

**Identifying Areas of Needed Support for Young Girls with Central Precocious Puberty  
(CPP)**

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**Abstract**

Identifying Areas of Needed Support for Young Girls with Central Precocious Puberty (CPP)

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We identified areas of needed support for young girls with Central Precocious Puberty (CPP) by conducting a secondary analysis of 14 semi-structured qualitative interviews with caregivers of girls diagnosed with idiopathic CPP. Questions elicited information about participants' perceptions regarding the initial signs of CPP, the impacts of CPP on their child before and after treatment in terms of behavior, relationships, and physical development, treatment selection and administration processes, and the ways in which CPP was explained to their child. Results indicated that the signs, behaviors, and events associated with the psychosocial and physical impacts of CPP pertained to either: *Key Theme #1) the decision to initiate medical treatment for CPP or Key Theme #2) the results of initiating medical treatment for CPP*. We also found variance of impacts across Key Themes by age of symptom appearance. Findings suggest that the effects of CPP go beyond the initial physical and psychosocial symptoms of the condition, affecting a patient's social and familial network, both before and after treatment has been initiated. The development of targeted strategies aimed at providing support and resources to families of girls diagnosed with CPP may alleviate the impacts of CPP on caregivers and patients alike.

## **I. Research Question and Specific Aims:**

Given a lack of research assessing psychosocial impacts of Central Precocious Puberty (CPP) on young girls, my broad research question is:

What are the most common impacts on girls diagnosed with CPP reported by caregivers prior to and after diagnosis and treatment?

To address this question, my specific aims are to:

1. Identify observable signs, behaviors, and events associated with psychosocial, and physical impacts of CPP diagnosis and treatment
2. Examine differences in impacts on girls with CPP by age of diagnosis

## **II. Background and Significance**

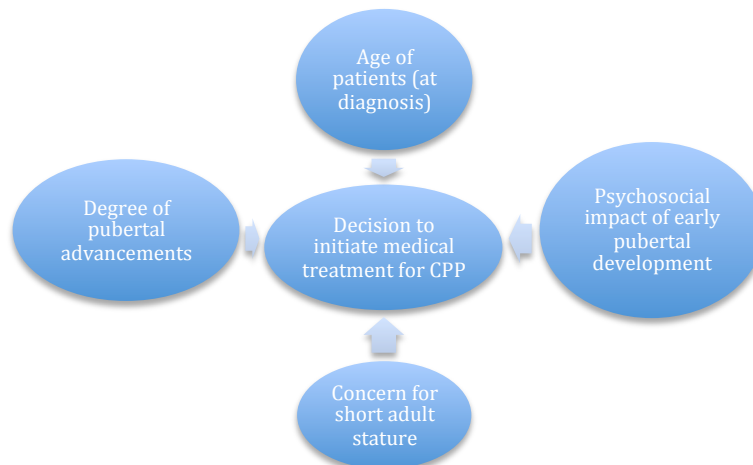
Puberty is defined as the period during which human development progresses to full sexual maturation with the capacity to reproduce. Pubertal development is typically triggered by the activation of the hypothalamic-pituitary-gonadal axis (HPGA), progressing with increasing pulsing secretions of gonadotropin-releasing hormone (GnRH), which precedes the rise in luteinizing hormone (LH) and follicle-stimulating hormone (FSH).<sup>1</sup> The first physical sign of pubertal development in females is typically the appearance of breast tissue (thelarche). This tends to be accompanied, or sometimes preceded, by an acceleration of growth velocity. The appearance of breast tissue is often followed by the appearance of pubic hair (pubarche).<sup>2</sup> In a landmark article by Marshall and Tanner (1969), the first signs of puberty were reported to appear between the ages of 8.5-13 years. In 95% of girls (sampled from a British population of girls used for the Harpenden Growth Study), the mean interval between initial signs of puberty and menarche (the first menstrual bleeding) was about 2.3 years.<sup>3,4</sup> In the last few decades, there has been a great deal of discussion, articles and reviews published debating the normal range of puberty in girls (and boys), given the historical reduction in the average age at which thelarche tends to occur.<sup>3,5-8</sup>

Central Precocious Puberty (CPP) is characterized by early pubertal changes, acceleration of growth velocity and rapid bone maturation that often results in reduced adult height.<sup>1,3,5,9</sup> CPP affects 1 in every 5,000 to 10,000 children (inclusive of boys and girls), but tends to occur more often in girls<sup>9</sup>, in whom it is usually idiopathic (i.e. having no known cause).<sup>10-12</sup> CPP can occur as the result of central nervous system (CNS) related issues that trigger the start of the hormonal releases that initiate the pubertal process. A number of studies have found higher rates of central precocious puberty in adopted girls.<sup>13,14</sup> In fact, a study of adopted children in Denmark found that foreign-adopted children originating from regions other than Korea had a 15- to 20-fold increased risk of precocious puberty compared to Danish-born children.<sup>13</sup> It is suspected that the effect of country of origin may be explained by genetic factors or by different environmental exposures and living conditions in different countries, but further research is needed.<sup>13-15</sup>

Precocious puberty is widely defined as the onset of secondary sexual characteristics before the age of 8 years in girls, based on a 2.5 standard deviation below the mean age of normal pubertal onset seen in girls.<sup>2</sup> Given recent studies regarding changing patterns of sexual

maturation,<sup>8</sup> the Drug and Therapeutics and Executive Committees of the Lawson Wilkins Pediatric Endocrine Society have suggested new guidelines for investigating pathologic etiology of precocious puberty for Caucasian girls 7 years of age and for African American girls 6 years of age.<sup>5</sup> There is consensus that girls should be evaluated in cases where there is: 1) unusual rapid progression of puberty resulting in rapid skeletal advancement (bone age >2 SD ahead of chronological age) with predicted height 2 SD (10cm) or more below genetic target height or <150 cm; 2) new CNS-related findings (which could indicate a possible cause for early puberty) and 3) child emotional state adversely affected by progression of puberty and the potential for early onset of menses.<sup>3</sup>

The primary motivations for treating CPP are to prevent compromised adult height and to avoid psychosocial or behavioral problems.<sup>1</sup> In the short-term, treatment aims to stop the progression of secondary sexual characteristics and menses in girls and to treat the underlying cause, when known. Long-term aims are to increase final adult height and promote psychosocial well-being.<sup>15</sup> Girls diagnosed with CPP have been shown to demonstrate decreased psychosocial functioning (as measured through social relationships, self-esteem, and mood and affect).<sup>1</sup> For instance, studies have found that girls at onset of idiopathic CPP and during treatment may experience a negative body image and low self-esteem.<sup>16,17</sup> Girls with CPP who have a short stature may tend toward neuroticism, an exaggeration of their physical appearance, and feel significantly more insecure than age-related females without CPP.<sup>18</sup> Additionally girls with CPP may suffer feelings of confusion or embarrassment about the physical changes they experience, such as getting their periods or developing breasts, significantly before their peers. As a result they may experience teasing and harassment by peers.<sup>7</sup> Girls with early puberty have also been found to suffer from higher rates of depression and anxiety,<sup>19,20</sup> lower quality of life,<sup>21</sup> higher rates of substance abuse, eating disorders,<sup>22,23</sup> and lower academic achievement.<sup>22,24,25</sup> The collection of evidence regarding the symptoms and impacts of early puberty suggest that the biologic and social changes that accompany puberty make young girls more at risk for the development of maladaptive coping mechanisms, presumably because they are developmentally underprepared to effectively deal with these changes.<sup>7</sup> Thus, the decision to initiate medical treatment for CPP is typically based on: a) the age of the patient, b) degree of physical pubertal advancements in the patient, c) caregiver and/or physician concern about short adult stature and d) the psychosocial impact of early pubertal development (Figure 1).<sup>1,15,20-25</sup> Of these factors, it is often the psychosocial impact of early pubertal development that drives the decision to proceed with treatment.<sup>1, 9, 20-25</sup>



## **Figure 1. Intervention Model for CPP**

Treatment for CPP aims to maintain constant levels of a drug that results in the continuous desensitization of GnHR receptors thus achieving complete hormonal inhibition.<sup>10,11,15</sup> While these drugs used to be administered one- to three-times daily, and eventually monthly, through subcutaneous injections, they are now replaced by depot preparations, which release an active compound in a consistent way over a long period of time.<sup>15</sup> This method has fewer compliance issues than previous forms of treatment, and provides the necessary hormonal suppression, thereby improving growth potential during the early phase of treatment.<sup>26</sup> Treatment delays the release of the relevant hormones until the child's family and medical team feel that the child is of an age that puberty can proceed as normal. Dosing regimens range from monthly to every three months or yearly.<sup>9,15</sup>

Side effects of treatments include menopausal symptoms such as nausea, insomnia, emotional lability, headache, and hot flashes.<sup>1</sup> Throughout and post-treatment, some of the common warning signs regarding girls' behavior that caregivers are advised to be aware of and discuss with the child's doctor include: poor grades, problems at school, loss of interest in daily activities, and depression.<sup>18</sup> Girls' adjustment to CPP and their coping mechanisms can be influenced by how their caregivers cope with the effects of CPP.<sup>27</sup> Caregivers are encouraged to facilitate a supportive environment and frequently praise achievements and participation in school, sports, or other events, rather than focus on appearance.<sup>27</sup>

### **III. Methods**

This study employed data collected for a previous study, the aim of which was to develop an outcomes instrument for assessing treatments for CPP in young girls.

#### ***A. Setting***

Participants were recruited from a Pediatric Endocrinology clinic at Swedish Hospital in Seattle, Washington.

#### ***B. Study Participants***

Caregivers of girls diagnosed with CPP ages 6-10 years were enrolled in the original study. The study recruiter examined the medical record to identify caregivers of eligible patients: 1) confirmed diagnosis of CPP, 2) 6-10 years of age, 3) female, 4) no underlying CNS pathology (as indicated by the absence of seizures, a normal brain MRI, and absence of symptomatology of central pathology). The age range was selected to encompass patients at various stages of treatment. A study recruiter from Swedish Health Services contacted families of eligible pediatric endocrinology patients being treated for CPP informing them of the study purpose and procedures and inquiring if they were interested in participating. At the time of the eligibility screening call with a caregiver, the following information was also collected: 1) caregiver and child race/ethnicity, 2) whether the child lived primarily with biological relatives, adoptive or foster family 3) child grade level, 4) caregivers' education level, and 5) child ability to understand and communicate in oral English.

The majority of interviews were conducted with a female caregiver (13), but one interview was conducted as a focus group that included a female/male caregiver pair, and two female caregivers from separate families. The focus group was conducted in person and the

remaining 13 interviews were conducted over the telephone. Given that there were 14 interviews conducted regarding 16 patients, and the focus group was recorded and analyzed as one unit, only the demographic information for the 13 patients whose mothers were interviewed independently were included in the subsequent summaries and analyses regarding relationships between particular codes and descriptors. The girls were in various stages of treatment, with one having yet to start treatment, and two having completed treatment.

### ***C. Study Design***

I used a thematic approach<sup>28</sup> to qualitatively analyze 14 interviews conducted with caregivers of girls diagnosed with CPP. Using this approach allowed me to better understand what challenges and impacts these caregivers observed in their daughters throughout the process of CPP diagnosis and treatment. This approach facilitated the identification of issues that may be worth further examination in relation to child impact, including age of diagnosis, method of diagnosis, treatment type, and when treatment started.

### ***D. Data Collection***

Data were collected through semi-structured qualitative telephone interviews conducted with 14 caregivers of girls diagnosed with CPP. Caregivers were screened for study eligibility by a recruiter and interviews were then scheduled with a study interviewer. One of the interviews was conducted in-person with two sets of caregivers answering questions in the presence of one another. The remaining interviews were conducted one-on-one over the telephone. The interview guide is contained in Appendix A. I was given access to the de-identified transcribed interviews by the study principal investigator (Dr. Edwards). The original study was approved by Western Institutional Review Board for Swedish Medical Center and the University of Washington.

### ***E. Data Analysis***

#### ***Coding and Identification of Interview Themes***

Dedoose, a web-based application designed for mixed methods research, was used to code and analyze the caregiver interview data. First, a priori codes based on a comprehensive literature review, were developed. The literature review revealed that while the physical effects of CPP, such as early pubertal development and accelerated skeletal growth can be problematic, the psychosocial impacts of these physical changes can be particularly impactful.<sup>1,9,15</sup> The a priori codes were used to code one of the caregiver interview transcripts and to develop and refine the codebook further. I selected excerpts of interviews text and tagged them with the code(s) I judged appropriate based on the code definitions. Figure 2 illustrates the a priori codes included in the initial codebook.

Code Label	Description
<b>Physical Impacts</b>	Issues related to breast development, accelerated skeletal growth, body odor, puebertal hair growth
<b>Psychosocial Impacts</b>	Issues related to mood swings, uncharacteristic emotions/emotional states, self-worth and self-confidence
<b>Communication/Relationship Impacts</b>	Issues related to changes in communication or relationship with <b>parents/family members</b> and with <b>peers</b> both prior to and after diagnosis and/or treatment
<b>-With parents</b>	Issues related to changes in communication/behaviors towards or relationships with parents/family members
<b>-With peers</b>	Issues related to changes in communication/behaviors towards or relationships with peers both prior to and after diagnosis and/or treatment
<b>Secondary Impacts of Conditions</b>	Issues related to the occurrence of CPP aside from the direct ones (perceived by the parents) to be experienced by the patient
<b>Coping Techniques</b>	Issues related to the ways in which patients cope with their condition, diagnosis, and/or treatment
<b>- Physical (e.g. treatment)</b>	Issues related to physical mechanisms of coping with CPP- such as having the treatment patch implanted
<b>- Psychosocial</b>	Issues related to the socioemotional mechanisms of coping with CPP- such as seeing a therapist, speaking with other patients, regularly discussing the reasons behind the changes the girl(s) are experiencing

**Figure 2. A priori codebook**

In the process of applying the codes, additional themes and sub themes were identified, leading to the refinement of the initial codes and the inclusion of additional codes and sub-codes. For instance, while it was anticipated that the psychosocial impacts of CPP would be discussed during caregiver interviews, it became clear that caregivers differentiated between the psychosocial impacts of CPP itself and the psychosocial impacts of the chosen form of treatment and the medical intervention process (i.e. undergoing tests to confirm diagnosis). Therefore, “psychosocial impacts of CPP” and “psychosocial impacts of treatment” were added as sub-codes to the primary code of “psychosocial impacts.” Additionally, the code “secondary impacts of condition” was intended to be a catch-all for any indirect impacts of CPP and/or the treatment of CPP on the affected girl and/or her family. In the coding of the interviews, 2 particular secondary impacts of the condition reoccurred: the financial impact of treating a child with CPP, and the stress experienced by the family as they searched for a diagnosis, dealt with the physical and psychosocial side effects of CPP, and explained the condition and what it meant to their child/children. Both financial burden and familial stress were added as sub-codes for the primary code “secondary impacts of condition.”

'Adoption' was added as a new code as it became clear that multiple girls in the sample were adopted (n=5). Given the higher rates of CPP in adopted girls<sup>13-14</sup>, this code was added to explore differential impacts in this population. Additionally, it became evident that when discussing the range of impacts that CPP and the treatment of CPP had on the girls and their families, caregivers tended to differentiate between struggles before and after diagnosis and before and after treatment, leading to distinctions between physical and psychosocial

impacts of conditions and physical and psychosocial impacts of the treatment, as reflected in the addition of new sub-codes.

The primary researcher coded all interviews. A selection of excerpts encompassing the range of codes and sub-codes used was selected to serve as a test for inter-coder reliability. Another qualitative researcher was recruited to take the test to ensure inter-coder reliability. Inter-code agreement was measured at 41%. This was thought to be the result of the second coder's incomplete understanding of the codebook and code application rules. Discrepancies in coding were discussed, and the codebook was further refined as a result. Excerpts that illustrated each code were selected and added to the codebook. Inter-code agreement was assessed again, using a test consisting of randomly selected excerpts (created by Dedoose software) spanning all codes in the codebook. Inter-code agreement for this selection was measured at 89%. Figure 3 depicts the final codebook used to code all caregiver interviews in this sample, including samples of coded text.

Code Label	Description	Sample Coded Text
<b>Physical Impacts</b>	Issues related to physical changes that result from the condition and/or its treatment	
Physical impacts of CPP	Issues related to breast development, accelerated skeletal growth, body odor, pubertal hair growth	"...And I noted she was growing a little bit of pubic hair"
Physical impacts of treatment	Soreness/pain around implant or injection site, and physical changes in pubertal development	"She is noticing that she doesn't need the deodorant as much and that her breast size has seems fine with that.;" "And that [treatment] day hurt, and the next day. It was like she had somebody punched her."
<b>Psychosocial (PS) Impacts</b>	Issues related to moods, emotional states, self-worth, confidence, and overall personality both before and after treatment	
PS impacts of CPP	Issues related to mood swings, uncharacteristic emotions/emotional states, self-worth and self-confidence	"[weird]...the term she used all the time, 'I feel weird. I feel different. I don't feel like play I don't feel like I'm normal.'"
PS impacts of treatment	Issues related to the treatment itself- anxiety towards doctors and injections; consequences of physical limitation like soreness following treatment, etc (i.e feeling emotionally isolated, singled out)	"My stomach doesn't feel good," which means she's nervous. She had butterflies in her stomach when she went to give her the second blood draw, we had put that numbing cream on, but she was
<b>Communication/Relationship Impacts</b>	Issues related to changes in communication or relationship with parents/family members and with peers both prior to and after diagnosis and/or treatment	
-With parents	Issues related to changes in communication/behaviors towards or relationships with parents/family members	"Kind of rolling her eyes at us, and stuff like that where it's like, she's always been a little bit kind of fun way, but there was a little bit more of a bite to it."
-With peers	Issues related to changes in communication/behaviors towards or relationships with peers both prior to and after diagnosis and/or treatment	"I'd ask her, 'Who do you play with,' and she'd say, 'Nobody,' more than one time. I don't through a point where she didn't want to really go out with friends or have play dates and then she went back to doing it again for a while"
<b>Secondary Impacts of Conditions</b>	Issues related to the occurrence of CPP aside from the direct ones (perceived by the parents) to be experienced by the patient	
-e.g. financial burden	Issues related to the financial burden of having a child with CPP- such as buying more clothes and shoes at a higher rate due to acceleration of growth in addition to the cost of treatment/insurance coverage etc	"It's incredibly expensive, so if I didn't have good insurance I probably would not be doing "You need to go and – and I'm sorry. I just bought her all underclothing last month. He's I shoes. Like what about her shoes? He's they're too tight. And he had to help me keep track I'm like buying her clothes every three months. And, meanwhile, the rest of her body is of "Really frustrated, because we didn't know how many kids we were gonna have have that think that's pretty rare for a family. And it takes time as they go through the early symptoms premature puberty before they can really do anything about it. We had to go through a watch watching our daughter go through this before we could even get to the point where we could And that was a very long, long year."
-e.g. familial stress	Issues related to the stress placed on families raising a child, or children, with CPP, such as struggling to explain to the child/children the physical and emotional changes they are experiencing; parental frustrations/concerns/anxieties	
<b>Coping Techniques</b>	Issues related to the ways in which patients cope with their condition, diagnosis, and/or treatment	
- Physical (e.g. treatment)	Issues related to coping with physical effects of CPP and CPP treatment	She was wearing inside-out socks. Panties and socks and tank tops were inside-out. That feel where they joined.
- Socioemotional	Issues related to the socioemotional mechanisms of coping with CPP- such as seeing a therapist, speaking with other patients, regularly discussing the reasons behind the changes the girl(s) are experiencing	"She said, 'Mama, I'm just afraid of everything,' and she is so not afraid of everything. She little kids I've ever met and I told her, 'Well, you know what? I don't agree with that, so I can do to help you remember this time as a bravery time.' So we made her a Bravery Brace appointment we go and get a charm, which she adds to her Bravery Bracelet."
<b>Age of Diagnosis</b>	Age at which the patient was diagnosed (not necessarily the age symptoms first appeared)	
- Elementary	Patient diagnosed in elementary school	"So our daughter at seven and a half was formally diagnosed, but when she was four and a the first change with her body."
- Prek	Patient diagnosed in preschool	"One four and a half and one seven and a half when we ended up trying to figure this out."
<b>Adopted</b>	References to adoption status and impact of status on process of diagnosis and treatment	"Well you know that was the problem was that we had put her at five years old when we how old she was and we based that on pictures to begin with because we really didn't have go by. So when she got here we said she was five years old and it was obvious that she was because she had all her teeth and everything."

**Figure 3. Sample Coded Text**

## RESULTS:

### Sample Characteristics

The racial/ethnic background of the girls enrolled in the study was: 10 Caucasian (Non-Hispanic), 2 Black (Ethiopian), 1 Asian, 1 Hispanic. Racial/ethnic identities were unavailable for 2 girls. One-third of the girls were adopted: two from Ethiopia, one from China, and another from an unknown country (Caucasian race). The majority of girls were diagnosed with CPP at age seven (44%) or eight (44%), with two girls diagnosed at age six (12%) (Table 1).

**TABLE 1. Characteristics of Index Girls with Central Precocious Puberty**

Patient Characteristic	n of 16 (%)
Age at diagnosis	
6 years old	2 (13)
7 years old	7 (44)
8 years old	7 (44)
Race/ethnicity	
Caucasian (Non-Hispanic)	10 (63)
Black (Ethiopian)	2 (13)
Asian	1 (6)
Hispanic	1 (6)
Missing	2 (13)

Adopted	4 (25)
Treatment type	
Implant only	8 (50)
Leuprolide only	1 (6)
Leuprolide IM Q3 months	2 (13)
Leuprolide + implant	1 (6)
Completed treatment	2 (13)
Untreated	1 (6)
Missing	1 (6)

### Key Themes

Psychosocial and physical impacts of CPP on the girls were observed by all caregiver participants. Identification of observable signs, behaviors, and events associated with psychosocial and physical impacts of CPP diagnosis and treatment (Specific Aim 1) occurred throughout the coding process. **These signs, behaviors, and events associated with the psychosocial and physical impacts of CPP pertained to either: Key Theme #1) the decision to initiate medical treatment for CPP or Key Theme #2) the results of initiating medical treatment for CPP.** The relevance and impact of the factors influencing the decision to initiate medical treatment and the results of this decision did not seem to vary by age of diagnosis (Specific Aim 2), a finding further discussed below.

### **Key Theme #1: The Decision to Initiate Medical Treatment for CPP**

As introduced in the Background, the decision to initiate medical treatment for CPP was based on: a) the age of the patient, b) degree of physical pubertal advancements in the patient, c) caregiver and/or physician concern about short adult stature and d) the psychosocial impact of early pubertal development (Figure 1). As per the intervention model introduced in the Background, the psychosocial impact and concern for short adult stature drove the decision to proceed with treatment.

Caregivers were asked how they found out their child had CPP, leading to discussion regarding the initial signs and symptoms they saw in their child and a discussion of the diagnostic process and clinical concerns (e.g. regarding short adult stature). The observable signs, behaviors, and events associated with the occurrence of CPP, and their role in influencing the decision to treat the symptoms of early puberty are described below.

### **Concern regarding short adult stature:**

Shortened adult stature specifically was described as a concern by only 21% of caregivers, while, rapid growth spurts and accompanying weight gain, common signs of CPP, were discussed by 64% of caregivers:

- *“[She would] gain a little weight, and then sprout up, and then she would lose a little bit, and then she’ll kind of gain a little, and I thought, ‘Well maybe she’s just kind of getting a little chubby or something.’” (7-year old, diagnosed age 7, Caucasian)*

### **Caregiver perception of appearance of CPP signs and degree of pubertal advancement:**

When asked how they first realized that their child may be experiencing early puberty, caregivers mentioned noticing breast bud development (79%) body odor (43%), growth

spurts (43%) appearance of pubic hair (36%), acne/oily skin (36%), sudden weight gain (29%), and/or underarm hair (14%).

In some cases (36%), psychosocial impacts were correlated with the appearance of physical indications of pubertal advancement:

- *“My daughter was very frustrated...a lot of the girls in her class were entirely fascinated with chest development...meanwhile her body is popping out all over the place. And she was pretty alarmed by it.” (13-year old, diagnosed age 7, race/ethnicity not reported)*

### **Psychosocial impacts of early pubertal development:**

The psychosocial impacts of CPP were discussed across 100% of caregiver interviews. Caregivers discussed the psychosocial impacts they observed in their daughters prior to diagnosis (100%), after diagnosis (100%) and during (93%) and after treatment (14%). One subtheme related to girls exhibiting severe mood swings and higher than usual irritability:

- *“She’d be happy and laughing one moment, and the next moment she’d be upset and crying, or mad, or she’d slam the door.” (10-year old, diagnosed at age 8, Caucasian)*

These psychosocial changes ranged in severity but affected patient relationships with her peers in 100% of cases, and relationships with parents in 86% of cases. The psychosocial impacts of CPP on peer relationships were primarily identified as negative, and stemming from the increased mood swings, emotional outbursts, and irritability exhibited by the girls. For some patients, this resulted in being bullied (14%) and feeling isolated and alone (43%):

- *“There were days that she’d say, “I didn’t feel like playing with anybody.” There were birthday parties that she got invited to and she was all excited about it, and the day of the party she’d say, “I don’t really want to go. I don’t want to go to the party. I don’t want to see anybody.” (13-year old, diagnosed at age 8, Hispanic)*
- *“Well, the friends that she lost were not really good friends. She had other peers around her that were good friends. So she just basically fell to a different position on the playground. She went from an assertive person who had lots of friends and was liked by everybody to someone who is like withdrawn and the kids and would like gravitate to her to bully her.” (13-year old, diagnosed at age 7, race/ethnicity not reported)*

In one interview, a caregiver described how the psychosocial changes her daughter exhibited led to her becoming a bully, rather than being the victim of bullying.

- *“She would just tease meanly. Like do hurtful things, although questionable whether she understands that it would mean or not. I’m not sure, but she tended to kind of go that route doing the things that you would see more of preteen girls doing when they gang up on another girl or they tease another girl. More of that type of behavior.” (9-year old, diagnosed at age 7, Caucasian)*

Changes in relationships with peers were also affected by the physical signs and symptoms of puberty (14%), leading to further psychosocial implications:

- *"...We had one incident probably when she was seven where she felt like – they were at a swimming pool and somebody made a comment about how hairy her legs were." (8-year old, diagnosed at age 8, Caucasian)*

One caregiver noted that while her daughter experienced changes in her relationships with her peers, the changes were largely positive:

- *"And so she's kind of a quiet leader now where before she was very outgoing and had no problems stating whatsoever. So, now, she just kind of considers everybody and kind of uses more predominant kids within the classroom to voice the opinions or she'll try to get kids together and insulate herself and standing up as a group to address an issue instead of just stand up alone like she did before." (13-year old, diagnosed at age 7, race/ethnicity unknown)*

Psychosocial impacts of CPP on the communication and relationship between patients and their caregivers, discussed by 86% of caregivers, were expressed in a different manner, compared to changes in relationships between patients and their peers. Communication with parents was often more unfiltered and expressive:

- *"When she'd go to school, she'd just encapsulate all these emotional feelings and everything and she'd come home and just rip and roar it at you, because she knew that her body was different. She knew that she had this chemistry box that was different. And she'd go to school and she'd just pull whatever it was in. And then when she came home, she was like I can't understand why so and so looked at me that way or said what she said or whatever." (13-year old, diagnosed at age 7, race/ethnicity not reported)*

Some caregivers (36%) expressed concerns about how other adults might draw conclusions because of these psychosocial impacts:

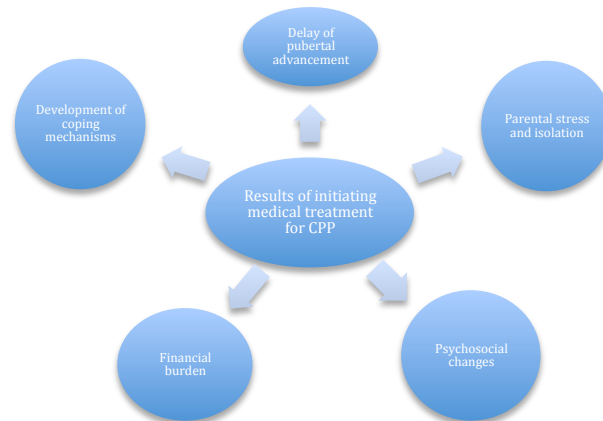
- *"I talked to the neighbors. I told the neighbors, you know, that we're not abusing her. We're not hitting her or anything like that, that she was going through tough times, because there were nights that I thought the police were gonna knock on my door any minute. She was very loud. I mean she's screaming. She was screaming out of control." (13-year old, diagnosed at age 8, Hispanic)*

A few caregivers (14%) stated that some of the physical changes caused by CPP led to positive psychosocial attitudes in their children, such as happiness about being tall and being able to use items such as deodorant.

### **Key Theme #2: Results of Initiating Medical Treatment for CPP**

Once medical treatment was initiated, a range of effects emerged, including: 1) delay of pubertal advancement, 2) increased caregiver stress and isolation, 3) positive and negative psychosocial changes in the girls, 4) increased financial burden on the family, and 5) development of positive coping mechanisms (Figure 4).

Caregivers were asked to comment on any changes in their child's physical and psychosocial condition during and after medical treatment for CPP. A number of indirect impacts of undergoing treatment were found, most notably, the development of caregiver coping mechanisms and family financial burdens associated with treatment. The impacts of medical treatment for CPP, derived from these interviews, are illustrated Figure 4.



**Figure 4. Impacts of medical treatment for CPP**

**Development of coping mechanisms:**

Most caregivers (93%) discussed how they overcame challenges throughout the processes of obtaining a diagnosis for CPP for their daughter and their daughter undergoing testing and treatment. Some coping strategies related to how to explain the symptoms, diagnosis and treatment process to their young daughters. This included using tools such as books and simplified explanations of medical processes:

- *“Well I think a lot of it is just kind of embarrassing...I got her a book, *The American Girl’s Guide*.” (9-year old, diagnosed at age 7, Caucasian)*
- *“Actually, what I ended up doing is the library has some really great preschooler books on the difference between boys and girls. And they’re geared towards little kids and they have pictures of your complete anatomy and they use appropriate language. And so I just let her first look at the book and then we talked about the difference between boys and girls. And then we talked about the fact that, for whatever reason, her pituitary gland had decided to wake up...” (6-year old, diagnosed at age 6, Ethiopian)*

Caregivers (43%) also gave examples of ways in which they helped their daughters cope with the fear associated with the treatment of CPP, particularly the fear of injections and blood draws. These coping mechanisms include the creation of “special words” and physical symbols of bravery, as explained in the excerpts below:

- *“She [the patient] coined the phrase ‘ex-scared’ which is being excited but scared about the first time she was going to the hospital for surgery for the implant. It was the anticipation about what it was gonna be like was very exciting and scare at the same time, but she wasn’t fearful.” (10-year old, diagnosed at age 8, Caucasian)*

- *“We made her a Bravery Bracelet, and after every appointment we go and get a charm, which she adds to her Bravery Bracelet.” (6-year old, diagnosed at age 6, Ethiopian)*

One caregiver explained how the demeanor and practices of the medical team helping her daughter served as a coping mechanism during medical intervention:

- *“The one thing – my hats off to how they treated her during the surgery. It’s the – I forget what it’s called, but where the specialist comes in and explains everything to her if she needs more explanation, but she actually stayed there during the surgery and sang to her, so P was so enthralled with this woman that was singing to her that she didn’t have any nervousness.” (10-year-old, diagnosed at age 8, Caucasian)*

#### **Delay of pubertal advancement:**

The initiation of medical treatment of CPP resulted in arrest of puberty amongst all patients in this sample, regardless of type of treatment implemented. The delay of pubertal advancement was seen in a range of ways, including:

- *“She’s had a reduction in her breast buds. She stopped growing out of things in a two-week period...her bone age has slowed down.” (8-year old, diagnosed at age 7, Asian)*
- *“Her body odor has gone almost completely...her hair is not nearly as greasy...” (9-year old, diagnosed at age 8, Caucasian)*

The delay of pubertal advancements was often accompanied by psychosocial changes as discussed further below.

#### **Psychosocial changes:**

Several caregivers whose daughters were in the process of undergoing treatment (81%), or who had completed treatment (13%), discussed the noticeable psychosocial changes that resulted from the treatment of CPP.

- *“I got my little girl back.’ That’s exactly what I felt like, that this little teenager who had entered our house was returned, had been restored to the sweet little Kindergartener...” (10-year old, diagnosed at age 8, Caucasian)*
- *“She’s just easy to laugh and easy to be around now, and it just seems like she wants to be around people.” (9 year old, diagnosed at age 8, Caucasian)*
- *“Our daughter has celebrated each regression in her physical development with the puberty...she’s like I want all my hair to fall out. And she would just go, ‘yes, I went down another bra size.’” (13-year old, diagnosed at age 7, race/ethnicity not reported)*

Of those caregivers whose children were being or had been treated, 31% observed psychosocial changes within 1-4 weeks after treatment was initiated,

- *"...I did notice that after the first couple, three weeks that it did start to even her out as far as her emotions and how she reacted to certain, different situations." (12-year old, diagnosed at age 8, Caucasian)*

Other caregivers (62%) noticed psychosocial changes after more than 1 month:

- *"When she got the implant, we noticed the effects about two months later. It took ten weeks. We counted them. They were long. And then that next day [snaps fingers], it was like, oh, we have her back." (10-year old, diagnosed at age 7, Caucasian)*

### **Financial burden:**

Many caregivers (50%) discussed the financial complications and burden associated with obtaining treatment for CPP. One caregiver stated that the "hardest part [of everything] was the financial aspect of it." With some of the caregivers (21%), the form of treatment they elected to have administered (implant or injection) and how frequently it was to be given, was determined by financial and insurance coverage factors:

- *"I think there was some fear on our part on whether or not our insurance company would pay for a designer drug." (13-year old, diagnosed at age 7, race/ethnicity not reported)*

In many instances (36%), caregivers expressed that they may not have elected to proceed with medical treatment of CPP if insurance did not cover the majority of costs. Even with insurance coverage, caregivers commented on how expensive the treatment was and the financial burden it posed.

- *"It's [treatment] is incredibly expensive, so if I didn't have good insurance I probably would not be doing this." (8-year old, diagnosed at age 7, Asian)*
- *"The payment process for the implant...is ridiculous...we have a co-pay assistance which the drug company offers and our insurance picks up a certain amount of it, like 80%, but it still leaves us paying between \$1600 and \$2000 or so..." (10-year old, diagnosed at age 8, Caucasian)*

### **Caregiver stress and isolation:**

It was common for caregivers (50%) to express experiencing feelings of stress around how to explain the CPP diagnosis to their child, as well as to teachers and other caregivers. The struggle to balance a desire for privacy and normalcy with necessary information sharing was a prevalent theme:

- *"We have several family members that don't know, because we ask her, you know, how much do you want to share about this? What do you - because grandma is a talker, [CHILD NAME]. And if you tell grandma, everybody will find out about it and then everybody - and we're like, I'm sorry, [CHILD NAME]. Its just grandma is kind of unusual. And she's like I don't want to share that much. And I said, well, we're gonna respect your views. And so grandma doesn't know. And we have an \$18,000.00 drug in my daughter's arm and grandma doesn't know [laughter]. It's kind of strange, you know?" (13-year old, diagnosed at age 7, race/ethnicity not reported)*

- *“We were very concerned that talking to other parents would stigmatize her in some way, so we kept it just within the family.” (10-year old, diagnosed at age 8, Caucasian)*

Another source of stress for some caregivers was the impact CPP had on their child’s relationships with her siblings (14%). They indicated that moodiness and irritability often led to friction between siblings.

- *“So if she’s [the patient] angry with her brother, she slams her door and she’ll just start screaming at him.”(9-year old, diagnosed at age 8, Caucasian)*

Caregivers (43%) also expressed a desire to want to connect with others experiencing similar struggles for support and understanding. One mother stated:

- *“But at the same time, I would have loved to have seen a mom face to face to help me go through that – help me, literally, me, go through some of the difficult pain of that, of having to go and buy bras for your girl and she doesn’t really want to wear them and her body is changing and she is so upset.” (13-year old, diagnosed at age 7, race/ethnicity not reported)*
- *“Gosh. I think it just would have been nice to have more resources available, more resources just explaining it to her. And that was one of the reasons we wanted to participate in the six-month treatment option, because we wanted to be able to help other children and families with it [the process of diagnosis and treatment].” (13-year old, diagnosed at age 7, race/ethnicity not reported)*

This desire to connect with other caregivers experiencing similar struggles was heightened by the lack of understanding about CPP and the ramifications of a CPP diagnosis, amongst other parents and colleagues:

- *“I would say that was one of the most heart wrenching parts of it in that parents said to her and to us all the time, ‘Oh my gosh, [NAME] has grown so much.’ We’d say yes, we know. They’d say, ‘No, but her face looks different. She’s just starting to look more grown up.’ When your daughter’s in first grade and you know what’s going on behind the scenes, that’s not a nice thing to hear. She’s a beautiful girl, she’s a striking girl, so people comment on it often. But to have people telling you your first or second grader looks like a super model – you know? To comment on how mature she looks and think that it’s a benign comment when it’s not is hard and something that has made me realize not to comment on other children.” (10-year old, diagnosed at age 8, Caucasian)*

Other caregivers (21%) found whatever resources they could using the Internet, and turned to those as a source of comfort and information. One such site was the MAGIC Foundation Mission (<https://www.magicfoundation.org>), a charitable non-profit organization created to provide support services for the families of children affected by a wide variety of chronic conditions, syndromes and diseases that affect children's growth. One mother explained how she used the MAGIC site to connect with others:

- *“On the MAGIC site, they had a listing of people with different conditions and you could actually contact them. And there was one and I did contact her. And her story was*

*different, but just to find out that there was somebody else out there. And we talked about meds and things..." (13-year old, diagnosed at age 7, race/ethnicity not reported)*

However, even resources like the MAGIC site had their limitations:

- *"But I could see other people here in our area on the site that had it, but they weren't contactable and that was really frustrating. Because for my peer group as an adult, I didn't have any friends around me [laughter] whose daughters had already gone through this and so I became kind of an expert [laughter]"*

Concerns about the sexual consequences of early puberty were an additional source of stress for some caregivers (14%):

- *"Promiscuity. Leading somebody on who is older than her and not having any kind of common sense about what she might be communicating physically to somebody else by climbing in their lap." (10-year old, diagnosed at age 8, Caucasian)*

Feelings of guilt were also identified as a source of caregiver stress, as some (14%) expressed how they were plagued by fears that their actions may in some way have triggered their child's condition, or worsened it in some way:

- *"The other part that we didn't talk about is just the guilt that you go through as a mom, because there is no known reason for why this came about. I can't tell you how long I went through this feeling of guilt and just racking my brain, what did I do? Because when she was born she was breastfed. We did organic. I've done hormone-free milk. You just go through everything that you've done as a parent. And then I start to think, well, maybe, it was all the water I drank from plastic bottles that now they're saying is not healthy for you. For me, at least speaking for myself, I went through that and I couldn't help but feel guilt." (12-year old, diagnosed at age 8, Caucasian)*

#### **Variance of impacts across Key Themes by age of diagnosis:**

Variance in CPP impacts by age of diagnosis did not follow a clear pattern, however, there were discernable patterns in impacts by age of first symptom appearance. Although only 13% of girls were diagnosed with CPP by age 6, 57% exhibited symptoms associated with CPP between the ages of 3 and 5. It is interesting to note that among the group of girls who first exhibited symptoms of CPP between the ages of 3-5, 50% were adopted.

#### **Variance of impacts across Key Themes by age of symptom appearance:**

Caregiver interviews suggest that the delay between symptom appearance and diagnosis was attributable to a lack of knowledge about the significance of these symptoms, misdiagnosis, and the need to track hormone and bone growth levels over time before obtaining a clinical diagnosis:

- *"I think it took awhile to put together more than a few clues that it was something I should be paying attention to. I think it didn't really click. She had things for several years... She's always had a lot of body odor for such a young girl, years ago before she had any other signs. We didn't really know what to make of that and didn't really*

*think it would mean anything whatsoever.” (7-year old, diagnosed at age 7, symptomatic at age 4, Caucasian)*

- *“She has had body odor for a really long time. Since she was about three. And no one would – our pediatrician just really didn’t bother with it. (9-year old, diagnosed at age 8, symptomatic at age 3, Caucasian)*
- *“They [doctors] monitor your blood levels for a couple of hours and that measures an exact – how much your brain is releasing, and that test is the one that’s proved that she’s 100 percent in central precocious puberty. But it took from the age of five until she was eight every three months going. And it’s just you go and they say, ‘Yes, she’s growing. Just watch it. The hormones aren’t present. There’s nothing we can do.’ So it was a wait and watch kind of thing. But her bone age was always about a year and half to two years advanced for her birth age.” (8-year old, diagnosed at age 8, symptomatic at age 5, Caucasian)*

Girls who were symptomatic before age 6 seemed to have little awareness or self-consciousness about the physical symptoms of CPP, compared to patients who experienced later emergence of symptoms:

- *“She’s not terribly shy about it [physical development]. She’s in this little dance team and you can tell the kids that are her age that are shy about it...So it’s not something she’s very conscious of... she’s willing to whip off her shirt and run around.” (8-year old, diagnosed at age 7, symptomatic at age 3-4, Asian)*
- *“...She’s very confident, and that [being stigmatized] wasn’t really an issue for us. She wasn’t feeling uncomfortable at all in her body, or anything. I mean, she’d offer – she’d kind of mention that she could tell she was getting breasts, and I said, “Oh Grace, you’re just – you’re still a little girl. (7-year old, diagnosed at age 7, symptomatic at age 5, Caucasian)*

A number of girls who were exhibiting signs of CPP before the age of 6 also seemed to have psychosocial impacts directly related to the treatment processes, rather than the direct effects of CPP (50%):

- *“Yeah, and she doesn’t really think about it [CPP] because I don’t think she feels that different yet at this age...But she – it’s only when she has to go for the shot that she kind of worries about it a little bit.” (9-year old, diagnosed at age 7, symptomatic at age 3, race/ethnicity not reported)*
- *She cries [before doctor’s appointments]. She just gets kind scared and cries over it. And \_\_\_ about – if we say we’re going to have to take you to the doctor tomorrow, she’ll – it’ll keep her up. She’ll be thinking about it and keep asking, ‘All we’re gonna do is this, right? We’re just gonna’ – very kind of \_\_\_ on the details of what’s gonna happen. (7-year old, diagnosed at age 7, symptomatic at age 5, Caucasian)*

Caregiver feelings of frustration, stress, and isolation seemed to be particularly prevalent amongst caregivers of patients who were symptomatic at an earlier age (i.e. 3-5 years old) (88%):

- *“Well it made me kind of sad...just sad that – well, to tell you the truth, that we had to deal with it. (7-year old, diagnosed at age 7, symptomatic at age 5, Caucasian)*
- *“...it takes time as they go through the early symptoms of the premature puberty before they can really do anything about it. We had to go through a whole year of watching our daughter go through this before we could even get to the point where we could have treatment. And that was a very long, long year.” (13-year old, diagnosed at age 7, symptomatic at age 4, Caucasian)*

## **DISCUSSION:**

This study indicated that observable psychosocial and physical impacts of CPP diagnosis and treatment pertain to either the decision to initiate medical treatment for CPP or the results of initiating medical treatment for CPP. Additionally, we found that the psychosocial impacts of CPP are far reaching, impacting patient relationships with peers and family members, and are affected by the diagnostic and treatment process associated with CPP, as well as the physical pubertal advancements associated with CPP. Also, medical treatment of CPP is correlated with the delay of pubertal advancement, increased caregiver stress and isolation, positive and negative psychosocial changes in patients, increased financial burdens, and the development of positive coping mechanisms. Variance exists in the impacts of CPP, by age of first symptom appearance. Patients symptomatic prior to age 6 appear to have little awareness or self-consciousness in relation to the physical symptoms of CPP, compared to those who experienced a later emergence of symptoms. Furthermore, patients symptomatic before age 6 appear to experience greater psychosocial impacts as a result of the treatment processes (e.g. doctors visits, blood draws, implant placement), rather than the impacts of CPP, compared to those who became symptomatic relatively later. These findings indicate that the effects of CPP go beyond the initial physical and psychosocial symptoms of the condition: CPP impacts a patient’s social and familial network, both before and after treatment has been initiated. Additionally, these findings provide support for development of targeted strategies to alleviate impacts of CPP on caregivers and patients alike. These efforts could be broadened to address impacts beyond physical and psychosocial ones, such as financial impacts, caregiver stress and isolation, and anxiety around diagnostic and treatment procedures.

The findings regarding the importance of addressing psychosocial aspects of CPP in the context of family and developmental factors are consistent with studies concluding that it is crucial for the management of precocious puberty to include counseling focused on the psychosocial aspects of developmental behavior.<sup>32, 33</sup> Findings are also consistent with literature emphasizing that, although treating CPP to stop and potentially reverse secondary sexual characteristics, prevent early onset of menses, and attenuate the loss of height potential is important, addressing the psychosocial aspects of CPP is just as essential to “enable the child and family to cope better with the ‘mismatch’ between physical and emotional development.”<sup>33(S7)</sup> Our findings support research indicating that CPP impacts occur in a larger context, affecting far more than simply the child with the condition.<sup>11, 14, 16,32,33</sup> Ultimately, girls with central precocious puberty have to cope with a body image that is “at variance with their chronological developmental stage within the context of their family, friends, and in education.”<sup>33(S7)</sup>

Furthermore, the findings of this paper support previous work emphasizing that services addressing the discrepancies between physical and emotional development of girls with CPP is an essential aspect of the treatment of the condition.<sup>33</sup> Many of the difficulties faced by participants and their daughters stemmed from problems caused by the mismatch between physical development and emotional experiences and development. These 'mismatches' often led to breakdowns in communication between the affected girls and their parents, siblings, peers, and teachers. The examples of sullenness, outbursts, moodiness, and withdrawn behavior cited in these interviews drive home previous research<sup>33</sup> that children with CPP are coping with early puberty in the context of family, friends, and in education.

Our findings support research on the consequences of early appearance of secondary sexual characteristics, such as behavioral disturbances and symptoms of depression and/or anxiety,<sup>34</sup> low self-esteem, feelings of isolation<sup>9,11,17</sup>, undesired attention due to physical changes, social problems, aggression, somatic complaints, and negative body image.<sup>35,36,37</sup> Previous research indicates that although changes in physical appearance that are caused by secondary sexual characteristics may be temporary, the "impact on the child's self-esteem and feelings of being set apart from the peer group could be significant."<sup>36, p.4</sup> The findings regarding familial stress related to accelerated physical development are also consistent with research concluding that the appearance of early breast development in a girl may draw attention from potentially abusive adults, and that the experience of early puberty increases the risk for sexual abuse or for early sexual debut (i.e. age of first sexual intercourse).<sup>36</sup> As such, parents of girls with accelerated physical development compared to others in their age range, will be affected by additional parental anxiety.<sup>37</sup>

Additionally, findings pertaining to varied impacts of CPP and treatment of CPP by age are consistent with literature concluding that in girls who experience accelerated skeletal maturation and in whom sexual development begins before age 6, treatment of CPP to arrest pubertal progression is the appropriate course of action and will effectively diminish the loss of height.<sup>36</sup> However, in children between 6 and 8 years of age, the ability to protect long-term growth potential is less effective, and as such, the treatment options must be individualized for girls in whom it will be most likely to be effective.<sup>36</sup>

Our findings indicate that caregivers have multiple areas in which further support and resources are needed: financial/insurance navigation, explaining CPP and treatment process to their young child, coping strategies to address psychosocial changes in their child, connecting with other caregivers and families experiencing the same process. Caregivers expressed an overwhelming desire to connect with other families with a child experiencing CPP, as a way to pool resources about how to cope with the signs and symptoms of CPP, learn more about the clinical options available to them, and have a general support system with others who have an intimate understanding of what it means to have a child with CPP. This underscores the importance of the need for clinicians to understand the significance of a support system for families on patient outcomes. By connecting caregivers with additional resources that will better equip them to handle the many facets of CPP (e.g. emotional outbursts, explaining the condition to their child, teachers, and other caregivers, physical changes, etc.), providers could help alleviate many of the psychosocial and secondary impacts of CPP. Interventions with parents of children who present with abnormal puberty include providing anticipatory guidance, supporting parent communication strategies, and providing support and information resources.<sup>38,39</sup>

Interviews with caregivers of adopted girls revealed that the psychosocial impacts of CPP, such as extreme mood swings, low self-esteem, and feelings of isolation and loneliness, were often correlated with the psychosocial impacts of adoption. The significance of this finding is underscored by research indicating that stressful transitions accentuate behavior problems among girls who were predisposed to behavioral problems earlier in childhood.<sup>40</sup> The impacts of CPP in adopted girls may be compounded by biological sensitivity to context and reproductive development.<sup>41</sup> Researchers have found that among children displaying heightened biological sensitivity to context (i.e. higher stress reactivity), higher quality parent-child relationships forecast slower initial pubertal tempo and later pubertal timing, whereas lower quality parent-child relationships forecast the opposite pattern.<sup>41</sup> Exploring CPP in the context of these theories could provide important insight into higher rates of CPP in adopted girls.<sup>14</sup> Further evidence exploring the role of context on emergence of CPP in adopted girls suggests a psychological influence on CPP and concludes that adoption, but not immigration, increases the risk of CPP.<sup>42</sup>

Study participants were recruited from the Greater Seattle area, meaning that findings may not fully encompass the experiences of all girls experiencing CPP. Furthermore, the high educational attainment levels of caregivers could have influenced the resources available to the patients and their families. Socioeconomic class and education levels of caregivers also could have influenced the development and ability to implement certain coping mechanisms, such as changing schools to avoid bullying and securing counseling services. Although one participant interview was conducted as a focus group, all others were conducted one-on-one, between a caregiver and a member of the research team. This led to the focus group interview being treated as a single interview in regards to code application, despite the presence of caregivers for three girls. This may have influenced the calculated prevalence of impacts among participants. Furthermore, treatment modality may impact the experiences of patients but treatment modalities reflect private practice preferences; therefore the high number of implants in this sample may not reflect standard pubertal suppression techniques in academic institutions. As such, variance of impact by treatment modality was not explored in this study.

Despite the aforementioned limitations of this study, there are a number of strengths apparent in this research. One such strength is the inclusion of a number of participants who are caregivers of girls adopted from developing nations, a population that is of particular interest in the study of CPP.<sup>13,14,16</sup> The semi-structured interview format employed by researchers allowed for participants to discuss a range of topics pertaining to CPP at various stages. This allowed us to elucidate the “bigger picture” of CPP– what happens before, during, and after treatment. The separation between the impacts of CPP and treatment of CPP provided valuable insight into ways in which clinicians may make the clinical experience of diagnosis and treatment less anxiety-inducing for the patients and caregivers, and the way in which they can support entire families throughout the process of diagnosis and treatment. An additional strength to this study is the inclusion of a wide age range, inclusive of patients that have completed treatment and those that have yet to start any treatment. This range of ages and experiences provided a glimpse into the impacts of CPP at various stages, for both patients and their caregivers.

Clinicians can use these findings to inform practices related to the diagnosis and treatment of CPP. Examples from participants regarding how caregivers and individual physicians and practices helped patients cope through age-appropriate explanations and soothing practices during treatment administration, among other tactics, could be scaled up and encouraged to

become standard protocol during the treatment process. Clinicians should aim to foster or create a support system for caregivers and patients currently experiencing or having experienced CPP as a way to alleviate the many secondary impacts of CPP, such as financial burdens and familial stress, as well as addressing psychosocial impacts of CPP on patients. Efforts to create and compile various coping strategies and examples of best practices and resources around how to talk to young girls about early puberty and how to discuss and explain symptoms and CPP overall to other caregivers, teachers, and athletic coaches, should be undertaken. The findings from this study should be used to inform additional research on the psychosocial impacts of CPP, including, any impacts triggered by the actual treatment process. Additional research regarding the psychosocial impacts of adoption and CPP, specifically addressing whether or not adopted children are more likely to experience negative psychosocial impacts (i.e. more severe feelings of depression and/or isolation), should also be carried out.

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## Appendix A. CPP Caregiver Interview Guide

We are doing interviews with caregivers in order to develop a questionnaire to find out how things are going for girls with early puberty. The results of the interviews will give us a final list of questions to be included in the questionnaire. This questionnaire will be useful for evaluating treatments for helping girls who are going

Our topic is about early puberty and how it affects the lives of girls ages 6-10 years. We want to know what life is really like for girls with early puberty.

You were selected to participate because you have a daughter with early puberty and are interested in sharing your insights about this topic.

- Can you tell me what you know about early puberty? [PROBES: doctor, other caregivers, other information sources]
- How did you first find out that your daughter had early puberty?
- How did you feel when you found out that your daughter has this condition? [PROBES: Concerns?]
- How did you talk to your daughter about what she was experiencing? [PROBES: Did you seek other sources of information to help you? If so, what kinds?]
- How did it affect her then (personal)? [PROBES: How her body looked? How it made her behave? Ability to cope socially and emotionally?] HOW DID YOU KNOW THAT? WHAT DID YOU SEE?
- How did it affect her then (social)? [PROBES: How other kids her age treated her? How adults treated her?] HOW DID YOU KNOW THAT? WHAT DID YOU SEE, HEAR, ETC.?
- How does it affect her now (personal)? [PROBES: How her body looks? How it makes her behave?] HOW DID YOU KNOW THAT? WHAT DID YOU SEE, HEAR, ETC.?
- How does it affect her now (social)? [PROBES: How other kids treat her? How adults treat her?] HOW DID YOU KNOW THAT? WHAT DID YOU SEE, HEAR, ETC.?
- Can you tell me about the treatments that your daughter has had for early puberty? [PROBES: Shots? Implant in arm?]
- How did you decide about what treatment options to choose for her? [PROBES: Treat or not to treat? Preferences? Concerns?]
- What is your understanding about how long this treatment will last and when your daughter can stop treatment? [PROBES: How will this decision be made?]
- Would you say the treatment she has had for CPP has helped her? What was different before and after she started treatment? What was different after she stopped

treatment? [PROBES: Concerns during expressed during follow-up?] HOW DID YOU KNOW THAT? WHAT DID YOU SEE, HEAR, ETC?

- Have you noticed anything different about how she behaves just before she has an appointment or has treatment (injection or implant)? HOW DID YOU KNOW THAT? WHAT DID YOU SEE, HEAR, ETC.?