pain to “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage” (Raja et al., 2020, p. 1976). The term chronic pain typically describes pain of longer than three months duration or pain that has exceeded expected tissue healing timeframes, without evidence of ongoing injury or biological markers (Abu-Arafeh & Abu-Arafeh, 2016; Campos et al., 2011; Collins et al., 2017). Chronic pain is not just continuous pain, children may also experience intermittent, yet, reoccurring episodes of pain over long periods (Bhatia et al., 2008; King et al., 2011). Chronic pain is often, but not always, precipitated by an injury or tissue damage. However, the onset and progression, or early trajectory of a chronic pain course is complex, and a wide range of biopsychosocial factors may contribute to its presentation (Swain & Johnson, 2014).

Prevalence of chronic pain in children range from 11% - 38%, increasing with age through childhood and adolescence (King et al., 2011). Between 2010 and 2014 the number of children admitted to paediatric hospitals in the USA for chronic pain related

conditions increased by 831% (Coffelt et al., 2013). These rates of prevalence of chronic pain amongst children raise concern for the consequences that follow through into adulthood (Tan et al., 2009).

There is limited data, however, on the rates of paediatric chronic pain in New Zealand, and only one study reporting chronic pain prevalence in New Zealand children was identified when implementing a database search strategy (Appendix A). Shipton et al. (2013) reported that 2.8% of audit data collected retrospectively over 18 months from the New Zealand, Burwood Pain Management Centre was related to individuals under 20 years of age. No other New Zealand prevalence data was able to be established from the literature search. It is unlikely Shipton et al.'s (2013) study reflects the true rate of paediatric chronic pain in New Zealand, as the Burwood Centre is located some distance from other cities in New Zealand and not all children would attend there. Moreover, children attending such a centre would likely have had well-established chronic pain conditions, and numbers may not represent the wider distribution of children with chronic pain.

Childhood chronic pain consequences are not just immediate, but can also have long-term social, emotional, physical and financial impacts (Bhatt et al., 2019; McClain & Suresh, 2009; Tan et al., 2009). A consistent pattern of childhood chronic pain negatively affects pain sensitivities and nociceptive thresholds into adulthood, creating a lifelong pain influence (Bhatt et al., 2019; McClain & Suresh, 2009; Tan et al., 2009). Over one quarter of the general New Zealand population is reported to experience chronic pain (Dominick et al., 2012; Swain & Johnson, 2014). Outside of New Zealand, up to 80% of adults with chronic pain described their symptoms as persistence of pain they had in their childhood (Hassett et al., 2013). Preventing chronicity of pain in children is not just critical for

knowledge of the bi-directional, non-linear interactions between all components in chronic pain conditions, the components are infrequently researched in concert (Wood, 1993).

The Social Context of Children's Chronic Pain: Family

For children, family is one of the most important social influences (Boettcher & Dammeyer, 2016; Palermo et al., 2014; Smith, 2013). Family is a child's most consistent social environment and also plays a crucial role in their chronic pain management (Wood, 1993). Children are largely reliant on adults, specifically parents, for care of their pain (McGrath et al., 2014), and, equally, family has long been understood to play a substantial role in the onset and early trajectory of childhood chronic pain. In 2005, Palermo and Chambers presented an 'Integrative Model of Parent and Family Factors in Paediatric Chronic Pain' (Palermo & Chambers, 2005, p. 3) illustrating what was known of the influences at that time. The model suggested bi-directional, psychophysiological processes associated with the individual child, their direct singular relationships with their parent(s), and broader family components (Palermo & Chambers, 2005). Importantly, the IASP pain definition outlines that components of pain are learnt through life experiences (Raja et al., 2020), and, with young children, family is recognised as a significant contributor to all learning (Miller, 2016). Therefore, sociocultural and social learning theories, along with neuropsychological theory, have been highlighted in this paper as relevant to childhood chronic pain.

Chronic Pain in Children and Developmental Considerations

This review focused specifically on chronic pain in younger children. Differences in the prevalence of chronic pain conditions and treatment responses between older and younger children, and practice considerations guided this focus. The adolescent age group shows a noticeable increase in chronic pain prevalence (Cservenka et al., 2015; King et al., 2011), suggesting different factors may be at play. Treatment for children's chronic pain has also shown greater effectiveness compared to older adolescents (Zernikow et al., 2018). Further, early interventions in primary care hold the possibility of interrupting the

influences, throughout a lifespan (Newman, 2016). These two components of development cannot be divided as discrete elements. Rather, the two components enable each-other (Boettcher & Dammeyer, 2016), and essentially shape learning through the interplay of biological maturation and socio-environmental factors (van Ooyen, 2003). Neuroplasticity is the dynamic neural variation in cortical networks and is essential for humans to respond to changing environmental pressures. The cortical changes associated with neuroplasticity result in adaptive learning and neural network modifications (Fine & Sung, 2014).

Alongside cognitive developmental theories, theory about neuroplasticity explains the emergence of cognitive capacities required for problem solving and adaptations to physical and social challenges (Newman, 2016), such as those experienced by children with pain. Learning and adaptation are central to all aspects of neuroplasticity and neuropsychological development (Turner-Cobb, 2014).

The extensive influence of neuroplasticity in a child's developing brain is another of the factors responsible for the developmental advances through to adulthood. Over 75% of brain maturation occurs after birth, highlighting the importance of learning and biological processes in development. Throughout childhood, the structure of the child's brain changes through synaptic pruning and improved myelination (Bhatt et al., 2019). Children's brain regions have been found to have lower levels of connectivity and communication which improve throughout development, supporting more complex cognitive functions. Early connections are primarily seen in the sensory and motor brain regions (Bhatt et al., 2019). In contrast, connections between the areas responsible for higher executive functions including the insula, posterior cingulate cortex and prefrontal cortex, develop later. Executive function, episodic memory, resilience and prospection domains are reported to follow rapid trajectories in development during the primary school years, followed by advanced refinement in adolescence and adulthood (Anderson, 2002; Best & Miller, 2010; Goldstein & Brooks, 2013). Similarly, another aspect of executive function, the ability to self-regulate behaviours, such as pain-related responses, begins in childhood, then continues to progress through to adolescence (Best & Miller, 2010). However, the

majority of development of the connections between the areas associated with more complex cognitive functions occurs during adolescence, especially in relation to growth in working memory. This includes the ability to predict consequences and the capacity to understand concepts such as pain (Bhatt et al., 2019; Zeltzer & Melamed, 2012).

Such understandings about children's neurophysiological and neuropsychological development suggests some new perspectives when considering children's responses to pain. Children have been reported to have exaggerated responses to pain due to immaturity of neurotransmitters causing lower thermal and mechanical thresholds, or increased neural excitability, compared to adults (Hathway, 2014). This neural excitability is seen as a factor potentially influencing pain catastrophising¹ in combination with less neural inhibitory pain control. However, pain catastrophising in children may not, necessarily, be dysfunctional coping as in adults. But may be more developmentally normal due to lack of executive brain functions needed to exhibit stability over the supraspinal controls (Feinstein et al., 2017; Hathway et al., 2012). This inhibitory control has been shown to be observed late in a child's development (McGrath et al., 2014), as have other executive functions (Feinstein et al., 2017). Likewise, children's cognitive and emotional understanding of pain, their appreciation of other's pain behaviour and insights into the social implications of pain behaviours, more advanced metacognitive skills, are not refined until early adolescence (Esteve & Marquina-Aponte, 2012).

What is clear, from a neuropsychological and neurophysiological perspective, is that children have 'critical' and 'sensitive' periods of development, in which they are rapidly and more efficiently adapting to influences, both positively and negatively (Fine & Sung, 2014; Hathway, 2014; Kuh et al., 2003; Miller, 2016). Knowledge of these periods of development and associated neuroplasticity processes in relation to complex conditions such as pain are emergent (Fine & Sung, 2014). Therefore, it is essential that critical time periods across development are acknowledged in research to improve the understandings

¹ Pain catastrophising is a response to pain characterised by helplessness, rumination and magnification of affective factors related to the pain experience (Leung, 2012).

for chronic pain development (Finley et al., 2014). Therefore, early and quality primary healthcare management has the potential to positively influence the trajectory of disability or recovery for children experiencing pain.

However, within primary care, a lack of training and understanding of child-specific pain conditions (Defenderfer et al., 2018) and their consequences in relation to children's development, and poor overall resources have been noted as reasons for poor management of childhood chronic pain (Bhatia et al., 2008). Additionally, a lack of clinical guidelines is highlighted as a reason for delays in diagnosis and numbers of tertiary referrals for children with chronic pain (Abu-Arafeh & Abu-Arafeh, 2016; Hinton & Kirk, 2016). Clinically, frustrations of parents who have children with chronic pain are high. Prior to arriving at tertiary interdisciplinary team management, families have reported low expectations for future interventions due to disappointment from their earlier healthcare interactions (McGrath et al., 2014). Whilst an integrated knowledge of the influences on the onset and early trajectory of children's chronic pain is vital, healthcare professionals also need to maintain an understanding of childhood development to avoid pathologizing aspects of pain presentations that may be developmentally normal (Sandberg & Spritz, 2010).

Summary

This chapter has provided an overview of how chronic pain in children is defined, prevalence data and the wider healthcare concerns related to childhood chronic pain. The relevance of the biopsychosocial model of chronic pain and the family context have been discussed. Sociocultural developmental theory, social cognitive developmental theory and advancement in neuropsychological and neurophysiological development understandings have been explained. Although it is not possible to provide a complete overview of childhood development, these abovementioned theories will provide a lens through which the literature exploring the biopsychosocial influences on the onset and early trajectory of

childhood chronic pain can be considered. Finally, the focus on primary healthcare as the initial contact for many children early in their chronic pain trajectory has been highlighted. Healthcare practitioners rely on thorough research to guide appropriate knowledge and management of the diverse components of a condition such as childhood chronic pain. However, the current available evidence relating to the influences on the onset and early trajectory of childhood chronic pain is diverse in focus, and appears divorced from foundational knowledge of children's development. Because this information is not integrated for healthcare professionals, intervention to prevent onset or to interrupt the early trajectory of chronic pain in children is not optimal. The prevalence of childhood chronic pain is increasing (Coffelt et al., 2013; King et al., 2011), and emerging evidence shows that chronic pain can create lasting effects for childhood developmental periods and in some cases, persisting to adult chronic pain (Hassett et al., 2013). It is essential that the body of knowledge about biopsychosocial influences on childhood chronic pain is integrated and explored through a developmental perspective to support early healthcare provider management of children with chronic pain. The aim of this review is to draw together and to critically analyse the research literature about the biopsychosocial factors influencing chronic pain onset and early trajectory in children through a childhood developmental lens. The next chapter will present the aims, methodology and methods utilised to undertake the review.

Chapter 2: Review Aims, Methodology and Methods

Chapter 1 provided a background to the review and introduced information about the context of childhood chronic pain and defined the terms utilised in this report. The biopsychosocial model, relevant developmental theories, the influence of parents and family and the context of primary healthcare in New Zealand in relation to childhood chronic pain have been outlined. Chapter 2 will outline the specific aims of the review as well as critically discuss the integrative review methodology. The review methods, data evaluation and search outcomes will also be explained.

Review Aims

This integrative review aims to draw together and to critically analyse the existing research literature about the biopsychosocial factors influencing chronic pain onset and early trajectory in children through a childhood developmental lens. Specifically, this review aims to 1) analyse and integrate findings from primary studies of biopsychosocial factors influencing chronic pain trajectory in children aged 5-11 years, and 2) discuss the factors influencing children's chronic pain in relation to theories of children's development.

Review Methodology

The aim of this integrative review is to draw together and to critically analyse the existing research literature about the biopsychosocial factors influencing chronic pain onset and early trajectory in children through a childhood developmental lens. An integrative review methodology was selected as being appropriate to achieve the aims of the review. The integrative review framework is based on the guidance provided by Russell (2005) and includes the following stages 1) formulation of the clinical problem; 2) comprehensive data collection; 3) data evaluation; 4) data analysis; and 5) interpretation and presentation of results (Russell, 2005; Torraco, 2016; Whittemore & Knaf, 2005).

The integrative review methodological approach supports a unique synthesis of a diverse range of primary study methodologies on a specific topic (Whittemore & Knaf, 2005). Integrative reviews allow all published primary research of experimental and non-

		years N=340; Mixed chronic pain conditions	months SD= 35.04	adolescents separately	Poorer parental global health indirectly related to child pain interference through higher parent pain catastrophising, then greater parent protective behaviours and child pain catastrophising.
(Carter, 2002)	Qualitative research, outpatient clinic; Nominated families from nurse practitioner; Not stated	N=3; 7-13 years (M=12.7 years); Mixed chronic pain conditions	3 months +	No	Main theme: 1) searching for a diagnosis, 2) professional dismissal, 3) medical communication. Families less focus on child's pain but more on difficulties with healthcare professionals. Parents used to communicate about their child's pain than the child themselves.
(Conte et al., 2003)	Case Control study, single outpatient clinic; USA	N=16 with JPFMS, N=16 with arthritis, N=16 healthy controls; 7.4-17.4 years	3-36 months (M=12 months)	No	JPFMS group lower mood, high anxiety and depression, irregular daily structure, withdrawal, somatic complaints, highly distractible when compared to the other two group. Significantly greater behavioural issues. Parents of children with JPFMS had higher levels of depression, anxiety. Parents reported for their children greater pain sensitivity than the other 2 groups.
(de Tommaso et al., 2017)	Cross sectional study, single outpatient tertiary clinic; Italy	N=151 (8-15 years); Chronic headache or migraine;	3 months +	No	Muscle pain/ peri-cranial tenderness intensity related to reduced duration of sleep. Loss of sleep may contribute to central sensitisation. Allodynia symptoms correlated to anxiety.
(Dell'Api et al., 2007)	Qualitative semi-structured interviews, single outpatient tertiary clinic; Canada	N= 5 (2 boys, 3 girls); 10-17 years, mixed chronic pain	6 months- 4+ years	No	Main theme: participation limitations; Main themes: Seeking understanding of pain, invisibility of pain, impact of encounters, future fears., negative perceptions of pain; Children felt disbelieved and dismissed. Lack of information regarding their pain, more likely to perceive pain as life threatening in children 10-12 years.
(Dunn et al., 2011)	Cohort Study prospective, Community Sample; USA	N= 1336; 11 years- 11 years 10 months initial sampling; Prevalence and trajectories of chronic pain measured.	Not stated, observational prevalence study	Pubertal development scale and age controlled.	Twelve percent of sample had persistent pain for at least one pain site. Persistent pain group primarily female, high baseline levels somatization and depression at age 11 and at end of study at 14 years.
(Erpelding et al., 2014)	Case control, outpatient clinic; USA	12 (9 females 3 males); 10-17 years, M 14.1 years with unilateral CRPS; CRPS	M= 13 months	No	Hb involvement in modulating responses of stress, reward-punishment and pain modulatory process which may contribute to CRPS symptoms including affective, cognitive, pain inhibition and motor processing. Reductions in fMRI between Hb and pain inhibitory systems.

		Controls (9 females 3 males); M 13.8 years, healthy				
(Fales et al., 2014)	Cross sectional study; outpatient clinic; USA & Canada	N= 210; 10-17 years (M= 14.23 SD 1.59) 73.9% female; mixed chronic pain conditions	3+ months	No		Low agreement between child and parent in regards to miscarried helping. Child and parent more likely to report miscarried helping with dysfunctional and less cohesive family network reports, greater reports of child depression.
(Finniss et al., 2006)	Case report, primary care; Australia	Single case study; 10-year-old male; CRPS	7 weeks	No		Pain, colour, swelling and temperature changes in foot; Nil trauma;
(Flack et al., 2017)	Cross sectional study, Inpatient & Outpatient; Germany	N= 40; 11-18 years; chronic headache & chronic abdominal pain.	IHSC, ICD-10 and Rome III criteria	No		Proximal interoceptive sensations caused greater fear-avoidance in chronic abdominal pain group. Lower task performance time in the associated threat task in both groups. Fear-avoidance behaviours were elicited when benign-threat tasks are applied near to the primary pain region. attention bias is anticipatory, not responsive.
(Heathcote et al., 2017)	Case control study; outpatient tertiary pain clinic patient group, controls 2 secondary schools; United Kingdom	N= 66 (55 female, 11 male) & 74 controls (42 female, 32 male); 10-18 years M= 13.97 years SD 2.13 / control group 11-18 years M 14.95 years SD 1.71; mixed chronic pain conditions.	5-170 months M= 45.7 months	No		Interpretation bias of ambiguous body threat tasks in chronic pain group, more likely to perceive threat. 87.9% had widespread MSK pain vs 12.1% single location.
(Ho et al., 2009)	Cross-sectional study, consecutive referrals tertiary pain service; Canada	N= 57 (46 females, 11 males); 8-18 years M= 14.64 SD 2.39; mixed chronic pain conditions.	M= 46.98 months SD 34.92	No		Above average scores on all cognitive and academic assessment measures.
(Huguet & Miró, 2008)	Prevalence cross-sectional study; Community sample; Spain	N= 561 8-16 years M=11.89 years SD 2.00	Prevalence study	No		Lower social Quality of Life Scores; Lower limb CP more common in boys (57% vs 19.65%) and multiple site CP more common in girls (50.6% vs 22.2%). Lower physical Quality of Life Scores. Abdominal pain, headache and lower limb complaints most common location of chronic pain; Prevalence of CP increased with increasing age M with CP=11.49 SD=2.08 vs M without CP=10.53 SD 1.86. Age not impacting functional disability or QoL measures in CP sample. 37.3% with chronic

					significantly higher levels of pain related impairment and was predictive of significant impairment.
(Lebel et al., 2008)	Cohort Study, Outpatient tertiary pain clinic; USA	N= 8 (all female); 9-18 years M=13.5 (1.63), CRPS, lower extremity unilateral.	M= 13.3 months (2.35)	No	Increased BOLD signal=Parietal lobe, bilateral SI, anterior and middle cingulate, anterior insula. Decreased BOLD signal= frontal lobe and parietal lobe, middle cingulate, middle temporal lobe, parahippocampus and hippocampus. Decreased signals in pain inhibition pathways. Contralateral/unaffected limb had almost double the increased BOLD signal and few regions showing decreased BOLD signal. Findings were similar when pain state had resolved; Notable central processing changes that are maintained after symptom resolution may be related to the developmental plasticity and have long lasting effects.
(Libby & Glenwick, 2010)	Cross sectional study; Outpatient tertiary rheumatology clinics; USA	N= 57 10-18 years (M=15.5); JPFMS	Not stated	No	School absence 2.5 days in past month (range 0-31 days). Daily hassles not related to pain ratings. Poor pain ratings, quality of life and depression scores with catastrophising. Self-efficacy positively influenced QoL, catastrophising, pain and depression scores; Social support from family and peers improved QoL and improved pain; 16% had a parent with fibromyalgia, 56% had a parent who had chronic pain. No significant differences existed between age group analysis of 10–14-year-olds and 15–18-year-olds and variables of pain, perceived social support, coping strategies, depression or self-efficacy.
(Linnman et al., 2013)	Cohort Study; Outpatient pain clinic, USA	N= 8; 9-18 years M=13.5 (1.6); CRPS	Not stated	No	Symptomatic and persistent cortical reorganisations- significant increased connectivity alterations anterior cingulate, postcentral gyrus, putamen, amygdala, caudate and thalamus. Alterations in multiple sensory, emotional and cognitive processing regions. The amygdala showed transient increased connectivity in BOLD signal analysis to the PCG.
(Logan et al., 2013)	Retrospective, cross-sectional case control study; single outpatient pain clinic; USA	N=101 CRPS (7-18 years M = 13.41 (0.24)). Comparisons N=103 abdominal pain, N=291 headache and N=119 back pain.	CRPS 13 months Headache 32.60 Abdominal Pain 28.14 Back pain 23.25	No	CRPS group fewer missed school days than other groups; CRPS group no greater anxiety, depression and relative to normative values; More females with CRPS proportionately than the other pain groups. CRPS group reported more somatic symptoms.

(Lynch et al., 2007)	Cross-sectional study; Outpatient pain clinic; USA	N= 272 (66% girls); 8-18 years, Mixed chronic pain	3-24 months	Analysis of children and adolescents separately	Boys more likely to participate in physical activity as a distraction from pain; Girls sought social support more than boys and expressed their pain and feelings more. Older children longer pain duration and become increasingly distressed and anxious with the long duration of their pain. Younger children rely heavily on social supports for pain related strategies and affirmations.
(Noel, Beals-Erickson, et al., 2016)	Cross-sectional study; Outpatient pain clinic; USA	N= 46 caregivers of children aged 10-18 years M=13.51 (2.00); 41 mothers and 1 grandmother. Mixed chronic pain	3-60+ months	No	Orientation with acceptance of diagnosis/ unresolved diagnosis beliefs showed correlation to resilience or distress cluster groups of parents. Parents in resilience narrative cluster were more likely to show humour, positive outlook and benefits with their child's pain. Parents reported higher levels of depression and anxiety. Extent of the child's functional disability did not explain the degree of parental distress levels.
(Noel, Wilson, et al., 2016)	Case control study; Outpatient pain clinic; USA	N= 95 chronic pain 10-17 M=15 (2.1), N= 100 controls M=14.3 (2.1); Mixed Chronic pain conditions.	3+ months	No	HRQoL lower in children with chronic pain compared to controls; CP group reported death and abuse as their most traumatic life event
(Pas et al., 2019)	Case control study, Inpatients; Belgium	39 FAP and 36 controls; 6-12 years M= 9	M= 24, median 28	No	Pressure pain thresholds significantly lower than controls, proposed lower endogenous pain control. No differences boys to girls CPM task; Parents of FAP group= greater pain related fear, catastrophizing, avoidance, helplessness, rumination (P= <0.001) and magnification (P= <0.012) about their child's pain; Children FAP group significantly more likely to have a parent with CP history.
(Pate et al., 2019)	Qualitative semi-structured interviews; community sample; Australia	8 chronic pain, 8 healthy peers; 8-12 year (median 10, 8.8-11.0 years)	Chronic pain group= 1-2 years= 63%, 3-5 years=25%, 6-10 years=13%	Explained age 8-12 inclusion for developmental reasons. Age analysis provided	Social constructs shown to have large impact on child's pain perception; Pain knowledge no differences between groups. Less certainty with 8- & 9-year-old participants and less abstract understanding. Children's focus on fixing the pain. Children with chronic pain more able to focus on the psychological, emotional and social impacts of pain.
(Pavlova et al., 2020)	Cohort Study, tertiary pain program past participants; Western Canada	N= 138; 9-18 years M= 14.29y (2.30), 75% female; Mixed chronic pain conditions	M= 39.17 months (38.66)	No	Older age poorer sleep, insomnia and shorter sleep duration; Older age >pain interference and PTS; PTS associated with increased pain interference over time, decreased duration of sleep; 47.2% =multiple pain areas; PTS greatest driver of pain

					interference. Worsening pain interference due to poor sleep quality
(Pavone et al., 2011)	Case series, outpatient pain clinic; Italy	N= 30 (12 female) 3-14 years M=8; growing pains	3+ months	No	Massaging pain site mostly relieved pain. Family history growing pains in 20%. Bilateral symptoms in 80% and linked to physical activity in 20%.
(Pearson et al., 2011)	Case report, primary case; Not stated	Single case report. 8-year-old female; CRPS	6-12 weeks	No	Periods of excessive emotional vulnerability; Parental anxiety increased, step father to be deployed on overseas duty.
(Perquin et al., 2000)	Cross sectional prevalence study, community sample; The Netherlands	0–18-year-olds. 5423 questionnaires completed and returned.	Prevalence study	Responses by age group categorised	25.0% reported chronic pain most commonly in age 12-15 years. Prevalence and multiple pain sites increased with age. Children up to 8 years= FAP most common pain 1/2 children with CP reported more than 1 location of pain.
(Seshia et al., 2008)	Cohort Study, Outpatient tertiary pain clinic; Canada	N= 70, 48 females, 22 males; 6-18 M male=12 M female= 14; Headaches	3-144 months M= 36 months	No	Sleep disruption 23%; Multiple environment stressors reported by 46%; Isolation 7%; School stress 10%; Family Hx= recurrent chronic headaches 70%, anxiety 7%, mood disorder 31%.
(Sieberg et al., 2011)	Cross sectional study, Outpatient pain clinic; USA	N= 157 8-17 years 87% female; M= 12.7 years (SD= 2.43), multiple chronic pain conditions	M= 25.92 months (13.79)	No	Parental factors: 30% reported significant global distress; Significant protective behaviours reported. Parental global stress, depression or anxiety did not directly influence level of child chronic pain disability, only parental pain related stress.
(Sinclair et al., 2020)	Cross sectional study, Outpatient pain clinic; Australia	N= 114 75 adolescents (68 girls, 7 boys) & 39 children (30 girls, 9 boys); Children 8-12 years & adolescents 13-18 years; multiple chronic pain conditions.	3 months + or CRPS criteria.	Analysis of children and adolescents separately	Sensory modulation associated with attachment low registration= > anxious and avoidant attachment Higher sensory sensitivity= lower anxious attachment & higher functional disability
(Soltani et al., 2020)	Case control study; Outpatient pain clinic; Canada	N= 155 (102 CP group 71% girls M=14.20 years (2.29, 53 controls, 50% girls M=13.49y (2.71)); 10-18 years; mixed chronic pain conditions.	3.38 years (3.25)	No	Initial and sustained Attentional bias for high level pain faces high in both groups whereas CP group more attention to low pain faces; Eye fixation measured on pain faces; fixation described as attentional bias to pain.
(Tan et al., 2008)	Cross sectional study, Outpatient pain clinic; The Netherlands	N= 78 children, N= 951 adults 85.9% children	M= 11.9 weeks	No	Time from injury to symptoms 0.57 weeks (longer than adults) Children specific results: 23.3% 1 upper extremity, 72.6% lower extremity and both 4.1%.; 28.2% had renewed CRPS 1 and

		female; Children= 5-16 years M=13; CRPS type 1.			many due to a new injury, 60% in the same extremity; CRPS type 1 more likely to develop after minor injury in comparison to adults.
(Wager et al., 2019)	Prospective Cohort Study, Primary Care; Germany	N= 266; 6-17 years M=11.2 (3.1); prospective of persistent pain	54.4 weeks	No	Poor pain perception at initial consult predicted treatment failure in primary care. Anxiety/ depression did not predict treatment failure but emotional burden did. 23.3% of cohort reported disabling chronic pain at 3 months, and continued to 6 months. Poor long-term prognosis is poor response to treatment 3 months in primary care. Older children greater risk for persistent pain; 1/2 mothers and 1/3 fathers reported chronic pain.
(Walker et al., 2002)	Cohort Study, Tertiary Pain clinic; USA	N=151; 8-18 years (M= 12.1 (2.5)) 57% Female; Chronic abdominal pain	3+ months	No	Reduced self-worth and low perceived academic performance increased symptom maintenance in combination with activity restriction. Punishment or pain disregard increased symptom maintenance. Activity avoidance not directly linked to pain intensity.
(Weiss et al., 2013)	Cohort Study, Outpatient Pain clinic; USA	N=112; 11-18 M= 15.47 (1.83) 76% female; mixed chronic pain conditions	3-144 months M= 37 (28)	No	Low pain acceptance, catastrophising, and depression predictive of functional disability and less goal orientated behaviours.
(Youssef et al., 2019)	Case control study, Outpatient tertiary pain clinic; USA	N= 52 & 52 controls- paediatric chronic cohort N=16 (10 females, 6 males M=14.3y (0.6y). CRPS	M=15 months	No	Shift in resting state circuits from sensory alterations in paediatric cases with widespread brain variations, including issues with sensory processing and descending pain inhibition. Grey matter atrophy in R) ACC region and thalamus connections.
(Zohsel et al., 2008)	Case control study, tertiary paediatric pain clinic and tertiary services; Germany	16 Chronic Migraine, 15 controls; 10-14 M=12 (1.5) 15 controls M= 12.3 (1.5)	M=5.7 years (1.7)	No	Attentional bias to painful and potentially harmful stimuli; Increased pain intensity at shorter latency in migraine group;

chronic pain compared to girls (Kaczynski et al., 2009). However, girls showed more affective symptoms associated with protective parental behaviours (Kaczynski et al., 2009). In summary, whilst it is not possible to rule out the additional effect of the biological developmental differences between boys and girls (Hoffnung, 2019), it can be seen how general gender schema and stereotypes, through sociocultural development might influence these gender specific findings.

Summary of Study Limitations

There were various limitations shared by majority of the studies in this review. The limitations affect the internal validity, and limit the generalisability of the study results to the wider population of children with chronic pain. General risks to the studies' internal validity included bias arising through parent proxy-reports, a risk of recall bias and a predominance of cross-sectional methodology (refer Table 2), which limited insights into changes in children's pain trajectories over time.

Many studies did not provide or analyse data about variables that had potential to act as confounders and bias the study results. Such variables included age at onset of chronic pain, pain duration (Lynch et al., 2007) and interventions children may have received. Lack of information about such variables also hampers generalisability and clinical application of the study information in practice.

Sampling bias was evident in the majority of studies, with homogenous samples of primarily Caucasian, middle-class children (refer Table 2). The sampling bias limits the generalisability of the results, especially within an ethnically diverse health care environment such as New Zealand. Generalisability of study findings to primary health care settings and to younger children was also constrained; most studies were undertaken in tertiary care and had a low representation of children under the age of 10 years, with some studies containing primarily adolescent data (refer Table 2). Study limitations are

Furthermore, outcome measures employed by de Tommaso et al. (2017) were not validated in young children.

The present review findings about the impact of psychological factors did highlight some variability, particularly in relation to children with a CRPS diagnosis. CRPS participants retrospectively, self-reported less anxiety and depression symptoms than comparative chronic pain groups suffering abdominal pain, headaches and back pain in a cross-sectional study by Logan et al. (2013). Abu-Arafeh and Abu-Arafeh (2016) also reported normal depression and anxiety scores in their prospective prevalence study of CRPS participants. However, in Logan et al. (2013) study, average pain duration in the CRPS group was only 13 months, compared with 28.14 months, 32.60 months and 23.25 months respectively. Additionally, Abu-Arafeh and Abu-Arafeh (2016) did not state their participants' pain duration, although the study was included in this review as the participants met the outlined Budapest Criteria for CRPS diagnosis. It is plausible that the lower psychological impairments are primarily due to low average pain duration and chronicity of symptoms. Furthermore, retrospective accounts are potentially influenced by recall bias and may have influenced the results for all groups.

Further studies shed light on the influence of anxiety and stress factors that relate to function and performance at school in participants with CRPS and mixed chronic pain conditions, yet show mixed results. Children with chronic pain showed higher than average school-functioning (Bayle-Iniguez et al., 2015; Ho et al., 2009). They had perfectionist tendencies, general anxiety and increased psychosocial stress compared to controls (Bayle-Iniguez et al., 2015). Conversely, Ho et al. (2009) found that pressures related to potential and actual school-achievement were not shown to directly influence chronic pain and functional disability (Ho et al., 2009). However, whilst Ho et al.'s (2009) cross-sectional study is able to show this association, it did not establish causation or prediction over the long-term, as in a prospective cohort study (Del Mar et al., 2017; Tilson, 2017). In contrast, Bayle-Iniguez et al. (2015) found in their case-control study of 76 participants with CRPS, that the strongest association with CRPS symptoms was with children being anxious and

being a good school performer. Developmental factors were not considered in either study, and wide age ranges of 5-16 years (Bayle-Iniguez et al., 2015) and 8-18 years (Ho et al., 2009) were considered in combination with their results. The broad age groupings across the various studies are not able to shed light on developmental changes, different school-related pressures and differing peer interactions across the extended age continuum (Hoffnung, 2019). Furthermore, recall bias might have influenced results from Bayle-Iniguez et al. (2015), with retrospective methodological design, where symptomatic participants are more likely to report higher risk factors compared to healthy peers (Sterne et al., 2019).

As with anxiety and stress, low pain acceptance³ has also been described as a psychological factor (Weiss et al., 2013), with potential to negatively influence the trajectory of chronic pain. Qualitative research with Australian children aged 8-12 years indicated that children's focus regarding management of their mixed chronic pain conditions revolved around 'fixing' the pain (Pate et al., 2019), indicating low pain acceptance. Alongside such findings, children who interacted more with healthcare professionals while continuing to seek resolution for their pain were reported to have poorer physical health and overall health satisfaction (Dell'Api et al., 2007). However, neither Pate et al. (2019) or Dell'Api et al. (2007) specifically explored pain acceptance.

In agreement, Weiss et al. (2013) specifically studied low pain acceptance as a factor, finding that it was significantly associated with fewer goal orientated behaviours, lower psychological flexibility, increased functional disability, pain catastrophising and greater depressive symptoms (Weiss et al., 2013). However, it is not possible to confirm the direction of the significant effect and whether these factors resulted from the low pain acceptance, or whether the low pain acceptance occurred because of the psychological factors (Weiss et al., 2013). Notably, Noel, Beals-Erickson, et al. (2016) found in their sample that 40% of parents of children with chronic pain continued to have unresolved

³ Pain acceptance encompasses recognising the existence of pain without adverse attempts to control it (Kalapurakkel et al., 2015).

setting and have not been validated for use in chronic pain (Soltani et al., 2020). Children's pain avoidance and attention bias is described as anticipatory to the potential of pain, not typically responsive to the sensation itself (Flack et al., 2017). It is possible that children's avoidance behaviour, such as those found in the above studies, is acquired via sociocultural or social learning. Avoidance behaviours will be applied to all similar experiences or environments that a child encounters where the same threat is associated with their prior learning (Flack et al., 2017).

Sensory modulation⁴ is established through the integration of multiple neural sensory inputs, past experiences and information about the current environment along with other complex multi-level cognitive organisations and attachment, mostly with a parent. In turn, sensory modulation influences pain behaviour responses (Sinclair et al., 2020). Children with high sensory seeking behaviours, for example specific signalling to enable a social response to their pain, tended to have more emotionally responsive parental support with their pain (Sinclair et al., 2020). Through Bandura's social learning theory, it can be seen that parents' responses and support provides reinforcement for the child's pain. In this way, the parent may help formulate such sensory seeking behaviour (Bandura, 1986, 2003). Consistent with this perspective, it was found that pain intensity did not influence sensory modulation behaviours, whereas attachment variables did in both children and adolescents (Sinclair et al., 2020). This suggests the relationship between parental responses and child sensory seeking behaviour may have been a key influence on chronic pain development.

Many of the above-mentioned studies reporting on psychological factors had cross-sectional designs (de Tommaso et al., 2017; Flack et al., 2017; Ho et al., 2009; Kashikar-Zuck et al., 2008; Konijnenberg et al., 2005; Noel, Beals-Erickson, et al., 2016), which can show associations, but are not suited to showing causality (Del Mar et al., 2017). Unlike longitudinal prospective studies, cross sectional studies are not well suited to identify

⁴ Sensory modulation is defined as "the ability to regulate and organise sensory input and to respond in an adaptive manner" (Whitcomb et al., 2015, p. 2).

features that can predict the outcome of interest over longer time frames, such as factors that might contribute to the onset or early trajectory of chronic pain (Tilson, 2017). Social context or developmental factors were given little consideration in these cross-sectional studies. Additionally, mean pain duration was not reported, making it difficult to determine if psychological factors were baseline influences or consequences of long-standing functional disability. It is plausible that many psychological factors could be a consequence of extended chronicity and maladaptive responses through children's cognitive development or learning during this lengthened period.

In contrast, a higher quality, prospective cohort study by Wager et al. (2019) indicated that only 9% of children initially presenting to primary healthcare appointments with unexplained pain had clinical levels of anxiety or depression (Wager et al., 2019). This rate is much lower than the other included studies which presented findings from specialised pain clinics. This variability could be caused by the different psychometric measures used by Wager et al. (2019). However, it is equally possible that these lower rates of negative psychological factors reflect the shorter pain duration in their primary care participants. Children have been reported to become increasingly distressed and anxious with the referral to specialised treatment following a long duration of their pain (Lynch et al., 2007). Developmentally, the longer that maladaptive behaviours exist and influence normal childhood developmental pathways, the less likely that full resolution of this will occur (Davies, 2011), highlighting how essential early, developmentally informed management will assist long-term positive outcomes.

Overall, the direct relationship between childhood chronic pain and affective symptoms is less than clear. Additional, unexplored, mediating factors may also contribute to the association between affective factors and pain, including pain duration and

efficacy skills may be key developmental factors influencing the onset or early trajectory of chronic pain in children and warrants more thorough investigation.

Participation Factors and Functional Disability

Participation and peer interaction is an integral part of childhood developmental learning. School absenteeism, where children may be isolated from their peers, was identified in this review, and was primarily associated with children with chronic pain and with higher levels of depression (Kanstrup et al., 2014; Kashikar-Zuck et al., 2010). Overall, children with JPFMS aged 11-18 years, missed on average 3 school days per month, compared to the population norm of 9 school days per year (Kashikar-Zuck et al., 2010). In addition, 43% of a mixed-condition chronic pain group, of a similar age range, were frequently absent for more than one day per week due to their pain (Kanstrup et al., 2014). School absences were reported to be enabled by families (Walker et al., 2002). Therefore, enabled school absenteeism reinforced illness behaviours and was interpreted by Walker et al. (2002) as positive attention for children's pain behaviours. Supporting this conclusion, actions that enabled children's activity restrictions, especially when they had low measures of self-worth, were shown to encourage symptom maintenance (Walker et al., 2002). Equally, children who had a poor view of their own health had significantly higher levels of pain related impairment (Konijnenberg et al., 2005). Only Kashikar-Zuck et al. (2010) evaluated the social influence of maternal pain history and its association with school absences, however, no link was established.

Children's feelings of support have an interesting association with symptom duration. Higher perceived support from family increased pain intensity (Libby & Glenwick, 2010). Negative reinforcement in the form of disregard also increased pain symptoms (Walker et al., 2002). Both findings can be explained by the concept of social learning,

whereby incentive or disregard prompts symptom maintenance (Miller, 2016). Influences of parents are discussed further, later in this review.

Consistently, neither activity avoidance nor participation levels were directly linked to pain intensity or symptoms (Beeckman et al., 2020; Walker et al., 2002). When examined through a developmental lens, participation limitation is concerning, especially if avoidance and chronic pain treatment occurs over an extended period of time, potentially influencing long-term developmental trajectories (Davies, 2011). Pain-related fear was the most central factor of activity avoidance and overall function (Beeckman et al., 2020) and is discussed in more detail below. However, children with chronic pain who rated their self-worth poorly, similarly responded with greater functional disability and activity limitations, especially with activities they expected themselves to perform poorly in (Walker et al., 2002). This concept of low self-worth may be related to self-efficacy (Bandura, 2003). The majority of functional activity limitations were enabled by families, or their direct social network (Walker et al., 2002). In line with Bandura's social cognitive theory, if the consequences of this functional avoidance are reinforced, this will provide further incentive for this avoidance behaviour in the future (Miller, 2016), and further influence low self-efficacy (Bandura, 2003).

Parent Factors Influencing Childhood Chronic Pain

Consistent with developmental learning theories, studies in the review suggested that parents play a central part in a child's understandings about pain, with potential to influence the onset and early trajectory of chronic pain. Illustrating this point, it has been found that children rely more strongly on their social support systems than themselves for pain related strategies and affirmations (Lynch et al., 2007). Vygotsky's social learning theory posited that parents' interpretation of events determines a child's response to an event. This may include the attention required to respond to the situation, and the behaviours to implement (Bergen, 2008). In this way, parents are reported as the central mediators to childhood pain behaviours (Akbarzadeh et al., 2018). As such, parental

influences on a child with chronic pain have been extensively examined in a wide range of studies in this review.

Firstly, findings in this current review show support for the notion that parents with chronic pain are an important social influence on the onset and trajectory of their children's chronic pain. Several of the studies reviewed in the present work reported the co-occurrence of parental or caregiver chronic pain and the development of childhood chronic pain conditions (Kashikar-Zuck et al., 2010; Pas et al., 2019; Wager et al., 2019). Further, if a family member experienced chronic pain, children were more likely to catastrophise their own pain (Dell'Api et al., 2007). Drawing from social learning theory precepts (Bandura, 1986, 2003; Miller, 2016), parental behaviours that relate to their own pain, or associated affective factors, are likely modelled and could be readily assumed by their children, defined as the caregiver-child dyad (Steck, 2016).

At a simple glance, parents mediate the way their children adapt to their pain (Akbarzadeh et al., 2018). Parents of children with chronic pain self-reported higher personal depression and anxiety rates (Conte et al., 2003; Noel, Beals-Erickson, et al., 2016) and greater fear of pain (Pas et al., 2019) compared to parents of children in healthy control groups. However, parental global stress, depression and anxiety did not directly influence levels of child chronic pain disability (Sieberg et al., 2011). Rather, studies indicate the link to child pain interference or functional disability involved multiple mediating factors (Birnie et al., 2020; Sieberg et al., 2011).

The present review found a complex interplay between the mediating factors of parental pain catastrophising (Akbarzadeh et al., 2018), parental protective behaviours, and parent pain-related stress, and child pain catastrophising and pain interference (Birnie et al., 2020; Sieberg et al., 2011). Children's perception of their pain is believed to be subsequently reinforced with increased attention to the pain experience from parents catastrophising about their child's pain (Akbarzadeh et al., 2018). Such findings thoroughly

support the relevance of social learning and sociocultural learning theories in understandings about childhood pain trajectories.

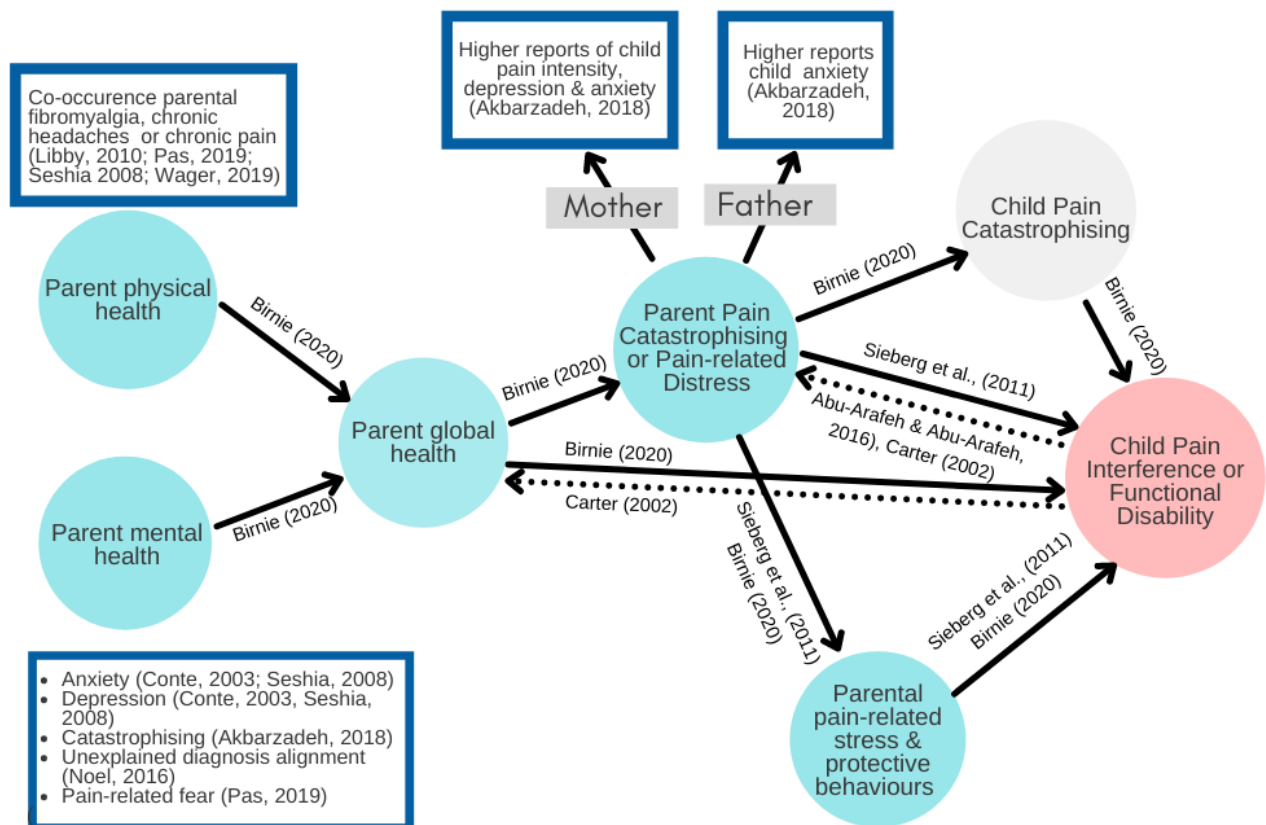
Drawing diverse study findings together, a path of influence is suggested where parental global health, including both physical and psychological concerns, contributes to parental pain catastrophising (Birnie et al., 2020); parent pain catastrophising or distress, in turn, contributes to child pain catastrophising (Birnie et al., 2020) and increased parental pain-related stress and protective behaviours (Birnie et al., 2020; Sieberg et al., 2011); and finally, child pain catastrophising (Birnie et al., 2020), parental pain related distress (Sieberg et al., 2011), and parental protective behaviours (Birnie et al., 2020; Sieberg et al., 2011) all contribute to child pain interference with varying inter-relating contributions. Integrating findings from the literature in the present review, a depiction of these potential pathways of parental influence on child pain from this is shown in Figure 2. It should be noted that a direct pathway from parental general health to child pain interference was shown to only occur in children aged 8-12 years (Birnie et al., 2020), highlighting the potentially greater influence of parent's function at this younger age. Furthermore, this direct link in this age group showed a lesser mediating influence of parental protective behaviours than in the adolescent age group (Birnie et al., 2020). Parental physical and emotional health also contribute factors to the pathway of influence on child pain as shown in Figure 2. Many studies outlined the co-occurrence of child chronic pain with parental chronic pain or psychological mood disorders (Conte et al., 2003; Libby & Glenwick, 2010; Pas et al., 2019; Seshia et al., 2008).

As seen in Figure 2, recent research by Akbarzadeh et al. (2018) provides additional, gender-specific details about the influence of parent catastrophising on children. Higher levels of maternal pain catastrophising increased the mother's report of their child's pain intensity, anxiety and depression. In contrast, high levels of a father's pain catastrophising only showed correlation to reports of their child's anxiety. Measures of mothers' catastrophising were significantly higher than those of fathers (Akbarzadeh et al., 2018). Akbarzadeh et al. (2018) work suggests that gender differences in reporting of

children's symptoms are a relevant limitation of many of the studies included in the present review. Many of the studies were based on parent proxy reports, which were primarily completed by mothers, who reported higher descriptive scores of all of their child's affective symptoms (Akbarzadeh et al., 2018). It is possible, therefore, that child affective influences on chronic pain have been overestimated. This overestimation could be through poor methodological designs, but also the lack of understanding of this substantial social influence on a child's pain experience and potential parental over-estimation of pain and associated gender influences.

Figure 2

Depiction of relationship between parental global health and child pain interference or functional disability in childhood chronic pain



Further adding to the complexity of these relationships (shown Figure 2), it appears that a child's pain impacts conversely on parent wellbeing (Carter, 2002), which, in turn, mediates the child's functional ability (Sieberg et al., 2011). In an effort to tease out this relationship further, Sieberg et al. (2011) found, that global parental distress associated

with general life did not influence their child's pain-related functional disability. Similarly, parental narratives when categorised into distress or resilience narratives did not show any association to children pain related functioning (Noel, Beals-Erickson, et al., 2016). Only parental pain-related stressors, parental global health and catastrophising increased child pain interference (Birnie et al., 2020; Sieberg et al., 2011), limiting overall functioning.

In this review parents did report increased stressors deriving from their child's pain, including adjustment of work, social restrictions, anxiety and worry (Abu-Arafeh & Abu-Arafeh, 2016). Moreover, through qualitative methodology, parents reported that their stress associated with their child's medical encounters was not present prior to the child's presenting pain complaint (Carter, 2002). Carter (2002) reported the viewpoints of the parents with a child with chronic pain, finding they had a greater focus on the frustrations that the child's pain caused than the pain itself. A main stressor reported by these parents were the encounters with medical professionals, medical misinterpretations, and lack of diagnosis or treatment plans for their child's pain (Carter, 2002).

Conversely, Hunfeld et al. (2002) reported that the stress impacting on a family resulting from a child with chronic pain was present, but was defined as mild. Hunfeld's et al (2002) child participants were an average of 8.4 years of age, compared to the contrasting findings from Abu-Arafeh and Abu-Arafeh (2016) CRPS sample with a mean age 11.9 years and Carter's (2002) mixed condition sample of average 12.7 years. Unfortunately, due to variation in outcome measures used, direct comparisons in these results are difficult to ascertain. However, it is possible that stress resulting from younger children with chronic pain has less of an impact on families.

Bearing in mind that the amount of the child's functional disability did not explain the degree of parental distress levels (Noel, Beals-Erickson, et al., 2016), it is possible that parental catastrophising is merely communicative to others, possibly to healthcare practitioners, seeking assistance for their child's pain. Parental catastrophising behaviours

may reflect the longevity of their child's symptoms, multiple healthcare practitioner visits and decreased expectations of resolution of symptoms (Carter, 2002; Dell'Api et al., 2007).

In conjunction with other studies in this review, the majority of the studies exploring parental influences included participants with longer than two years of child pain duration. Therefore, it is difficult to ascertain if these parental affective factors are a consequence of long-term stressors relating to their child's pain, or whether they are baseline causative factors. It seems reasonable that parents are going to respond in a protective and hypervigilant manner if their children have chronic pain. Further, longitudinal research is required to establish if stress or other affective symptoms are initially present and/or increase in parents over time with increased child pain chronicity.

Despite the mixed methodologies adopted by the various studies, and despite the studies' focus on numerous chronic pain complaints, parental influences on child chronic pain were evident throughout the included studies. It is apparent that there are likely multiple, complex factors mediating the relationship between parental protective behaviours, parental catastrophising and child pain responses. There is a host of social interactions that young children learn through, but the greatest of these influences is their parents (Birnie et al., 2020). However, there is a need of a greater depth of understanding of these interactions and their influence to gain a more relevant clinical picture for practitioners and families.

A parent's desire is to help their child who is suffering pain. However, occasionally, this synergistic process between a parent and a child can become unconsciously negative. One study that particularly explored the changing and interactive environment of the relationship between parents and children with chronic pain focused on a concept defined as miscarried helping (Fales et al., 2014). This concept was only reported in one study but may be another relevant parent factor impacting on the onset and early trajectory of a child's chronic pain. Fales et al. (2014) found in their multi-centre, cross sectional study of mixed chronic pain conditions, miscarried helping was defined as "a transactional process whereby a caregiver's desire to be helpful inadvertently contributes to negative

parent-child interactions regarding health behaviours, ultimately resulting in poorer health and adjustment over time” (Fales et al., 2014, p. 428). The context of this relationship was the influence of each other’s views, emotions and behaviours.

Whilst the concept of miscarried helping holds promise for explaining the ways parents might influence the onset and early trajectory of a child’s chronic pain, the study findings should be treated cautiously. There was minimal congruency between parental and child reports of miscarried helping (Fales et al., 2014). Results showed variances in outcomes when child participants had lower pain intensity but higher activity restrictions. Furthermore, miscarried helping occurred when parents reported their child to have higher depression scores (Fales et al., 2014). As stated above, parent gender influenced the parent-reporting of affective symptoms (Akbarzadeh et al., 2018). In Fales et al. (2014) sample, 90% of the participant caregivers answering the questionnaires were mothers (Fales et al., 2014). Additionally, one of the main outcome measures, the Helping for Health Inventory, has only been validated in the families of adolescent diabetics (Fales et al., 2014).

Nonetheless, miscarried helping was found to describe an interaction that adjusts over time, from a supportive, compatible relationship, through to where the child becomes more and more resistant to support. This resistance is proposed to occur with increased chronicity and increased desire for autonomy over their condition (Fales et al., 2014). Such desire for autonomy is, however, consistent with developmental perspectives (Hoffnung, 2019), although the findings were not explored in the context of normal child developmental changes. Similar findings were reported in Libby and Glenwick (2010) in their JPFMS participants, where high levels of youth stress, combined with increased social support from parents, increased depression scores.

Fales et al. (2014) also used cross-sectional methodology, involving participants aged 10-17 years with chronic pain duration greater than 3 months. Despite an initial theoretical understanding that the miscarried helping phenomenon changes over time, no developmental methodological considerations were employed in this study, nor were

participants stratified by children's pain chronicity. This appears a significant omission given the definition provided for miscarried helping developing over time. In line with this critique, Birnie et al. (2020), found that parental protective behaviours only significantly influenced child pain interference in their adolescent group, not the child group aged 8-12 years. They proposed that parental protective behaviours were less developmentally appropriate at the older age group (Birnie et al., 2020). The inconsistencies between parent and child reports of miscarried helping highlight the need to explore both child and parent reports of pain perspectives, whilst being aware of potential gender, developmental, reporting, and measurement biases likely influencing results. Therefore, in light of the inconsistencies and potential limitations, the concept of miscarried helping will likely require further investigations in future research.

Association of Sleep and Childhood Chronic Pain

A number of studies in this review provided valuable insights into the relationship of sleep disturbances with pain sensitivities and affective symptoms. Shorter sleep duration was associated with increased central sensitisation in children suffering from migraines (de Tommaso et al., 2017). Children with chronic pain were shown to wake more frequently (Konijnenberg et al., 2005; Pavlova et al., 2020), with insomnia more common in older children and adolescents (Kanstrup et al., 2014; Pavlova et al., 2020). Insomnia explained the variance between chronic pain and functional disability, pain interference and depression symptoms (Kanstrup et al., 2014; Pavlova et al., 2020). Higher ratings of baseline pain interference influenced greater sleep disturbances, and poor sleep quality was considered a major factor of pain symptom maintenance at 3-month follow-up in children aged 10-18 years with various chronic pain conditions (Pavlova et al., 2020). However, the average pain duration at baseline of participants in Pavlova et al's (2020) study was over 3 years with tertiary pain clinic participants. Therefore, the generalisability to onset or early trajectory of chronic pain in primary healthcare settings is limited. Of note, both Kanstrup et al. (2014) and Pavlova et al. (2020) utilised retrospective questionnaires

within their data collection methods. Retrospective recall of pain and symptomology tends to overestimate results (van den Brink et al., 2001) and caution should be used when interpreting these results.

Association of Trauma and Stress with Chronic Pain

Early traumatic experiences can influence the future responses of children's pain and stress response systems (Turner-Cobb, 2014). Theory holds that neurophysiological processes affect the way pain and stress are interpreted through integration of both sensory and affective information (Steck, 2016). However, the interpretation of pain and stress is also influenced by social and developmental learning contexts (Steck, 2016; Turner-Cobb, 2014). Developmental theory indicates that an impact on brain structures and neurotransmitters by stress-response systems, via a trauma or sustained stressful experience, will likely influence later chronic health issues (Davies, 2011). It is thought that physical injury and pain enhance an individual's stress response system, designed as a threat system for survival measures (Turner-Cobb, 2014). For children, trauma also has potential to influence the trajectory of their development, with newly advanced development the most susceptible to disruption as a result of adversities (Davies, 2011). Moreover, sustained trauma is likely to influence children's long-term stress responses and emotional regulation (Davies, 2011; Steck, 2016), lending insight into the way post-traumatic stress (PTS)⁵ might be associated with the onset and early trajectory of chronic pain.

Within this integrative review, only two studies were identified that explored the associations between trauma, chronic pain and children's development (Noel, Wilson, et al., 2016; Pavlova et al., 2020). Additionally, a small number of studies were obtained which explored factors associated with children's chronic pain and stress symptoms. Pavlova et al. (2020) reported the combined occurrence of poor-quality sleep, PTS and pain, where sleep

⁵ Post-traumatic stress disorder symptoms (PTS) are severe symptoms as a reaction to trauma or traumatic experiences (Kaminer et al., 2005).

is proposed to be the mediating factor. Additionally, higher PTS correlated with increased pain intensity, pain impact, poorer quality of life (Noel, Wilson, et al., 2016) and poor sleep (Pavlova et al., 2020).

Supporting Turner Cobb's (2014) contention as to the importance of context when studying children's stress responses, in this review, over 50% of Bayle-Iniguez et al. (2015) 73 participants reported increased stress caused by family conflict, death of a close family member, school issues or sexual abuse preceding their CRPS diagnosis. Pearson et al. (2011) reported on a single case where an 8-year-old female participant developed CRPS with reported increased parental anxiety due to her step-father being deployed on overseas military duty. Further, in other studies, both children with chronic pain and their parents presented with high levels of PTS (Noel, Wilson, et al., 2016; Pavlova et al., 2020), highlighting the relevance of the social learning models, whereby modelling or support from family may shape children's stress levels, and behavioural responses to pain and adversity.

At this stage, the studies in this review lend emergent insights into the associations between trauma, stress and other factors, and are consistent with theoretical understandings, but further research is needed to provide sound evidence as to the role played by stress. It may be that affective concerns are related to stress responses and pain mediation through parallel cortical links. Future prospective studies utilising advanced imaging techniques, and emerging developmental and neuroscientific research, may help advance understanding of the various impacts of stress, pain, sleep, affective factors and childhood development.

Neuro-Biological Factors Associated with Childhood Chronic Pain

Until relatively recently, the understanding of psychological, cognitive and biological factors in health conditions and in children's development was largely observational and descriptive without consideration of fundamental cortical changes (Blakemore et al., 2011; Munakata et al., 2004). Advanced studies in the field of neuroscience and in brain imaging

techniques have provided improved awareness and understanding of supraspinal, cortical changes in children with chronic pain (Steck, 2016). Plasticity, or change in responses to various stimuli or experiences is also essential in human development (Hoffnung, 2019; Steck, 2016). Functional Magnetic Resonance Imaging (fMRI) has allowed exploration and comparison of the functional communications within cortical regions in children with a current CRPS diagnosis and after symptom recovery (Linnman et al., 2013).

Four studies that met the inclusion criteria for this review used fMRI to investigate neurobiological circuits in children with CRPS. Each study concurrently reported evidence for cortical reorganisation (Erpelding et al., 2014; Lebel et al., 2008; Linnman et al., 2013; Youssef et al., 2019) and grey matter atrophy (Youssef et al., 2019) with CRPS.

Collectively the studies suggest brain plasticity and changes in the developing brain structure (Hoffnung, 2019) in response to children's experience of pain. Substantial alteration of sensory, motor, emotional, cognitive and descending controls have similarly been identified in paediatric CRPS fMRI studies through measurements of Blood-Oxygen-Level-Dependent (BOLD) signals⁶ (Youssef et al., 2019). It is unclear how alterations in these neurological factors might impact on children in terms of their influence on chronic pain trajectories, or, indeed, on their functional development, although they are acknowledged as important contributors to children's development and learning (Bergen, 2008; Steck, 2016).

Children included in three of these studies had an average pain duration of 13.3 (Lebel et al., 2008), 15 (Youssef et al., 2019), and 13 months (Erpelding et al., 2014). The authors of one study, Linnman et al. (2013), did not state their participants' CRPS pain duration. Children in all four studies were all recruited from tertiary or specialist care settings. It is unknown, therefore, if the included studies' findings would be similar at an earlier period of chronicity, say three month-mark of defined chronicity. Due to the relative

⁶ Blood-Oxygen-Level-Dependent (BOLD) signals measure the levels of functional connections between brain or cortical regions through visualising haemodynamic alterations inducing changes in the magnetic fields (Gatchel et al., 2007).

uniformity of the diagnoses in the four included studies, it is also unknown if these results are relevant for the wider childhood chronic pain population, or just CRPS populations. Therefore, the wider applicability of these findings should be utilised with caution.

The four included studies that focused on the neuro-biological influences on the paediatric CRPS population (Erpelding et al., 2014; Lebel et al., 2008; Linnman et al., 2013; Youssef et al., 2019) also linked the 'physical' diagnostics of fMRI to the earlier psychological risk factors reported in this review's findings sections above. For example, reduced BOLD signals in the anterior cingulate cortex (ACC), middle cingulate cortex and parietal cortex highlighted issues with descending pain inhibition, changes in sensory processing and increased pain catastrophising (Erpelding et al., 2014; Lebel et al., 2008; Youssef et al., 2019). The habenula thalamic brain region is a main relay region for pain processing, stress responses, sleep-regulation, analgesia, reward-punishment and affective conditions such as anxiety and depression (Erpelding et al., 2014). Children with CRPS also showed reduced functional connectivity of the habenula, motor control and movement brain regions compared to controls. This was proposed to be due to limb disuse over time or a CRPS related dysfunction in movement planning. Furthermore, reductions in resting state functional connections between the habenula and affective and pain inhibitory systems were reported (Erpelding et al., 2014). Such neurobiological findings lend support to findings about negative influences of psychological factors, but also provide some initial insights into neurological contributors underlying the relationships.

Erpelding et al.'s (2014) findings of connectivity reductions in the habenula and motor areas contrasted with an earlier study where increases in connectivity were noted in the posterior and anterior cingulate cortex and the temporal lobe, with stimulation of the affected limb of participants compared to stimulation of their unaffected limb. Such increases were apparent in both symptomatic and recovered CRPS participants (Linnman et al., 2013). BOLD signal increases have also been reported between the primary somatosensory cortex and the thalamus both in the symptomatic and recovered CRPS groups (Lebel et al., 2008; Linnman et al., 2013). These findings suggest relative longevity

of structural cortical changes and connectivity patterns after symptom resolution (Lebel et al., 2008; Linnman et al., 2013). Mechanisms proposed for this persisting increase in connectivity included learning processes from the trauma of CRPS symptoms and ongoing nociceptive recognition (Linnman et al., 2013). However, no known studies in children have ascertained the period of time over which these connective changes resolve. In our included studies the cortical modifications were still present in varying periods post symptom recovery (Lebel et al., 2008; Linnman et al., 2013).

Specific cortical regions that show BOLD signal changes are believed to be directly linked to affective and behaviour adaptations associated with childhood chronic pain. In children with CRPS, the anterior cingulate cortex (ACC) and postcentral gyrus (PCG) cortical regions showed hyper-connectivity BOLD signal alterations to multiple sensory, emotional and cognitive processing regions (Lebel et al., 2008; Linnman et al., 2013). Evidence of these heightened connections lends unique insights into, and support for, the interrelationships amongst biological, psychological and social processes in CRPS pain responses. For example, BOLD signal connectivity was reported to be higher between the thalamus and ACC with increased uncertainty or fear of pain. The amygdala, which is thought to be linked to conditioned fear and associated stimulus uncertainty, showed transient increased connectivity in BOLD signal analysis to the PCG (Linnman et al., 2013).

Conversely, decreased BOLD signals in children with symptomatic CRPS, compared to post-recovery measurements, suggest cortical changes affecting pain inhibition, limb neglect and integration of sensory information (Lebel et al., 2008). Lebel et al. (2008) found BOLD signal decreases in frontal and parietal lobe regions associated with cognitive and emotional control of inhibitory pain processes. Additionally, Erpelding et al. (2014) found lower connections between habenula thalamic regions and the ACC, potentially linking CRPS states and areas with roles in pain inhibition, modulation and control (Erpelding et al., 2014). Furthermore, grey matter density was found to be decreased in the right ACC region in resting states, in absence of painful stimuli in children

with CRPS (Youssef et al., 2019). Youssef et al. (2019) reported prevalent grey matter atrophy in general sensory-emotional, motor, cognitive and sensory-descending modulating brain regions, and a high degree of plastic cortical reorganisation was described in the thalamus connections. Since the thalamus is a main relay station for ascending sensory neural connections, these structural alterations would likely have implications for various brain region connections and heightened pain responses (Erpelding et al., 2014; Youssef et al., 2019). So, the trajectory of chronic pain might be affected by early cortical changes, but it cannot be ascertained how early these changes may begin to take place. Furthermore, the lack of current evidence of any resolution of cortical modifications makes it difficult to draw conclusions as to how these changes might reflect or influence the early trajectory of chronic pain in children.

Two of the fMRI studies included used cross sectional methods (Erpelding et al., 2014; Youssef et al., 2019). Cross-sectional evidence of fMRI studies with case controls creates multiple questions regarding the reliability of the conclusions. Due to the 'snapshot' nature of cross-sectional methods, pain-related and developmental changes in brain structure and connectivity over longer periods of time are unable to be ascertained. Future studies might usefully adopt prospective case control methodology with several fMRI data sets of a child over an extended period of their development or chronic pain experience. This will likely provide a depth of information to shed more light on the linkages of physical and cognitive development with the biopsychosocial factors influencing the early trajectory of chronic pain. Although it has been recommended information from fMRI studies be applied cautiously, the body of research is building, and findings are consistent with studies into psychological factors (Gatchel et al., 2007).

Currently, however, there is limited research in children exploring how the psychosocial factors associated with acute pain or early chronic pain might influence the plastic changes in the associated brain regions and resting state networks. Further research is also needed to establish the neurobiological changes throughout the typical

timeline of multiple chronic pain conditions and whether these factors are causative or predictive of the onset and early trajectory of chronic pain conditions. An understanding of the neurobiological changes across the chronic pain trajectory, and at different stages of children's development will enable a basis for quality clinical guidelines and treatment pathways to be established.

Development of Children's Understandings About Their Pain

Neuropsychological developmental theory suggests that children's understandings of their pain and the way they adapt and regulate their responses will not be static but will relate to the stages of their cognitive development. Progressions in children's executive function may be of particular relevance, with development of insight, the ability to think and reason in abstract, and self-regulation skills building throughout childhood and into adolescence (Anderson, 2002; Best & Miller, 2010). Whilst quantitative studies in this review provided information about affective, sleep and trauma factors that influenced the onset and trajectory of children's chronic pain, few of those studies specifically explored these influences from a developmental perspective. However, a small number of qualitative studies highlighted the importance of considering age-related influences on children's ability to understand their pain experiences, and these are discussed next.

Perhaps responding to concerns over children's understandings, it is parents who are regularly addressed in medical encounters (Carter, 2002). However, qualitative research has found that children feel that they can contribute to discussions regarding their pain (Carter, 2002; Dell'Api et al., 2007). Moreover, in an Australian, qualitative study, children with chronic pain, aged 8-12 years, were able to reflect on their own experiences to describe the concept of pain. When observing vignettes, the children were able to focus more on the psychological, emotional and social impacts when describing pain, compared to pain-free controls (Pate et al., 2019). Their greater appreciation of psychological, emotional and social impacts suggests that children this age were able to learn and

reason, applying information from their experiences to gain insight into others' pain experiences (Pate et al., 2019).

Pate et al. (2019) conceptualised the main themes and influences on children's understandings about pain. Data were analysed from 16 children aged 8-12 years, eight with persistent pain, and eight without pain. The study findings are displayed in a diagrammatic pain puddle, depicting the child's concept of pain and the multitude of factors, including personal factors that 'feed' this puddle. Findings suggest that children aged 8-12 years do have understandings about the concept of pain. From a cognitive developmental perspective, these understandings are an important influence, because they have implications for the way in which to provide education and interventions for children with chronic pain, or to children who have not yet developed chronic pain. Although Pate et al. (2019) did not utilise any formal developmental theories in their conceptual framework, the methodology and age-related analysis of their participants did conceptualise pain understanding and the way a child constructs their concept of pain. Age related differences in children's ability to account their knowledge about pain were acknowledged. However, it is unclear how well younger children would understand or be able to talk about abstract pain concepts. Of note, many children had difficulty communicating about the emotional aspects of pain. However, it was only the children with pain who had learned cognitive strategies to manage their pain (Pate et al., 2019).

The findings from Pate et al's (2019) study highlight the importance of experiential learning about pain. This type of learning has significant implications for practitioners managing the onset or early trajectory of chronic pain and the importance to provide appropriate education to children and their family early so that experiences do not negatively shape learning about pain.

In this section, the factors that influence the onset and early trajectory of childhood chronic pain were drawn together and critically analysed. Often, it seems that factors might be associated with or result from chronic pain, but that their direct influence is less clear. While critiquing the factors with a developmental lens, it is apparent that childhood

development influences childhood pain in multiple dimensions. These developmental factors will be discussed in conjunction with biopsychosocial influences in the following chapter along with their implications for primary healthcare practice.

Chapter 4: Discussion

This integrative review aimed to draw together and critically analyse the existing research relating to the biopsychosocial factors influencing chronic pain onset and early trajectory in children aged 5-11 years through a childhood developmental lens. Chapter 3 provided an in-depth synthesis of the current research literature. The literature has been critically discussed in relation to key developmental theories, including social learning theory, sociocultural developmental theory and neuropsychological and neurophysiological developmental theory.

The relationship amongst biopsychosocial influences and developmental theories in childhood chronic pain has been given limited consideration in the current literature, with a lack of information to inform practitioners in primary care settings about the onset and early trajectory of chronic pain, particularly for younger children. This review is innovative in its use of systematic methods to search for, screen and analyse this literature, and in its critical discussion of information both from a methodological perspective and in light of developmental theories. The empirical research in the review does not provide an adequate framework or unified evidence to guide developmentally appropriate clinical management in early chronic pain trajectories for children. Nonetheless, the review findings provide an initial basis to inform practice for a range of health care professionals working with younger children with pain conditions in primary healthcare. To our knowledge, this is the first study to integrate information about biological, psychological and social influences with childhood developmental theories in relation to childhood chronic pain.

In this final chapter, the clinical importance of conceptually integrating developmental theory with the various biopsychosocial components involved in the onset and early trajectory of childhood chronic pain will be discussed. The implications of the review findings for primary healthcare practice will be explored, highlighting the importance of quality, child and family-centred interactions in positively improving the early trajectory of childhood chronic pain. The practical implications of the influences on childhood chronic pain are considered in primary healthcare. The various biopsychosocial factors are woven together to

portray the complexities of the evidence and the indeterminate influences on childhood chronic pain. Finally, limitations of this current review and suggestions for future research are presented.

The Utilisation of the Biopsychosocial Model in Children's Chronic Pain Research

Framed by the biopsychosocial model (Engel, 1977), this integrative literature review draws together and provides insights into the current literature about childhood chronic pain. Diverse biopsychosocial aspects, such as psychological factors (both positive and negative), parental impacts, sleep quality, trauma history, stress and neuro-biological factors, notwithstanding temporal factors such as age at onset and pain duration, were suggested as having potential to influence chronic pain onset and early trajectory in children. Limitations were evident in the research where, for the most part, various biological, psychological and social factors were researched as discrete influences rather than considering the involvement of multiple, interactive forces (Alonso, 2004). Addressing this would require researchers to consistently gather knowledge about the full range of factors that are involved, and to examine the influences and their interactions and effects using multivariate analyses (Tilson, 2017). This could be done with a prospective study over time, or at a single time point, but with a large sample involving different age groups. The predominant use of cross-sectional methodologies with relatively small samples, or where a range of ages were not included, could not fully inform us to the influence of developmental changes in the factors over time.

The biopsychosocial model has served well as a basis for generating evidence about adult chronic pain. But this review suggests that for children, a more nuanced, developmentally informed view of the influences may be appropriate. Nonetheless, the extensive range of biopsychosocial factors revealed in this review highlight the importance of

a holistic acknowledgement of all factors by healthcare practitioners and researchers alike for a child and family-centred approach to chronic pain.

The Utilisation of Cognitive Development Theories in Children's Chronic Pain

Research

Sociocultural developmental theory and social learning theory were utilised in this review to provide insights into the ways social and cultural contexts of learning and development might be associated with the influences on children's chronic pain. Additionally, neuropsychological developmental texts were integrated to provide a foundation for understanding how development of executive function, resilience, prospection and self-regulation (Anderson, 2002; Best & Miller, 2010; Goldstein & Brooks, 2013; Powell & Voeller, 2004) might relate to children's chronic pain experiences (refer Appendix B). Whilst these developmental influences received limited discussion or acknowledgement within the included studies, it is important to consider that such factors may have been reflected in the study findings.

In 2020, the ISAP modified their definition of pain to further highlight the social and experiential learning contributors to a pain experience. Sociocultural and social learning theory suggest children's learning about how to respond to pain evolves and changes. Learning develops through problem solving and support from others (Koenig & Sabbagh, 2013; Miller, 2016; Vygotskiĭ, 1978), and by observed learning and appraisal of situations, emotions and social interactions (Bandura, 1986, 2003; Miller, 2016; Smith, 2013). From this learning come complex and increasingly advanced abstract thinking and insight into one's own and other's behaviours (Miller, 2016; Smith, 2013). Some studies provided valuable insights into parental influences on children's learned responses to pain (Akbarzadeh et al., 2018; Birnie et al., 2020; Dell'Api et al., 2007; Sieberg et al., 2011), including factors such as affirmations, behaviours, functional disability and coping strategies.

Whilst a small number of the studies usefully analysed children's age as a factor in their chronic pain (Birnie et al., 2020; Dunn et al., 2011; Kanstrup et al., 2014; Lynch et al.,

2007; Pate et al., 2019; Perquin et al., 2000; Sinclair et al., 2020), analysis of the age-related data relied, for the most part, on broad age-group means. Further, many studies involved largely adolescent populations. Cross-sectional methodology as used in the majority of studies in this review, whilst providing insights into relationships amongst variables at a particular time point for some broad age groupings, is less suited to explain the way children's understandings of and responses to chronic pain change as they grow and learn (Tilson, 2017). In these ways, many of the studies showed limited understanding or neglect of the periods of change and variability that occur within a child's development.

Another key critique of the included studies in this review was the clear lack of consideration of the cognitive developmental differences between a young child, an adolescent and an adult (Bergen, 2008; Best & Miller, 2010). Analysis of children's cognitive skills, essential to learning, were only present in a small number of studies (Lynch et al., 2007; Pate et al., 2019). Such factors are important in consideration of how they might support a child's understanding of their pain and shape their responses to pain over their development and the pain trajectory. Greater knowledge of child cognitive and neuro-biological development could inform age-appropriate treatment methods, and are required to empower clinical applications and improve children's pain experiences.

Primary Healthcare and Practice Implications

The reasoning for the focus of this review to be on onset and early trajectory of chronic pain in children was two-fold. Firstly, my physiotherapy practice is based in a primary healthcare setting, predominantly working with children with acute or early in the trajectory of chronic pain. Secondly, as with the role of primary healthcare, our focus should be on prevention or early, quality interventions with aim to avoid chronicity or severity of disease processes (*The Primary Health Care Strategy*, 2001). The prognosis of chronic pain is thought to be determined from initial treatment effectiveness (Simons et al., 2018; Wager et

al., 2019; Zernikow et al., 2018), where primary care is the most common initial contact (Mallen et al., 2007).

This synthesised research in this review suggested affective factors, parental influence, post-traumatic stress and sleep showed some association or influence on childhood chronic pain. However, there are various methodological limitations present within a large portion of the studies. These may limit the internal validity and the broader generalisability of the findings to the wider, clinical, childhood chronic pain population. Specific limitations included the predominance of tertiary and specialist pain centre settings with children who had longstanding durations of their pain. Additionally, much of the research was with adolescents. The research in the review is, therefore, limited in its ability to inform primary healthcare practitioners about factors that should be considered in the onset and early trajectory of chronic pain in younger children. Whilst treating the study findings cautiously due to methodological limitations, the information indicates a need for primary care practitioner understanding that pain is experienced through physical, psychological and social realms, all needing to be appropriately managed for successful outcomes (Gatchel et al., 2007). Treatment of a single causative factor is unlikely to be successful (Malleon et al., 2001).

The review findings also suggest that a child with pain that is continuing beyond 3 months, or beyond expected tissue healing time, should be examined by gaining a thorough history, including obtaining information about psychological factors, functional disability, sleep quality, stress and trauma history. Information should be gathered in a way that recognises the child's level of cognitive development (Hoffnung, 2019; Sandberg & Spritz, 2010; Smith, 2013), and how their cognitive development might relate to their pain responses (Feinstein et al., 2017; Pate et al., 2019). Furthermore, children should not be assessed in isolation. The relationship of parental global health, parental catastrophising and protective behaviours on a child's pain interference needs consideration (Birnie et al., 2020; Sieberg et al., 2011). In this way it is also important to explore any family history of pain and family understandings about pain. Drawing together specific expertise from a wider

interprofessional team, particularly psychology practitioners, but also clinicians experienced in paediatrics early in the pain trajectory would support such assessment. Practitioners in primary care settings would benefit from assessment and intervention guidelines, informed by research into biopsychosocial influences and relevant developmental knowledge to positively influence or interrupt children's chronic pain trajectories.

Listening to children's stories enables an understanding of their environment and their pain (Carter, 2004). Children feel that they can contribute to healthcare interactions regarding their pain (Carter, 2002; Dell'Api et al., 2007) and have understanding of the concept of their own pain (Pate et al., 2019). Since pain is a personal experience (Hinton & Kirk, 2016), it should be the child that is addressed in a primary healthcare consultation, whilst acknowledging the significant social support and information from parents and caregivers. Furthermore, awareness of factors such as miscarried helping (Fales et al., 2014) and variances between mothers and fathers reports of their child's pain intensity, depression and anxiety (Akbarzadeh et al., 2018). Healthcare interactions are also part of a child's experiential learning about their pain experience (Dell'Api et al., 2007; Pate et al., 2019). Consultation in primary healthcare may draw on the opportunity to educate the child and their relevant social network, at cognitively appropriate levels, about the factors that can influence the child's pain experience and strategies that can be used. Parents may benefit from support in their interactions with their child (Noel, Beals-Erickson, et al., 2016). Furthermore, younger children's difficulty with the abstract concept of pain should also influence education approaches (Pate et al., 2019).

A consistent pattern of childhood chronic or reoccurring pain can negatively influence endogenous pain modulation into adulthood, creating a lifelong pain influence (Bhatt et al., 2019; McClain & Suresh, 2009; Tan et al., 2009). Within this review, both Lebel et al. (2008) and Linnman et al. (2013) showed BOLD signal variations equally in symptomatic and recovered child participants with CRPS. It is currently unknown how long these cortical network connectivity changes persist (Lebel et al., 2008; Linnman et al., 2013) and whether they are present in other chronic pain conditions. However, wider

research reporting pain conditions that commence as a child (Hassett et al., 2013), and that remain in adults following childhood pain, it is possible that resolution of these changes does not occur. Consistent with developmental neurological change processes (Steck, 2016), children appear to have greater capacity for plasticity of their pain responses than adults (Campos et al., 2011; Jan et al., 2010). It is unknown at this stage, however, if this more modifiable response is due to sensitive periods of development (Fine & Sung, 2014; Kuh et al., 2003). Alternatively, children's responses may reflect developmental differences in engaging descending inhibitory pathways and modulating techniques (Bhatt et al., 2019; Feinstein et al., 2017). It is also unknown whether children experience earlier chronic pain cortical changes (Campos et al., 2011). Therefore, quality, primary healthcare interventions and interprofessional team involvement at the onset and early trajectory of chronic pain should be a healthcare priority to prevent negative long-term changes. Further evidence is required into how to address factors in acute pain episodes to prevent the onset of chronic pain, or interrupt its trajectory in the early stages.

As a result of this review, outcomes can be drawn together to inform practitioners on how to optimise primary healthcare input with children presenting with chronic pain. Holistic and early healthcare delivery, acknowledging the complex interactions of the biopsychosocial factors and childhood development impacts influencing chronic pain trajectories are essential.

Psychological Influences of Childhood Chronic Pain and Practice Implications

Avoidance of pain and the perceived dangers of pain is a defence behaviour linked directly to survival (Hadjistavropoulos et al., 2011; Hermann et al., 2008) and is likely influenced by the acquisition of credible evidence that pain is a significant threat. Child participants in the studies in this review struggled to move their attention away from a potentially threatening stimulus (Zohsel et al., 2008) and were more perceptive to all aspects of pain (Soltani et al., 2020). Pain responses were found to be anticipatory rather than sensory (Flack et al., 2017), indicating higher central processes involved with pain

interpretation. Both sociocultural and social cognitive theories are implicated as relevant influences of fear avoidance and attentional biases through past experiences, observations and constructed learning practices. Children are likely to acquire how to respond to the experience of pain, the fear of this unpleasant sensation and acquire the skills of inhibitory pain control, management and understanding through structured learning and observations (Bandura, 1986, 2003; Bergen, 2008; Miller, 2016; Turner-Cobb, 2014; Vygotskiĭ, 1978). Key findings from an earlier review by Evans et al. (2008) showed children with pain were more likely to have observed their parent in pain and then model those precise behaviours in their own pain experience (Evans et al., 2008). This contention was supported by the studies included in the present review with several studies reporting the co-occurrence of parental and child chronic pain (Kashikar-Zuck et al., 2010; Pas et al., 2019; Wager et al., 2019).

From a social learning perspective, it is possible that pain catastrophising (Dell'Api et al., 2007; Libby & Glenwick, 2010; Weiss et al., 2013) and fear-avoidance behaviours (Beeckman et al., 2020; Flack et al., 2017; Heathcote et al., 2017) communicate children's uncertainty and reflect their prior observations of others in pain. In terms of effective practice, catastrophising and fear avoidance might usefully be reconceptualised as worry or anxiety, and searching for reassurance and understanding from parents and healthcare professionals (Levy et al., 2007).

This review also found that children were more perceptive to pain displays and had difficulty realigning their attention from a potential painful sensation (Soltani et al., 2020; Zohsel et al., 2008). Flack et al. (2017) concluded that children's attention bias and avoidance behaviours towards pain were anticipatory rather than reactive to the sensation. Therefore, primary healthcare providers should seek to understand what fears are creating anxiety, catastrophising or avoidance behaviours. Pain education and reassurance should be main focuses of interventions with children presenting with heightened attention to pain. The review equally suggested a number of factors that could support positive outcomes (Beeckman et al., 2020; Libby & Glenwick, 2010). Psychological flexibility and the ability to cognitively shift attention elsewhere positively mediated goal orientated behaviours,

decreased depression symptoms and reduced functional disability (Beeckman et al., 2020). However, these are skills that may not have been attained by young children (Best & Miller, 2010). Additionally, self-efficacy, and the ability of the child to believe in their ability to overcome adversity (Bandura, 2003), may positively influence pain attention (Soltani et al., 2020; Zohsel et al., 2008), avoidance (Beeckman et al., 2020), pain-related fear (Flack et al., 2017; Heathcote et al., 2017; Pas et al., 2019), depression and stress (Bayle-Iniguez et al., 2015). Intercepting attention bias and avoidance behaviour whilst enhancing psychological flexibility and supporting engagement in achievable and valued activities may be viable strategies to positively influence chronic pain trajectories in primary health care practice. Implementing such strategies would benefit from an interprofessional approach in working with children, parents, teachers, and healthcare practitioners with expertise in these areas. However, it is important to acknowledge, the skills of psychological flexibility, sensory modulation and resilience reflect neuropsychological development of executive functions (Best & Miller, 2010). Therefore, developmentally appropriate interventions should always be considered in conjunction with a child's social support systems to promote skill development (Lynch et al., 2007; Maciver et al., 2010).

Stress, Pain Trauma and Poor Sleep Influences on Childhood Chronic Pain and Practice Implications

A number of studies in this review provided insights into the relationships of stress, trauma and sleep, with pain sensitivities and affective symptoms in childhood chronic pain presentations (Bayle-Iniguez et al., 2015; de Tommaso et al., 2017; Kanstrup et al., 2014; Konijnenberg et al., 2005; Noel, Wilson, et al., 2016; Pavlova et al., 2020; Pearson et al., 2011). All these factors showed similar associations with pain and all potentially required intervention. Shedding light on factors that might particularly contribute to the onset of chronic pain, such as family conflict, a father's military deployment, death of a close family member, school issues and sexual abuse were reported as preceding children's pain presentations (Bayle-Iniguez et al., 2015; Noel, Wilson, et al., 2016; Pavlova et al., 2020;

Pearson et al., 2011). However, these studies only provided emerging insights into the association between prior trauma or stress and the development of chronic pain conditions.

The stress effects of sleep duration and frequent waking were reported within this review and related to pain intensity, pain interference and affective symptoms (Kanstrup et al., 2014; Pavlova et al., 2020). Furthermore, decreased sleep duration has been proposed to increase central sensitivity in children with migraines (de Tommaso et al., 2017).

Periods of sustained sleep deprivation are known to create systemic stressors on the body and to impact long-term development of children (Jan et al., 2010; Lewandowski et al., 2010).

Optimal development, cognitive function and overall health are associated with 10.2 hours of sleep for 6–12-year-olds (McLaughlin Crabtree & Williams, 2009), whilst sleep duration of less than 6.5 hours has been defined as extreme deprivation for youth (Lewandowski et al., 2010).

Wider, adolescent chronic pain literature indicated that 52% of adolescents with various chronic pain conditions reported less than 6 hours sleep and pain was specifically associated with time awake after sleep onset (Lewandowski et al., 2010).

Furthermore, this review noted bi-directional relationship between childhood pain and sleep (de Tommaso et al., 2017; Kanstrup et al., 2014; Konijnenberg et al., 2005; Pavlova et al., 2020) disturbances originally theorised by Lewin and Dahl (1999). Yet, the

understanding of general sleep deprivation in younger children, its links with sustained trauma or pain, and implications for children's development pathways remains limited (Jan et al., 2010). Education on the importance of sleep, and interventions to modify sleep behaviours may be beneficial in the early stages of chronic pain trajectories in children.

Further, interventions to limit the systemic stress of sleep deprivation may influence central sensitisation (de Tommaso et al., 2017), functional disability and depression symptoms (Kanstrup et al., 2014; Pavlova et al., 2020).

Broadly, persistent or recurrent pain may be influenced by prior stress and trauma, but may also be considered a foundation of stress and trauma. Recurrent pain experiences, of all intensities and associated levels of functional disability, are types of

'micro-traumas' (Kao et al., 2017). Trauma in children is defined as "events and conditions in which the child experiences or repeatedly experiences, in a prolonged and uncontrolled manner, circumstances that they perceive as being likely to be significantly life-threatening for themselves" (Delima & Vimpani, 2011, p. 43). Catastrophising behaviours, excessive pain attention bias, including to benign threats, reported in this review (Flack et al., 2017; Heathcote et al., 2017; Soltani et al., 2020; Zohsel et al., 2008) could, conceivably, reflect recurrent trauma for a child. Furthermore, Dell'Api et al. (2007) reported that children whose pain remained unexplained were more likely to interpret their pain as life threatening, in line with the definition of trauma.

Neural plasticity or reorganisation of cortical networks is an essential human process to adapt and adjust to various environmental demands. Activation of stress-response systems is normal to brief adversities. However, sustained trauma or stress on a developing child during critical periods sensitises the body's stress-response system (Delima & Vimpani, 2011; Fine & Sung, 2014; Zilberstein, 2014) and can lead to long-term maladaptive functioning with sustained or recurrent adversities (Fine & Sung, 2014; Zilberstein, 2014). It is understood that the modulation of distress and the experience of pain are mediated by similar central cortical processes (Kao et al., 2017; Landa et al., 2012). Chronic pain could be regarded as a type of PTS, through hyperarousal symptoms and overwhelmed stress responses (Kao et al., 2017), all relating to sustained trauma to the developing brain. Supporting this contention, various brain regions associated with processing fear, catastrophising, sleep-responses, affective conditions, reward-punishment, uncertainty and descending pain modulation were shown to have connectivity changes compared to healthy peers (Erpelding et al., 2014; Youssef et al., 2019). Furthermore, the timeline for any resolution of these cortical modifications has not been established with changes remaining after CRPS symptom resolution (Lebel et al., 2008; Linnman et al., 2013). It is imperative that this neurophysiological stress-response system and potential adaptations are understood by practitioners providing care in the onset and early trajectory of chronic pain in children. Psychological interventions to manage stress or

trauma in relation to pain in this early stage have potential to reduce long-term maladaptation in pain-stress-response networks.

This review reported emerging evidence of the influences of stress, trauma and sleep disturbances on chronic pain in children. Yet, more evidence is required to enhance our understanding into these associations. Greater understanding is important as children's developmental trajectories are at risk when stress or trauma influences their ability to manage their daily tasks (Smith, 2013) and this is plausible for periods of childhood chronic pain. Adolescents have greater cognitive and modulatory skills for managing traumatic experiences (Zilberstein, 2014). This is consistent with understandings of the development of executive function and refinement in adolescence (Best & Miller, 2010). Whereas, younger children, the focus population of this review, are likely at greater risk for increased aversive cortical adaptations to trauma (Zilberstein, 2014) or chronic pain (Bhatt et al., 2019). The increased application of fMRI has allowed the identification of even small neurobiological changes compared to healthy participants and can be utilised to further inform research in this field in relation to chronic pain (Bhatt et al., 2019). Whilst the majority of trauma-based research in children is focused on neglect, violence and abuse, (Delima & Vimpani, 2011; Shrivastava et al., 2017; Zilberstein, 2014) further research is required to ascertain whether recurrent or chronic pain in childhood has similar lifelong neurobiological developmental effects.

Parent Factors and Family-Centred Care in Practice with Childhood Chronic Pain

Consistent with sociocultural and social learning theories, this review highlighted that parents are central mediators of children's pain responses, suggesting that at least some of the responses are learned (Akbarzadeh et al., 2018; Birnie et al., 2020; Sieberg et al., 2011). However, the review also found that the relationships between parents and children's

chronic pain were complex, and, at times, bidirectional; for example, the influence of pain on the wider family was also identified in the review.

It is established in the wider literature, as well as in the studies in this review, that family history of chronic pain can influence childhood chronic pain (Kashikar-Zuck et al., 2010; McKillop & Banez, 2016; Pas et al., 2019; Wager et al., 2019), yet the mechanisms of such transition are recognised as complex and unclear (Dario et al., 2019; McKillop & Banez, 2016). Of importance clinically, parents who have chronic pain are more likely to seek healthcare interventions for their children for pain related complaints (Clementi et al., 2019). Several of the reviewed studies discussed the co-occurrence of parental chronic pain and their child having chronic pain (Kashikar-Zuck et al., 2010; Pas et al., 2019; Wager et al., 2019). If parents are hypervigilant to their children's pain due to their own experiences, the potential for reinforcement of child pain behaviours can be appreciated through socio-cultural and social learning theories (Bandura, 1986, 2003; Miller, 2016; Vygotskiĭ, 1978). Parents may establish particular cultural behaviours around management of pain, for example, assisting a child in avoiding activities to avoid further pain (Walker et al., 2002) or being hypervigilant in attending to their child's pain (Sinclair et al., 2020).

Parents can, through teaching behavioural responses and modelling, increase a child's functional disability. Conversely, parents can provide the required support for modification of pain behaviours and recovery (Maciver et al., 2010). It is essential that parents are not blamed by practitioners for their child's pain (Maciver et al., 2010). However, educating family networks of the influence of a parent's responsiveness is a potential management intervention in primary healthcare.

It is plausible that parental protective behaviours and pain-related stress are an adaptive response to their child's suffering, and feelings of failure to fix their child's pain (Carter, 2002; Maciver et al., 2010; Vasey et al., 2019). Healthcare professionals should be acutely aware of the multifaceted relationship between parental pain related stress (Birnie et al., 2020; Sieberg et al., 2011), reinforcement of child pain through increased parental attention and parental catastrophising thoughts (Akbarzadeh et al., 2018) and wider

sociocultural and social learning theory influences (Bandura, 2003; Miller, 2016; Vygotskiĭ, 1978). Furthermore, the contention of miscarried helping, where a child becomes more resistant to support (Fales et al., 2014) and gender influences of parent reports their child's symptoms (Akbarzadeh et al., 2018) requires insight in healthcare interactions.

Parent pain-related stress, and their catastrophising, helping and protective behaviours was found to be key influences on child pain interference (Birnie et al., 2020; Sieberg et al., 2011). Therefore, a key role of healthcare professionals is to ensure that assessment and subsequent interventions are aligned with reducing parental pain-related stressors. However, the review findings also point to the need for practitioners to support parents to gain insight into their own responses, and to learn positive strategies they can, instead, adopt to support their child's adaptation and function.

Parent pain responses in terms of how to feel and respond to pain, and the potential of reinforcement of pain are delicate, but potentially modifiable factors (Evans et al., 2008). Parents should be encouraged to actively contribute to educating children on pain and assisting in their rehabilitation (Finley et al., 2014), however, also need to be appropriately educated and reassured to enable this process. It is essential that healthcare professionals create positive development and learning opportunities for both children and parents in initial primary care interactions to positively influence the long-term trajectory of chronic pain (Wager et al., 2019).

Future Research

Research into childhood chronic pain remains in its infancy. There is limited research investigating pain interpretation or pain experience in relation to age or cognitive development, especially in pre-adolescent children. As a result of this review, it can be seen that childhood pain researchers need to embrace the complexity of childhood development to assist in establishing robust practice guidelines. A formal interplay between research and developmental theory is required to urgently advance our clinical knowledge in this area (Huguet et al., 2011). Once models are established in empirical research, treatment

applications need to be explored through evidence-based practice models (Davies, 2011). However, the complexity of an individualised, developmentally informed, biopsychosocial treatment approach needs to be explicitly acknowledged for practical applications.

Of urgent importance is creating a standardised method where chronic pain is defined (Lewandowski Holley et al., 2017). Within this review, chronic pain was defined as a duration of 3 months or longer, as per the ICD-11 definition (Treede et al., 2015). However, many studies were excluded from this review due to the requirement of this definition in the primary study methodologies. A global definition of chronic pain, clear definitions and further validation of outcome measures for children with chronic pain (McKillop & Banez, 2016), will allow uniformity of research methodologies to allow more succinct and systematic analysis of childhood chronic pain influences.

The current lack of longitudinal prospective studies creates a current gap in knowledge. The predominance of smaller, cross-sectional and small, 'snap-shot' methodologies does not allow an adequate causative understanding of childhood chronic pain trajectories. Future studies need to ascertain whether chronic pain conditions and central cortical changes resolve, whether there are variances in psychological influences with increased chronicity, and therefore, establish conclusive timelines for intervention effectiveness. Information is particularly lacking in relation to the onset of chronic pain in children aged under 12, and their early pain trajectories, with much of the current information focused on those with well-established chronic pain diagnoses. This gap in the research suggests a need for research in primary healthcare settings, in the early stages of children's pain conditions. Longitudinal prospective research methodologies would allow research to adopt the construct of the biopsychosocial model combined with developmental theories, providing analysis of participants changes over time. Moreover, within longitudinal studies, it will be important to gather and analyse full information, not

only about the child, but also about temporal features of the pain, the family, and wider contextual variables such as interventions provided, and participation in school.

Neuroscientific research to date has advanced the understanding of pain experience (Steck, 2016). Functional MRI has furthered our recognition that various factors create interpersonal variations to the pain experience (Hadjistavropoulos et al., 2011; Steck, 2016). Psychological, behavioural, cognitive and social influences are mediated by the brain (Hadjistavropoulos et al., 2011; Steck, 2016). Therefore, advancements in neuroscience may aid in linking the non-linear, complex interactions between all components (Steck, 2016). These imaging advances have also shown the longevity of cortical connectivity networks and grey matter adaptations in children with CRPS, which exist long after symptom resolution (Bhatt et al., 2019; Lebel et al., 2008; Linnman et al., 2013). Large, longitudinal studies are required to establish when these cortical changes occur within a chronic pain trajectory, whether these changes are unique to CRPS presentations or multiple chronic pain centralised pain states and what the long-term effects are from the adversity of chronic or recurrent pain in children.

Neuropsychological and neurophysiological literature included in this review suggests that further neuroscientific research might usefully investigate possible sensitive or critical developmental periods in children (Delima & Vimpani, 2011; Fine & Sung, 2014; Steck, 2016; Zilberstein, 2014) that could influence greater pain chronicity, PTSD, pain-related fear or any of the multitude of biopsychosocial factors influencing chronic pain onset or trajectories. Future studies might adopt prospective case control methodology with several fMRI data sets of a child over an extended period of their development or chronic pain experience. Whilst ethical considerations would be paramount, inclusion of fMRI data holds promise for linking understandings of childhood development with the biopsychosocial factors influencing the trajectory of chronic pain.

In this review, only one, higher quality quantitative study examined the influence of early care of chronic pain conditions in children (Wager et al., 2019), despite the understanding of worsening functional outcomes with increased chronicity (Finley et al.,

2014). Evidence about the early stages of onset and initial engagement in primary healthcare settings need to be addressed with more longitudinal prospective studies or life course epidemiological studies (Kuh et al., 2003).

Limitations of the Review

When considering the applicability of this review, it is essential to reflect on the limitations of the data presented and weigh these against the apparent strengths. Although formal quality-appraisal of each included study was not undertaken as part of this integrative review (Torraco, 2016; Whittemore & Knafl, 2005), the studies were considered critically. However, one of the limitations is that the findings of this review are constrained by the quality of studies that were included. There were various methodological limitations present within a large portion of the studies which may limit the internal validity and the broader generalisability of the findings to the wider, clinical, childhood chronic pain population. Key limitations included the emphasis on tertiary and specialist pain centre settings within the included studies and the predominance of older children and adolescents in the samples. These and other identified limitations have been outlined within this review. Therefore, the information presented in the review should be applied with caution to populations of younger children in primary healthcare settings where onset and early trajectory of chronic pain is encountered clinically.

Whilst developmental theories provide valuable insights into childhood learning and cognitive development, they do have limitations. Primarily, theories are just that, assumptions based on beliefs that methodically relate to a phenomenon (Bergen, 2008). For this reason, no one theory should direct our whole understanding of development (Miller, 2016). Within this review the following theories were utilised to provide a developmental lens for analysis of the existing biopsychosocial research. Lev Vygotsky's sociocultural theory (Vygotskiĭ, 1978) and Bandura's social cognitive theory (Bandura, 1986) along with neuropsychological and neurophysiological developmental theories. Tenets from these theories were identified as well placed to inform practitioner knowledge and research as to

children's learning processes regarding pain and behavioural responses to pain experiences. However, various other theoretical views could also have been utilised and could also provide a basis for future practice guidelines.

For a true, holistic assessment of school-aged children, the increasing influence of peers and their interaction with childhood learning should be acknowledged (Davies, 2011; Eccleston et al., 2008). The social influences of peers were not explored within this review, primarily because peer social influences were not reported within the included studies of this younger school-age-group. Peer relationships stimulate development of emotional adjustment and behaviours that are not always possible within a family, due to the unequal social standing of the parent-child relationship (Hoffnung, 2019). Whilst peer social influences have received little attention to date in the research, the review found a small amount of evidence indicating an association between perceived support from friends, levels of distress and chronic pain in children (Finley et al., 2014). The lack of such studies examining peer influences is a potential limitation of this review, as peers are likely a key chronic pain or pain behaviour influences in pre-adolescent children.

As a practising physiotherapist, it is well accepted that establishing the biological, psychological and social aspects of a child's pain is essential for assessment of the condition (Campos et al., 2011). However, our physiotherapy training remains substantially within the physical or biological component, with limited formal training in psychological and social interventions (Driver et al., 2017). On reflection, to enhance the application of holistic, biopsychosocial physiotherapy interventions, learning related to wider, psychological and social aspects of pain should form an important part of physiotherapy programmes. Given the prominence of psychological concerns highlighted for parents and children in this review, the benefits of including a paediatric psychologist alongside physiotherapists as part of an interprofessional team are apparent.

Finally, the initial objective of this integrative review was to provide a basis for developmentally informed practice, to aid in minimising the unnecessary chronicity of childhood chronic pain. However, the current lack of developmentally informed literature and

a focus on discrete of biopsychosocial influences in research was greater than initially envisioned. The use of integrative review methodology, whilst making a useful contribution, may be viewed as a limitation. Linking the diverse and complex interactions of various biopsychosocial factors was challenging. Furthermore, isolating the information to children in an area of research dominated by studies of adolescence added extra complexity. The lack of evidence informed by childhood development theories in the included studies meant limited, research-based developmental information was available to provide a solid foundation for practice recommendations.

However, various implications for practice have been highlighted in Chapter 4. These include 1) an awareness of how a child's cognitive development may relate to their pain responses; 2) recognition of the interacting physical, psychological and social realms of childhood chronic pain; 3) investigating the potential influences of stress, pain trauma and poor sleep negatively influencing neural plasticity; 4) ensuring cognitively appropriate education approaches to both children and parents; 5) consideration of parental global health, parental catastrophising and protective behaviours on a child's pain interference; 6) utilising specific expertise from a wider interprofessional team and; 7) acknowledging the importance of initial treatment effectiveness for childhood chronic pain outcomes.

The conclusions of this integrative review, I hope, will challenge existing researchers and healthcare practitioners to broaden their enquiry into developmental factors, be more aware of the extensive changes across childhood and give the dynamic interplay of the biopsychosocial factor's greater consideration. Whilst the included studies shed some light on the relationships between developmental factors and biopsychosocial influences, this integrative review also promotes the need for further empirical research and guidelines to support effective practice.

Conclusion

This integrative review aimed to draw together and to critically analyse the existing literature about the biopsychosocial factors influencing chronic pain onset and early

trajectory in children through a childhood developmental lens. It integrated and critically analysed existing biopsychosocial empirical research along with developmental theory to build a more holistic understanding of evidence to date, and to provide an overview of practical healthcare applications. Conclusions revealed the urgency for researchers and healthcare practitioners to increase their enquiry into the interactions of childhood cognitive development with biopsychosocial influences of childhood chronic pain. The consequences of childhood chronic pain do not just have an immediate impact on a child's function.

The understandings about what may be developmentally appropriate behaviours, heightened sensitivities at particular developmental stages, and cortical reorganisation are of concern, yet are currently under-researched. This review draws attention to the neglect of developmental theories and understandings about children's developmental changes in relation to the onset and early trajectory of chronic pain.

Younger children's pain is encompassed within continually changing cognitive, physical and affective developmental stages. Children's social and family systems add further complexity to their pain experience. Adopting a conceptual understanding of children's pain in relation to their development would generate evidence that is better placed to inform practice. From a primary healthcare perspective, it is imperative that practitioners have holistic intervention guidelines, informed by latest evidence of biopsychosocial influences and combined with relevant developmental understandings to positively influence or interrupt children's chronic pain trajectories.

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Appendix A

Database Search Strategy of Prevalence of Paediatric Chronic Pain in New Zealand

Database & Sites Searched	Search Terms	Limits Used	Number of Hits	Articles identified with prevalence data
EBSCO Health - Cinahl - Medline	Child* OR pediatric* OR paediatric* OR adolescen* OR youth OR "School age*" or "school-age" OR kid* OR young AND prevalence or incidence or epidemiology or frequency or occurrence AND new zealand or aotearoa or nz AND "persistent pain" OR "chronic pain" OR "complex regional pain syndrome" OR "neuropathic pain" OR "pain syndrome*" OR "secondary hyperalgesia" OR "central hyperexcitability" OR CRPS OR "somatoform pain" OR "unexplained pain"	English Published date All All child; age 0-18; age 6- 12	52	1

Appendix B

Supporting Childhood Development Texts

Assessment and development of executive function (EF) during childhood (Anderson 2002).
Bandura's social cognitive theory: An introduction (Bandura, 2003).
A developmental perspective on executive function (Best & Miller, 2010).
Human development: Traditional and contemporary theories (Bergen, 2008).
Child development: A practitioner's guide (Davies, 2011).
Handbook of resilience in children (Goldstein & Brooks, 2013).
Lifespan development (4th Australasian ed.) (Hoffnung, 2019).
Theories of developmental psychology (6th ed.) (Miller, 2016).
Theories of human development (2nd ed.) (Newman, 2016).
A clinician's guide to normal cognitive development in childhood (Sandberg & Spritz, 2010).
Understanding children and childhood: A New Zealand perspective (5th ed.) (Smith, 2013).
Brain and mind: Subjective experience and scientific objectivity (2nd ed.) (Steck 2016).
Child health psychology: A biopsychosocial perspective (Turner-Cobb, 2014).
