

# Treatment Goals for Achondroplasia: A Qualitative Study with Parents and Adults

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## Research

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# Abstract

## Background:

Achondroplasia is characterized by disproportionate short stature accompanied by other changes to the musculoskeletal system. Individuals with this condition typically experience a variety of medical complications. Pharmacologic treatments are being developed for the treatment of achondroplasia. It is important to understand the goals for pharmacologic treatment among those affected by achondroplasia and factors that shape these views.

## Methods:

This qualitative study is based on semi-structured interviews with 19 parents of children with achondroplasia and 5 adults with achondroplasia in the United States. We employed thematic analysis using an iterative process to identify themes across the interviews.

## Results:

Participants had two goals for pharmacologic treatment of achondroplasia: ameliorating complications associated with the condition and increasing stature to overcome functional limitations and psychosocial challenges. Complications of particular concern were chronic pain and surgeries to repair spinal, ENT, and neurological sequelae. Increased height would enhance independence, fitting in socially, and avoiding social stigma. Despite many challenges, parents and adults with achondroplasia expressed that they found ways to adapt and emphasized satisfaction and the positive aspects of their lives. Concerns about medical treatment included fear of loss of their identity as a little person.

## Conclusions:

This study offers evidence about how individuals affected by achondroplasia think about pharmacologic treatment of this condition, including both the benefits of ameliorating complications and increasing height. The findings can offer practical insights for parents of children considering treatment, treating physicians and decision makers evaluating coverage decisions for treatment of achondroplasia.

## Background

Achondroplasia, a skeletal dysplasia, is the most common form of disproportionate short stature<sup>1,2</sup>. It is an autosomal dominant condition caused by a pathogenic gain of function variant in the fibroblast growth factor receptor 3 (*FGFR3*) gene, leading to an inhibition of endochondral bone growth<sup>1-3</sup>. Achondroplasia is a rare condition, occurring in approximately 1 in 25,000 births<sup>3,4</sup>. Estimates suggest that 80% of cases are the result of a spontaneous pathogenic variant and that most individuals are born to parents of average stature<sup>3</sup>. Occurrence increases with paternal age<sup>3</sup>. Mortality rates are higher in this population across all ages, and average life spans are shorter<sup>5</sup>

The physical features of achondroplasia are characterized by changes in the musculoskeletal system that include short stature, decreased length of the proximal section of limbs (rhizomelic shortening), macrocephaly, frontal bossing with midface hypoplasia, and atypical development of the mandible<sup>6,7</sup>. In addition, individuals with this condition may have hypotonia and kyphosis of the spine in infancy and then lordosis when they begin walking. They may also develop a smaller than normal chest size; shortened fingers with a trident hand shape; hypermobility of hips; and leg bowing<sup>2</sup>.

A number of secondary medical complications, some of which can be life threatening or have serious health consequences, are associated with achondroplasia. They emerge in infancy, and many continue into adulthood<sup>8,9</sup>. Unger et al (2017)<sup>10</sup> grouped complications into four areas: 1) ENT problems including hearing loss; 2) sleep apnea and other pulmonary related concerns; 3) neurologic problems; and 4) orthopedic problems<sup>1,11</sup>. Problems tend to occur in predictable age groups and age-specific surveillance is recommended<sup>1,2,10,11</sup>. Complications associated with achondroplasia often result in multiple surgeries over the lifetime<sup>12</sup>. Chronic pain is common and increases with age<sup>13,14</sup>.

Functional limitations can result from the various physical features and complications associated with achondroplasia. Delays in motor development are associated with anatomic differences such as disproportionately short limbs, stiff elbow, hypermobility of other joints and macrocephaly<sup>2</sup>. Children need assistance with self-care including perineal hygiene, grooming, bathing, and dressing<sup>10,15</sup>. Other functional limitations include difficulties with locomotion such as climbing stairs, transferring on to and off of chairs, walking or running, and sitting in chairs without leg support<sup>16,17</sup>. These challenges lead children with this condition to achieve independence, on average, later than non-affected children<sup>16</sup>. Difficulties around social engagement, emotional wellbeing and school participations can arise<sup>13,18</sup>. Pfeiffer (2020)<sup>17</sup> notes the importance of finding adaptations or assistance in the home and at school. In adulthood, people with achondroplasia may face limited educational and career choices, despite normal intellectual capacities<sup>19</sup>.

Children and adults with achondroplasia can experience lower quality of life (QOL) than do their counterparts without this condition<sup>13,20-25</sup>. QOL is influenced by a number of factors including disease severity, height, pain, age, self-esteem, social support, and perceived stigmatization<sup>13,19,20</sup>. Several studies, however, did find that while scores related to the physical function domain were lower than in reference populations, mental or emotional components scores were not<sup>22,23</sup>.

Concerns about medical complications, functional limitations, and overall quality of life have led to an interest in treatment of this condition. To date, the most commonly available treatments have been surgical interventions to lengthen limbs. These procedures involve multiple surgeries and prolonged recovery<sup>11,24</sup>. As an understanding of the pathogenesis of achondroplasia improves, attention is turning to pharmacologic treatments<sup>6,25,26</sup>. While the potential benefit of pharmacologic treatment is documented in the clinical literature, little is understood about how patients and families view the use of

medications to improve endochondral bone growth in order to increase stature and, potentially, to ameliorate complications.

The purpose of this study is to address this gap in knowledge. It examines the treatment goals of parents of children with achondroplasia and adults with the condition. In addition, the study aims to understand the challenges individuals with achondroplasia face in performing daily tasks, their adaptations to these challenges, their social experiences, and how these challenges influence thoughts about pharmacologic treatment.

## **Methods And Materials**

### **Study Design**

For this qualitative study we report on semi-structured interviews with 19 parents of children with achondroplasia and five adults living with the condition. We used thematic analysis to examine the interview transcripts<sup>27,28</sup>. All participants signed an informed consent document prior to the interview. The study was approved by the Ethical and Independent Review Services IRB.

### **Recruitment**

Since the goal of this qualitative study was to explore life experiences of people living with this rare condition, we used purposive sampling to recruit parents and adults from a range of age groups<sup>29</sup>. Due to the rare nature of the condition, we sought to recruit enough participants in both categories to allow us to reach content saturation.

Parents and adults with achondroplasia were recruited through patient advocacy groups such as Little People of America and a list of individuals from a website (achondroplasia.com) who agreed to be contacted for research activities. Parents were eligible to participate in the study if they had a living child with achondroplasia who was under the age of 18. Adults aged 18 years or older and diagnosed with achondroplasia were also eligible. Exclusion criteria were participation in an achondroplasia clinical trial in the preceding 12 months.

### **Data Collection**

Two professional interviewers, experienced in qualitative methods, completed the interviews. Questions for parents and adults covered their background and family life; how achondroplasia affected their lives including the social and functional effects of the condition; the complications they experienced, primary concerns for themselves or their child; their goals for treatment; and the perceived benefits of treatment.

The interviews were conducted and recorded through an online meeting space. Identifying information and names were erased from the recording. Interviews were 60 minutes in length. The interview recordings were transcribed verbatim. Upon completing an interview, participants received \$75.

## Analysis

Thematic analysis followed an iterative and a consensual process<sup>27,28,30,31</sup>. Inductive or open codes were identified through an initial reading of the transcripts. Deductive or a priori codes were informed by an earlier internal study (unpublished, 2021). To begin, a lead coder (SM) read and identified salient concepts for each transcript. Second, two members of the coding team (SM and JN) independently read the same set of ten transcripts. A third coder served as an auditor, reviewing a subset of transcripts. After each set of transcripts was coded, the team met to reconcile differences, revise the code list, and recode. Joint coding and reconciliation broadened the capture of salient constructs, while ensuring the codes were consistently applied. Following an iterative process, team members reviewed and synthesized the text captured for each code to identify patterns and to summarize underlying concepts<sup>28</sup>. They grouped the concepts into higher order categories, identifying cross-cutting themes.<sup>30</sup> NVivo was used to facilitate coding and analysis<sup>32</sup>.

To enhance readability of verbatim quotes, we removed verbal hesitations or repetitions. Quotations in the text are identified with a number to indicate the speaker's participant group: C for parent and I for adult.

## Results

### Study population

The study population included 19 parents who had a child with achondroplasia and 5 adults with this condition. The parents were predominantly female; white; had college or post-graduate education; and worked fulltime (Table 1). None of the parents had this condition themselves. All respondents in the parent cohort had only one child with achondroplasia. Their children ranged in age from 1-13 years; 10 were 5-12 years old. Ten of their children were male.

The five adults with achondroplasia ranged in age from 27 to 67 years; 3 were female; and all were white. Four had a college education or more, and three were employed (Table 1). Three of these adult participants had a child (or children) and/or a spouse with achondroplasia. Four mentioned that their parents were of average stature.

### What Shapes Treatment Goals

Participants emphasized two goals for treatment: 1) ameliorating or preventing complications; and 2) easing their lives through increased stature. We begin with a description of three factors underlying these goals: 1) the medical complications they experienced; 2) their ability to carry out daily activities and necessary adaptations; and 3) variations in the medical and psychosocial impact of the condition by age.

#### 1. Experiences with the Medical Complications of Achondroplasia

Experiences with medical complications fell on two dimensions: concerns about their severity and efforts to lead normal lives despite their symptoms. Participants described a variety of complications and their severity, including some which were serious or even life-threatening, but while acknowledging the medical effects of achondroplasia, some participants nonetheless stressed their good fortune.

**A broad range of medical complications.** Children and adults with achondroplasia experienced a broad range of complications; many required medical attention and caused notable worry. All but one parent described their child's ear, nose, and throat (ENT) problems or their worry that these problems would occur in the future. Hearing loss, a result of repeated ear infections, affected social engagement. An adult with achondroplasia described her husband's hearing loss.

*I think that really affects his ability to communicate with people and hear people. Because if he doesn't hear what someone says, he won't ask them what they say. He'll just nod his head. He might have missed something important. So, I think that is a really big issue, ear tubes and hearing loss. (I10)*

Other complications among children commonly noted by parents were sleep apnea, foramen magnum stenosis, kyphosis, and leg bowing. Among adults with the condition, ENT problems, spinal stenosis, and leg bowing were frequently mentioned.

Both parents and affected adults mentioned one or more surgeries for a variety of problems including ear tube placements, tonsillectomies, spinal decompression, orthopedic surgery for leg bowing, or spinal surgery for spinal stenosis. In many instances, these surgeries were required at a very young age. One parent described the two surgeries her child had before he was one year old.

*...Those two surgeries, it improved the sleep apnea that was being caused by the compression of the part of the brain that controls the breathing....That was all before one-year-old. (C27)*

Chronic pain affected daily lives and limited physical activities or social participation. A mother said that her son '*was going to the nurse to get [painkiller] during the day ...*' (C25), and she assumed that these visits limited his classroom time. She noted that she hoped his pain would diminish when the surgery for correcting leg bowing was completed.

**Feeling fortunate.** Although parents and adults in this sample described multiple complications, at the same time, some tended to downplay or even minimize these problems. Minimizing was expressed in three ways: as "feeling lucky"; feeling that their child was doing "better than expected"; and noting that their problems were simply part of life.

Feeling lucky was a common refrain. Participants felt lucky for a number of reasons. First, parents whose children experienced very few complications, or fewer than they anticipated initially, felt lucky. Second, participants felt lucky when the frequency of complications diminished over time and *became 'a minimal part of our life that we don't have to constantly worry about it.'*(C16) Feeling lucky was possible even if a child had experienced multiple surgeries or other problems.

*...He's been pretty lucky. He's had the tube placements and adenoids, tonsils... and then he had like major leg surgery, but he hasn't had to have back surgery and he hasn't had to have anything really with his spine... So, we've been lucky, but my hope is that he continues to stay healthy. (C25)*

Good fortune was relative, noticeable in contrast to others with this condition who might be experiencing more difficulty. An adult counted his blessings, despite experiencing surgery and chronic pain because others might not be able to be as active as he had been.

*...I had surgery in 2003. I couldn't believe that I walked around in pain like I did all my life until I had this surgery. That is the most major surgery that I've ever had, and it was a success. I count my blessings because there are little people who can't walk, who can't do half the things I do. I walk 10,000 steps a day. I treadmill. I walk outside. I exercise. ...For being my age, I'm very active...(I15)*

When their children were first born, parents said that they were told about myriad potential complications that might arise and described having considerable anxiety about the future. However, later, when their children had avoided or recovered from medical problems, these parents experienced relief. This response is particularly prominent for parents of average height who did not have prior experience with achondroplasia.

*I expected her to have more complications. I expected it to be maybe a bigger part of our life, having to kind of manage any kind of medical issues that she might have. That really hasn't come to fruition. We haven't really had to worry about that at all. (C16)*

Finally, chronic complications, such as pain became “one of those things” that one learns to tolerate. A mother talked about her son who had chronic pain.

*And his pain is different from my pain...his is pretty consistent. It's just something that he lives with and that we manage, or he manages with my supervision. So, I think he'll just be used to that. I think that's just one of those things. (C22)*

## **2. Experiences with Functional Limitations and Adaptations**

Functional limitations, resulting primarily from short stature and limb disproportionality, presented ongoing challenges for people with achondroplasia. Limitations affected how they carried-out daily tasks of living and their social activities. Below we show how participants characterized these limitations and their adaptations.

Functional limitations had a broad effect both on life in and outside the home. Reaching, carrying, climbing stairs and even traversing public spaces could present challenges. For example, reaching a toilet, sink, or shower faucet required use of a stool or lowering or re-sizing the bathroom fixtures. To use public restrooms, they had to bring a stool.

Some adaptations could be burdensome, both physically and psychologically. A mother described her daughter's embarrassment about using adaptive devices in school because they drew unwanted attention. She reported that her daughter said:

*'I don't like having to have this special chair at my school. I don't like it. And then that chair has to follow me. Mom, the chair looks horrible. You don't understand what it's like. I don't like having to have a stepping stool every time I go to use the restroom.' Or, 'I don't like having to have to carry these wipes with me when I use the bathroom because people ask questions.' [She says], 'Sometimes I just hate it when people ask or point at me'... 'What are you pointing at? (C33)*

Participants reported difficulty reaching counter tops or shelves in stores, handles of shopping carts, pushing elevator buttons, or using ATMs. Stair risers were too high to climb or doors too difficult to open. One adult said: *'I hate going to the grocery store, where I can't reach the items. If they don't have low carts or short carts, I have to practice as to how I'm going to layer the groceries in the cart so I can get them out.'* (I15)

Carrying large or heavy items was difficult. For example, children had difficulty using a school backpack. A mother with achondroplasia described her difficulty with carrying her own children. *'It really affects the way I carry my son and hold my son ...I can't carry him for long periods of time because he gets heavy. My back starts hurting.'* (I10)

Smaller stature made walking long distances difficult. A mother explained: *'...for every one step that an average child takes, he probably takes two or three. So, it's more of a physical exertion for him to just do everyday things.'* (C22) To cover distances in an airport quickly, a parent described how they had their 10-year-old child ride in a stroller, something the child found humiliating and resented: *'... I can tell it's starting to bother him.'* (C25)

Participants mentioned enjoyment of outdoor physical activity and sports, but short stature sometimes required children to adapt by finding alternative forms of participation in group sports. For example, a child found a way to be involved in water basketball by directing the play from the edge of the pool rather than engaging in the water.

*We were just on vacation, and there were some kids playing basketball on the water, and he was doing pretty well. He was treading water and throwing, but all these other kids could stand and he couldn't. ... And then after a while, he got out and started like coaching and directing everybody on what to do. So, he always finds a way to kind of make it work and still be involved in things (C25).*

Concern about possible injury, especially to the spine, worried parents from infancy and throughout childhood, leading families to change aspects of their lives. Parents modified how they held their infants, used a stroller, or a car seat because *'the spine was so unstable'* (C22), or changed childcare arrangements because they *'worried about other people handling [their child] correctly.'* (C32) As children grew older, parents wrestled with wanting to protect their children from injury while allowing them to enjoy

physical activity. They carefully weighed how much they had to supervise their children. Finding the right balance was difficult.

Despite challenges, individuals and families were often able to adapt to physical limitations. Some families made extensive changes to their homes such as lowering light switches, lowering counters, and re-arranging closets. Others made only limited changes in the hopes that their children would learn to function independently in environments built for persons of average height. As one adult participant remarked: *'... [It's] the only life that I've known, and so you kind of learn to adapt. You learn to especially when it comes to things with school or even in the real-world setting, like how do I brush my teeth or things like that, you find solutions.'* (I06) Adaptations enabled families to do many of the same things as individuals of average stature, as one said: *'...we can do absolutely anything anyone else can do. It just might be harder.'* (I10)

### 3. Variations in the Physical and Social Concerns by Age

The participants in this study talked about the variation in medical complications and social concerns across age groups. In their view, the trajectory followed a U-shaped curve (Figure 1). The most acute, or troubling complications such as foramen magnum stenosis or repeated ENT problems were more common in the youngest age group (infancy into early childhood). As individuals grew into childhood and adolescence, they observed that medical complications tended to diminish in severity and frequency. In adulthood, complications, particularly related to the spine and chronic pain, became more prominent again. An adult commented on this phenomenon saying: *'And they face even more concerns, at least initially, and then will face similar concerns as they age as well.'* (I06)

In the view of participants, age trajectory for social concerns also changed with age but the curve followed an inverse shape (See Figure I). Psychosocial concerns in the youngest age group centered around parents' needs and family concerns; participants expressed less anxiety about immediate social and emotional needs among the younger children. Such concerns increased as the children entered school. As individuals settled into adulthood social and emotional concerns largely receded in importance. In the following section we describe the variation in social and medical concerns by age group.

Study participants described early childhood as the period when people with achondroplasia were likely to experience the greatest number of complications, many of which could be acute or severe. A mother reviewed a litany of potential complications but ended her list by noting that her daughter was getting past this most *"dangerous age"* and in her view would be less likely to experience medical problems: *'She's almost two, so we are passing the more dangerous age...'* (C17)

Parents of children approaching the end of the *"dangerous"* period expressed relief that their child had made it through the worst and seemed to be healthy. At this point, their anxiety about medical complications diminished.

*...He's doing incredibly well, and he's very, very healthy right now. And kind of getting over the hump of age two or age three without any major things going wrong is really a huge, huge relief. There's a lot of anxiety and a lot of worry with these kiddos the first couple years of life. And so, it was not easy, and it was kind of scary just knowing that any of these really major things could kind of happen and pop up at any time (C28).*

When children entered school, concerns shifted to the emotional and social needs of their children. At this age, children became increasingly aware of differences in height and functional abilities. An adult recalled: *"And so then it wasn't till probably grade school that it became aware from my perception that I was different (I06)."* While they spent more time with peers, children and began to experience stigma and bullying. Parents reported that their children were called names, laughed at, or physically bullied by classmates or people they encountered in the community. They described experiencing inappropriate attention such as staring, or asking to take a photograph. A mother explained:

*... People would look at her and immediately like run up to her and be like, 'Oh, you're a little person. Can I take a photo with you?', which is something I've seen happen multiple times or friends of ours have told us about (C30)*

A mother described how she found that *'...Sometimes adults talk down to him because he does look younger, but that his intelligence is off the charts. He's a smart kid.'* (C25)

Although these problems were noted in adolescence and adulthood, they were most difficult for school-aged children who were still learning how to manage difficult interactions. One mother noted that, in her view, this could be a particular problem for children: *'When they're children, I think they do experience some bullying and, I guess, being treated differently because of their stature.'* (P23)

Entry to school required finding accommodations for a child's functional limitations. This transition presented emotional challenges for parents. They had concerns, for example, about how their children would use the toilet in school. A mother explained: *'Starting school was very stressful for me. I was concerned with self-care at the school.'* (C31)

During adolescence concerns became largely psychosocial in nature. As might be expected for adolescents with achondroplasia, concerns about friendship, fitting in, and dating became prominent. A mother of a young child anticipated the shift: *'... I worry as he gets older...the height difference continues to be really be obvious. I worry about ...him social.'* (C13) She wondered what it will be like for her son when he wants to join the school marching band, go to the prom, or drive. Another mother worried about the potential detrimental effects 'physically standing out', particularly for her daughter's *'mental health through her preteen and teen years too and her self-esteem.'* (C16) One parent expressed concerns about the difficulty her child might face as she became interested in dating, *'...Its going to be really hard when you get to the age of crushes and all that.'* (C20)

In adulthood, both parents and adults reported that medical problems resurface, primarily in the form of joint and back pain, particularly associated with spinal stenosis and related back surgery. A parent explained: *'I know people who were totally fine and had no medical complications, and then they turned 38 and all of a sudden couldn't walk one day and had spinal stenosis.'* (C28) Parents worried about the need for future surgeries and the associated pain, concerns, that a mother said were problems that were *'associated with aging that I worry about.'* (C16)

Despite the increase in focus on medical problems in adulthood, social stigma; and discrimination was also a concern. Some reported limited career options. An adult participant reported,

*I had to meet this new administrator who questioned me like how was I going to reach things. "Well, I'll stand on a stool." "Well, what if you fall off the stool?" "I won't fall off the stool." I said, 'I'm not a safety hazard.' He wasn't going to hire me, and I was the only degreed person. (I15)"*

Although they were aware of the age trajectory, participants recognized that the age and frequency with which complications occurred was variable and the future was unknown. Some found this uncertainty to be anxiety provoking: *'It's totally hard to predict. So, there's never a point where like, you get to age 10, and you haven't had this, you're totally fine. There's always kind of a worry.'* (C28) An adult similarly emphasized the uncertainty of medical needs as people with achondroplasia age:

*...There are things outside of your control, right? You're going to have spinal compression—the risk for any kind of spinal compression or joint and leg pain or neck pain can be kind of out of your control. And you really don't know how you will be when you're older, because you're going to naturally age. So how is that wear and tear going [show up] for you? (I06).*

## Treatment Goals

Participants had treatment goals related to two outcomes: easing their lives by increasing height and preventing or ameliorating complications. In addition, we also found that some participants were doubtful about the benefits of treatment, and some who were less enthusiastic about increasing height because they were happy with themselves and wanted to maintain their identity as a little person. In this section we describe the themes for each of these four areas.

### 1. Increasing height

Increasing height was not necessarily an end in itself. Rather, increased height would help them in three ways: 1) creating an independent life in an average height world by removing functional limitations; 2) fitting in socially; and 3) minimizing discrimination and stigma.

**Fitting into an average height world and greater independence.** Increasing height would facilitate the ability of individuals with achondroplasia to carry out daily activities, helping them to function more easily because, as they noted, this *'... world is built for people for average height. It's not for people with achondroplasia.'* (C17) Parents commented that they hoped that increased height would help their

children with *'just normal activities that you do day in and day out. I just don't want her to always have to think every day, 'Oh, I can't...'*(C31) One parent hoped that treatment would *'Really just provide the growth so that he could be closer in height to an average height. When you think about it, everything in this world is designed for that certain height.'* (C01) Parents cited examples such as:

*...If you gain a few inches, maybe you can drive a car without having all the equipment. Reach out to a door opening and opening a window. ...They're daily things that you could perhaps avoid by doing a treatment that's safe, that's giving me reason to do it (C12).*

One parent thought increased height would help: *'...in terms of toileting, that's huge. Just access in stores, in the workplace, in public transportation, in her own transportation. It's every moment of your day, it would impact.'* (C20) With additional inches in stature, it would be: *'feminine hygiene, making her bed...I think driving a car will be easier for her, and she'll need less accommodation there.'* (C16) For another mother, increased height would have enabled her daughter to be *'a more free kid.'* She said her daughter: *'could have ridden [a bike] when she was little with all the other kids, or gotten to do the bounce houses.'* (C31)

**Fitting in socially.** There were multiple dimensions to the benefits of fitting in socially that would make life “easier” or help their child to be *“fully embraced and sort of accepted (C18).”* These dimensions included the ability to find friends, life partners, and employment. An adult speculated about how increased height through limb lengthening might have changed her life:

*Maybe it would have been easier socially to make friends. And if I wanted to marry an average sized person, it probably would have made that easier. It might have been easier to become more of an athlete or drive a car without pedal extenders or not need so many stools. So, I can definitely see how it could have made life easier. (I10).*

In some cases, fitting in socially meant simply looking like an average person. A mother described how distraught her child was when she learned that she would never grow to be the same height as her parents. A mother said her daughter was upset to learn she would not be average stature. *'...She did get really upset and start[ed] crying and said, 'But I want to be big like you.'* (C20)

Another parent observed that sometimes being little can affect social interactions because little people cannot look average-stature people directly in the eye when they converse standing up. This mother noted that a friend chose to have limb lengthening surgery in part because of these types of challenges. She said: *'...one of the things she said was when she would speak to someone, ...she was eye level to their crotch. I'm not a little person, so I wouldn't even think of that. And I'm like, 'Oh my gosh.' Like she would always have her head down. She would never look up.'*(C26)

Parents recognized the potential psychological benefits of fitting in. A mother summarized saying: *'the social, emotional, mental health benefits to her would be big'*, later elaborating this would be because their child would, *'stand out less from her peers.'* (C16)

**Avoiding stigma and discrimination.** Closely related to the desire to be socially accepted were experiences with being stigmatized or discriminated against at school, work, or in the community.

Parents believed that their children might avoid negative social experiences with increased height. For example, a parent hoped that a height increase might improve career opportunities. *'...She would be less likely to face potential discrimination due to her size if she was able to have more growth.'* (C16) Another felt that an increase in height could help prevent unwanted attention and bullying. She said: *'To be closer to at least the bottom range of the average height people so that he doesn't stand out. People don't always point at him and... bully him.'* (C21)

## 2. Ameliorating or Preventing Complications

Preventing or ameliorating complications was important to all participants. They hoped that treatment would help to lessen or avoid complications in childhood, or prevent them as individuals age. In particular, four benefits of treatment were noted, benefits that reflected the most troubling complications described above. In addition, where a child along the age trajectory influenced views on treatment.

**Preventing or ameliorating spinal problems.** Concerns about issues related to the spine were prominent: *'Anything that can prevent issues with his spine, those are very strong selling points for me.'* (C27) Another parent said:

*... if they had come to me and said, 'Oh, this medication is going to widen her foramen magnum and ... she's not going to need a neck surgery or shunt surgery', of course, that would be something that my husband and I would have totally talked about and considered (C9).*

**Preventing pain.** The desire to keep their children from experiencing pain, including joint pain, and pain as a result of surgeries was an important benefit of treatment. A mother hoped,

*That there wouldn't be the back pain, the leg pain, the knee pain, the neck pain, the surgeries. ...that would be the most important. That it would take care of just that pressure being put on her body as she would grow (C14).*

**Preventing surgery.** In commenting on the value of treatment, a mother exclaimed that if a treatment had been available that could prevent many of the complications her child experienced, she would have started treatment as soon as her daughter was born.

*... She had decompression surgery. She's had four sets of tubes. She's had her adenoids out twice. If that all could be avoided, yep. If somebody had said to me at 33 weeks pregnant, 'the day your baby is born, we can give them medicine that could help with avoiding all of that.' I would have started day one. I would not have hesitated (C31).*

**Age Trajectory Shaped Treatment Views.** A child's age, or where a child fell in the age trajectory of achondroplasia influenced parents' considerations about treatment. One parent talked about how

receptive they would have been to pharmacologic treatment when their child was facing serious problems. As these problems diminished the parents also thought less about treatment.

*I would say when we were going through the really scary times about a year ago when they thought he was going to have major brain and spine surgery, we were both more on the fence of like, 'Let's do this. If anything can help us, if anything can prevent this from happening again... let's roll the dice (C28).'*

This parent went on to explain that if their son was experiencing more severe problems, they would have done *"Anything possible to prevent surgery: [I] think if the last three years were different for us, I could imagine wanting to do anything possible to prevent horrifying medical surgery (C28)."*

**Preventing problems in adulthood.** Finally, preventing problems in adulthood could be a motivator for parents. A mother said: *'I want to decrease the chances that my kid's going to be using a walker in her late fifties or have surgeries or pain...'* (C20)

For a few participants, ameliorating or preventing complications was more important than increasing stature. They believed that treatment would not be beneficial if it only increased stature; they would be most focused on preventing complications and pain. As one adult said:

*Not just the height. That is not something that I really care about. I care more about [whether] it will improve the size of the thoracic cavity and also the shape of the facial structure and also the foramen magnum, because there are some kids that have a recurring narrowing of the foramen magnum even though they had already had the surgery done. So, if those are positive things that that drug can solve, I will consider it. (C27).*

### 3. Doubt and Negative Views

Doubt about the range of benefits that pharmacological treatment could offer patients was expressed by some. This skepticism was driven by two concerns. First, they believed that despite treatment, a patient would still have achondroplasia. Second, some wanted more information about the potential effectiveness of treatment beyond height benefits.

**My child will still have achondroplasia.** While recognizing that treatment could increase height, they anticipated that it would not change the fact that their child has achondroplasia, or as one parent said they will *'still have the gene. (C09)*. Another speculated that increasing height may not change other phenotypic features of the condition: *'...Sure, you're getting some height, but you're not really addressing a lot of the other phenotype characteristics. Like, the trident hand, your feet, the larger head and frontal embossing.'* (I06) A mother had similar concerns:

*I'm just trying to be a realist. I don't think it really will change much how he looks because achondroplasia is a condition that is the only dwarfism that is disproportional. Like your head, a regular-sized trunk, but shorter limbs. They look different, and I don't know how much really will change that. And also, adding the fact that he has hydrocephalus. His head is even larger (C27).*

**Height is part of our identity, and there is nothing wrong with being little.** Being a little person was an important part of identity for many and they liked who they were as little people. One parent explained simply that their child, 'likes being small.' (C12). An adult echoed this sentiment, pointing out that his experiences with achondroplasia helped him to see the world in a different way, helping him to be more creative.

*I think a lot of that has actually led to my creativity, which has helped me from a professional standpoint of always looking at problems from a different lens or always thinking how can we better improve different things from a professional perspective (I06).*

Suggesting that they would want to increase their height was seen by some as being offensive and critical of who they were. In their view, the world should learn to accept them as they are. One parent said: '... [Little People] kind of want society to be better instead of—they don't think they should try and change for society, and that's kind of how we feel (C09).' She noted that height is not a concern for her and her family. Another parent said:

*...I think people just need to realize that just because someone is short in stature, that's it... There's no cognitive delays or things like that. So, I think it's just a matter of people becoming familiar with achondroplasia and with dwarfism in general and just treating people like people and not be so affected by the height difference (C14).*

## Discussion

Our study showed that treatment goals with potential pharmacologic agents centered around two features of life with achondroplasia: 1) medical complications; and 2) limitations to physical function and social adaptation due to short stature. While the benefits of addressing both features were apparent to participants, doubts and some negative views also were noted, particularly the importance of identity as a little person.

The results of this study illustrate the importance of the age trajectory on how individuals experience achondroplasia. The medical literature describes the manner in which medical complications vary by age<sup>7,8,33</sup> but there is little in the literature about the trajectory of social concerns, with the exception of the report by Pfeiffer et al (2020)<sup>13</sup> in which the authors offer a description of social concerns across different age groups of children. Our study adds to this knowledge by underscoring the inverse relationship between medical complication and social concerns by age.

In many respects, the experience of achondroplasia is one of contradictions. Participants described their worries about the severity of medical complications yet also minimized the implications of the condition. While many said they liked who they were as little people, they also recognized the potential benefits of increasing height and preventing complications. While many participants did not see height as a primary treatment outcome, they did recognize benefits related to increasing one's stature in terms of increased accessibility, independence, and acceptance. This finding is consistent with the report of Matsushita et al

(2019)<sup>21</sup> that increased height is associated with higher scores on physical components HRQoL measures.

Contradictory views can be understood through the framework of the “disability paradox”<sup>34</sup>. In that framework, individuals with disabilities may report a high level of wellbeing or happiness with their circumstances, regardless of the challenges they may face. Albrecht (1999)<sup>34</sup> argued that people with disabilities aim to find a balance across three inter-related domains: “body” or physical function; “mind” or intellectual capacities; and “spirit” or sense of self and higher purpose. Those who can achieve this balance find a way to define themselves within their social world and physical environment. Their capacity to manage their lives with this condition can be rewarding and satisfying<sup>34,35</sup>. The participants in this study who believed that they were lucky, or that life was better than expected, were adjusting how they saw themselves within their current circumstances. They were exercising “salutogenesis” in contrast to pathogenesis,<sup>34</sup> focusing on what they had, in contrast to what they did not have, or could not do. A more systematic exploration of this phenomenon among individuals living with achondroplasia would enhance the understanding of the disability paradox in this population.

Our study did not set out to assess quality of life, rather we focused on understanding how people affected by achondroplasia think about their experiences and how they perceive whether they may or may not benefit from treatment. Our findings do point to the importance of going beyond a single QoL measure to understand the range of experiences and views of persons affected by achondroplasia. Stature and complications are two separable domains of life experience and should be treated as such in measures to assess the effect of treatment or QoL measures. This finding is consistent with the results of the concept elicitation reported by Pfeifer et al (2020)<sup>17</sup>.

Some QOL studies indicate that not all individuals affected by achondroplasia have had negative life experiences<sup>21-23</sup>. Our findings reflect this. While our participants do face medical complications and physical limitations, positive views about identity as a person with achondroplasia were evident. Being of shorter stature is part of their identity; and for the most part, they are happy with that and want to be accepted and valued as little people. In general, children are encouraged and supported by their parents to learn to accept themselves and their challenges. This finding might help to explain why Witt et al (2019)<sup>22</sup> found that children with achondroplasia did not have lower scores on the emotional domain of QOL compared to their counterparts. It is possible that the children in this study arrived at self-acceptance and were happy with themselves.

Consistent with the quality-of-life literature we found that having achondroplasia does affect function and social experiences<sup>17</sup>. Clearly particular social challenges such as stigma and discrimination were a concern for study participants. Such experiences can affect a sense of well-being and are consistent with the items suggested by Pfeiffer (2020)<sup>17</sup> for the Achondroplasia Child Experience Measure (ACEM). While many individuals found ways to adapt to an average height world, some continued to experience difficulties with functional limitations. Increased height might help to address some of these challenges.

**Limitations and strengths.** Like many qualitative studies the sample was small and not designed to represent the full population. The study participants were largely white, employed and highly educated. As such they may have greater resources to adapt to functional limitations. This study only draws on participants in the United States who were affiliated with patient groups or were actively seeking information about achondroplasia. While one strength of the study sample was the inclusion of views from two sets of stakeholders in the achondroplasia community - parents and adults; however, despite our best attempt, we were not successful in recruiting adolescents whose views may differ from those of parents. The in-depth nature of the interviews yielded rich data that offer insights into views on treatment and the factors that help to shape these views. To our knowledge, this is the first examination of treatment goals among those affected by achondroplasia. The results suggest hypotheses that can be explored in future quantitative studies.

## **Conclusions**

The study findings describe the spectrum of views about the benefit of pharmacologic treatment of achondroplasia. The benefits of increasing height included making it easier to function in an average height world, and increasing independence, fitting in socially, and avoiding stigma and discrimination. Participants hoped that pharmacologic treatment would prevent pain, surgery, problems of the spine, and problems in adulthood. Contrary to views about the benefits of increasing height was the notion that short stature was an important part of identity as a little person.. Age trajectory was important and shaped views on treatment.

The results offer practical insights for parents of children with achondroplasia, physicians treating these patients as well as decision makers evaluating coverage decisions for achondroplasia treatment. Parents may be more receptive to the benefits of treatment early in a child's life when they have the highest level of concern about complications and what the future will bring for themselves and their children.

## **Declarations**

### **Competing Interests**

E. Chen and A. Abrahamson Larkin are employees of BioMarin Pharmaceutical, Inc. None of the other authors have competing interests.

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## Authors Contributions

S. McGraw, J. Henne, E. Chen, and A. Abrahamson Larkin contributed to the design of the study and developed the interview guide. S. McGraw and J. Henne were involved in the data collection. S. McGraw and J. Nutter conducted the data analysis and interpretation of results, and drafted the manuscript. J. Henne, E. Chen and A. Abrahamson Larkin contributed a critical review of the manuscript. All authors read and approved the manuscript.

## Ethics approval

Ethics approval for this study was obtained from the Ethical & Independent Review Services. Informed consent was obtained from all study participants.

## Availability of data and materials

Data supporting the findings in the manuscript are included within the manuscript. Further data is available from the corresponding author.

## Consent for publication

All participants gave written consent to use study data in publications.

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## Tables

*Table 1: Characteristics of parents of children and adults with achondroplasia*

Parents N= 19	n (%)	Adults N=5	n (%)
<b>Gender</b>			
Female	16 (84)	Female	3 (60)
Male	3 (16)	Male	2 (40)
<b>Ethnicity</b>			
White	16 (84)	White	5 (100)
Black	1 (5)	Black	0
Latinx	2 (11)	Latinx	0
API	0	API	0
<b>Education</b>			
Some high school or GED	3 (16)	Some high school or GED	0
Some college/technical	2 (11)	Some college/technical	1 (20)
Four-year degree	6 (32)	Four-year degree	3 (60)
Postgraduate	8 (42)	Post graduate	1 (20)
<b>Employment Status</b>			
Full-time	11 (58)	Full-time	3 (60)
Part-time	5 (27)	Part-time	0
Homemaker	1 (5)	Homemaker	0
Unemployed	2 (11)	Unemployed	1 (20)
Retired	0	Retired	1 (20)
<b>Others in family with achondroplasia</b>		<b>Others in family with achondroplasia<sup>a</sup></b>	
Partner	0	Partner	3
Sibling	0	Sibling	1
Children	0	Child(ren)	3

<sup>a</sup> 3 of the 5 adults with achondroplasia had others in their family with the condition.

## Figures

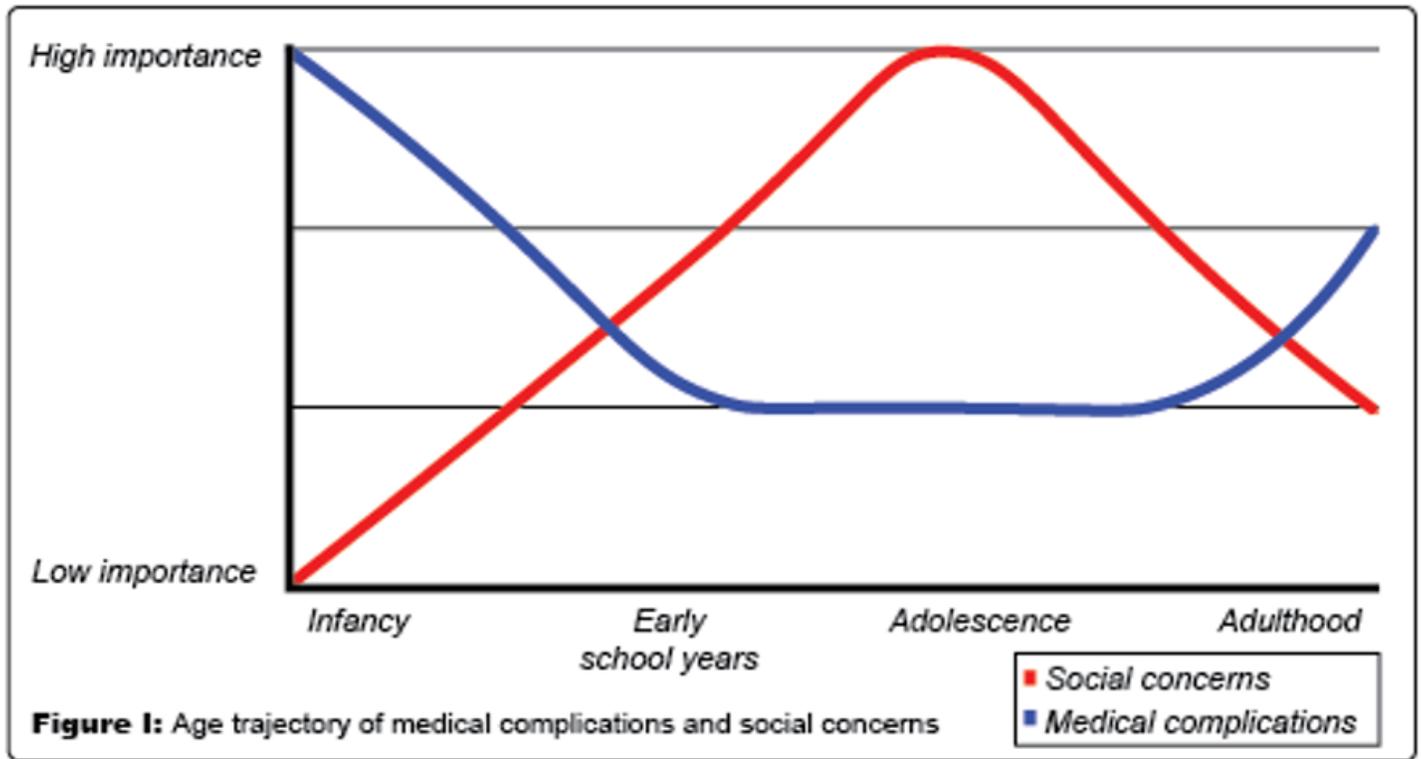


Figure 1

See image above for figure legend.