**Title:**  *Perceived Diagnostic Uncertainty in Pediatric Chronic Pain*

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In this review, we argue that perceived diagnostic uncertainty in idiopathic pediatric chronic pain patients and their parents is critically important for understanding pain cognitions, behavioral responses to pain, treatment choices, and outcomes during this developmental period. We include evidence from children (under 12 years) and adolescents (12-18 years). This period sets the stage for future experience of pain: two thirds of children and adolescents with chronic pain will become adults with chronic pain [30]. The prevalence of pediatric chronic pain is rising, and has been described as a growing epidemic [11]. Better understanding of this core issue through well-designed research with pediatric populations is therefore crucial.

***What is diagnostic uncertainty?***

Diagnostic uncertainty is a complex phenomenon, which relates to clinicians’ inability to provide a clear pathological cause and label that explains symptoms and leads to a selection of an intervention to cure a problem. It has recently been defined as a *"subjective perception of an inability to provide an accurate explanation of the patient's health problem”* [1]*.*  However, diagnostic uncertainty can also refer to patients’ perceptions that such a label and explanations are missing, or that the one given is incorrect. While we know little about the factors leading to this perception, the consequences can be devastating to patients, resulting in worry, helplessness, and an elusive and unrelenting search for a cure.

***Diagnostic uncertainty in adults***

Perceived diagnostic uncertainty has been reported in adults, irrespective of diagnoses, explanations, and labels offered by their clinicians. In a recent study, over 40% of patients with chronic back pain reported having received a diagnosis, but also that they believed that there was something else, undetected and serious, causing their pain [27]. In the absence of a clear diagnosis and biological cause for pain, many patients feel that their pain is not legitimate [9] and subsequently, some patients feel guilty [17,22,26], diagnostic uncertainty is associated with emotional distress [6], depression and anxiety [28], disability [6], pain intensity [6,28], and pain catastrophizing [6]. Patients with high diagnostic uncertainty also show a recall bias for negative health-related stimuli, independent of levels of disability and depression [27]. Such biases reflect patients’ pre-occupation with the consequences of their illness and have been associated with poor coping [7,20]. Diagnostic uncertainty in adults often results in a search for a clear or correct diagnosis and/or biological causes, preventing patients from engaging in life fully, and it may place a heavy and unnecessary burden on health services [17,26].

Considering the evidence in adults, which strongly supports an association between perceived diagnostic uncertainty and poorer prognosis and adjustment, the impact of perceived diagnostic uncertainty in children with idiopathic chronic pain and their parents merits investigation. Receiving, understanding, and accepting explanations for pain within different stages of cognitive and social development adds an extra layer of complexity to interactions with clinicians. Parental involvement and influence on pediatric patients’ behaviors, adherence, and self-efficacy to manage their problem complicate matters further. In addition, there is evidence suggesting that the presence of unhealthy beliefs and behaviors in parents is strongly associated with medically unexplained symptoms in their children [4]. This means that there is a need to study perceived diagnostic uncertainty in parents in parallel to their children.

***Diagnostic uncertainty in pediatric pain***

A systematic review of the construct of illness uncertainty in caregivers and youth (including both children, adolescents and young adults) with a variety of chronic illnesses (e.g., asthma, diabetes, medically unexplained symptoms, cancer, cystic fibrosis, rheumatic disease, etc.) found that illness uncertainty was associated with illness distress and poorer psychological functioning [29]. Diagnostic uncertainty in the context of childhood and adolescent idiopathic chronic pain is likely fundamental to the patient and parental experience (e.g., adjustment, acceptance, responsiveness to intervention) of this condition. Nevertheless, this topic has been largely overlooked with the exception of a small number of studies.

The salience of the experience of diagnostic uncertainty was examined in a narrative study of 53 children and adolescents with chronic pain. Children and adolescents reported a sense of doctors being unable to identify and provide an explanation for their pain and associated symptoms that was satisfactory to them [14]. A recent Swedish qualitative study of parents and adolescents who presented with medically unexplained symptoms in the previous 6 months (all of which included unexplained pain) reported that the need for a label and an explanation was, for some parents so overwhelming that they wished that the symptoms were due to a serious pathology [16]. For parents, this would offer more specific care options, and for adolescents, it would provide justification to their peers [16]. Both parents and adolescents reported that the lack of receipt of any medical explanation for their symptoms added additional strain to existing stresses associated with managing their condition and raised difficult questions around the authenticity of the unexplained symptoms. In some cases, fears about lack of legitimacy and justification for pain may be understandable, as health care providers may resort to psychiatric labeling in the absence of clear organic pathways [15].

In a cross-sectional, observational study, Noel and colleagues [18] examined the pain narratives of 46 mothers of children aged between 10-18 with chronic pain at the outset of a problem-solving skills training intervention targeting parent distress. The content and affective tone of narratives was coded for aspects of pain-related vulnerability (negative affect, anger, pessimism) and resilience (positive affect, humour, optimism, benefit finding). Narratives were also coded for the degree to which parents were ‘resolved’ or ‘unresolved’ with respect to their child’s diagnosis of chronic pain [21,23]. A ‘resolved’ orientation was characterized by expressing a change in feelings since the time of their child’s diagnosis; for example, by moving on from the trauma or disorganization and no longer searching for an alternative diagnosis. Conversely, an ‘unresolved’ diagnosis reflected minimal change in thoughts/feelings since diagnosis or a preoccupation with their emotional response since that time. These parents often described ‘being stuck in the past’, actively searching for an alternative diagnosis in the face of contradictory evidence, and believing that their child would grow out of chronic pain. Among parents, all of whom were entrenched within a tertiary level chronic pain (i.e., and therefore had received a diagnosis and engaged in treatment), nearly 40% were ‘unresolved’ about their child’s diagnosis. In other words, they did not ‘buy in’ or accept the diagnosis or were actively still grieving or expressing anger about it. Parents who provided ‘resilience’ (‘versus distress’) narratives tended to be ‘resolved’ (i.e., certain) about their child’s diagnosis, and this narrative typology was linked to less parental helplessness regarding child pain.

Similarly, in an ethnographic study of family experiences in a pediatric pain clinic, one mother explained how she devoted substantial time to searching for the ‘right’ help to manage her son’s pain despite the existence of a clear diagnosis of complex regional pain syndrome [3]. This urgent and all-consuming parental quest for an alternative or ‘correct’ diagnosis was also identified in a qualitative study of 17 parents of adolescents with chronic pain [10]. Parents reported an unrelenting, exhausting and resource intensive search for an explanation for their child’s pain. Some parents conveyed a sense of desperation for clinical certainty in the form of a specific diagnosis for their child: Even if indicative of substantial pathology, a ‘correct’ diagnosis was considered to be the ‘holy grail’. Perhaps most interestingly, some parents in the Jordan et al. [10] study reported a continued search for diagnostic certainty, even after their adolescent had received a diagnosis of idiopathic pediatric chronic pain. For these parents, a medically provided diagnosis and explanation of their child’s pain was insufficient to allay fears that a more sinister condition could have been overlooked. Missing for these parents was the existence of an accurate and accepted explanation for their child’s pain. Whilst parents in this study focused specifically on the search for a diagnosis, it is possible that other factors such as the typically non-specific treatment recommendations with unspecified targets may also play an important role in explaining parental uncertainty in the context of adolescent chronic pain.

Study findings have also examined the wider social context of diagnostic uncertainty, highlighting that both healthy peers and teachers question the legitimacy of pain in children and adolescents with chronic pain [5,12]. Specifically, studies have highlighted that teachers report feeling uncertain about a child’s chronic pain condition in the absence of medical documentation [12] and offer more support to children with medically diagnosed rather than unexplainable pain conditions [13].

***Priorities for research, changes in the process of care, and interventions.***

Research has only begun to uncover the phenomenon and impact of diagnostic uncertainty in the context of pediatric chronic pain. The prevalence of diagnostic uncertainty among pediatric patients and parents of children and adolescents with chronic pain is not known and diagnostic uncertainty has not been systematically assessed in pediatric pain research. Nevertheless, if the observational narrative findings are generalizable, up to 40% of parents of patients aged 10-18 in tertiary level chronic pain programs are uncertain about their child’s diagnosis [18]. These rates are consistent with adult findings [27]. Assessment and screening of diagnostic uncertainty in pediatric populations is needed to determine its influence on treatment engagement and responsiveness. Serbic and Pincus [26] developed a brief measure of perceived diagnostic uncertainty for adults with back pain, which we have adjusted here to reflect any pain condition. The items include:

1. I have been given a clear label/diagnosis for my pain
2. I have been given a clear explanation about why I have pain
3. I think there is something else happening with my pain which the doctors have not found out about yet

These items should not be treated as a questionnaire, as items do not tally. They are instead a tool to help practitioners and researchers establish whether patients have received a diagnosis and explanation for the problem and whether these are credible and acceptable to patients. The final item is particularly informative *(“I think there is something else happening with my back which the doctors have not found out about yet”*), because it can capture catastrophic thinking and concerns even when patients report having received a clear diagnosis/explanation.

Children themselves need to orient towards their diagnosis and ‘buy in’ in order to engage in the process of self-management and recovery. Yet, it is currently unknown how children’s rapidly evolving cognitive development may influence their understanding of a chronic pain diagnosis, and how clinicians can best tailor their explanations to achieve certainty. Diagnostic uncertainty is likely a *dynamic process* that unfolds over time. Specifically, longitudinal investigations are needed to study change in the impact of diagnostic uncertainty and reassurance needs across age, cognitive comprehension, identity formation, and autonomy development. Beyond these developmental processes, research should examine the influence of diagnostic uncertainty on the child’s developing sense of identity and trust in the healthcare system. Past experiences with and memories of interactions with healthcare providers, for both parents and children, will likely influence their acceptance of a diagnosis and engagement with treatment focused on this diagnosis.

Based on the evidence presented here, we postulate that the interactions that children, adolescents and parents have with professionals are the index event to adjustment: In the presence of diagnostic uncertainty we hypothesise that communication becomes ambiguous and confusing. We know from previous research that above all else, patients find clear explanations about cause and prognosis the most reassuring (Holt et al., 2016) [8], but in the presence of uncertainty, such reassurance is difficult to convey. The consequences of this perceived diagnostic uncertainty can then cascade to all aspects of the child’s life, and define how peers and teacher respond to their problem.

*Treatment implications.*

If children, adolescents, and parents are devoting significant efforts and resources to searching for an elusive ‘organic’ cause for pain due to a belief that a serious pathology is being missed, how is it possible for them to meaningfully engage with treatment that does not address their perceived explanation of pain? Currently, there are no specific interventions to address the issue of diagnostic uncertainty in children and adolescents with chronic pain and their parents, and the influence of diagnostic uncertainty on one’s readiness to change and engage in treatment is not known. Results of a recent meta-analysis of 21 psychological intervention studies for children and adolescents with functional unexplained somatic symptoms identified some success of psychological interventions for reducing symptom load, disability, and school absence [2]. Such results are promising but might be enhanced by addressing the specific issue of diagnostic uncertainty. Of primary importance is clear communication about diagnosis and treatment plan, including specific actions and targets. Indeed, reducing ambiguity in proposed care through clear communication about the nature of chronic pain (and underlying neural changes and activation) is implied.

It may be that psycho-educational interventions (e.g., pain neuroscience education) designed to increase understanding and ‘buy-in’ of parents and children to the diagnosis of chronic pain, will more directly influence diagnostic uncertainty [24]. In the absence of a diagnosis or explanation, recommendations include the exclusion of significant organic disease, education about psychosomatic mechanisms and providing reassurance to parents about recognition of stressors [4]. These recommendations, however, are not evidence-based, and the effective provision of reassurance remain poorly understood [19]. Possibly approaches based on acceptance might be more effective [31], as they do not include assumptions about somatic origins to the pain, which might be perceived as judgemental, delegitimizing, and patronizing [25] .

Assessment of diagnostic uncertainty from the time of receiving a diagnosis, entry into a chronic pain program, and over the course of treatment is needed to determine if, how, and why uncertainty changes over time. Finally, studies are needed to examine the response of diagnostic uncertainty to interventions, and in particular, which interventions, with whom, and in what settings diagnostic uncertainty is most amenable to change. Future research should examine how to match clinicians’ language to pediatric patients’ level of comprehension (e.g., through the use of visual and memory aids) and how to provide effective information in a sufficient time frame that allows exploration of concerns.

Acknowledgment:

Dr Noel is supported by the Vi Riddell Pain Initiative and the Alberta Children's Hospital Research Institute. The research on effective reassurance was supported by Eurospine. The authors have no conflict of interest.

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