Development of a pilot questionnaire to evaluate parental health-related quality of life, caregiving burden, mental stress, and individual resources in caring for children with idiopathic short stature or isolated growth hormone deficiency

Dissertation

zur Erlangung des akademischen Grades eines
Doktors der Medizin (Dr. med.)

an der

Medizinischen Fakultät der Universität Hamburg

vorgelegt von

Lea Carlotta Lackner

aus

Hamburg

2024

Betreuer:in / Gutachter:in der Dissertation: Prof. Dr. Julia Quitmann

Gutachter:in der Dissertation: Prof. Dr. Ania C. Muntau

Vorsitz der Prüfungskommission: Prof. Dr. Ania C. Muntau

Mitglied der Prüfungskommission: Prof. Dr. Laura Inhestern

Mitglied der Prüfungskommission: PD Dr. Christine Blome

Datum der mündlichen Prüfung: 24.11.2025

Table of Contents

frontiers | Frontiers in Endocrinology

TYPE Original Research
PUBLISHED 17 March 2023
DOI 10.3389/fendo.2023.1093983

Check for updates

OPEN ACCESS

EDITED BY
Ahmed Khattab,
Rutgers, The State University of New Jersey, United States

REVIEWED BY
Margaret F. Keil,
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NIH), United States
Mumtaz M. Mazicioglu,
Erciyes University, Türkiye

*CORRESPONDENCE
Stefanie Witt
s.witt@uke.de

SPECIALTY SECTION
This article was submitted to Pediatric Endocrinology, a section of the journal Frontiers in Endocrinology

RECEIVED 09 November 2022
ACCEPTED 30 January 2023
PUBLISHED 17 March 2023

CITATION
Lackner L, Quitmann JH and Witt S (2023) Caregiving burden and special needs of parents in the care of their short-statured children – a qualitative approach. *Front. Endocrinol.* 14:1093983. doi: 10.3389/fendo.2023.1093983

COPYRIGHT
© 2023 Lackner, Quitmann and Witt. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Caregiving burden and special needs of parents in the care of their short-statured children – a qualitative approach

Lea Lackner, Julia Hannah Quitmann and Stefanie Witt*

Department of Medical Psychology, Center for Psychosocial Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Purpose: To explore caregiving burden, health-related quality of life (HRQOL), stress, and individual resources of parents in the care of children with isolated growth hormone deficiency (IGHD) or idiopathic short stature (ISS).

Methods: Focused interview analysis of previously, within the *Quality of Life in Short Stature Youth* (*QoLISSY*) project, conducted structured focus group discussions (n=7) with parents (n=33) of children with IGHD/ISS aged 4 to 18 years were performed.

Results: 26 out of the 33 parents reported mental stress due to their child's growth disorder. Social pressure and stigmatization were also mentioned as being demanding. Some parents reported having trouble with human growth hormone (hGH) treatment. Several parents wished for parent support groups with other like-minded parents of short-statured children.

Conclusion: For physicians, it is essential to understand the parents' caregiving burden, stress, and individual resources in caring for IGHD/ISS children. If an impaired HRQOL is detected, psychological intervention for these parents may be scheduled, and coping mechanisms may be discussed. Furthermore, it seems essential for parents to be educated by their healthcare provider about the possible side effects of hGH treatment or to know where to find evidence-based information about it.

KEYWORDS

health-related quality of life, short stature, caregiving burden, children and parents, isolated growth hormone deficiency, idiopathic short stature

1 Introduction

Short stature is a chronic health condition defined as a height below the 3rd percentile based on sex, age, and population. Alternatively, the standard deviation score (SDS) can be used to define short stature (1). The causes of short stature can be both a norm variant of growth and a primary or secondary acquired pathological disorder or idiopathic (2). The

diagnosis of short stature includes various anthropometric, biochemical, and radiological assessments, such as nutritional and hormonal assessment and an estimation of the children's bone age (3).

However, isolated growth hormone deficiency (IGHD) and idiopathic short stature (ISS) are most common and, therefore, especially relevant for everyday clinical practice (4).

IGHD is diagnosed when short stature is due to substantiated growth hormone (GH) deficiency. Characteristically, IGHD is defined as a growth rate below the 25th percentile and evidence of retardation of bone age (5). Insulin-like growth factor I (IGF-1) and IGF binding protein 3 (IGF-BP-3) below -2 SD indicate IGHD. Clarification is usually conducted using two GH stimulation tests (6); a nocturnal GH secretion profile can be obtained as an alternative to a stimulation test. Without human GH (hGH) treatment, affected individuals achieve a mean final body height of 4.7 SD below the population mean (7). The gain in body height with hGH treatment is an average of 1.5 to 2.0 SD and, in extreme cases, up to 3.5 SD (7).

ISS refers to a heterogeneous group of patients without a known cause for their short stature. It is a diagnosis that requires complex diagnostics and, if necessary, genetic testing to exclude other (rare) causes (8). ISS includes familial short stature, where body height in adulthood is usually within the familial target height range (9).

IGHD and ISS are not life-threatening diagnoses for children but can still lead to an impaired health-related quality of life (HRQOL) and effect the well-being of the short-statured children, their caregivers, and even the whole family (4, 10–12).

HRQOL is a multidimensional concept of physical, psychological, and social dimensions, including general perceptions of life satisfaction in the context of health (13). The development nd well-being of children with chronic health conditions are directly related to the HRQOL of their parents (14, 15). Thus, exploring and understanding potential reasons for an impaired HRQOL and the caregiving burden that may arise from the child's health condition is essential.

A child's chronic health condition requires a future-oriented approach, which aims to teach the children to be independent and successfully integrate the treatment into daily life (16). Studies show that the better adaption of the condition to the family's everyday life, the less burdensome the disease is perceived and classified by the affected family member (17, 18). The personal responsibility of those involved is fundamental and directly influences the medical prognosis (19). Both parents are affected by the child's chronic health condition, although mothers are often more involved in caregiving and mainly report to be the primary caregiver (20–22). Mothers consider themselves more psychosocially burdened (23). Mothers and fathers experience disadvantages compared to parents of healthy children regarding personal needs (24, 25). For parents, a chronic health condition of their child results in challenges regarding the balance of care and support on the one hand and the support of independence on the other hand (26, 27).

Chronic conditions in children and adolescents are often associated with significantly poorer HRQOL and a higher caregiving burden on the children's parents (24, 28–31). The family's dealing with the health condition depends on the experienced caregiver burden and influences the affected child's assessment of the HRQOL and treatment adherence (32–34).

Therefore, we aimed to describe the parental caregiving burdens, HRQOL, stress, and individual resources in the care of IGHD/ISS children to address the unmet needs of parents of short-statured children and improve the HRQOL of all family members. The better parents deal with their child's chronic condition, the better they can meet the child's development tasks and their own needs (27).

2 Materials and methods

2.1 QoLISSY project

This analysis used data from the *Quality of Life in Short Stature Youth* (*QoLISSY*) project. This project was a multicenter study in five European countries (Sweden, Spain, France, the United Kingdom, and Germany). The *QoLISSY* study aimed to develop and establish a cross-cultural condition-specific HRQOL instrument for IGHD/ISS children and adolescents. The QoLISSY questionnaire contains self-reports for children ages 8 to 18 and proxy-reports for children ages 4 to 18 (35).

The project was divided into three phases: 1. focus group discussions, 2. pilot testing and cognitive debriefing, and 3. psychometric testing (field and retest). The current analysis used the German statements from the parent's focus group discussions. The regional ethics board approved the study before it started (PV3184). A regional ethic board achieved an additional ethic statement for the re-analysis of this data (LPEK-0579a).

2.2 Focus groups

As part of the QoLISSY study, seven structured focus group discussions were conducted with 33 parents of children with IGHD/ISS aged 4 to 18. Parents were recruited through the cooperating clinical centers in Bonn, Erlangen, Hamburg, and Munich. Participants received verbal and written information about the study and had to sign the informed consent before focus group participation. Two trained moderators led the focus groups and followed a semi-structured interview guideline. The focus groups were tape-recorded after receiving the informed consent of the participants (4).

We included parents for interview participation if they met the following inclusion criteria (1): parents of a child with a confirmed diagnosis of IGHD or ISS, independently of treatment status (2), parents of a child aged between 4 and 18 years, and (3) sufficient German language skills to participate in an interview. Parents were excluded if other health conditions of the child were the focus of attention. No additional clinical data were collected.

2.3 Data analysis

The interviews were transcribed verbatim all names of the participants and names mentioned by the interviewees were pseudonymized with either letters or names. Based on the interview data, a computer-assisted focused interview analysis (36) was conducted using MaxQDA-Software (MaxQDA 2020). Categories

for the coding guide were defined deductively and inductively. The deductive categories and their definitions are based on the interview guideline and a previously performed systematic review (submitted). In addition, inductive main categories and subcategories were added based on the qualitative data.

After the coding process, a reliability check of the focus group statements was conducted to ensure that the results were reproducible. A second coder (SW) coded 20% (n = 2) of the focus groups. An agreement of a minimum of 70% was set previously as the lowest limit. After the first run, there was a 65% intercoder agreement. By discussing difficult sections and then optimizing the coding guideline, we achieved an intercoder agreement of 81%.

3 Results

3.1 Sample description

A total of 33 parents participated, having at least one child diagnosed with IGHD or ISS - three parents had two children with growth problems, including one mother with identical twins. The participating parents reported about 36 children and adolescents with IGHD or ISS; 26 were male, and ten were female. Three of the 33 parents participated as parent pairs, and 27 participated without their partners (Table 1).

3.2 Category system

Five hundred and nine growth-related statements from parents with IGHD/ISS children were coded, resulting in eight main categories related to parents' caregiving burdens, HRQOL, stress, and special needs due to the child's short stature (1): *social problems, (2) mental stress, (3) everyday life, (4) growth hormone treatment, (5) special support, (6) future worries, (7) special needs*, and *(8) individual resources.*

3.2.1 Social problems

The category *social problems* includes statements about parental stress from social situations, structures, and relationships due to the child's growth disorder. These problems mainly cover stigmatization and social pressure some parents experienced throughout their child's short stature. Statements about social problems related to hGH treatment were coded into the *growth hormone treatment* category.

Parents mainly reported problems due to their child's growth disorder depending on concrete social situations, structures, and relationships. They felt stressed about comparing their child to peers of the same age in size and skills (n=11; 33%). Some interviewees, for example, found it upsetting that their child was only able to ride the walking bike at the age of five, while other children could already ride the bicycle by then. Other parents mentioned their child's shorter body height compared to their peers as challenging (n=11; 33%).

"And when my son did not really grow along with his friends of the same age, that has been depressing me for all these years." (Mother of an 18-year-old adolescent with IGHD)

Some parents (n=6; 18%) also distinguish between boys and girls. From their point of view, girls with a growth disorder had a much easier time in daily life than boys, which also made interacting with their social environment easier. One mother said that society expects men to be taller than women.

Parents also reported getting stigmatized because of their child's short stature, and they mentioned the ignorance of society about short stature. For example, some interviewees (n=7; 21%) outlined that other people thought their child was short because the parents did not provide sufficient food for their child. Some parents (n=9; 27%) mentioned that social standards are demanding.

"But that's exactly how I felt, I felt like I had a bad child because she didn't fit the standard. In society, much emphasis is placed on the standard, and this is quite awful." (Mother of a 7-year-old child, ISS)

In some cases, the social environment tried to force the parents of short-statured children to act. Parents (n=7; 21%) reported that other people tried to advise them on what would be best to do. Few parents (n=4; 12%) reported having no social problems, mainly because their surroundings ignored the topic.

3.2.2 Mental stress

Statements were coded into the category *mental stress* when they addressed parents' mental stress due to their child's growth problems. If the reported problems were influenced or caused by the social environment, these statements were coded into the category *social problems.*

Almost all the interviewees mentioned their psychological well-being getting affected by their child's growth problem (n=26; 79%). Often other people's reactions and behavior toward the parents' child were the cause for them feeling frustrated. Parents experienced frustration because their children were treated according to height and not age (n=11; 33%).

Parents also reported that they witnessed or heard their children being bullied by peers resulting in isolation and feelings of rejection (n=11; 33%). These experiences negatively affected the parents' well-being and mental health. Some parents stated that they felt excluded from society because of the growth disorder of their children (n=7; 21%).

TABLE 1 Sample size of parents divided into their children's age groups, and the children's diagnosis.

Childrens' age groups	4-7 years		8-12 years		13-18 years		Total
Diagnosis	IGHD	ISS	IGHD	ISS	IGHD	ISS	
participating mothers	4	4	4	3	6	7	28
participating fathers	1	–	1	–	2	1	5
total amount of parents	5	4	5	3	8	8	33

"And now I just felt that this hurts me in part, because for me, what I experience with my daughter is really an enrichment, actually. It really makes my life more beautiful. But often it is not seen, and I notice over and over again that one point with us is really also loneliness. […]. That we lead such a different life. That she very often notices that she is not taken seriously." (Mother of a 12-year-old child, ISS)

Some parents felt helpless because they could not permanently protect their children from challenging situations concerning their short stature (n=11; 33%).

"When I see that she suffers [from her short stature], when she is always asked about it. And at some point you no longer know how you can help her […]." (Mother of a 13-year-old adolescent, ISS)

Children's body height was another concern influencing parents' psychological well-being. Parents mentioned they struggled to determine their child's estimated future height (n=12; 36%). Some parents mentioned setbacks in gaining height as a problem for their children and themselves. Sometimes the parents had the impression they were more concerned about the child's height than the children themselves.

Another aspect mentioned by the participating parents was problems within the family (n=8; 24%). Parents described the children's grandparents having problems accepting their grandchildren's growth disorder. From the parents' perspective, some grandparents were ashamed of their grandchildren's short stature; others accused the parent's children of overrating the growth problem. In addition, some parents themselves felt bad because they initially underestimated the growth disorder.

"I also thought that [his height] is normal and you can't speed it up, and he has to live with it, and the more it's discussed, the worse it gets for him. Because he then also looks for excuses because he is so small. And that's why we tended to ignore it until it was no longer possible to ignore." (Mother of a 15-year-old adolescent, IGHD)

Additionally, getting a final diagnosis was accompanied by good feelings for most parents, who felt relieved after receiving their child's diagnosis (n=29; 88%).

3.2.3 Everyday life

The category *everyday life* includes statements about everyday life in the care of short-statured children. Assertions mainly concerned the domains of school, leisure activities, and the home environment, but also physical restrictions on behalf of the parents. If parents reported what special support they had provided for their child in everyday life, this statement was coded into the category *special support*.

Parents mentioned everyday situations from school or kindergarten, especially regarding the contact with professionals, e.g., teachers and pedagogues. Some parents talked to their child's teacher about the growth disorder and reported having no problems at school (n=6; 18%). Others mentioned having trouble, especially at school, because of a lack of understanding from teachers and peers (n=8; 24%).

"So I think that [clarification about the growth disorder] is actually the job of the teachers or educators. But they don't dare to do it, because they don't know anything about this topic; they are simply afraid of it." (Mother of a 10-year-old child with IGHD)

Some parents emphasized that their children had disadvantages in physical education (PE) classes because of their short stature (n=14; 42%). For many parents, this meant they had to mentally support their children intensively when they returned disappointed from PE classes. Parents reported being disappointed because their child had disadvantages because of their short stature in the evaluation of PE, for example, in the high jump.

Parents mentioned shopping trips with their short-statured children (n=17, 52%). Especially problems with buying clothes and bicycles were discussed. Pants were too long, shoes too wide, and many clothes that would fit were inappropriate in style. For these reasons, several interviewees stated that shopping trips are problematic and time-consuming. One mother recounted that she had to shorten all the pants she bought for her short-statured son.

"Yeah, so that's all kind of…. When I think about buying the bike. Bikes are ridden by everyone now, but you'll get them in her size only in pink, which is absolutely babyish. […]. These are such things … these are problems." (Mother of a 13-year-old adolescent, IGHD)

Other parents reported that many playgrounds were not designed for small children (n=12, 36%). Often the children would encounter limitations when playing, which was frustrating and burdensome for some parents to watch. One mother mentioned feeling bad because her daughter was too weak to ride a tricycle.

One topic that was not explicitly asked about but raised by a mother was physical limitations. Due to back problems, she could not meet all the demands of everyday life caused by her daughter's short stature. For example, she could not lift her daughter to have a better view of the zoo animals.

3.2.4 Growth hormone treatment

The category *growth hormone treatment* covers all kinds of parental experiences with hGH treatment, like concerns and stresses, but also positive experiences. Many interviewees' children were treated with hGH, so parents' viewpoints regarding hGH therapy were discussed in detail.

Some of the parents whose children were treated with hGH mentioned they were concerned about the side effects of the treatment (n=5; 15%). For example, parents suspected that it could affect the whole body of their child. One mother was afraid of her child getting edema from hGH treatment.

"For me, for example, it was incredibly horrifying because there was also something about water retention, which can also take place in the head, and then I thought, "Wow, I wouldn't want to have such a water head child." (Mother of a 7-year-old child, ISS)

Many parents reported that the potential side effects did frighten them during decision-making for or against the hGH treatment (n=10; 30%). One father mentioned that he decided for hGH treatment because he wanted to spare his son disadvantages in future life due to his short stature.

Some parents whose children got hGH treatment said, they had difficulties administering the hGH by injection to their children (n=7; 21%). For example, many children feared the injection, which was a problem for the parents because most had to inject their children themselves.

"But actually, it was really the fear - "Oh God, I still have to inject her." And then it started, and then you really had to hold her. I had to inject her for weeks [in the clinic], because I couldn't do it on my own. So the fear of doing it myself, not myself, but in general, no matter who did it. She really resisted." (Mother of a 12-year-old child, IGDH)

A few parents mentioned that hGH's application improved after a while, and their children were more relaxed about the injection. One

mother stated that special child-friendly injections made it more fun and straightforward for her child and, at the same time, for herself.

Another topic focused on organizational issues (n=6; 18%). Parents mentioned they had issues going on vacation because the hGH injections need to be cooled all the time. Also, class trips were mentioned as being a problem due to the treatment. One single mother said she had organizational issues when she wanted to go out on a date.

"So for me it was a problem with the treatment because I'm a single parent, and if I wanted to do something on the weekend, I couldn't get a normal babysitter, but I always needed a nurse to take over the injection. Now he does it himself, so the issue is settled, but in the beginning, it was bad. […]." (Mother of a 13-year-old adolescent, IGHD)

One-third of the interviewees whos children were treated with hGH, raised the issue of the pediatrician's disease handling (n=7; 21%). Many were unsatisfied because their pediatrician trivialized their child's growth disorder and discouraged the parents from starting with hGH treatment. Some pediatricians even approached the parents with prejudice because the child was short. For example, parents were asked about the abuse of drugs or alcohol while pregnant.

Beyond that, parents mentioned they were happy with hGH treatment (n=5; 15%). Some reported that giving injections became routine, and they were satisfied with their child's growth success and future prognosis. Parents also mentioned that the hGH treatment got simplified once their child could inject the hGH independently.

3.2.5 Special support

Statements dealing with special care due to the children's short stature were coded into the category *special support.* The code was assigned when, for example, parents mentioned how they support or treat their short-statured children in a certain way because of their body height, including deliberate "normal" treatment.

Parents' perception of the need to offer special support to their short-statured child showed an inconsistent picture. On the one hand, parents reported intensive support (n=16; 48%); on the other hand, they reported treating their short-statured children the same way as, for example, healthy siblings (n=11; 33%).

Approximately half of the parents gave social-emotional support to their short-statured children, mainly because of their children's experiences of being bullied at school resulting in the need for intensive emotional support (n=16; 48%). Parents also mentioned that they strengthen their children's self-esteem.

"Yes, you build them up again and again like "You're strong, you can do it" or "You're great" or that you also praise small things that don't matter so much to others that you would praise that." (Mother of a 7-year-old child, IGHD)

One mother reported that she only wears flat shoes because her son does not like his mother to be taller than him.

Some parents mentioned treating their short-statured children differently than their siblings (n=14; 42%). For example, they tended to be more overprotective and helpful. One mother said she often helped her short-statured daughter with tasks because otherwise, it would take too much time if her daughter would do it herself.

"As a mother, you sometimes have the tendency, or I have actually had it, to protect the smaller child a bit against the bigger child because of its short stature." (Mother of a 14-year-old adolescent, IGHD)

Other parents reported no difference in treating their short-statured children because they felt that the most regular treatment would help their children prepare for future life (n=11; 33%). For example, some parents said they would hardly discuss the topic of short stature so their children would not feel different from others.

3.2.6 Future worries

Parents' worries due to the future perspective of their short-statured children were coded into the category *future worries*. Parents focused on their children's career prospects but also on their later private life and starting a family. Several parents were concerned about their children's success in these areas of life.

Parents reported worrying about how and whether their children will cope with limitations and restrictions caused by their short stature later in life (n=6; 18%). For example, one mother mentioned she was frightened her short-statured child would not be able to keep up with the others regarding body height and skills. Parents also mentioned that they were concerned their children would not develop properly because they would consistently be underestimated and treated regarding their height and not their age. From the parents' perspective, short-statured children do not get the opportunity to gain much independence.

"[His brother] always relieves everything from him, and that is not an advantage for such small children, because they have to develop and do their own thing." (Mother of a 7-year-old, IGHD)

Parents reported also being concerned about their children's future personal life and mentioned that finding a love-mate might be difficult for short-statured children, especially boys (n=4; 12%). Another aspect concerns the independence of short-statured children, and parents mentioned concerns about short-statured children's possibility of getting a driver's license.

A few parents discussed occupational disadvantages because of their children's short stature (n=5; 15%). Parents reported worries about their children's prospects in the labor market, and one mother worried about the disadvantages in work pay.

"Where again, starting from me, you think it's all okay now, but let the boy come into puberty, and he's so small or he doesn't get taller than 1.66 m. I think for a man, that's already a problem. So many things. I have also informed myself a bit that there are studies in America that say that small men earn less in the same job, for example." (Mother of a 14- years-old (IGHD) and 12-year-old (ISS) adolescents)

Furthermore, one mother stated being worried about the growth development of her second child. The mother reported she is afraid that her daughter might also be short-statured and therefore controls the development of growth very intensively.

3.2.7 Special needs

We coded statements about special needs into the category *special needs*. In this category, statements were coded when parents expressed their wishes and needs regarding how their child's growth disorder should be handled. Statements mainly concerned the parent's desire for a society more aware of the needs of short-statured people and their families.

Many interviewees reported intense wishes that other people would not treat their children differently than their peers (n=16; 48%). Even if their children are shorter than others, parents perceived the special treatment of short-statured children by the social

environment as unhelpful and made them feel discontented. Several parents mentioned they would be happier if their children would be treated like any other child.

"[…]. If you don't say anything to him, there is no problem. I think that would be the very best if you treat him just like everyone else, and that's it." (Father of a 15-year-old adolescent, ISS)

Some parents said they wished that pediatricians, teachers, pedagogues, and the industry would be more considerate of the needs of short-statured people and their families (n=8; 24%). For example, some mentioned that the industry should also produce smaller schoolbags because the normal ones were too big for short-statured children, which made it difficult to buy a suitable one. Some interviewees expressed being upset about how the pediatrician treated their child, so they mentioned the desire that pediatricians would be more aware of growth disorders and treat the children more age-appropriate.

Some parents wished for an exchange with other parents of short-statured children (n=4; 12%). They said it would help them better manage upcoming growth disorder issues. One mother said she would appreciate not being alone with short stature associated difficulties and challenges.

"I mean, it is also an interesting topic. Above all, it's nice when you're not so alone with it. Otherwise, you always have no one to talk to. […]." (Mother of 5-year-old identical twins, both, ISS)

A few parents suggested establishing a discussion group for parents of short-statured children, so they could exchange experiences with other parents of short-statured children and find solutions for problems together (n=4; 12%). Some said it would help them cope with the entire situation.

Moreover, some parents reported wishing their children would find ways to compensate for their growth disorder (n=4; 12%). For example, finding a peer group who accepts them how they are. Several interviewees stated that it would make them feel contented seeing their child getting accepted and integrated by other peers.

"[…]. I would be very happy for him if he finally found someone who has exactly these character traits, where you say, okay, now you've found your partner." (Mother of a 13-year-old adolescent, ISS)

Other parents reported the idea of additional psychosocial support for their children when visiting the physicians for medical check-ups (n=6; 18%). Professional psychosocial support might ease coping with the health condition and its associated treatment or consequences. From the parents' point of view, a connection to regular care would be associated with the advantage of an additional trusted person and reduced travel distances, relieving the parents.

Some parents talked about wanting their children to grow more (n=4; 12%). Parents said this would give them hope for the future and make them happy. Others felt the need to defend their children from bullies because they felt helpless. Furthermore, a few parents expressed the wish for more understanding and greater societal tolerance for growth disorders. They mentioned it would make life easier for them and their children if other people would approach them, for example, openly and without bias about the growth disorder.

3.2.8 Individual resources

The category *individual resources* covers parental sources of strengths or resources in dealing with the child's growth problems. Parents addressed straightforwardness about growth problems, optimism, or getting support as power sources.

Some interviewees reported that it helps them cope with their child's chronic condition when dealing with this topic openly (n=7; 21%). For example, some expressed how it helps them to talk unconcealed about their child's growth disorder with other people. One mother mentioned that being open-minded about this topic helped her find other parents with short-statured children.

"And then I also deal with it quite openly and then also talk to people quite openly, because I think that is still a taboo subject with some people." (Mother of a 4-year-old child, IGHD)

Parents mentioned education about the growth disorder and support from their pediatrician and other family members as key factors in coping with their child's condition (n=6; 18%). Parents stated they were more confident about the short stature when their pediatrician educated them about short stature and the therapy with hGH. Furthermore, parents reported that optimism about body growth helped both parents and their children deal with the issue.

"But in the meantime, I've really learned to say: okay, it comes as it comes, I have to take it as it is. And when it's good, it's good, then we make the best of it. And if we have a bad phase, we also have to make the best of it. But it took me a long time, I have to be honest. It takes time to reach that point, you can't do it overnight." (Mother of a 7-year-old child, ISS)

In addition, parents mentioned positive perceptions regarding the growth disorder by establishing an emotional distance from the topic of short stature (n=5; 15%). For example, parents stated it was relieving and helpful when adolescents were in charge of all the organizational issues, like executing the hGH injections themselves. A few parents mentioned that observing their children's success in gaining height and physical development was helpful.

Parents reported feeling positive when their children succeed, for example, in sports (n=5, 15%). One mother reported being very proud that her son could qualify for a swimming competition, making it easier for her to deal with the short stature and its requirements in daily life.

4 Discussion

The parents in our sample reported experiencing a caregiving burden mainly due to the requirements of hGH treatment and mental stress due to their child's growth disorder. Over half of the parents felt stressed about treatment with hGHs, mainly because they feared side effects or struggled with applying hGH via injections. The injections cause parental stress because parents struggle with causing their children pain, and organizational issues regarding the daily injections result in daily life challenges (37).

Many participants mentioned they adapted to the treatment application after some time but still had difficulties correctly interpreting the risks and side effects. They expressed being unsure where to search for valid information if not given by their pediatrician. Parents were concerned about the side effects of hGH treatment and reported hGH treatment having a big or extreme impact on their decision to seek medical treatment for their child's short stature in a quantitative cross-sectional study (38). Accordingly, responsible healthcare providers need to educate their patients'

parents about possible side effects of hGH treatment and advise them on where to find evidence-based information. This professional support seems even more critical as the adherence of short-statured children and, therefore, the effectiveness of children's treatment mainly depends on the parent's psychological well-being and attitudes towards treatment (17). Knowing about treatment details could also help parents adjust their life to hGH treatment, as the daily injections often interfere with daily life routines (39).

Parental mental stress mainly results from frustration because of the reactions and behavior of the social environments toward their children (40). Additionally, parents were relieved when they received the children's final diagnosis, emphasizing the great pressure parents experience by uncertainties, waiting times, and the diagnostic process. When comparing the anxiety levels of mothers of short-statured children with an IGHD diagnosis and mothers of children without a diagnosis, mothers of undiagnosed children report significantly higher anxiety levels (17). Waiting for the disclosure of a final diagnosis results in parental anxiety and concerns (37). These findings suggest that parents could benefit from psychological support during their children's diagnostic process (17), and professional accompaniment, especially when no diagnosis can be made.

Our results confirm earlier findings on parents' multiple caregiving burdens, stress, and impaired HRQOL in the care of IGHD/ISS children (17, 30, 37, 41, 42). The associations between children's chronic health conditions and children's and whole families' well-being need to be considered in the healthcare and treatment of short-statured children (26, 29–31, 43).

Parents of male children/adolescents reported more problems and mental burdens due to the societal expectations of boys/men being tall. Parental worries regarding the additional challenges of short-statured males (44, 45) might result from societal expectations and norm orientations. From the parents' perspective, society and the social environment emphasize standards, making short-statured children and their parents feel excluded. Getting stigmatized and bullied because their children failed to grow was demanding for parents. Stigmatization is often associated with physical and mental stress for the bullied children and their parents (46, 47).

Additionally, the distribution of parents of male and female children is very uneven, with a strong emphasis on boys. Although no gender differences were reported in the prevalence of short stature defined as a height below -2.25 SD, hGH treatment is more often indicated in males than females (48). Regardless of whether physicians indicate the more frequent indication for hGH treatment in boys or whether parents solicit this, it is clear that small body height is viewed as more negative for boys compared to age- and gender-adjusted norms. Parents of short-statured children reported being less able to accept the pathological short stature in boys than in girls (45). This may also be a reason for the disproportionate participation of parents of male children. A selection bias is also the exchange with other parents with similar experiences, which is perceived as support. This exchange with like-minded people is an essential resource for many parents, but also for affected children and adolescents, in dealing with the disease, the treatment, and the consequences in everyday life (49).

Impaired HRQOL of short-statured children's parents due to stigmatization and other issues can cause additional problems. The positive link between parents' stress levels and children's well-being (50) highlights the need for parental support. Parents advise their children on coping strategies, serve as role models and help them adapt to their chronic health condition in the best possible way (51). So assuring parents can handle the caregiving burden will influence their children's abilities to cope with their health-related burdens (52).

There is little research about parental HRQOL in the context of IGHD and ISS. The QoLISSY study group, an international research team, aimed to develop a patient-reported outcome measure to assess the children's HRQOL and included two domains in the proxy-report focusing on the effects on parents and parents' future worries (35). Parents mentioned future worries, especially in the context of their children's perspective in the labor market (51, 53). Brodt et al. (40, 42) focussed on the burden of hGH treatment from the child's perspective and the impact of the children's treatment on the parents. In qualitative telephone interviews, parents reported their emotional impacts from their children's IGHD; including worry for their child, anger or frustration over the reactions of others about their child's height, relief when receiving a final diagnosis, and pressure in managing treatment for their children (40).

Several parents wished for parent support groups with other parents of short-statured children. Expansion and reinforcement of societal acceptance of diversity are required to meet the parents' (and children's) desire for regular care, including age-appropriate in contrast to height-appropriate treatment in daily life. Problems within the families, like ashamed grandparents leading to conflicts and disappointment in the parents, only mainly arose when other people made an issue out of the children's growth disorder. Therefore, education and tolerance are crucial to support families of short-statured children.

5 Limitations

Our results are based on a small national sample, making the results hardly generalizable for all parents of IGHD/ISS children. Furthermore, it needs to be considered that people who participate in the interviews may not be representative. Hence, the parents' attitudes and viewpoints might differ from other parents of IGHD/ISS children. Mainly mothers participated in the focus group discussions, and fathers were underrepresented. This can be explained by the fact that mothers are more often the primary caregivers than fathers (39).

Furthermore, parents of short-statured boys participated more often than those of girls. We did not collect any clinical data, so we cannot consider the time between the final diagnosis and the interviews or the duration of hGH treatment. Similarly, we were unable to consider sociodemographic factors when analyzing the interviews. However, it can be assumed that the fact that only parents who spoke sufficient German were included represents a bias. The parental experiences of short stature in the context of culture and parental gender need to be considered in future studies.

6 Conclusion

The influence of the child's growth disorder due to IGHD/ISS on the parents and the whole family should not be underestimated. For

physicians, it is essential to understand the parents' caregiving burden, stress, and individual resources to initiate psychosocial intervention or parent support groups, if needed, and provide support and evidence-based information for parents having difficulty with hGH treatment. Healthcare and medical treatment in pediatric endocrinology should be family-centered. The parents especially strongly influence their children's well-being and adaptation to the growth disorder by serving as role models. Therefore, one aim in the care of short-statured children has to be the appropriate support of parents resulting in confident parenthood and thus promoting the healthy development of these children.

Data availability statement

The datasets analyzed during the study are not available publicly. This was done to keep the interview transcripts confidential. Requests to access these datasets should be directed to s.witt@uke.de.

Ethics statement

The original QoLISSY study was reviewed and approved by the regional ethics board (PV3184) before it started. A regional ethics board achieved an additional ethics approval for re-analyzing the data (LPEK-0579a).

Author contributions

SW and JQ developed the study concept and the design. LL and SW developed the coding guideline and coded the interviews. LL wrote the first draft of the manuscript. SW critically reviewed and revised the first draft for important intellectual content. All authors have critically revised subsequent drafts of the manuscript. All authors contributed to the article and approved the submitted version.

Funding

The original QoLISSY study, in which we collected the qualitative data, was funded by Pfizer. The funder was not involved in the study design, analysis, interpretation of data, the writing of this article or the decision to submit it for publication.

Acknowledgments

We want to thank all participating parents for sharing their experiences with us. Further, we thank the QoLISSY-study group for their support and Pfizer for funding the original QoLISSY project.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Ranke MB. Towards a consensus on the definition of idiopathic short stature. *Horm Res* (1996) 45 Suppl 2:64–6. doi: 10.1159/000184851

2. Oostdijk W, Grote FK, de Muinck Keizer-Schrama SM, Wit JM. Diagnostic approach in children with short stature. *Horm Res* (2009) 72(4):206–17. doi: 10.1159/000236082

3. Warrier V, Krishan K, Shedge R, Kanchan T. *Height assessment*. StatPearls. Treasure Island (FL: StatPearls Publishing (2022).

4. Quitmann J, Rohenkohl A, Sommer R, Petzold S, Bullinger-Naber M. [How do affected children and adolescents experience their short stature, and what is the point of view of their parents?]. *Prax Kinderpsychol Kinderpsychiatr*. (2014) 63(8):635–48. doi: 10.13109/prkk.2014.63.8.635

5. Deutsche Gesellschaft für Kinderendokrinologie und -diabetologie e.V. (DGKED). *Zweite revision der leitlinie diagnostik des wachstumshormonmangels im kindes- und jugendalter. AWMF registernummer 174-002* (2022). Available at: https://www.awmf.org/leitlinien/detail/ll/174-002.html.

6. Growth Hormone Research Society. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: Summary statement of the GH research society. *J Clin Endocrinol Metab* (2000) 85(11):3990–3. doi: 10.1210/jcem.85.11.6984.

7. Wit JM, Kamp GA, Rikken B. Spontaneous growth and response to growth hormone treatment in children with growth hormone deficiency and idiopathic short stature. *Pediatr Res* (1996) 39(2):295–302. doi: 10.1203/00006450-199602000-00018

8. Cutfield WS, Albert BB. Growth hormone treatment for idiopathic short stature. *Pediatr Endocrinol Rev* (2018) 16(Suppl 1):113–22. doi: 10.17458/per.vol16.2018.ca.ghidiopathicshortstature.

9. Cohen P, Rogol AD, Deal CL, Saenger P, Reiter EO, Ross JL, et al. Consensus statement on the diagnosis and treatment of children with idiopathic short stature: A summary of the growth hormone research society, the Lawson Wilkins pediatric endocrine society, and the European society for paediatric endocrinology workshop. *J Clin Endocrinol Metab* (2008) 93(11):4210–7. doi: 10.1210/jc.2008-0509

10. Naiki Y, Horikawa R, Tanaka T. Assessment of psychosocial status among short-stature children with and without growth hormone therapy and their parents. *Clin Pediatr Endocrinol* (2013) 22(2):25–32. doi: 10.1297/cpe.22.25

11. Sandberg DE, Voss LD. The psychosocial consequences of short stature: a review of the evidence. *Best Pract Res Clin Endocrinol Metab* (2002) 16(3):449–63. doi: 10.1053/beem.2002.0211

12. Valero-Moreno S, Pérez-Marín M, Montoya-Castilla I, Castillo-Corullón S, Ramírez-Aguilar A, Escribano-Montaner A. Emotional distress in family caregivers of adolescents with bronchial asthma: Analysis of its predictors. *Arch Argent Pediatr* (2018) 116(2):e234–e40. doi: 10.5546/aap.2018.eng.e234

13. Revicki DA, Kleinman L, Cella D. A history of health-related quality of life outcomes in psychiatry. *Dialogues Clin Neurosci* (2014) 16(2):127–35. doi: 10.31887/DCNS.2014.16.2/drevicki

14. Cousino MK, Hazen RA. Parenting stress among caregivers of children with chronic illness: a systematic review. *J Pediatr Psychol* (2013) 38(8):809–28. doi: 10.1093/jpepsy/jst049

15. Crandell JL, Sandelowski M, Leeman J, Havill NL, Knafl K. Parenting behaviors and the well-being of children with a chronic physical condition. *Fam Syst Health* (2018) 36(1):45–61. doi: 10.1037/fsh0000305

16. Beacham BL, Deatrick JA. Children with chronic conditions: Perspectives on condition management. *J Pediatr Nurs.* (2015) 30(1):25–35. doi: 10.1016/j.pedn.2014.10.011

17. Majewska KA, Stanisławska-Kubiak M, Wiecheć K, Naskręcka M, Kędzia A, Mojs E. Maternal anxiety in relation to growth failure and growth hormone treatment in children. *Med (Baltimore).* (2020) 99(37):e22147. doi: 10.1097/MD.0000000000022147

18. Eccleston C, Fisher E, Law E, Bartlett J, Palermo TM. Psychological interventions for parents of children and adolescents with chronic illness. *Cochrane Database Syst Rev* (2015) 4(4):Cd009660. doi: 10.1002/14651858.CD009660.pub3

19. Whitehead L, Jacob E, Towell A, Abu-Qamar M, Cole-Heath A. The role of the family in supporting the self-management of chronic conditions: A qualitative systematic review. *J Clin Nurs* (2018) 27(1-2):22–30. doi: 10.1111/jocn.13775

20. Caicedo C. Families with special needs children: family health, functioning, and care burden. *J Am Psychiatr Nurses Assoc* (2014) 20(6):398–407. doi: 10.1177/1078390314561326

21. Craig L, Mullan K. Parenthood, gender and work-family time in the united states, Australia, Italy, France, and Denmark. *J Marriage Family.* (2010) 72(5):1344–61. doi: 10.1111/j.1741-3737.2010.00769.x

22. de Silva KS, de Zoysa P. Assessment of the psychological status of children with growth hormone deficiency and their parents. *Ceylon Med J* (2011) 56(2):59–61. doi: 10.4038/cmj.v56i2.3110

23. Macedo EC, da Silva LR, Paiva MS, Ramos MN. Burden and quality of life of mothers of children and adolescents with chronic illnesses: An integrative review. *Rev Lat Am Enfermagem.* (2015) 23(4):769–77. doi: 10.1590/0104-1169.0196.2613

24. Cohn LN, Pechlivanoglou P, Lee Y, Mahant S, Orkin J, Marson A, et al. Health outcomes of parents of children with chronic illness: A systematic review and meta-analysis. *J Pediatr* (2020) 218:166–77.e2. doi: 10.1016/j.jpeds.2019.10.068

25. Golics CJ, Basra MK, Salek MS, Finlay AY. The impact of patients' chronic disease on family quality of life: an experience from 26 specialties. *Int J Gen Med* (2013) 6:787–98. doi: 10.2147/IJGM.S45156

26. Anderson T, Davis C. Evidence-based practice with families of chronically ill children: a critical literature review. *J Evid Based Soc Work.* (2011) 8(4):416–25. doi: 10.1080/15433710903269172

27. Hentinen M, Kyngäs H. Factors associated with the adaptation of parents with a chronically ill child. *J Clin Nurs.* (1998) 7(4):316–24. doi: 10.1046/j.1365-2702.1998.00154.x

28. Hatzmann J, Heymans HS, Ferrer-i-Carbonell A, van Praag BM, Grootenhuis MA. Hidden consequences of success in pediatrics: Parental health-related quality of life–results from the care project. *Pediatrics* (2008) 122(5):e1030–8. doi: 10.1542/peds.2008-0582

29. Kazak AE. Families of chronically ill children: A systems and social-ecological model of adaptation and challenge. *J Consult Clin Psychol* (1989) 57(1):25–30. doi: 10.1037/0022-006X.57.1.25

30. Palermo TM, Valrie CR, Karlson CW. Family and parent influences on pediatric chronic pain: a developmental perspective. *Am Psychol* (2014) 69(2):142–52. doi: 10.1037/a0035216

31. Quittner AL, Opipari LC, Espelage DL, Carter B, Eid N, Eigen H. Role strain in couples with and without a child with a chronic illness: associations with marital satisfaction, intimacy, and daily mood. *Health Psychol* (1998) 17(2):112–24. doi: 10.1037/0278-6133.17.2.112

32. Gau SS, Shen HY, Chou MC, Tang CS, Chiu YN, Gau CS. Determinants of adherence to methylphenidate and the impact of poor adherence on maternal and family measures. *J Child Adolesc Psychopharmacol* (2006) 16(3):286–97. doi: 10.1089/cap.2006.16.286

33. Manne SL, Jacobsen PB, Gorfinkle K, Gerstein F, Redd WH. Treatment adherence difficulties among children with cancer: the role of parenting style. *J Pediatr Psychol* (1993) 18(1):47–62. doi: 10.1093/jpepsy/18.1.47

34. Shorer M, David R, Schoenberg-Taz M, Levavi-Lavi I, Phillip M, Meyerovitch J. Role of parenting style in achieving metabolic control in adolescents with type 1 diabetes. *Diabetes Care* (2011) 34(8):1735–7. doi: 10.2337/dc10-1602

35. Bullinger M, Quitmann J, Power M, Herdman M, Mimoun E, DeBusk K, et al. Assessing the quality of life of health-referred children and adolescents with short stature: Development and psychometric testing of the QoLISSY instrument. *Health Qual Life Outcomes.* (2013) 11:76. doi: 10.1186/1477-7525-11-76

36. Rädiker S, Kuckartz U. *Focused analysis of qualitative interviews with MAXQDA. step by step*. Berlin: MaxQDA Press (2020).

37. Marini MG, Chesi P, Mazzanti L, Guazzarotti L, Toni TD, Salerno MC, et al. Stories of experiences of care for growth hormone deficiency: The CRESCERE project. *Future Sci OA* (2016) 2(1):Fso82. doi: 10.4155/fso.15.82

38. Hitt T, Ginsburg KR, Cousounis P, Lipman TH, Cucchiara AJ, Stallings VA, et al. Concerns and expectations of parents seeking subspecialist care for their child's short stature. *Horm Res Paediatr* (2019) 92(5):311–8. doi: 10.1159/000506739

39. Quitmann J, Bloemeke J, Dörr HG, Bullinger M, Witt S, Silva N. First-year predictors of health-related quality of life changes in short-statured children treated with human growth hormone. *J Endocrinol Invest.* (2019) 42(9):1067–76. doi: 10.1007/s40618-019-01027-4

40. Brod M, Alolga SL, Beck JF, Wilkinson L, Højbjerre L, Rasmussen MH. Understanding burden of illness for child growth hormone deficiency. *Qual Life Res* (2017) 26(7):1673–86. doi: 10.1007/s11136-017-1529-1

41. Backeljauw P, Cappa M, Kiess W, Law L, Cookson C, Sert C, et al. Impact of short stature on quality of life: A systematic literature review. *Growth Horm IGF Res* (2021) 57-58:101392. doi: 10.1016/j.ghir.2021.101392

42. Brod M, Højbjerre L, Alolga SL, Beck JF, Wilkinson L, Rasmussen MH. Understanding treatment burden for children treated for growth hormone deficiency. *Patient* (2017) 10(5):653–66. doi: 10.1007/s40271-017-0237-9

43. Halleran DR, Lane VA, Leonhart KL, Fischer B, Sebastião YV, Chisolm DJ, et al. Development of a patient-reported experience and outcome measures in pediatric patients undergoing bowel management for constipation and fecal incontinence. *J Pediatr Gastroenterol Nutr* (2019) 69(2):e34–e8. doi: 10.1097/MPG.0000000000002348

44. Quitmann J, Giammarco A, Maghnie M, Napoli F, Di Giovanni I, Carducci C, et al. Validation of the Italian quality of life in short stature youth (QoLISSY) questionnaire. *J Endocrinol Invest.* (2017) 40(10):1077–84. doi: 10.1007/s40618-017-0667-1

45. Rotnem D, Cohen DJ, Hintz R, Genel M. Psychological sequelae of relative "treatment failure" for children receiving human growth hormone replacement. *J Am Acad Child Psychiatry* (1979) 18(3):505–20. doi: 10.1097/00004583-197922000-00008

46. Link BG, Phelan JC. Stigma and its public health implications. *Lancet* (2006) 367 (9509):528–9. doi: 10.1016/S0140-6736(06)68184-1

47. Wang B, Li X, Stanton B, Fang X. The influence of social stigma and discriminatory experience on psychological distress and quality of life among rural-to-urban migrants in China. *Soc Sci Med* (2010) 71(1):84–92. doi: 10.1016/j.socscimed.2010.03.021

48. Grimberg A, Huerta-Saenz L, Grundmeier R, Ramos MJ, Pati S, Cucchiara AJ, et al. Gender bias in U.S. pediatric growth hormone treatment. *Sci Rep* (2015) 5(1):11099. doi: 10.1038/srep11099

49. Witt S, Schuett K, Wiegand-Grefe S, Boettcher J, Quitmann, CARE-FAM-NET study group. Living with a rare disease - experiences and needs in pediatric patients and their parents. *Orphanet J Rare Dis.* (under review).

50. Preston A, Storch EA, Lewin A, Geffken GR, Baumeister AL, Strawser MS, et al. Parental stress and maladjustment in children with short stature. *Clin Pediatr (Phila).* (2005) 44(4):327–31. doi: 10.1177/000992280504400407

51. Visser-van Balen H, Sinnema G, Geenen R. Growing up with idiopathic short stature: psychosocial development and hormone treatment; a critical review. *Arch Dis Child.* (2006) 91(5):433–9. doi: 10.1136/adc.2005.086942

52. Grootenhuis MA, Bronner MB. Paediatric illness! family matters. *Acta Paediatr* (2009) 98(6):940–1. doi: 10.1111/j.1651-2227.2009.01321.x

53. Haverkamp F, Noeker M. 'Short stature in children–a questionnaire for parents': A new instrument for growth disorder-specific psychosocial adaptation in children. *Qual Life Res* (1998) 7(5):447–55. doi: 10.1023/a:1008862021532

International Journal of
Environmental Research and Public Health

MDPI

Review

Health-Related Quality of Life, Stress, Caregiving Burden and Special Needs of Parents Caring for a Short-Statured Child—Review and Recommendations for Future Research

Lea Lackner, Julia Quitmann, Kaja Kristensen and Stefanie Witt *

Department of Medical Psychology, Center for Psychosocial Medicine, University Medical Center Hamburg-Eppendorf, Martinistraße 52, W26, 20246 Hamburg, Germany
* Correspondence: s.witt@uke.de

Abstract: Children with short stature can experience a range of burdens due to their chronic condition. However, little is known about parents' experiences dealing with their child's short stature and the potential caregiving burdens and concerns they may face. We aim to review the literature on health-related quality of life (HRQOL), caregiving burden, and special needs among parents caring for a child with isolated growth hormone deficiency (IGHD) or idiopathic short stature (ISS). Using pre-defined inclusion and exclusion criteria, we systematically searched for literature using PubMed and Web of Science from its inception to December 2022. We identified 15 articles assessing HRQOL, special needs, or caregiving burdens in parents of IGHD/ISS children. The main problems included concerns about the future, organizational issues, side effects from growth hormone treatment, and social stigmatization. Furthermore, two studies assessed parents' special needs to cope with caregiving stress, mainly the dialogue between them and their families or parent support groups. This review outlines parental burdens, needs, and resources when caring for an IGHD/ISS child. Furthermore, it provides information about previously used measures appraising parents' special needs and underlines the need for disease-specific measurements.

Keywords: health-related quality of life; stress; caregiving burden; special needs; parents; short-statured children

check for updates

Citation: Lackner, L.; Quitmann, J.; Kristensen, K.; Witt, S. Health-Related Quality of Life, Stress, Caregiving Burden and Special Needs of Parents Caring for a Short-Statured Child—Review and Recommendations for Future Research. *Int. J. Environ. Res. Public Health* **2023**, *20*, 6558. https://doi.org/10.3390/ijerph20166558

Academic Editor: Marta Tremolada

Received: 23 March 2023
Revised: 13 July 2023
Accepted: 8 August 2023
Published: 11 August 2023

Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

Short stature is defined as a disorder in which the height of an individual is more than two standard deviations (SD) below the corresponding mean height for a given age, sex, and population group. It is associated with many different diseases, such as genetic or endocrine ones [1], whereas the most common causes are growth hormone deficiency, hypothyroidism, Turner syndrome, and celiac disease [2]. Isolated growth hormone deficiency (IGHD) is an endocrine disease caused by a lack or insufficiency of growth hormone (GH) secretion [3] and therefore leads to short stature. Besides IGHD, many children fit the definition of short stature but have no underlying pathogenesis or etiology for being short [1,4]. In these cases, idiopathic short stature (ISS) is diagnosed [1]. In 2019, it was estimated that 144 million children worldwide under five years were short-statured, according to United Nations Children's Fund (UNICEF) et al. [5]. A study that examined the data of the Pfizer International Growth Study (KIGS®®) from Europe, Asia, and Japan revealed that 46.9% of the sample with short stature (n = 83,803) exhibited short stature as a result of IGHD, while 8.2% presented with ISS [6]. This finding underscores the significance of IGHD and ISS in children within the medical system. Another study highlights that short stature is one of the most frequent concerns pediatric endocrinologists and other physicians caring for children must deal with [4]. Given that this topic affects many children and their families, several studies have been conducted to investigate the IGHD/ISS children's well-being and health-related quality of life (HRQOL). This was also reinforced by the fact that the impact of

chronic conditions on children and their families has gained importance in recent years [7,8]. Most studies assume that short-statured children have a lower HRQOL compared to their normal-statured peers [9] and have low self-esteem [10], primarily because of short-statured children being bullied at school. Worries about their height, feeling inferior about their shortness, and negative comparison with peers were additional results retrieved in the studies on IGHD/ISS children's HRQOL [11–13].

A chronic pediatric health condition affects the child and the entire family [14,15]. Especially the parents of children with a chronic condition are often responsible for maintaining the functioning of the family by emphasizing the positive aspects of the development of their children and helping them cope with their chronic illness [16,17]. Socioecological factors such as a good functioning parent–child relationship and parental adaptation are some of the main protective factors for these children [18,19]. Moreover, studies have shown that high caregiving stress levels can affect children by causing depression, anxiety, and feeling desolate [20]. Therefore, it is crucial to investigate parental HRQOL, burdens, and special needs throughout their children's short stature and to understand how they are affected by caring for a short-statured child because parents can modulate their children's intrapersonal emotional attitude towards themselves with social support and coping strategies [21,22]. The better the parent can deal with the caregiving burden, the better the child will be able to cope with their health-related burdens [23]. Parents' HRQOL is essential as it significantly affects the parent reports on their children's HRQOL [21]. That is essential to keep in mind since parents' perception of the well-being and functioning of their child might affect treatment decision making and healthcare utilization [24].

Although numerous studies have been conducted on short stature in general and its impact on children, only a limited number of studies have addressed the impact of pediatric IGHD/ISS on parents, and the results are inconclusive [25]. It is important to differentiate between the different etiologies of short stature, as they require different medical treatments and also have different prognoses. IGHD and ISS can be treated with GH injections, although this treatment option is only approved in the USA and may only be used off-label in Germany and other countries [26].

This research aims to review the current literature and find out how parents are challenged throughout caregiving for a child with IGHD/ISS. We also intended to find out about the parents' HRQOL and what kind of special needs they might have. Another aim was to detect how the included studies assessed parents' caregiving burden and HRQOL and if they used a disease-specific or generic approach. In this context, special needs mean the requirements parents might need to cope with the caregiving burden. HRQOL is defined as the subjective perception of health, including physical, social, and emotional well-being [27]. Over the years, it has become an outcome indicator in the medical field [28]. Furthermore, the caregiving burden can be defined as the strain on a person caring for a chronically ill or disabled family member [29]. Understanding the aspects of the caregiving burden is crucial as it is connected to the well-being of the individual and the caregiver [30]. Therefore, we aim to understand the aspects of the caregiving burden in short-stature youth and identify patient-reported outcomes measures (PROMs) assessing the caregiving burden and parental quality of life for use in routine care and research by conducting a scoping review.

2. Materials and Methods

We conducted a literature review in December 2022 using PubMed and Web of Science (Core Collection) without any limitation on the year of publication, the language employed, or the accessibility of full-text articles. Furthermore, sources in the included articles were searched for additional materials (hand searching). We followed the methodological framework of Arksey and O'Malley [31] for scoping reviews. This framework includes five stages, as well as an optional sixth stage: (1) identifying the research question; (2) identifying relevant studies; (3) study selection; (4) charting the data; (5) collating, summarizing, and reporting the results; and (6) a consultation exercise [31].

Publications up to the search date, including information about HRQOL, caregiving burden, or special needs of parents of IGHD/ISS children, were identified. Text word searches and Mesh-Terms, only available on PubMed, were used to avoid missing relevant articles. We used a combination of keywords and database-specific search terms. The search term included a combination of keywords and MeSH terms combined with the Boolean operators "AND" and "OR": For the diagnosis ISS, we used the following term: "Growth Disorders"[Mesh] OR "Growth disorder*"[tw] OR "short stature"[tw] OR "idiopathic short stature"[tiab] OR "Dwarfism"[Mesh] OR "rare condition*"[tiab]; for the diagnosis of IGHD we used this term: "Dwarfism, Pituitary"[Mesh] OR "Dwarfism, Pituitary/psychology"[Mesh] OR "Hypopituitarism"[Mesh] OR "Pituitary insufficiency"[tiab] OR "Insulin-Like Growth Factor II/deficiency"[Mesh] OR "Insulin-Like Growth Factor I/deficiency"[Mesh] OR "Insulin-like growth factor-I Deficiency"[tiab] OR "Human Growth Hormone/deficiency"[Mesh] OR "Growth Hormone/deficiency"[Mesh] OR "Growth Hormone-Releasing Hormone/deficiency"[Mesh] OR "growth hormone deficiency" [tw]. Those terms were connected to the following terms with "AND": "Parents"[Mesh] OR "Parents/psychology"[Mesh] OR "Caregivers"[Mesh] OR Parent*[tw] OR mother*[tw] OR father*[tw] OR caregiver*[tw] AND "Cost of Illness"[Mesh] OR "costs of illness"[tw] OR "Quality of Life"[Mesh] OR "quality of life"[tw] OR "parental quality of life"[tw] OR "Mental Health"[Mesh] OR "mental health"[tw] OR "Parent–child Relations"[Mesh] OR "Family Conflict"[Mesh] OR "well being "[tw] OR "well being "[tw] OR "emotional drain"[tw] OR "caregiving stress"[tw] OR "caregiving burden"[tiab] OR "parental burden"[tw] OR "parent reported outcome*"[tw] OR "psychosocial outcome"[tw] OR "psychosocial need*" [tw] OR "burden of disease"[tw] OR "health related quality of life"[tw] OR "health outcome"[tw].

The process of publication selection followed the PRISMA statement [32]. We used predefined inclusion and exclusion criteria to screen titles and abstracts (Figure 1). Included in this study were research papers that encompassed parents of children diagnosed with IGHD or ISS within the age range of 0–21 years. Studies examining parents' QoL, mental health, or general well-being were considered for inclusion, as well as those investigating the parental burdens associated with their child's chronic condition. Additionally, studies exploring parental needs and resources were included. Furthermore, the inclusion criteria involved peer-reviewed journals, cross-sectional studies, clinical trials, prospective studies, longitudinal studies, qualitative studies, and case reports. Excluded from this study were research papers that focused on parents of children with causes of short stature other than IGHD/ISS, such as achondroplasia, small for gestational age, Turner syndrome, skeletal dysplasia, or psychosocial dwarfism. The only exception was made for studies that included the largest number of participants who were parents of children with IGHD/ISS and evaluated them separately. Studies that solely compared treatment and non-treatment groups, focusing on the effectiveness of growth hormone therapy, were also excluded. Additionally, studies that solely examined the child's HRQOL were excluded. Conference abstracts, reviews, and meta-analyses were also excluded from the study.

We removed duplicated publications after the initial search in December 2022 using the above-mentioned search term. In the next step, a title and abstract screening were conducted by one researcher. Two independent raters screened eligible full texts to ensure an unbiased selection. Outcomes sought for this review were caregiving burden, HRQOL, stress, and special needs of parents caring for an IGHD/ISS child.

We charted the data using Microsoft Excel (version 2016, Microsoft Corporation, Redmont, WA, USA) and identified the relevant data on the sample (population and country of origin), the study design used, the aim of the studies and the PROMs used, and the main results from all included publications.

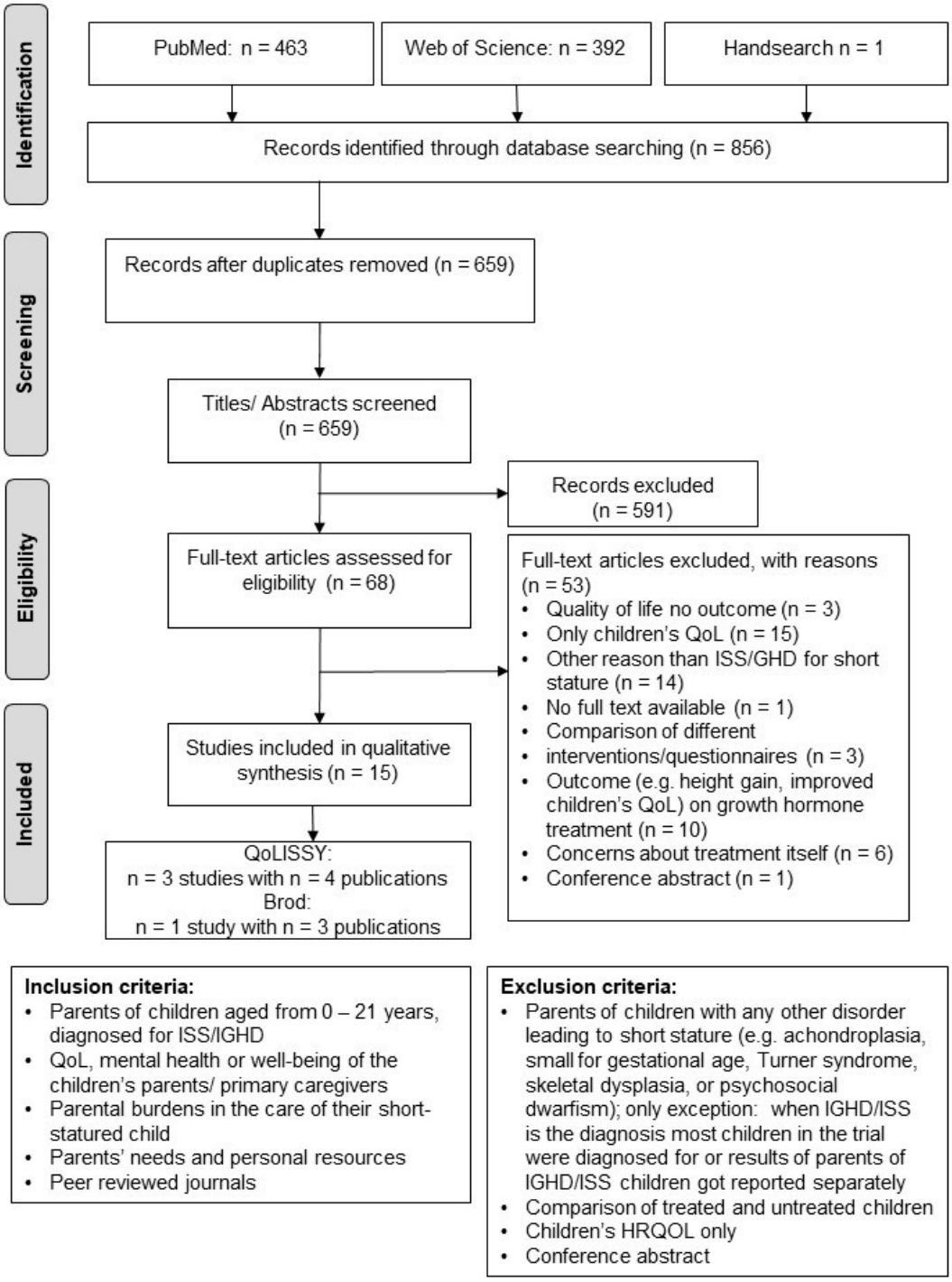

Figure 1. Prisma Flow Chart [32], search date 17 December 2022.

3. Results

3.1. Study Characteristics

We included 15 publications (published 1979–2022) for qualitative synthesis [16,19,25,33–44] (Table 1).

Table 1. Overview of the included 15 publications.

Authors	Population; Country	Study Design	Aim of the Study and Measure Method	Results
Casana-Granell, Lacomba-Trejo, Montoya-Castilla and Perez-Marin [44]	145 principal caregivers of short-statured children aged 12–17 years; Spain	Cross-sectional study	Measuring stress levels of parents using PIP and their emotional distress using HADS	HADS: 47.6% showed symptoms of anxiety, 17.2% showed symptoms of depression. PIP: 44.2–62.7% showed high stress levels concerning caregiving.
Majewska, Stanisławska-Kubiak, Wiecheć, Naskręcka, Kędzia and Mojs [37]	101 mothers of children aged 5–16 years with IGHD or unknown cause for growth failure; Poland	Cross-sectional study	Assessing anxiety levels in mothers using the STAI	Trait anxiety: low in all recruited mothers; state anxiety: medium levels; mothers of children without diagnosis presented significantly higher levels of anxiety than mothers of children without diagnosis, as did mothers of younger children.
Brod, Rasmussen, Alolga, Beck, Bushnell, Lee and Maniatis [43]	243 parents of IGHD children aged 4 to <13 years; UK and the USA	Non-interventional	Describing the psychometric validation data for the three measures, namely GHD-CTB-Child, GHD-CTB-Observer, and GHD-PTB	Mean scores of the GHD-PTB ranged from 0.35 to 1.28. Treatment-naïve participants improved for the Emotional and Overall domains (−16.6 and −8.6 points) after 12 weeks.
Brod, Alolga, Beck, Wilkinson, Højbjerre and Rasmussen [35]	31 parents of children aged from 4–13 years with IGHD; Germany, the UK, and the USA	Cross-sectional study	Focus groups or telephone interviews guided by a semi-structured interview guide to understanding emotional well-being of parents of IGHD children	47% of parents worried for their child, 38% felt angry/frustrated over the reaction of others, 29% felt relieved receiving diagnosis, 12% were pressured in parenting and managing treatment for their child.
Brod, Højbjerre, Alolga, Beck, Wilkinson and Rasmussen [40]	31 parents of IGHD children aged 4–13 years treated with growth hormone; Germany, the UK, and the USA	Cross-sectional study	Focus groups or telephone interviews guided by a semi-structured interview guide to explore the parents' burden of hGH treatment	Parents worried about hGH treatment administration (59%), causing pain to their child (38%), and medication costs (15%); 12% were affected in daily activities; 50% felt limited in family travel, 32% needed time to prepare child for injection.
Marini, Chesi, Mazzanti, Guazzarotti, Toni, Salerno, Officioso, Parpagnoli, Angeletti, Faienza, Iezzi, Aversa and Sacchetti [39]	72 parents of children aged 8–17 years with IGHD; Italy	Cross-sectional study	Narrative-based approach to collect stories from parents to understand their points of view	"Waiting for diagnosis": 55% lived with anxiety; "difficulties of hGH treatment": 33% had organizational issues, for 21% it was painful task; "expressed worries": 67% worried about side effects of hGH treatment.

Table 1. *Cont.*

Authors	Population; Country	Study Design	Aim of the Study and Measure Method	Results
Quitmann, Rohenkohl, Sommer, Petzold and Bullinger-Naber [19]	31 parents of IGHD/ISS children aged 4–18 years; Germany	Cross-sectional study	Developing measurement tool to capture HRQOL in IGHD/ISS children and the view of the parents with focus group discussions	Main burdens expressed: comparison of height, everyday problems, future anxieties, and social stigmatization through others.
Silva, Bullinger, Sommer, Rohenkohl, Witt and Quitmann [25]	238 parents of IGHD/ISS children aged 8–18 years; France, Germany, Spain, Sweden, and the UK	Cross-sectional study	Levels of caregiving stress and HRQOL of parents were raised by parents reporting on their HRQOL via EUROHIS-QOL-8 Index and caregiving stress via QoLISSY scale "effects on parents"	Parents of currently short-statured children: greater caregiving stress than parents of children with normal height; significant indirect effect of children's psychosocial functioning on parents' HRQOL via caregiving stress ($p < 0.01$).
Bloemeke, Silva, Bullinger, Witt, Dörr and Quitmann [42]	Parents of children aged 4–18 years with IGHD (n = 65) or SGA (n = 58) starting hGH treatment; ISS children (n = 31) and the parents served as he control group (T0: n = 152 parents; T1: n = 126 parents); Germany	Prospective observational study	Evaluating the QoLISSY questionnaire as a health-outcome indicator of hGH interventions by assessing HRQOL before the start of hGH treatment (baseline, T0) and at 12 months after the start (T1) with KIDSCREEN-10 Index and QoLISSY questionnaire	QoLISSY questionnaire detected changes in parents' HRQOL between treated and untreated patients. Parents of untreated children: higher HRQOL at T0 in domain "future" than parents of children in treated group; improvement on "effects on parents" from T0 to T1 for both intervention and control groups on QoLISSY.
Quitmann, Giammarco, Maghnie, Napoli, Di Giovanni, Carducci, Mohn, Bullinger and Sommer [34]	20 parents of IGHD/ISS children aged 4–18 years; Italy	Cross-sectional study	Testing the QoLISSY questionnaire in Italy by undergoing focus group discussions and a cognitive debriefing-process	"Effects on parents": second-largest category with about 20% of codes. HGH treatment organization was main concern; 10 out of 31 parents expressed future anxieties.
Visser-van Balen, Geenen, Kamp, Huisman, Wit and Sinnema [41]	38 parents of children aged 11–13 years with ISS (n = 26) or SGA (n = 12); Netherlands	Cross-sectional study	Structured interviews and CBCL to understand the motives of parents for choosing hGH treatment	Two out of three parents: worries about future opportunities; 44.5% expected their child to have lower prospects in the labor market; 39% expected their child to have a lower prospect of finding a spouse.
Hitt, Ginsburg, Cousounis, Lipman, Cucchiara, Stallings and Grimberg [36]	166 parents of children with IGHD/ISS (6–16 years) seeking EP; USA	Cross-sectional study	Exploring factors that influence parental decision making to seek hGH treatment for their short-statured child by utilizing a survey	Efficacy and side effects concerned most parents (64%), 60% were concerned about comparison of their child with others, 54% about health in general.

Table 1. *Cont.*

Authors	Population; Country	Study Design	Aim of the Study and Measure Method	Results
de Silva and de Zoysa [38]	74 parents of children aged 8–18 years with IGHD; Sri Lanka	Cross-sectional study	Gathering mental health difficulties of parents using the GHQ-30	54% of parents seemed to have mental health difficulties, 70% of them were mothers.
Haverkamp and Noeker [33]	442 parents of children (mean age 10.6 years) with different pathological growth disorders (IGHD n = 79, ACH n = 47, TS n = 225, FSS n = 38, CDPG n = 53); Germany	Cross-sectional study	Testing new questionnaire for parents of short-statured children with four dimensions: "suffering", "future anxieties", "behavioral problems", and "coping efforts"; comparison between IGHD and ACH	Parents of IGHD children scored low on all scales; 15.2% feared secondary psychological problems due to hGH treatment, future anxieties stressed 13.9%. Parents' main sources of energy: good relationships with medical staff, medical intervention, and family.
Rotnem, Cohen, Hintz and Genel [16]	Families of hypopituitary IGHD children with a mean age of 11.3 years (n = 11 parents); USA	uncontrolled before-and-after study	Structured and open-ended interviews with parents before and during one year of hGH treatment about experiences and resources	Doubts about maternal competence and overprotectiveness. Defenses: denial, rationalization, and reaction formation through incorporation with organizations.

Abbreviations: IGHD = isolated growth hormone deficiency; ACH = achondroplasia; TS = Turner syndrome; FSS = familial short stature; CDPG = constitutional delay of puberty and growth; hGH = human growth hormone; ISS = idiopathic short stature; QoLISSY = Quality of Life in Short Stature Youth; PIP = Pediatric Inventory for Parents; HADS = Hospital Anxiety and Depression Scale; HRQOL = health-related quality of life; EP = endocrine subspecialist care; STAI = Spielberger State-Trait Anxiety Inventory; GHQ-30 = General Health Questionnaire-30; SGA = small for gestational age; CBCL = Child Behavior Checklist; UK = United Kingdom; USA = United States of America; GHD-CTB-Child = Growth Hormone Deficiency-Child Treatment Burden Measure; GHD-CTB-Observer = Growth Hormone Deficiency-Child Treatment Burden Measure-Observer: GHD-PTB = Growth Hormone Deficiency-Parent Treatment Burden Measure.

Three studies resulting in four publications were conducted within the QoLISSY project [19,24,34,42], and another study with three publications was carried out by the Brod Group [35,40,43].

The publications were conducted in Germany [19,33,42], Italy [34,39], the United States of America (USA) [16,36], Spain [44], Poland [37], Sri Lanka [38], and the Netherlands [41]. Four publications were conducted multi-nationally [25,35,41,43].

The age of the children with ISS and IGHD included in the publications ranged from 4 to 18 years. Sample sizes ranged from n = 11 parents [16] to n = 243 parents [43]. Out of the 15 selected publications, 12 were cross-sectional, one utilized a prospective observational design, another used a non-interventional design, and the remaining used an uncontrolled before-and-after design. Seven of these publications were multi-center trials, and five were single-center trials. Eight publications approached parental burdens using a quantitative approach [25,33,36–38,42–44]. Moreover, one publication reported structured interviews to capture parental burdens [16]. Another publication utilized a mixed-method approach using questionnaires and interviews [41]. Two publications carried out focus group discussions [19,34]. Another two publications combined structured interviews and focus group discussions [35,40]. A narrative-based approach was implemented in one publication [39].

3.2. Parents' HRQOL, Stress, Caregiving Burdens, and Special Needs

Casana-Granell, Lacomba-Trejo, Montoya-Castilla and Perez-Marin [44] examined stress levels and emotional distress at 145 principal caregivers of short-statured children, most likely ISS children aged 12–17.

This study utilized the Pediatric Inventory for Parents (PIP) to assess the caregivers' stress levels, a chronic–generic questionnaire for parents with chronically ill children. In addition, this study used the Hospital Anxiety and Depression Scale (HADS) to evaluate the principal caregivers' emotional distress by analyzing possible symptoms of anxiety and depression. According to the PIP, 44.2% to 62.7% of the principal caregivers showed high stress levels. The resistance and always-returning care situation especially contributed to these high stress levels (57.3% of centiles > 50).

Furthermore, 15.2% (n = 22) of the principal caregivers expressed a clinically significant problem with overall emotional distress on the HADS. Additionally, 47.6% (n = 69) showed anxiety symptoms (22.8% most likely had an anxiety disorder, 24.8% had a clinical anxiety disorder), and 17.2% seemed depressed. Casana-Granell, Lacomba-Trejo, Montoya-Castilla and Perez-Marin [44] emphasized that almost every principal caregiver was the mother of the short-statured child, which confirmed earlier findings [45]. The authors did not address the risk of bias within their study.

Majewska, Stanisławska-Kubiak, Wiecheć, Naskręcka, Kędzia and Mojs [37] assessed anxiety levels in 101 mothers of children with growth failure due to IGHD or unknown causes. The children were aged 5 to 16 years, and of them, 70 were diagnosed with IGHD and received human growth hormone (hGH), and 31 were undergoing the diagnostic process to determine the short stature etiology.

The Spielberger State–Trait Anxiety Inventory (STAI) was used to assess mothers' anxiety levels. Anxiety as a trait was low in all recruited mothers; nevertheless, it was higher in mothers whose children did not get diagnosed yet. Anxiety as a state was presented with medium anxiety levels, whereas mothers without a diagnosed child showed higher values. Overall, the mothers of children without diagnosis or treatment presented significantly higher anxiety levels ($p = 0.001$). The risk of bias was not addressed by the authors. The small sample size and the limitation of only mothers of short children being included must be considered as limitations within this study.

The Brod Group recruited thirty-one parents of IGHD children aged between 4 and 13 years to develop a model of the impact of IGHD [35] and assess the burden of GHT on children and parents [35]. They conducted four focus group discussions and 52 telephone interviews with IGHD children and their parents/guardians.

Within this one study, the Brod Group published the three following papers.

Brod, Alolga, Beck, Wilkinson, Højbjerre and Rasmussen [35] aimed to develop a model of the impact of IGHD to support a disease-specific patient-reported outcome (PROM) and an observer-reported outcome (ObsROM) measure. Parents (n = 31) reported their emotional impacts from their children's IGHD. Nearly half of the parents reported worry for their child (n = 16, 47%), anger or frustration over the reactions of others about their child's size (n = 13, 38%), relief when a diagnosis was made (n = 10, 29%), and pressure in managing treatment for their children (n = 4, 12%). The limitations addressed by the authors were the generalizability of the findings. Although it was a large sample size for qualitative research, these findings may not be generalizable to parents of IGHD children in other countries or ethnic groups.

Brod, Højbjerre, Alolga, Beck, Wilkinson and Rasmussen [40] assessed the burden of GHT from the child's perspective and the impact of the children's treatment on the parents. Parents (n = 31) reported being emotionally impacted by hGH treatment for their children. Of these, 62% (n = 21) noted their worry, including worry about treatment administration (n = 20, 59%), causing pain to their child (n = 13, 38%), and medication costs (n = 5, 15%). The second treatment burden identified for parents was the "interference" domain. Half of the parents (n = 17, 50%) reported that hGH treatment interferes with family travels. Thirty-two percent (n = 11) of the parents noted that preparing their child for the injection took time. For 12% (n = 4) of parents, the hGH treatment interfered with their daily and social life. An attempt to minimize recall bias for those taking treatment was made by having a relatively short duration (no more than 12 months).

Brod, Rasmussen, Alolga, Beck, Bushnell, Lee and Maniatis [43] aimed to describe the psychometric validation data for three measures generated through a concept elicitation phase beforehand. The elicitation consisted of a literature review, interviews with clinical experts, four focus groups organized in Germany, and 52 telephone interviews in the UK and the US. The Growth Hormone Deficiency-Parent Treatment Burden Measure (GHD-PTB) was one of the three generated measures. The assessment tool is a PRO that evaluates the treatment burden experienced by parents/guardians of children aged 4 to <13 years with IGHD.

To conduct the psychometric validation for the GHD-PTB, n = 243 parents/guardians of IGHD children aged 4 to <13 years completed the GHD-PTB. Parent/guardian mean age was 41.6 years (range 22–66), with most coming from the US (91.8%). Of the parents/guardians, 80.7% were mothers, and 88.1% were married.

The average scores of the eight items in the GHD-PTB ranged from 0.35 to 1.28 on a response scale ranging from 0 ("Not at all/Never") to 4 ("Extremely/All of the time"). In the group that started hGH treatment within this study, significant improvements were observed in the Emotional and Overall domains, with scores decreasing by 16.6 and 8.6 points, respectively, on a 0-to-100-point scale. One limitation addressed by the authors was the sample. Most participants were from the US and white, so the results may not be generalizable.

Marini, Chesi, Mazzanti, Guazzarotti, Toni, Salerno, Officioso, Parpagnoli, Angeletti, Faienza, Iezzi, Aversa and Sacchetti [39] aimed to understand illnesses of children and teenagers with IGHD and their families' experiences through a narrative-based approach.

Some parents (n = 48) wrote about waiting for the diagnosis. Over half of them spent time living with anxiety and concerns (n = 26, 55%). Many mentioned the communication of hGH treatment in their narratives (n = 51 answers). One-third were worried and unconvinced about the treatment (n = 16, 30%). Most parents (n = 89 answers) wrote about the treatment difficulties: 33% (n = 29) had organizational issues because of the daily injections. For 21% (n = 19) of parents, it was painful to cause pain to their affected child. Asking the parents about their worries, over half of them (67%, n = 28) were worried about the side effects of hGH treatment, and 14% (n = 6) of parents feared the therapy would not work. No differences showed up throughout the parents' narratives depending on the children's gender. The authors did not address limitations within their study.

The QoLISSY project was a multi-center study conducted simultaneously in five European countries (France, Germany, Spain, Sweden, and the United Kingdom (UK)). They aimed to develop a disease-specific HRQOL instrument for children and adolescents aged 8–18 with IGHD/ISS and for parents of IGHD/ISS children aged 4–18. In total, three studies were conducted, which resulted in the following four publications.

Quitmann, Rohenkohl, Sommer, Petzold and Bullinger-Naber [19] executed focus-group discussions with item generation for the QoLISSY project in Germany.

The study aimed to identify important aspects of children's HRQOL from parents' and children's perspectives. Although the primary aim was to focus on children's HRQOL, parents expressed personal burden due to their child's short stature. Specifically, parents described everyday problems concerning their child's height and future anxieties concerning the short body height of their children. Problems in treatment were another burden for parents of short-statured children, and the treatment organization appeared to be a main concern. Social stigmatization also played a significant role in talking about hGH treatment. Parents were frustrated by the lack of knowledge of others.

Silva, Bullinger, Sommer, Rohenkohl, Witt and Quitmann [25] aimed to compare the levels of caregiving stress and HRQOL of short-statured children's parents between different clinical groups of diagnosis, treatment status, and current height deviation. Furthermore, the authors examined the direct and indirect links between children's psychosocial functioning and their parents' HRQOL by using caregiving stress as an indicator.

The authors took advantage of the "effects on parents" scale of the QoLISSY questionnaire to assess caregiving stress. In total, parents of children/adolescents with ISS reported greater caregiving stress than parents of IGHD children. Parents of children with current short stature reported greater caregiving stress than those who achieved normal height.

A significant effect of children's psychosocial functioning was found on caregiving stress (ß = −0.53, $p < 0.01$). According to this, caregiving stress directly affected parents' QoL (ß = −0.37, $p < 0.01$). The indirect effect of children's psychosocial functioning on parents' QoL via caregiving stress was statistically significant (ß = 0.20, $p < 0.01$; BC 95% CI = 0.11/0.31).

Bloemeke, Silva, Bullinger, Witt, Dörr and Quitmann [42] conducted a prospective observational study to evaluate the QoLISSY questionnaire as a health-outcome indicator of human growth hormone (hGH) interventions.

The authors used the generic KIDSCREEN-10 and the QoLISSY questionnaire. Raw QoLISSY scores were transformed into 0 to 100 scores, whereas higher values represented a higher HRQOL.

Comparing the treated and untreated group at baseline on the QoLISSY questionnaire showed that parents of untreated children reported a significantly higher HRQOL in the domain "future" than parents of children in the treated group (parents of treated children (IGHD/SGA): M = 53.93, parents of untreated children (ISS): M = 68.57).

Overall, the results displayed a trend of HRQOL scores improving in all QoLISSY domains in the treated sample while decreasing in the untreated sample. These differences were not statistically significant. Furthermore, the generic KIDSCREEN-10 instrument could not detect changes in HRQOL, whereas the QoLISSY questionnaire detected changes in HRQOL between the treated and untreated groups in this sample. Endocrine short stature is a rare disease; the sample size was large but still very selective because they were all looking for treatment options in the growth clinics. So the sample might not be representative of the overall target population.

Quitmann, Giammarco, Maghnie, Napoli, Di Giovanni, Carducci, Mohn, Bullinger and Sommer [34] adapted and validated the existing QoLISSY questionnaire for Italian patients and parents by undergoing focus group discussion and a cognitive debriefing process.

"Effects on parents" was the second-largest category, with about 20% of codes. Parents described the effect of their children's growth deficit as being sad and wishing for a better life for their children. Fifteen percent of the parents addressed hGH treatment as a burden

of treatment administration or expressed concerns about possible side effects. Limitations within this study were the small sample size due to unforeseen difficulties in recruitment, which makes generalizing the results to other ethnic groups difficult.

Visser-van Balen, Geenen, Kamp, Huisman, Wit and Sinnema [41] assessed parental stress about their child's future and their worries about the children's psychosocial functioning to understand parents' motives for choosing hGH treatment. A psychologist interviewed parents about their consideration of their child having equal chances in the labor market compared to people of normal height and the children's prospect of finding a spouse (yes, doubtful, no), and 44.5% of the parents expected their child to have a lower prospect in the labor market as an adult (39% of boys, 48% of girls), while 39% of the parents considered their child to have a lower prospect of finding a spouse (77% of boys, 17% of girls). This difference between boys and girls was significant ($p < 0.01$).

Furthermore, the CBCL was utilized in this study. Two out of three parents reported worries about future opportunities or observed psychosocial problems in their children. One limitation of this study is the sample size. It was sufficiently large to conclude with a comparison with normative data but too small to examine other possible roles in modulating the results with sufficient power.

Hitt, Ginsburg, Cousounis, Lipman, Cucchiara, Stallings and Grimberg [36] explored factors influencing parental height-related decision making to seek medical treatment for their child. Using a five-point Likert scale, parents answered the following question: "how much of an impact would each of the following issues make on your decision whether to do something medical for your child's height?".

Most parents were concerned about the efficacy and side effects of hGH treatment. This was illustrated by 64% of the parents rating "treatment characteristics" as having a big or extreme impact on their decision to seek medical treatment for their child's short stature. Sixty percent of the parents were concerned that their child's height was short relative to their peers and demonstrated a strong focus on external comparisons of their children to others. In third place came the category "health", rated by 54% of the parents as having a significant impact on their decision. The survey consisted of two additional questions to assess the parents' opinions on how much hGH treatment could improve their HRQOL. Seventy-six percent of the parents rated hGH treatment as potentially improving any QoL issue related to their child's short height. The authors mentioned a response bias (the desire to give the socially preferred answer) within their study, which may have contributed to a reduced rating of specific categories of concern.

De Silva and de Zoysa [38] assessed mental health difficulties in 74 parents of children with IGHD. The authors used the General Health Questionnaire-30 (GHQ-30) to examine the parents' mental health. A score of 4 or above identifies the respondent as having mental health difficulties.

Fifty-four percent (n = 40) of the parents with an IGHD child scored at or above 4, indicating that more than half the parents showed evidence of mental health difficulties. Seventy percent (n = 28) of them were mothers. A limitation of this study was the small sample size and hence the generalizability and the statistical power of the study are limited. Furthermore, the results were preliminary, so no conclusion on causality can be made. On top of that, the GHQ-30 has not been validated in Sri Lanka. Because de Silva and de Zoysa only focused on parents' mental health as an outcome and reported very concisely on their results, the results section of this study is brief.

Haverkamp and Noeker [33] assessed the psychosocial stress factors of parents associated with short stature. The authors invented a new disease-specific parental questionnaire to inquire about the parents' short-stature-associated stress factors. The questionnaire includes four scales: "suffering", "future anxieties", "behavioral problems", and "coping efforts".

In general, the parents scored low on all four scales. Of the parents of IGHD children, 21.5% were anxious about possible hGH treatment side effects. Parents reported being stressed by future anxieties concerning their child's professional career (13.9%). On top of

that, the primary sources of energy for parents of IGHD children were good relationships with medical staff (38%) and medical intervention (35.4%). Another confidence booster named by 20.3% of the parents was their family. The authors controlled for parental misattributions using background information such as socioeconomic status.

Rotnem, Cohen, Hintz and Genel [16] investigated the subjective experiences and special needs of parents whose children failed to grow normally due to IGHD.

All parents expressed confusion about how to relate to their short-statured child. Most parents had been aware of their tendency toward overprotectiveness and not-age-appropriate expectations toward their children. However, they continued to react to their children according to size rather than age. It was more difficult for mothers and fathers to accept pathological short stature in boys than girls. Defenses most often used by these parents were denial, rationalization, and reaction formation through incorporation with Human Growth Foundation, Little People of America, or parent support groups. Limitations within this study include the small sample size of families, making generalization difficult.

3.3. Validated Tools to Assess Parents' HRQOL, Stress, Caregiving Burdens, and Special Needs

In the studies identified and summarized above, eight different tools were used to assess parental HRQOL, caregiving burden, and special needs of parents with short-statured children; five of them were generic (PIP, HADS, STAI, GHQ-30, and EUROHIS-QOL-8) and three short-stature-specific (GHD-PTB, QoLISSY, and "Short stature in children—a questionnaire for parents").

The PIP assesses 42 potentially stressful situations for parents of children with chronic illnesses. It measures the difficulty and frequency of each situation across four domains: medical care, communication, emotional functioning, and role function. Scores are obtained for each subscale by adding up the item scores. The PIP showed high internal consistency reliability using Cronbach's alpha between 0.80 and 0.96. Its origin was developed in a sample of pediatric oncology patients in English in 2001 [46]. The instrument has been used in studies focusing on various illnesses, including, e.g., diabetes [47], cancer [48], short stature [20], and congenital malformations [49]. The PIP has been translated into, e.g., German [50] and Spanish [51].

The HADS, developed in 1983, is a tool used to assess anxiety and depression in a general medical population and consists of seven items for anxiety and seven items for depression [52]. Cronbach's alpha for the subscale of anxiety (HADS-A) ranges from 0.68 to 0.93, and for the subscale of depression (HADS-D), Cronbach's alpha varies between 0.67 and 0.90 [53]. Cut-off values are available for both scales. The HADS is available in many languages, e.g., German [54], Italian [55], Chinese [56], or Arabic [57].

The STAI is a psychological assessment comprising 40 self-report items on a four-point Likert scale. It measures two types of anxiety: state anxiety and trait anxiety. The inventory is divided into separate sections for each type, with 20 questions dedicated to each. Higher scores on the inventory indicate higher levels of anxiety. The STAI is available in over 40 languages [58], e.g., German [59], Spanish [60], and French [61]. Cut-off values are available [62]. The STAI demonstrates high internal consistency, with median alpha coefficients of 0.93 for state anxiety and 0.90 for trait anxiety [63].

The GHQ is a tool for assessing general mental health and well-being in non-psychiatric populations. The GHQ measures psychological distress through subscales such as somatic symptoms, anxiety and insomnia, social dysfunction, and severe depression. It comprehensively assesses an individual's mental health status [64]. The reliability and validity of the GHQ-30 show values of Cronbach's alpha of 0.95 for the GHQ-30. The GHQ is available in different versions consisting of 12, 28, 30, or 60 items and different languages, e.g., Spanish [65], German [66], and Italian [67].

The EUROHIS-QOL eight-item index, developed by the WHOQOL group, serves as an economic screening measure. It has been validated using data from multiple European countries, including France, Germany, the United Kingdom, Lithuania, Latvia, Croatia,

Romania, Slovakia, the Czech Republic, and Israel. The index is conceptually derived from the original WHOQOL-BREF, with two items selected from each domain (physical, psychological, environmental, and social). The study's findings revealed consistent and satisfactory internal consistencies across the countries studied [68,69].

The GHD-PTB is an eight-item PROM for parents/guardians of children aged 4 to <13 years with IGHD. The score is calculated by summing the individual item scores and converting them into a standardized score ranging from 0 to 100 points, where a higher score demonstrates a higher caregiver burden. The eight items result in two domains (parental emotional and parent interference) and one total score. Internal consistency reliability was acceptable and ranged between 0.60 and <0.70. The GHD-PTB is currently available in the English language [43].

The QoLISSY questionnaire is a PROM to assess the HrQol of short-statured children using self-reports (8–18 years) and proxy-reports (4–18 years) and consists of 50 items resulting in six subscales. The proxy version comprises two additional subscales: future (5 items) and effects on parents (11 items) [70]. Cronbach's alpha varies between 0.65 and 0.95 [42]. The QoLISSY questionnaire is validated for ISS, IGHD [70], achondroplasia [71], and Small-for-Gestational Age [72] and is available in various languages, e.g., German, Englisch, Spain, Frech, Swedish [70], Italian [34], or Greek [73].

The questionnaire "Short stature: a questionnaire for parents" was developed by [33] in a sample of parents of patients with IGHD, achondroplasia, Turner syndrome, familial short stature, and constitutional delay of puberty and growth. This tool consists of 34 items, resulting in four scales (Suffering, Future anxieties, Behavioral problems, and Coping efforts). Cronbach's alpha ranges from 0.60 to 0.91.

4. Discussion

Parenthood represents an incisive and momentous experience. The transition to parenthood will be assumed not only as a crisis but also as a normative event; it is often underestimated [74]. It has to be noticed that parenthood is a decades-long developmental task, resulting in various challenges. Parents/primary caregivers of young children especially experience a relinquishment of autonomy, personal liberty, occupational identity, and social and leisure activities [75]. In addition to increased requirements [51], mothers report multiple changes in their lives, which are experienced as stressful [76–78]. These challenges include mental health costs, such as time, physical and emotional well-being, conflicts of social roles, and economic restrictions [76–78]. Additionally, aspects of, e.g., the changes in responsibility and feelings of loss [79] were mentioned.

With the diagnosis of a child's chronic health condition, parents/primary caregivers are confronted with additional responsibilities and tasks that may affect their quality of life [23,80]. Parents/primary caregivers of a child diagnosed with a chronic health condition may experience higher levels of emotional pressure than parents caring for a healthy child. Next to the primary responsibilities of parents/primary caregivers, they have to deal with additional disease-specific tasks to enable the healthy development of their child. Some studies examining the situation of families with a pediatric chronic disease highlighted that these parents have to adjust to restrictions in their social life, job perspective, and psychosocial well-being as their everyday life is decisively determined by the responsibilities for the child's care [23,80]. The parental adaptation to the new situation of having a chronically ill child often happens without much support for coping with the child's diagnosis. Supplies of psychosocial support are rarely offered, making it hard to assimilate the new family situation [80].

Children with IGHD/ISS do not need regular invasive medical interventions except daily injections, which is why their parents' burdens are often questioned and minimized [44]. Therefore, this review investigated the caregiving burden, special needs, HRQOL, and stress in parents of IGHD/ISS children. The 15 included publications used various approaches to assess these domains; questionnaires, narrative-based approaches,

structured interviews, and/or focus group discussions. Some authors also assessed the parents' main sources of energy [16,19,33].

Most publications utilized questionnaires to assess the parents' caregiving burden, special needs, HRQOL, and stress [25,33,36–38,42–44]. Various questionnaires were used, but most were generic and thus not sensitive enough to cover disease-specific aspects. While generic instruments are extensively validated and enable comparisons among different populations, they frequently fall short in identifying subtle yet clinically meaningful changes in HRQOL over time. This limitation arises from the absence of disease-specific aspects in the lives of affected patients that significantly influence their HRQOL [42]. Hitt, Ginsburg, Cousounis, Lipman, Cucchiara, Stallings and Grimberg [36], and Haverkamp and Noeker [33] engendered disease-specific questionnaires to assess parents' concerns. Unfortunately, both only covered small domains, such as factors influencing parents' decision-making for hGH treatment [36]. Bloemeke, Silva, Bullinger, Witt, Dörr and Quitmann [42] and Silva, Bullinger, Sommer, Rohenkohl, Witt and Quitmann [25] used the disease-specific QoLISSY questionnaire. Brod, Rasmussen, Alolga, Beck, Bushnell, Lee and Maniatis [43] implemented the disease-specific PRO GHD-PTB. Moreover, they developed two disease-specific measures for assessing children's treatment burden. Structured interviews and focus group discussions were implemented in several publications [16,19,34,35,40,41]. Some developed a semi-structured interview guide [15,28,30,35] but still focused on different domains of parental concerns.

The QoLISSY Group and the Brod Group used the same interview guide for their studies, making the results more comparable.

The included publications reported various burdens, special needs, and HRQOL of the parents. On the one hand, hGH treatment and all the issues coming along with it were expressed as having a massive impact on the parents and their families. Organizational issues were especially mentioned by the parents/primary caregivers as a main burden [34–36,39,40]. Nevertheless, most parents still decided on hGH treatment for their children because the suggested benefits outweighed the possible side effects and daily injections. On the other hand, Brod, Rasmussen, Alolga, Beck, Bushnell, Lee and Maniatis [43] found that most parents had little to no problems with their children's hGH treatment. Thus, the results on parental burden through hGH treatment are inconsistent and need further exploration.

Furthermore, parents mentioned future anxieties as being a major concern. Many were stressed about their children's future because they believed that short-statured children had a lower prospect in the labor market and of finding a spouse as an adult due to their short stature [19,33,34,40].

Social stigmatization and comparison of height to their children's peers appeared to be another caregiving burden for parents of IGHD/ISS children [19,35,36]. Some parents wished for psychological treatment besides the medical treatment option and were convinced they would have fewer problems if those in their environment knew about the parents' and their children's special needs and opportunities [19]. There were concerns that parents seemed to have high stress levels and symptoms of anxiety [37,44] and that the children's psychosocial functioning significantly affected parents' HRQOL via caregiving stress [24].

Many publications did not address parents' special needs to cope with caregiving stress. Nevertheless, the dialogue between the parents and their families or parent support groups appeared to be a good coping mechanism for parents [12,20]. This domain needs to be explored in depth in further explorations.

Parents of children diagnosed with IGHD/ISS can have an impaired HRQOL, have special needs, and face various caregiving burdens and stress. The adaptation of these parents has a significant impact on other family members and their well-being, but parents need time and resources to adapt to a child's chronic disease [81]. Once they have adapted, parents can increase their children's well-being, and health-related outcomes may improve [23]. A crucial risk factor for parents' impaired HRQOL is caregiving stress, which

links the positive association between children's psychosocial functioning and parents' outcomes [25]. Besides stress mechanisms, a child's development can be influenced by the feedback children with chronic diseases receive from their families [82,83]. Psychological support could be a huge benefit for the parents [32], but it is essential to discern those for whom this will be necessary to ensure positive feedback.

A further-developed disease-specific measurement besides the parent domain of the QoLISSY questionnaire [19] and the GHD-PTB [43] would be beneficial to find out more about the parents' special needs, burdens, and HRQOL in the care of an IGHD/ISS child. If those dimensions are assessed and the parents are offered psychological counseling, their children could also benefit from the changed perception of their parents if needed. As earlier findings have shown, parental frustration can be transferred to their children [20,84]; in addition, good family functioning appears to be an essential protective factor for short-statured children [18].

Limitations

The limitations of this study include the fact that we only used two databases for our search. While we believe that we identified all relevant articles through our search, we cannot definitively exclude the possibility that including additional databases would have yielded further results. Additionally, we did not assess the quality of the studies, making it challenging to compare their findings. Moreover, the included studies had very different designs that were not directly comparable. Furthermore, the included studies primarily focused on mothers, making it difficult to generalize the results to parents in general. Comparing the results is complicated because the studies were conducted in different healthcare systems. Cultural differences are also likely to influence the assessment of burdens and concerns. Most publications were from Europe and the USA, with only one from Sri Lanka. Another limitation of our review is that the included studies employed different recruitment strategies, often purposive sampling, which introduces a potential bias. Nonetheless, our review highlights parental burdens in dealing with IGHD/ISS children and draws attention to the limited research on this topic.

5. Conclusions

Parenthood itself is a decades-long task with various challenges. Parents/primary caregivers of children with chronic health conditions face additional challenges. While IGHD and ISS are not life-threatening health conditions, these challenges are often understated, and parents/primary caregivers rarely seek help in processing the diagnosis and in day-to-day tasks. In contrast, this review points out that parents of IGHD/ISS children can have various burdens, anxiety, special needs, and an impaired HRQOL in caring for their short-statured child. Clinicians should remember that parental support may positively affect the child's development.

On top of that, our results support earlier findings concerning the limited use of disease-specific measures. Still, most measurements are generic and hence not very sensitive. However, the Brod Group has contributed towards disease-specific measures for parents of IGHD/ISS children with the development of the GHD-PTB. Further studies should aim to develop measures for all domains of affected parents' lives. For children, especially those with a chronic condition, family support is a major protective factor and helps children cope with their disease. Therefore, assessing the caregiving burden, HRQOL, and special needs of parents and families of IGHD/ISS children is crucial, because once the parents/families are adapted to the child's short stature, they can increase their child's health-related outcomes and well-being.

Author Contributions: Conceptualization, J.Q. and S.W.; methodology, L.L. and S.W.; formal analysis, L.L. and S.W.; writing—original draft preparation, L.L.; writing—review and editing, J.Q., K.K. and S.W.; visualization, S.W.; supervision, J.Q.; project administration, J.Q. and S.W. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Ranke, M.B. Towards a consensus on the definition of idiopathic short stature. *Horm. Res.* **1996**, *45* (Suppl. S2), 64–66. [CrossRef]
2. Barstow, C.; Rerucha, C. Evaluation of Short and Tall Stature in Children. *Am. Fam. Physician* **2015**, *92*, 43–50. [PubMed]
3. Argente, J.; Abusrewil, S.A.; Bona, G.; Chiarelli, F.; Kelnar, C.J.; Skordis, N. Isolated growth hormone deficiency in children and adolescents. *J. Pediatr. Endocrinol. Metab.* **2001**, *14* (Suppl. S2), 1003–1008. [CrossRef] [PubMed]
4. Cohen, P.; Rogol, A.D.; Deal, C.L.; Saenger, P.; Reiter, E.O.; Ross, J.L.; Chernausek, S.D.; Savage, M.O.; Wit, J.M. Consensus Statement on the Diagnosis and Treatment of Children with Idiopathic Short Stature: A Summary of the Growth Hormone Research Society, the Lawson Wilkins Pediatric Endocrine Society, and the European Society for Paediatric Endocrinology Workshop. *J. Clin. Endocrinol. Metab.* **2008**, *93*, 4210–4217. [CrossRef] [PubMed]
5. United Nations Children's Fund (UNICEF); World Health Organization; International Bank for Reconstruction and Development/The World Bank. *Levels and Trends in Child Malnutrition: Key Findings of the 2020 Edition of the Joint Child Malnutrition Estimates*; World Health Organization: Geneva, Switzerland, 2020.
6. Ranke, M.B.; Lindberg, A.; Tanaka, T.; Camacho-Hübner, C.; Dunger, D.B.; Geffner, M.E. Baseline Characteristics and Gender Differences in Prepubertal Children Treated with Growth Hormone in Europe, USA, and Japan: 25 Years' KIGS® Experience (1987–2012) and Review. *Horm. Res. Paediatr.* **2017**, *87*, 30–41. [CrossRef]
7. Fitzgerald, C.; George, S.; Somerville, R.; Linnane, B.; Fitzpatrick, P. Caregiver burden of parents of young children with cystic fibrosis. *J. Cyst. Fibros.* **2018**, *17*, 125–131. [CrossRef]
8. Piran, P.; Khademi, Z.; Tayari, N.; Mansouri, N. Caregiving burden of children with chronic diseases. *Electron. Physician* **2017**, *9*, 5380–5387. [CrossRef]
9. Quitmann, J.; Bloemeke, J.; Silva, N.; Bullinger, M.; Witt, S.; Akkurt, I.; Dunstheimer, D.; Vogel, C.; Böttcher, V.; Kuhnle Krahl, U.; et al. Quality of Life of Short-Statured Children Born Small for Gestational Age or Idiopathic Growth Hormone Deficiency Within 1 Year of Growth Hormone Treatment. *Front. Pediatr.* **2019**, *7*, 164. [CrossRef]
10. Ayadi, H.; Cherif, L.; Hadjkacem, I.; Kammoun, W.; Khemakhem, K.; Khemekhem, S.; Moalla, Y.; Kammoun, T.; Hachicha, M.; Ghribi, F. Self-Esteem in Children and Adolescents with Growth Hormone Deficiency. *Iran. J. Pediatr.* **2018**, *28*, e4617. [CrossRef]
11. Naiki, Y.; Horikawa, R.; Tanaka, T. Assessment of Psychosocial Status among Short-stature Children with and without Growth Hormone Therapy and Their Parents. *Clin. Pediatr. Endocrinol.* **2013**, *22*, 25–32. [CrossRef]
12. Sandberg, D.E.; Voss, L.D. The psychosocial consequences of short stature: A review of the evidence. *Best Pract. Res. Clin. Endocrinol. Metab.* **2002**, *16*, 449–463. [CrossRef] [PubMed]
13. Voss, L.D.; Mulligan, J. Bullying in school: Are short pupils at risk? Questionnaire study in a cohort. *BMJ* **2000**, *320*, 612–613. [CrossRef] [PubMed]
14. Kazak, A.E.; Kassam-Adams, N.; Schneider, S.; Zelikovsky, N.; Alderfer, M.A.; Rourke, M. An integrative model of pediatric medical traumatic stress. *J. Pediatr. Psychol.* **2006**, *31*, 343–355. [CrossRef] [PubMed]
15. Schor, E.L. Family pediatrics: Report of the Task Force on the Family. *Pediatrics* **2003**, *111*, 1541–1571. [PubMed]
16. Rotnem, D.; Cohen, D.J.; Hintz, R.; Genel, M. Psychological Sequelae of Relative "Treatment Failure" for Children Receiving Human Growth Hormone Replacement. *J. Am. Acad. Child Psychiatry* **1979**, *18*, 505–520. [CrossRef] [PubMed]
17. Logan, D.E.; Scharff, L. Relationships between family and parent characteristics and functional abilities in children with recurrent pain syndromes: An investigation of moderating effects on the pathway from pain to disability. *J. Pediatr. Psychol.* **2005**, *30*, 698–707. [CrossRef]
18. Visser-van Balen, H.; Sinnema, G.; Geenen, R. Growing up with idiopathic short stature: Psychosocial development and hormone treatment; a critical review. *Arch. Dis. Child.* **2006**, *91*, 433–439. [CrossRef]
19. Quitmann, J.; Rohenkohl, A.; Sommer, R.; Petzold, S.; Bullinger-Naber, M. How do Affected Children and Adolescents Experience their Short Stature, and what is the Point of View of their Parents? *Prax. Kinderpsychol. Kinderpsychiatr.* **2014**, *63*, 635–648. [CrossRef]
20. Preston, A.; Storch, E.A.; Lewin, A.; Geffken, G.R.; Baumeister, A.L.; Strawser, M.S.; Silverstein, J.H. Parental stress and maladjustment in children with short stature. *Clin. Pediatr.* **2005**, *44*, 327–331. [CrossRef]
21. Witt, S.; Kolb, B.; Bloemeke, J.; Mohnike, K.; Bullinger, M.; Quitmann, J. Quality of life of children with achondroplasia and their parents—A German cross-sectional study. *Orphanet J. Rare Dis.* **2019**, *14*, 194. [CrossRef]
22. Wheeler, P.G.; Bresnahan, K.; Shephard, B.A.; Lau, J.; Balk, E.M. Short stature and functional impairment: A systematic review. *Arch. Pediatr. Adolesc. Med.* **2004**, *158*, 236–243. [CrossRef] [PubMed]
23. Grootenhuis, M.A.; Bronner, M.B. Paediatric illness! Family matters. *Acta Paediatr.* **2009**, *98*, 940–941. [CrossRef] [PubMed]
24. Quitmann, J.; Rohenkohl, A.; Bullinger, M.; Chaplin, J.E.; Herdman, M.; Sanz, D.; Mimoun, E.; Feigerlova, E.; DeBusk, K.; Power, M.; et al. Parental perception of health-related quality of life in children and adolescents with short stature: Literature review and introduction of the parent-reported QoLISSY instrument. *Pediatr. Endocrinol. Rev.* **2013**, *11*, 147–160. [PubMed]

25. Silva, N.; Bullinger, M.; Sommer, R.; Rohenkohl, A.; Witt, S.; Quitmann, J. Children's psychosocial functioning and parents' quality of life in paediatric short stature: The mediating role of caregiving stress. *Clin. Psychol. Psychother.* **2018**, *25*, e107–e118. [CrossRef]
26. Richmond, E.; Rogol, A.D. Current indications for growth hormone therapy for children and adolescents. *Endocr. Dev.* **2010**, *18*, 92–108. [CrossRef] [PubMed]
27. Bullinger, M. Assessing health related quality of life in medicine. An overview over concepts, methods and applications in international research. *Restor. Neurol. Neurosci.* **2002**, *20*, 93–101.
28. Higginson, I.J.; Carr, A.J. Measuring quality of life: Using quality of life measures in the clinical setting. *BMJ* **2001**, *322*, 1297–1300. [CrossRef]
29. Edlund, B.J.; Lufkin, S.R.; Franklin, B. Long-term care planning for baby boomers: Addressing an uncertain future. *Online J. Issues Nurs.* **2003**, *8*, 3.
30. Liu, Z.; Heffernan, C.; Tan, J. Caregiver burden: A concept analysis. *Int. J. Nurs. Sci.* **2020**, *7*, 438–445. [CrossRef]
31. Arksey, H.; O'Malley, L. Scoping Studies: Towards a Methodological Framework. *Int. J. Soc. Res. Methodol. Theory Pract.* **2005**, *8*, 19–32. [CrossRef]
32. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* **2021**, *372*, n71. [CrossRef] [PubMed]
33. Haverkamp, F.; Noeker, M. 'Short stature in children—A questionnaire for parents': A new instrument for growth disorder-specific psychosocial adaptation in children. *Qual. Life Res.* **1998**, *7*, 447–455. [CrossRef] [PubMed]
34. Quitmann, J.; Giammarco, A.; Maghnie, M.; Napoli, F.; Di Giovanni, I.; Carducci, C.; Mohn, A.; Bullinger, M.; Sommer, R. Validation of the Italian Quality of Life in Short Stature Youth (QoLISSY) questionnaire. *J. Endocrinol. Investig.* **2017**, *40*, 1077–1084. [CrossRef]
35. Brod, M.; Alolga, S.L.; Beck, J.F.; Wilkinson, L.; Højbjerre, L.; Rasmussen, M.H. Understanding burden of illness for child growth hormone deficiency. *Qual. Life Res.* **2017**, *26*, 1673–1686. [CrossRef] [PubMed]
36. Hitt, T.; Ginsburg, K.R.; Cousounis, P.; Lipman, T.H.; Cucchiara, A.J.; Stallings, V.A.; Grimberg, A. Concerns and Expectations of Parents Seeking Subspecialist Care for Their Child's Short Stature. *Horm. Res. Paediatr.* **2019**, *92*, 311–318. [CrossRef]
37. Majewska, K.A.; Stanisławska-Kubiak, M.; Wiecheć, K.; Naskręcka, M.; Kędzia, A.; Mojs, E. Maternal anxiety in relation to growth failure and growth hormone treatment in children. *Medicine* **2020**, *99*, e22147. [CrossRef]
38. de Silva, K.S.; de Zoysa, P. Assessment of the psychological status of children with growth hormone deficiency and their parents. *Ceylon Med. J.* **2011**, *56*, 59–61. [CrossRef]
39. Marini, M.G.; Chesi, P.; Mazzanti, L.; Guazzarotti, L.; Toni, T.D.; Salerno, M.C.; Officioso, A.; Parpagnoli, M.; Angeletti, C.; Faienza, M.F.; et al. Stories of experiences of care for growth hormone deficiency: The CRESCERE project. *Future Sci. OA* **2016**, *2*, Fso82. [CrossRef]
40. Brod, M.; Højbjerre, L.; Alolga, S.L.; Beck, J.F.; Wilkinson, L.; Rasmussen, M.H. Understanding Treatment Burden for Children Treated for Growth Hormone Deficiency. *Patient* **2017**, *10*, 653–666. [CrossRef]
41. Visser-van Balen, H.; Geenen, R.; Kamp, G.A.; Huisman, J.; Wit, J.M.; Sinnema, G. Motives for choosing growth-enhancing hormone treatment in adolescents with idiopathic short stature: A questionnaire and structured interview study. *BMC Pediatr.* **2005**, *5*, 15. [CrossRef]
42. Bloemeke, J.; Silva, N.; Bullinger, M.; Witt, S.; Dörr, H.G.; Quitmann, J. Psychometric properties of the quality of life in short statured youth (QoLISSY) questionnaire within the course of growth hormone treatment. *Health Qual. Life Outcomes* **2019**, *17*, 49. [CrossRef] [PubMed]
43. Brod, M.; Rasmussen, M.H.; Alolga, S.; Beck, J.F.; Bushnell, D.M.; Lee, K.W.; Maniatis, A. Psychometric Validation of the Growth Hormone Deficiency-Child Treatment Burden Measure (GHD-CTB) and the Growth Hormone Deficiency-Parent Treatment Burden Measure (GHD-PTB). *Pharmacoecon Open* **2023**, *7*, 121–138. [CrossRef]
44. Casana-Granell, S.; Lacomba-Trejo, L.; Montoya-Castilla, I.; Perez-Marin, M. Emotional discomfort and stress in primary caregivers of pediatric patients with low stature. *Calid. Vida Salud* **2016**, *9*, 93–103.
45. Gaite, L.; García Fuentes, M.; González Lamuño, D.; Alvarez, J. Needs in rare diseases during paediatric age. *An. Sist. Sanit. Navar.* **2008**, *31* (Suppl. S2), 165–175.
46. Streisand, R.; Braniecki, S.; Tercyak, K.P.; Kazak, A.E. Childhood illness-related parenting stress: The pediatric inventory for parents. *J. Pediatr. Psychol.* **2001**, *26*, 155–162. [CrossRef] [PubMed]
47. Monaghan, M.; Clary, L.; Stern, A.; Hilliard, M.E.; Streisand, R. Protective Factors in Young Children With Type 1 Diabetes. *J. Pediatr. Psychol.* **2015**, *40*, 878–887. [CrossRef]
48. Kearney, J.A.; Salley, C.G.; Muriel, A.C. Standards of Psychosocial Care for Parents of Children With Cancer. *Pediatr. Blood Cancer* **2015**, *62*, S632–S683. [CrossRef]
49. Pierpont, E.I.; Wolford, M. Behavioral functioning in cardiofaciocutaneous syndrome: Risk factors and impact on parenting experience. *Am. J. Med. Genet. A* **2016**, *170*, 1974–1988. [CrossRef] [PubMed]
50. Vrijmoet-Wiersma, C.M.; Hoekstra-Weebers, J.E.; Margreet de Peinder, W.M.; Koopman, H.M.; Tissing, W.J.; Treffers, P.D.; Bierings, M.B.; Jansen, N.C.; Grootenhuis, M.A.; Egeler, R.M. Psychometric qualities of the Dutch version of the Pediatric Inventory for Parents (PIP): A multi-center study. *Psychooncology* **2010**, *19*, 368–375. [CrossRef]

51. del Rincón, C.; Remor, E.; Arranz, P. Estudio psicométrico preliminar de la versión española del Pediatric Inventory for Parents (PIP). *Int. J. Clin. Health Psychol.* **2007**, *7*, 435–452.
52. Zigmond, A.S.; Snaith, R.P. The hospital anxiety and depression scale. *Acta Psychiatr. Scand.* **1983**, *67*, 361–370. [CrossRef] [PubMed]
53. Bjelland, I.; Dahl, A.A.; Haug, T.T.; Neckelmann, D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J. Psychosom. Res.* **2002**, *52*, 69–77. [CrossRef] [PubMed]
54. Herrmann, C.; Scholz, K.H.; Kreuzer, H. Psychologic screening of patients of a cardiologic acute care clinic with the German version of the Hospital Anxiety and Depression Scale. *Psychother. Psychosom. Med. Psychol.* **1991**, *41*, 83–92. [PubMed]
55. Costantini, M.; Musso, M.; Viterbori, P.; Bonci, F.; Del Mastro, L.; Garrone, O.; Venturini, M.; Morasso, G. Detecting psychological distress in cancer patients: Validity of the Italian version of the Hospital Anxiety and Depression Scale. *Support. Care Cancer* **1999**, *7*, 121–127. [CrossRef]
56. Leung, C.M.; Wing, Y.K.; Kwong, P.K.; Lo, A.; Shum, K. Validation of the Chinese-Cantonese version of the hospital anxiety and depression scale and comparison with the Hamilton Rating Scale of Depression. *Acta Psychiatr. Scand.* **1999**, *100*, 456–461. [CrossRef]
57. Malasi, T.H.; Mirza, I.A.; el-Islam, M.F. Validation of the Hospital Anxiety and Depression Scale in Arab patients. *Acta Psychiatr. Scand.* **1991**, *84*, 323–326. [CrossRef]
58. Tilton, S.; Charles, D.; Lushene, R.E.; Jacobs, G.A. Review of the State-Trait Anxiety Inventory (STAI). *News Notes* **2008**, *48*, 1–3.
59. Laux, L.; Glanzmann, P.; Schaffner, P.; Spielberger, C.D. *Das State-Trait-Angstinventar. Theoretische Grundlagen und Handanweisung*; Beltz Test: Weinheim, Germany, 1981.
60. del Río Olvera, F.J.; Santamaría, F.C.; Cabello García, M.A.; Vela, J.A. Cuestionario de Ansiedad Estado Rasgo (STAI): Análisis psicométrico y funcionamiento en una muestra de drogodependientes y controles. [State Trait Anxiety Inventory (STAI): Psychometric analysis and functioning in a sample of drug addicts and controls]. *Univ. Psychol.* **2018**, *17*, 1–10.
61. Spielberger, C.D.; Bruchon-Schweitzer, M.; Paulhan, I. *STAI-Y Inventaire D'anxiété État-Trait Forme Y*; Editions du Centre de psychologie appliquée: Paris, France, 1993; Volume 1.
62. Spielberger, C.; Goruch, R.; Lushene, R.; Vagg, P.; Jacobs, G. *Manual for the State-Trait Inventory STAI (Form Y)*; Mind Garden: Palo Alto, CA, USA, 1983.
63. Spielberger, C.; Sydeman, S.; Maruish, M. State-trait anxiety inventory and state-trait anger expression inventory. In *The Use of Psychological Testing for Treatment Planning and Outcome Assessment*; Lawrence Erlbaum Associates, Inc.: Hillsdale, NJ, USA, 1994; pp. 292–321.
64. Goldberg, D.P.; Hillier, V.F. A scaled version of the General Health Questionnaire. *Psychol. Med.* **1979**, *9*, 139–145. [CrossRef]
65. Lobo, A.; Pérez-Echeverría, M.J.; Artal, J. Validity of the scaled version of the General Health Questionnaire (GHQ-28) in a Spanish population. *Psychol. Med.* **1986**, *16*, 135–140. [CrossRef]
66. Klaiberg, A.; Schumacher, J.; Brähler, E. General Health Questionnaire 28 (GHQ-28): Teststatistische Überprüfung einer deutschen Version in einer bevölkerungsrepräsentativen Stichprobe. *Z. Klin. Psychol. Psychiatr. Psychother./Im. Auftr. Görres-Ges.* **2004**, *52*, 237–251.
67. Piccinelli, M.; Bisoffi, G.; Bon, M.G.; Cunico, L.; Tansella, M. Validity and test-retest reliability of the Italian version of the 12-item General Health Questionnaire in general practice: A comparison between three scoring methods. *Compr. Psychiatry* **1993**, *34*, 198–205. [CrossRef] [PubMed]
68. Schmidt, S.; Mühlan, H.; Power, M. The EUROHIS-QOL 8-item index: Psychometric results of a cross-cultural field study. *Eur. J. Public Health* **2005**, *16*, 420–428. [CrossRef] [PubMed]
69. Rocha, N.; Power, M.; Bushnell, D.; Fleck, M. The EUROHIS-QOL 8-item index: Comparative psychometric properties to its parent WHOQOL-BREF. *Value Health J. Int. Soc. Pharmacoecon. Outcomes Res.* **2012**, *15*, 449–457. [CrossRef]
70. Bullinger, M.; Quitmann, J.; Power, M.; Herdman, M.; Mimoun, E.; DeBusk, K.; Feigerlova, E.; Lunde, C.; Dellenmark-Blom, M.; Sanz, D.; et al. Assessing the quality of life of health-referred children and adolescents with short stature: Development and psychometric testing of the QoLISSY instrument. *Health Qual. Life Outcomes* **2013**, *11*, 76. [CrossRef]
71. Rohenkohl, A.C.; Bullinger, M.; Quitmann, J. Quality of life in children, adolescents, and young adults with achondroplasia. *Orthopade* **2015**, *44*, 212–218. [CrossRef]
72. Sommer, R.; Blömeke, J.; Bullinger, M.; Quitmann, J. The psychometric evaluation of the quality of life in short stature youth (QoLISSY) instrument for German children born small for gestational age. *J. Endocrinol. Investig.* **2018**, *41*, 1185–1191. [CrossRef]
73. Drosatou, C.; Vlachopapadopoulou, E.-A.; Bullinger, M.; Quitmann, J.; Silva, N.; Salemi, G.; Pavlopoulou, I.; Michalacos, S.; Tsoumakas, K. Validation of the Greek version of the Quality of Life in Short Stature Youth (QoLISSY) questionnaire. *J. Pediatr. Endocrinol. Metab.* **2019**, *32*, 215–224. [CrossRef]
74. Petch, J.; Halford, W.K. Psycho-education to enhance couples' transition to parenthood. *Clin. Psychol. Rev.* **2008**, *28*, 1125–1137. [CrossRef]
75. Hoffenaar, P.J.; van Balen, F.; Hermanns, J. The Impact of Having a Baby on the Level and Content of Women's Well-Being. *Soc. Indic. Res.* **2010**, *97*, 279–295. [CrossRef]
76. Evenson, R.J.; Simon, R.W. Clarifying the relationship between parenthood and depression. *J. Health Soc. Behav.* **2005**, *46*, 341–358. [CrossRef] [PubMed]

77. UMBERSON, D.; GOVE, W.R. Parenthood and Psychological Well-Being:Theory, Measurement, and Stage in the Family Life Course. *J. Fam. Issues* **1989**, *10*, 440–462. [CrossRef]
78. Nomaguchi, K.M.; Milkie, M.A. Costs and rewards of children: The effects of becoming a parent on adults' lives. *J. Marriage Fam.* **2003**, *65*, 356–374. [CrossRef]
79. Keating-Lefler, R.; Wilson, M.E. The experience of becoming a mother for single, unpartnered, Medicaid-eligible, first-time mothers. *J. Nurs. Sch.* **2004**, *36*, 23–29. [CrossRef]
80. Nehring, I.; Riedel, C.; Baghi, L.; Moshammer-Karb, T.; Schmid, R.; Kries, R.V. Psychosocial situation of families with chronically ill children: A survey of parent initiatives. *Gesundheitswesen* **2015**, *77*, 102–107. [CrossRef]
81. Hentinen, M.; Kyngäs, H. Factors associated with the adaptation of parents with a chronically ill child. *J. Clin. Nurs.* **1998**, *7*, 316–324. [CrossRef] [PubMed]
82. Wallander, J.L.; Varni, J.W. Effects of pediatric chronic physical disorders on child and family adjustment. *J. Child. Psychol. Psychiatry* **1998**, *39*, 29–46. [CrossRef] [PubMed]
83. von Hagen, C.; Schwarz, H.P. *Psychische Entwicklung bei Chronischer Krankheit im Kindes-und Jugendalter*; Kohlhammer Verlag: Stuttgart, Germany, 2009.
84. de Schepper, J. Listening to the parents of short stature children: The role of the pediatrician. *Pediatrie* **1990**, *45*, 71–73.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

2 Summary Presentation of the Publication

2.1 Introduction

The concept of health-related quality of life (HRQOL) has emerged as a pivotal outcome criterion in the domain of medical care over the past decades (Bullinger and Quitmann, 2014). As children's chronic conditions may impair not only the children's HRQOL but also the whole family (Kazak, 1989), disease-specific patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs) have been developed for chronically ill children and their parents. Despite the potential for children with chronic conditions to experience a fulfilling life, they may encounter disadvantages in education, the workforce, and social interactions (Spencer et al., 2015, Newacheck and Halfon, 1998, Fauconnier et al., 2009). Especially given the increasing prevalence of chronic conditions in childhood (Perrin et al., 2007), it is crucial to support children and their families in addressing their needs and identifying where assistance is required. The total prevalence of chronic diseases in childhood is subject to fluctuations due to the existence of different definitions for the same condition and divergent inclusion criteria. Approximately 25% of children in the United States of America (USA) fit the definition of a chronic disease (Van Cleave et al., 2010), whereas in Germany, as part of the Children and Adolescents Health Surveys (KiGGS), 39% of surveyed children and adolescents reported at least one chronic health condition (Scheidt-Nave et al., 2008).

Short stature is considered a chronic condition, with 2.3% of the population fitting the definition of a height -2 standard deviations (SD) below their reference group (Chinoy and Murray, 2016). The prevalences of two main causes of short stature - isolated growth hormone deficiency (IGHD) and idiopathic short stature (ISS) - vary widely in the literature, likely due to significant global differences and varying disease definitions. The prevalence of IGHD is estimated to be approximately 1:400 (Vimpani et al., 1977), while 60-80% of short statured children meet the diagnostic criteria for ISS (Lindsay et al., 1994). Nevertheless, only a few studies have investigated the effects of children's IGHD/ISS on parents and families (Silva et al., 2018). Given that good family functioning and parents' adaptation are major protective factors for short-statured children (Visser-van Balen et al., 2006, Hentinen and Kyngäs, 1998), it is crucial to investigate and understand their parents' caregiving burden, mental stress, and personal resources. The examination of these topics will contribute to the advancement of knowledge regarding the factors that influence the adaptation of families, with a particular focus on parents of IGHD/ISS children (Casana-Granell et al., 2016).

Consequently, the objective of this work was to develop a pilot questionnaire to assess parents' HRQOL, caregiving burden, mental stress, and individual resources in caring for an IGHD/ISS child.

PROMs and PREMs

PROMs are used to assess the patient's perceptions of their general health status, with a particular focus on HRQOL and mental and physical health (Kingsley and Patel, 2017, Noonan et al., 2017). In essence, PROMs are used to measure the 'outcome' of the condition or intervention (Halleran et al., 2019). PREMs are questionnaires that mirror the process and the patient's experiences while receiving medical care (Kingsley and Patel, 2017, Halleran et al., 2019). PROMs and PREMs are proper measurements that can help improve the quality of care. This is achieved by measuring the patient's perceptions of their health and experiences throughout the entire medical care process without any interpretation by a clinician (Kingsley and Patel, 2017, US Food and Drug Administration, 2009).

HRQOL

The concept of HRQOL is not straightforward to define, as the majority of existing definitions lack the precision required to distinguish it from health and/or Quality of Life (QoL) (Karimi and Brazier, 2016). In psychological terminology, HRQOL is a multidimensional construct comprising emotional, mental, physical, and social dimensions of well-being and functioning, as perceived by the individual in question, whether that be the patient themselves or another observer (Bullinger, 2002, WHOQOL Group, 1995, Ravens-Sieberer et al., 2006). The importance of HRQOL measurements in the clinical setting has increased in recent years, as they focus on the emotional state of patients rather than solely on the success of treatment (White et al., 2020).

IGHD/ISS

Short stature is defined as a height below -2 SDs, which refers to a height below the 2.3 percentile of the corresponding mean height for a given age, sex, and population group (Wit et al., 2008). For the diagnoses IGHD and ISS, the affected individuals experience proportional short stature. IGHD is caused by a lack of growth hormone (GH) action (Hernández et al., 2007); ISS is diagnosed when there is no identifiable disorder for the short stature present (Ranke, 1996). Nevertheless, the phenotype and symptoms of afflicted individuals in both diseases are strikingly similar, which is why the caregiving burdens of their parents can be considered collectively. A notable distinction, however, is that ISS in children can only be treated off-label with recombinant human GH (rhGH) in Europe,

whereas rhGH is an approved therapy option for patients with IGHD (Quitmann et al., 2023, Ranke and Wit, 2018).

2.2 Methods

The development of a questionnaire to capture the caregiving burden, stress, HRQOL, personal needs, and resources of parents of IGHD/ISS children takes place in 4 phases, following the methodology of PRO instrument development of United States Food and Drug Administration (US Food and Drug Administration, 2009):

1. Literature research
2. Development of a pilot questionnaire (using statements of earlier conducted focus group discussions)
3. Pilot testing, including cognitive debriefing with new focus group discussions
4. Field- and Re-Tests for psychometric testing and validation of the questionnaire

Phase 1 consisted of a systematic literature research and the composition of a systematic review (Lackner et al., 2023a). The review summarizes all study results that existed up to December 2022 on HRQOL, caregiving burden, mental stress, and individual resources of parents of IGHD/ISS children.

Phase 2 implied the development of a pilot questionnaire based on focus group discussions within the Quality of Life in Short Stature Youth (*QoLISSY)* project (Bullinger et al., 2013).

Phase 3 consists of a preliminary version testing to ensure the understanding of the pilot questionnaire. Therefore, the questionnaire will be tested among the previous focus group participants. The pilot questionnaire will be modified based on the results of the cognitive debriefing.

Phase 4 implies a field test, where the questionnaire will be administered to newly identified study participants. Furthermore, the validation process of the questionnaire will follow.

This project covers phases 1 and 2; further steps (phases 3 and 4) will be conducted in future projects.

Literature Research

To assess the current state of research on HRQOL, caregiving burden, mental stress, and individual resources in parents of children with IGHD/ISS, I conducted a systematic literature search on 17/12/2022. Therefore, PubMed and Web of Science (Core Collection) were searched without limitations to the year or the language employed by the publications. Abstracts and full texts were screened using pre-defined inclusion and exclusion criteria. Two independent raters (Lea Lackner (LL) and Stefanie Witt (SW)) screened the eligible full

texts for an unbiased selection. Based on this review, the first categories for the coding guide were identified deductively.

Development of the Pilot Questionnaire

In phase 2, the items for the pilot questionnaire on parental HRQOL, caregiving burden, mental stress, and individual resources were developed. For this purpose, the German focus group discussions from the *QoLISSY* study were used. The *QoLISSY* project was a multinational project across several European countries (Sweden, Spain, France, United Kingdom (UK), and Germany) to assess the HRQOL of short-statured children and the view of their parents (Quitmann et al., 2013). For this doctoral thesis, only the German statements from the parents' focus group discussions were used. There are two ethics votes for the *QoLISSY* project, one from the original ethics committee (PV3184) and one from the re-analysis committee (LPEK-0579a).
The focus group discussions were transcribed verbatim using MaxQDA-Software (MaxQDA 2020), and all names of the participants and names mentioned by the interviewees were pseudonymized with either letters or names. To develop specific items for the questionnaire, a computer-based focused interview analysis of the focus groups was conducted according to the approach of Kuckartz (Kuckartz and Rädiker, 2020). In addition to the deductively built categories based on the systematic review, inductive categories were created throughout the focused interview analysis process.

Item Selection Process

The pilot questionnaire items were generated using anchor examples from the respective category, based on the coding guide from the focused interview analysis. A total of 47 items were developed in this way and arranged into seven scales. Items within the categories *individual resources,* and *special treatment* were redistributed among other appropriate scales during the revision process. In contrast, items pertaining to the category *special needs* within the coding guide were included in a separate section of the questionnaire. The responses to these items will not be included in the overall score for the pilot questionnaire.

2.3 Results

This section will describe the results retrieved from the systematic literature research and the focused interview analysis of the focus group discussions. Furthermore, the coding guide will be presented. Detailed results can be found within the systematic review (Lackner et al., 2023a) and the original article (Lackner et al., 2023b). The following results are roughly summarized:

Literature Research

The initial search retrieved n = 856 publications, of which n = 659 were excluded by screening for pre-defined exclusion criteria. Sixty-eight full texts were read in their entirety; n = 15 articles met the inclusion criteria and were included in the qualitative synthesis.
The age range of the children included in the 15 publications (published 1979 – 2022) ranged from four to 18 years; sample sizes ranged from n = 11 parents to n = 243 parents. Finally, the systematic review was written to extract previously recorded HRQOL, caregiving burden, mental stress, special needs, and individual resources of parents of children with IGHD/ISS (Lackner et al., 2023a).
The review outlines that no uniform disease-specific measurement exists to assess for HRQOL of parents of short-statured children. At the same time, many publications reported high anxiety levels, future concerns, and an overall impaired HRQOL of parents caring for IGHD/ISS children. Parents also reported social stigmatization and comparison of height being stressful in their everyday lifes. Another caregiving burden emphasized by some studies was growth hormone treatment (GHT). Many parents struggled with the application via injection, and organizational issues were mentioned. Furthermore, parents seemed to benefit from parent support groups and/or the dialogue with other parents of IGHD/ISS children. Based on these results, the first main categories of the coding guide were created deductively.

Coding guide

A reliability check was performed to ensure the results will be reproducible. A second coder (SW) recoded 20% (n = 2) of the focus groups. An agreement of a minimum of 70% was set previously as the lowest limit. After the first run, there was a 65% intercoder agreement. After discussing difficult sections and optimizing the coding guideline, an intercoder agreement of 81% was achieved. In the end, five hundred and nine growth-related statements about HRQOL, caregiving burden, special needs, and individual resources from parents with IGHD/ISS children were coded.

Eight thematic main categories were derived: *social problems, mental stress, everyday life, growth hormone treatment, special support, future worries, special needs,* and *individual resources* **(Table 1).**

Table 1: Main- and subcategories resulting from the focus group discussions

Social problems	4. Home	Special needs
1. No problems	5. Physical disadvantages	1. Conventional treatment
2. Comparison	Growth hormone treatment	2. Sensitization
3. Stigmatization	1. No problems	3. Child's coping mechanisms
4. Social pressure	2. Decision-making	4. Open approach
5. Acceptance	3. (Side)-effects	5. Like-minded people
Mental stress	4. Application	6. Growth success
1. Frustration	5. Disapproval	7. Vigilant justice
2. Child's body height	6. Health care system	Individual resources
3. Helplessness	7. Organizational issues	1. Open-minded
4. Family difficulties	Special treatment	2. Enlightenment and help
5. Diagnosis	1. Social-emotional support	3. Optimism
6. Misconduct	2. Special treatment	4. Achievements
7. Fears	Future worries	5. Distance
Everyday life	1. General	
1. School	2. Child's personal life	
2. Shopping	3. School	
3. Leisure	4. Occupational disadvantages	

Sample Size

Within the *QoLISSY* project, 33 parents (n = 28 mothers, n = 5 fathers) of IGHD/ISS children participated in the German focus group discussions. Of the 33 parents, three parent pairs attended together; the other 27 participated without their partners. Nine parents from children's age group 4 to 7 years were present, eight parents of children ages 8 to 12 years, and 16 parents of adolescents between 13 and 18 years participated.

Focused Interview Analysis

The parents discussed the primary caregiving responsibilities associated with GHT and the associated mental stress. Many parents reported difficulties in administering the rhGH, with some citing organisational challenges. The mental stress experienced by parents often arose from frustration based on how other people treated their children. Furthermore, social issues such as stigmatisation were mentioned by some parents as being stressful and harmful. Another topic that several parents discussed was how their pediatrician handled

the child's growth disorder. A significant proportion of parents reported that their pediatrician did not take their child's growth problems seriously.
When asked about special needs, the majority of parents expressed a preference for conventional treatment for their short-statured child. Additionally, some parents expressed a desire for joint meetings with other parents of IGHD/ISS children. Several parents also discussed their coping strategies. Some parents reported that maintaining an optimistic outlook about their child's growth was beneficial, while others expressed satisfaction when they observed their child making progress in their development.

> *"And now I just felt that this hurts me in part, because for me, what I experience with my daughter is really an enrichment, actually. It really makes my life more beautiful. But often it is not seen, and I notice over and over again that one point with us is really also loneliness. [...]. That we lead such a different life. That she very often notices that she is not taken seriously."* (Mother of an 12-year-old adolescent with ISS).

Pilot Questionnaire

The pilot questionnaire consists of 47 items using a 5-point Likert scale: *do not agree at all*, *do not agree*, *neither agree nor disagree*, *agree*, and *fully agree*. It is subdivided into thematic scales, which represent the main categories of the coding guide (Appendix: Pilot questionnaire).

2.4 Discussion

Chronic health conditions in children, such as IGHD and ISS, mostly have a significant impact on the family unit, particularly on the caregivers (Quitmann et al., 2014). Parents, and in particular mothers, are required to assume a multitude of special circumstances in raising a chronically ill child, including the application for medicine, doctor visits, and special care. Although IGHD and ISS are not life-threatening diseases, societal standards can lead to parents of short-statured children feeling marginalised. Within this project, this was identified as one of the major burdens parents of IGHD/ISS children have to face. Parents of IGHD/ISS children reported feeling hopeless due to their inability to protect their child from being bullied. Some parents reported feeling stigmatized due to their child being short, while others expressed frustration at the lack of understanding and support they received. Finally, some parents expressed anxiety about their child's future. As anxiety, lack of support, and hopelessness are predictors for reduced HRQOL (Smith et al., 1999, Mitchell et al., 2005), these parents should receive professional support if necessary.
This is the rationale behind our aim to develop a pilot questionnaire for parents of IGHD/ISS children to assess their HRQOL, caregiving burden, mental stress, and individual resources.

The questionnaire is designed to facilitate the provision of support to parents who experience difficulties adapting to their child's short stature. This is a crucial aspect, as parents who adapt well to their child's chronic condition are better able to address their child's developmental tasks and their own needs, which in turn enhances their own and their children's HRQOL (Beacham and Deatrick, 2013).

Furthermore, Smits et al. (2022) emphasised that the period before receiving a diagnosis can be especially demanding for both parents and their children. At this point, the physician must offer assistance to these parents. Some parents of the focus group discussions also expressed this perception. Some were relieved after receiving their children's diagnosis, which underlines the great pressure parents of IGHD/ISS children can encounter while undergoing the diagnostic process.

It is noteworthy that parents in our sample had already proposed potential solutions to meet their needs and suggestions on how the healthcare system could support them in the care of an IGHD/ISS child. A few parents indicated that parent support groups with other parents in similar circumstances could assist them in coping with the caregiving burdens and stress. These findings align with those reported by Pelentsov et al. (2015), who investigated the needs of parents caring for a child with any rare disease. One potential challenge in establishing support groups for parents of children with chronic illnesses is that some parents may perceive that their circumstances are not adequately addressed by healthcare professionals (Smits et al., 2022).

Overall, our findings reiterate the significance of considering the entire family unit within the context of pediatric care (Kim et al., 2010). This is because children tend to exhibit fewer psychological and behavioural issues when their families maintain healthy relationships and minimise conflicts (Landolt et al., 2002, Crandell et al., 2018). To foster such relationships, parents of chronically ill children should receive interventions to enhance their resilience in dealing with their child's chronic illness and to impart coping mechanisms to their children.

Conclusion

The results of this work underscore the significance of awareness regarding the HRQOL, caregiving burden, mental stress, and individual resources of parents of IGHD/ISS children. Only by comprehending the areas in which parents of IGHD/ISS children require assistance can early intervention be feasible and family resilience strengthened to enable effective coping with the chronic illness. In conjunction with the pilot questionnaire, affected parents can access professional assistance in the future if necessary. Further research will be required to develop the final questionnaire for parents of children with short stature. However, the foundation for this was established with this project and the development of the pilot questionnaire.

2.5 References

BEACHAM, B. L. & DEATRICK, J. A. 2013. Health care autonomy in children with chronic conditions: implications for self-care and family management. *Nursing Clinics,* 48**,** 305-317.

BULLINGER, M. 2002. Assessing health related quality of life in medicine. An overview over concepts, methods and applications in international research. *Restor Neurol Neurosci,* 20**,** 93-101.

BULLINGER, M. & QUITMANN, J. 2014. Quality of life as patient-reported outcomes: principles of assessment. *Dialogues Clin Neurosci,* 16**,** 137-145.

BULLINGER, M., QUITMANN, J., POWER, M., HERDMAN, M., MIMOUN, E., DEBUSK, K., FEIGERLOVA, E., LUNDE, C., DELLENMARK-BLOM, M., SANZ, D., ROHENKOHL, A., PLEIL, A., WOLLMANN, H. & CHAPLIN, J. E. 2013. Assessing the quality of life of health-referred children and adolescents with short stature: development and psychometric testing of the QoLISSY instrument. *Health Qual Life Outcomes,* 11**,** 76.

CASANA-GRANELL, S., LACOMBA-TREJO, L., MONTOYA-CASTILLA, I. & PEREZ-MARIN, M. 2016. Emotional discomfort and stress in primary caregivers of pediatric patients with low stature. *Calidad De Vida Y Salud,* 9**,** 93-103.

CHINOY, A. & MURRAY, P. G. 2016. Diagnosis of growth hormone deficiency in the paediatric and transitional age. *Best Pract Res Clin Endocrinol Metab,* 30**,** 737-747.

CRANDELL, J. L., SANDELOWSKI, M., LEEMAN, J., HAVILL, N. L. & KNAFL, K. 2018. Parenting behaviors and the well-being of children with a chronic physical condition. *Fam Syst Health,* 36**,** 45-61.

FAUCONNIER, J., DICKINSON, H. O., BECKUNG, E., MARCELLI, M., MCMANUS, V., MICHELSEN, S. I., PARKES, J., PARKINSON, K. N., THYEN, U., ARNAUD, C. & COLVER, A. 2009. Participation in life situations of 8-12 year old children with cerebral palsy: cross sectional European study. *Bmj,* 338**,** b1458.

HALLERAN, D. R., LANE, V. A., LEONHART, K. L., FISCHER, B., SEBASTIÃO, Y. V., CHISOLM, D. J., LEVITT, M. A., WOOD, R. J., MINNECI, P. C. & DEANS, K. J. 2019. Development of a Patient-reported Experience and Outcome Measures in Pediatric Patients Undergoing Bowel Management for Constipation and Fecal Incontinence. *J Pediatr Gastroenterol Nutr,* 69**,** e34-e38.

HENTINEN, M. & KYNGÄS, H. 1998. Factors associated with the adaptation of parents with a chronically ill child. *J Clin Nurs,* 7**,** 316-324.

HERNÁNDEZ, L. M., LEE, P. D. & CAMACHO-HÜBNER, C. 2007. Isolated growth hormone deficiency. *Pituitary,* 10**,** 351-357.

KARIMI, M. & BRAZIER, J. 2016. Health, Health-Related Quality of Life, and Quality of Life: What is the Difference? *Pharmacoeconomics,* 34**,** 645-649.

KAZAK, A. E. 1989. Families of chronically ill children: a systems and social-ecological model of adaptation and challenge. *J Consult Clin Psychol,* 57**,** 25-30.

KIM, K. R., LEE, E., NAMKOONG, K., LEE, Y. M., LEE, J. S. & KIM, H. D. 2010. Caregiver's burden and quality of life in mitochondrial disease. *Pediatric neurology,* 42**,** 271-276.

KINGSLEY, C. & PATEL, S. 2017. Patient-reported outcome measures and patient-reported experience measures. *Bja Education,* 17**,** 137-144.

KUCKARTZ, U. & RÄDIKER, S. 2020. Fokussierte Interviewanalyse mit MAXQDA. 1st ed. Wiesbaden: Springer VS.

LACKNER, L., QUITMANN, J., KRISTENSEN, K. & WITT, S. 2023a. Health-Related Quality of Life, Stress, Caregiving Burden and Special Needs of Parents Caring for a Short-Statured Child-Review and Recommendations for Future Research. *Int J Environ Res Public Health,* 20**,** 6558.

LACKNER, L., QUITMANN, J. H. & WITT, S. 2023b. Caregiving burden and special needs of parents in the care of their short-statured children - a qualitative approach. *Front Endocrinol (Lausanne),* 14**,** 1093983.
LANDOLT, M. A., GRUBENMANN, S. & MEULI, M. 2002. Family impact greatest: predictors of quality of life and psychological adjustment in pediatric burn survivors. *Journal of Trauma and Acute Care Surgery,* 53**,** 1146-1151.
LINDSAY, R., FELDKAMP, M., HARRIS, D., ROBERTSON, J. & RALLISON, M. 1994. Utah Growth Study: growth standards and the prevalence of growth hormone deficiency. *J Pediatr,* 125**,** 29-35.
MITCHELL, A. J., BENITO-LEÓN, J., GONZÁLEZ, J. M. & RIVERA-NAVARRO, J. 2005. Quality of life and its assessment in multiple sclerosis: integrating physical and psychological components of wellbeing. *Lancet Neurol,* 4**,** 556-566.
NEWACHECK, P. W. & HALFON, N. 1998. Prevalence and impact of disabling chronic conditions in childhood. *Am J Public Health,* 88**,** 610-617.
NOONAN, V. K., LYDDIATT, A., WARE, P., JAGLAL, S. B., RIOPELLE, R. J., BINGHAM III, C. O., FIGUEIREDO, S., SAWATZKY, R., SANTANA, M. & BARTLETT, S. J. 2017. Montreal Accord on Patient-Reported Outcomes (PROs) use series–Paper 3: patient-reported outcomes can facilitate shared decision-making and guide self-management. *Journal of Clinical Epidemiology,* 89**,** 125-135.
PELENTSOV, L. J., LAWS, T. A. & ESTERMAN, A. J. 2015. The supportive care needs of parents caring for a child with a rare disease: A scoping review. *Disability and Health Journal,* 8**,** 475-491.
PERRIN, J. M., BLOOM, S. R. & GORTMAKER, S. L. 2007. The increase of childhood chronic conditions in the United States. *Jama,* 297**,** 2755-2759.
QUITMANN, J., ROHENKOHL, A., BULLINGER, M., CHAPLIN, J. E., HERDMAN, M., SANZ, D., MIMOUN, E., FEIGERLOVA, E., DEBUSK, K., POWER, M., WOLLMANN, H. & PLEIL, A. 2013. Parental perception of health-related quality of life in children and adolescents with short stature: literature review and introduction of the parent-reported QoLISSY instrument. *Pediatr Endocrinol Rev,* 11**,** 147-160.
QUITMANN, J., ROHENKOHL, A., SOMMER, R., PETZOLD, S. & BULLINGER-NABER, M. 2014. [How do Affected Children and Adolescents Experience their Short Stature, and what is the Point of View of their Parents?]. *Prax Kinderpsychol Kinderpsychiatr,* 63**,** 635-648.
QUITMANN, J. H., BINDER, G., WITT, S., BULLINGER, M., BLÖMEKE, J., FRICKE-OTTO, S., HAUFFA, B., KAHRS, S., PARTSCH, C.-J. & ROHENKOHL, A. 2023. Lebensqualität von kleinwüchsigen Kindern und Jugendlichen und Wachstumshormontherapie. *Monatsschrift Kinderheilkunde***,** 1-7.
RANKE, M. B. 1996. Towards a consensus on the definition of idiopathic short stature. *Horm Res,* 45**,** 64-66.
RANKE, M. B. & WIT, J. M. 2018. Growth hormone - past, present and future. *Nat Rev Endocrinol,* 14**,** 285-300.
RAVENS-SIEBERER, U., ERHART, M., WILLE, N., WETZEL, R., NICKEL, J. & BULLINGER, M. 2006. Generic health-related quality-of-life assessment in children and adolescents: methodological considerations. *Pharmacoeconomics,* 24**,** 1199-1220.
SCHEIDT-NAVE, C., ELLERT, U., THYEN, U. & SCHLAUD, M. 2008. Versorgungsbedarf chronisch kranker Kinder und Jugendlicher. *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz,* 51**,** 592-601.
SILVA, N., BULLINGER, M., SOMMER, R., ROHENKOHL, A., WITT, S. & QUITMANN, J. 2018. Children's psychosocial functioning and parents' quality of life in paediatric short stature: The mediating role of caregiving stress. *Clin Psychol Psychother,* 25**,** 107-118.
SMITH, K. W., AVIS, N. E. & ASSMANN, S. F. 1999. Distinguishing between quality of life and health status in quality of life research: a meta-analysis. *Qual Life Res,* 8**,** 447-459.

SMITS, R. M., VISSERS, E., TE PAS, R., ROEBBERS, N., FEITZ, W. F. J., VAN ROOIJ, I., DE BLAAUW, I. & VERHAAK, C. M. 2022. Common needs in uncommon conditions: a qualitative study to explore the need for care in pediatric patients with rare diseases. *Orphanet J Rare Dis,* 17**,** 153.

SPENCER, N. J., BLACKBURN, C. M. & READ, J. M. 2015. Disabling chronic conditions in childhood and socioeconomic disadvantage: a systematic review and meta-analyses of observational studies. *BMJ open,* 5**,** e007062.

US FOOD AND DRUG ADMINISTRATION. 2009. *Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims* [Online]. Available: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf [Accessed].

VAN CLEAVE, J., GORTMAKER, S. L. & PERRIN, J. M. 2010. Dynamics of obesity and chronic health conditions among children and youth. *Jama,* 303**,** 623-630.

VIMPANI, G. V., VIMPANI, A. F., LIDGARD, G. P., CAMERON, E. H. & FARQUHAR, J. W. 1977. Prevalence of severe growth hormone deficiency. *Br Med J,* 2**,** 427-430.

VISSER-VAN BALEN, H., SINNEMA, G. & GEENEN, R. 2006. Growing up with idiopathic short stature: psychosocial development and hormone treatment; a critical review. *Arch Dis Child,* 91**,** 433-439.

WHITE, B. E., DRUCE, M. R., GROZINSKY-GLASBERG, S., SRIRAJASKANTHAN, R., GAMPER, E. M., GRAY, D., MUJICA-MOTA, R. & RAMAGE, J. K. 2020. Health-related quality of life in neuroendocrine neoplasia: a critical review. *Endocr Relat Cancer,* 27**,** R267-r280.

WHOQOL GROUP 1995. The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. *Soc Sci Med,* 41**,** 1403-1409.

WIT, J. M., CLAYTON, P. E., ROGOL, A. D., SAVAGE, M. O., SAENGER, P. H. & COHEN, P. 2008. Idiopathic short stature: definition, epidemiology, and diagnostic evaluation. *Growth Horm IGF Res,* 18**,** 89-110.

3 Abstract

One of the most common reasons for parents to take their children to a pediatrician is because of their child's short stature. Two of the most prevalent appearances of disproportionate short stature are isolated growth hormone deficiency (IGHD) and idiopathic short stature (ISS). For children and their families affected by these conditions, the chronic nature of the disease can be highly stressful. Parents of children with short stature may experience anxiety, feel overwhelmed by the therapy, or face stigmatisation from their social environment.

In order to gain a more comprehensive understanding of the health-related quality of life (HRQOL), caregiving burden, mental stress, and individual resources of these parents, focus group discussions were conducted with 33 parents of children with IGHD/ISS as part of the Quality of Life in Short Stature Youth (QoLISSY) project. In the present study, the focus group discussions were analysed through a focused interview analysis, with statements classified in pre-defined categories. This was followed by the development of a pilot questionnaire. The pilot questionnaire is designed to encompass all the areas identified as burdensome in the focus group discussions.

During the discussion groups, parents mentioned stigmatization, worries about the future, anxiety, and the challenges of implementing growth hormone therapy (GHT) as the primary caregiving burdens. Some parents expressed a desire for parent support groups for those with children who are short in stature, while others would appreciate greater sensitivity from their social environment regarding the issue of short stature or more serious consideration from their attending physicians regarding the growth problem.

Subsequent phases, which are not included in this work, will involve further development and adaptation of the pilot questionnaire in order to ultimately utilise it as a diagnostic tool. This will facilitate the early identification of stressed parents of children with IGHD/ISS and the provision of professional support. This is crucial because well adjusted parents can pass on their coping mechanisms to their affected child, thereby creating a supportive environment for both the child and the whole family.

4 Zusammenfassung

Kleinwuchs stellt einen der häufigsten Gründe dar, weshalb Eltern mit ihren Kindern eine Kinderärztin oder einen Kinderarzt aufsuchen. Proportionaler Kleinwuchs äußert sich besonders häufig in Form eines isolierten Wachstumshormonmangels (IGHD) oder dem idiopathischen Kleinwuchs (ISS). Die chronische Erkrankung kann für die betroffenen Kinder, aber auch für deren Eltern und die gesamte Familie mit einer hohen Belastung einhergehen. Die elterliche Belastung kann sich in Ängsten, einer Überlastung durch die Wachstumshormontherapie oder einer Stigmatisierung durch das soziale Umfeld manifestieren.

Um die gesundheitsbezogene Lebensqualität, die pflegerische Belastung, den mentalen Stress sowie die individuellen Ressourcen dieser Eltern genauer erfassen zu können, wurden im Quality of Life in Short Stature Youth (QoLISSY) Projekt Fokusgruppendiskussionen mit 33 Eltern von Kindern mit IGHD/ISS durchgeführt. Im Rahmen der vorliegenden Arbeit wurden die Diskussionen anhand einer fokussierten Interviewanalyse ausgewertet, Aussagen in vorab definierten Kategorien eingeordnet und darauf aufbauend ein Pilotfragebogen entwickelt. Der entwickelte Pilotfragebogen zielt darauf ab, sämtliche Bereiche abzudecken, die in den Fokusgruppendiskussionen als belastend identifiziert wurden. Als Hauptbelastungen wurden Stigmatisierung, Zukunftssorgen, Ängste sowie die Durchführung der Wachstumshormontherapie angeführt. Einige der befragten Eltern äußerten den Wunsch nach Gesprächsgruppen mit weiteren betroffenen Eltern, während anderen ein taktvolleres Umfeld sowie eine ernsthaftere Auseinandersetzung mit der Wachstumsproblematik durch die behandelnden Ärztinnen und Ärzte helfen würden. In den nachfolgenden Phasen, welche nicht mehr Gegenstand dieser Arbeit sind, erfolgt eine Weiterentwicklung und Anpassung des Pilotfragebogens, sodass eine Anwendung als diagnostisches Instrument möglich wird. Dadurch kann in Zukunft eine frühzeitige Erkennung von belasteten Eltern von Kindern mit IGHD/ISS gewährleistet werden, um ihnen professionelle Unterstützung anzubieten. Dies ist von Bedeutung, da gut adaptierte Eltern ihre Copingmechanismen an ihr betroffenes Kind weitergeben und somit ein sicheres Umfeld für das Kind schaffen.

5 Declaration of Own Contribution

This doctoral thesis was conducted in the Quality of Life Research Group at the Institute and Polyclinic for Medical Psychology at the University Medical Center Hamburg-Eppendorf under the direction of PD Dr. Julia Quitmann. The focus group discussions employed in this study were performed previously under the direction of PD Dr. Quitmann (Bullinger et al., 2013). The doctoral thesis was developed in collaboration with PD Dr. Quitmann, Dr. Witt and myself. The literature review was conducted by Dr. Witt and myself, as well as the composition of the systematic review. I undertook the transcription of the focus group discussions and the coding process. Dr. Witt acted as the second rater of the coding. I conducted the analysis, evaluation, and illustration of the generated data. Dr. Witt and I collaborated on the development of the pilot questionnaire. I wrote the preliminary manuscript and subsequently underwent a peer-review process with the assistance of PD Dr. Quitmann and Dr. Witt.

6 Acknowledgement

First and foremost, I would like to extend my gratitude to all the parents of IGHD/ISS children who participated in the focus group discussions. Without their willingness and contributions, this work would not have been feasible. Special acknowledgement is due to my doctoral supervisor, PD Dr. Julia Quitmann, who guided me through this captivating topic. I am also deeply thankful for my advisor, Dr. Stefanie Witt, who provided the most crucial support throughout this entire project and was consistently available to address my queries. Furthermore, I wish to express my gratitude to my own parents, who supported me throughout with great strength, good food, and the determination never to give up. Special thanks are also owed to Paul, who supported me in pursuing my objectives and uplifted me during challenging times.

7 Curriculum Vitae

Persönliche Daten

Name, Vornamen:	Lackner, Lea Carlotta
Adresse:	Eppendorfer Weg 252, 20251 Hamburg
Geburtsdatum:	26.03.1999

Ausbildung

2020 – 2024	Dissertation in der medizinischen Psychologie
2018 – heute	Studium der Humanmedizin *Universitätsklinikum Hamburg-Eppendorf*
2021	Physikumsäquivalent: sehr gut
2024	Zweite Ärztliche Prüfung: gut
2017	Abitur *Gymnasium Bondenwald, Hamburg*

Publikationen

2024	LACKNER, L., ZYRIAX, B. C., & STEPHAN, B. 2024. To what Extent does Vitamin D and its Serum Levels Influence the Severity of Hidradenitis Suppurativa: A Literature Review. *Acta dermato-venereologica*, *104*, adv40321.
2023	LACKNER, L., QUITMANN, J., KRISTENSEN, K. & WITT, S. 2023a. Health-Related Quality of Life, Stress, Caregiving Burden and Special Needs of Parents Caring for a Short-Statured Child-Review and Recommendations for Future Research. Int J Environ Res Public Health, 20, 6558. LACKNER, L., QUITMANN, J. H. & WITT, S. 2023b. Caregiving burden and special needs of parents in the care of their short-statured children - a qualitative approach. Front Endocrinol (Lausanne), 14, 1093983.

Famulaturen und Praktisches Jahr (PJ)

12/24 – 04/2025	PJ Pflichttertial: Innere Medizin *Agaplesion Diakonieklinikum, Hamburg*
09 – 12/2024	PJ Pflichttertial: Chirurgie *Universitätsklinikum Hamburg-Eppendorf*

05 – 09/2024	PJ Wahltertial: Dermatologie *Universitätsklinikum Schleswig-Holstein, Lübeck*
08 – 09/2023	Ambulante Famulatur Zentrale Notaufnahme *Amalie Sieveking Krankenhaus*
03/2023	Stationäre Famulatur Dermatologie *Elbeklinikum Buxtehude*
08/2022	Stationäre Famulatur Dermatologie *Juntendo University Hospital Tokio (Japan)*
09 – 10/2021	Stationäre Famulatur Unfallchirurgie *Universitätsklinikum Hamburg-Eppendorf*
08 – 09/2021	Hausarztfamulatur *Internisten am Klosterstern (Dr. Thuneke)*

<u>Stipendien</u>

2022 – heute	Deutschlandstipendium

8 Affidavit

Ich versichere ausdrücklich, dass ich die Arbeit selbständig und ohne fremde Hilfe, insbesondere ohne entgeltliche Hilfe von Vermittlungs- und Beratungsdiensten, verfasst, andere als die von mir angegebenen Quellen und Hilfsmittel nicht benutzt und die aus den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen einzeln nach Ausgabe (Auflage und Jahr des Erscheinens), Band und Seite des benutzten Werkes kenntlich gemacht habe. Das gilt insbesondere auch für alle Informationen aus Internetquellen.
Soweit beim Verfassen der Dissertation KI-basierte Tools („Chatbots“) verwendet wurden, versichere ich ausdrücklich, den daraus generierten Anteil deutlich kenntlich gemacht zu haben. Die „Stellungnahme des Präsidiums der Deutschen Forschungsgemeinschaft (DFG) zum Einfluss generativer Modelle für die Text- und Bilderstellung auf die Wissenschaften und das Förderhandeln der DFG“ aus September 2023 wurde dabei beachtet.
Ferner versichere ich, dass ich die Dissertation bisher nicht einem Fachvertreter an einer anderen Hochschule zur Überprüfung vorgelegt oder mich anderweitig um Zulassung zur Promotion beworben habe.
Ich erkläre mich damit einverstanden, dass meine Dissertation vom Dekanat der Medizinischen Fakultät mit einer gängigen Software zur Erkennung von Plagiaten überprüft werden kann.

27.10.2024
Datum

Unterschrift

9 Appendix: Pilot questionnaire

Kategorie	Ankerbeispiele	Item	Stimme überhaupt nicht zu	Stimme nicht zu	Stimme weder zu noch lehne ab	Stimme zu	Stimme voll und ganz zu
Soziale Probleme							
1	Ja also in unserem Umfeld ist das jetzt nicht so, da haben wir jetzt nicht so Probleme.	Ich erlebe durch die Kleinwüchsigkeit meines Kindes **keinerlei** Probleme in meinem sozialen Umfeld.					
2	Es belastet mich auch, weil ich es ehrlich gesagt eine Frechheit finde. Ich kann doch keinen betiteln, weil er gelb ist, weil er rot ist keine Ahnung, weil er ein Ausländer ist, so nach dem Motto "du bist schlecht". Aber genau so kam ich mir vor, ich kam mir vor als hätte ich ein schlechtes Kind, weil es nicht der Norm entspricht. Und es wird in der Gesellschaft viel auf die Norm geschaut und das ist ganz schlimm.	Mir wird von anderen das Gefühl vermittelt, mit meinem kleinwüchsigen Kind nicht in die gesellschaftliche Norm zu passen.					
3	Und ich gehe damit dann auch ganz offen mit um und rede dann auch Leute mal ganz offen an, weil ich denke, das ist doch bei manchen noch ein Tabuthema.	Ich kann offen mit anderen Menschen über die Wachstumsproblematik meines Kindes sprechen.					

4	Also bei uns war dann auch immer das Problem, dass es hieß: ,,Das braucht man ja nicht, hast ja selber etwas verkehrt gemacht." So dieses Unterschwellige, du hast etwas verkehrt gemacht in der Schwangerschaft und deshalb ist das Kind so klein. Also das hört man dann oft, auch von Ärzten.	Mein Umfeld gibt mir das Gefühl, dass ich schuld an der Kleinwüchsigkeit meines Kindes bin.					
5	[...]. Wir haben ganz viele Leute, die dadurch sagen: ,,Ja ihr müsst mal etwas machen." Also ich selber hätte da vielleicht gar nichts gemacht, weil ich mir da eigentlich am aller wenigsten Gedanken gemacht habe, aber jeder hat etwas gesagt. Und irgendwann kriegt man dann so ein schlechtes Gewissen, dass man dann denkt - jetzt sollte man vielleicht doch nochmal etwas machen, weil dann jeder nervt.	Ich fühle mich wegen der Kleinwüchsigkeit meines Kindes durch mein Umfeld unter Druck gesetzt, z.B. bei der Inanspruchnahme einer Behandlung.					

6	Und ich denke mit den Kindern, die wir haben, wir haben ja viel Leid erlebt und wir können doch echt stolz sein, dass wir so viel erreicht haben und das wird aber einfach nicht wertgeschätzt. [...] Also man kriegt diesen Rückhalt nicht und darüber bin ich eigentlich mehr sauer. [...] ich bin einfach sauer, wie die Gesellschaft damit umgeht. Das finde ich schon sehr sehr schade.	Ich erhalte von meinem sozialen Umfeld Rückhalt im Umgang mit der Kleinwüchsigkeit meines Kindes.					
Psychische Belastungen							
7	[…] weil die kommen ja mit den anderen Kindern nicht mit. Das ist nicht nur die Größe, das ist halt alles. Das ist die Kraft, das ist die Muskulatur. Das merkt man beim Fußballspielen.	Ich fühle mich dadurch belastet, dass mein Kind kleiner ist als andere Kinder im gleichen Alter.					
8		Ich fühle mich dadurch belastet, dass mein Kind körperlich benachteiligt ist, verglichen mit anderen Kindern im gleichen Alter.					

9	Was mir noch aufgefallen ist, viele ältere Menschen, also da ist es ja auch ganz schlimm. Manche wollen sie dann so extrem beschützen und sagen dann sie wäre noch zu klein für die große Rutsche. Aber die kann das, sie kann da runter rutschen. Das ist halt echt ein gesellschaftliches Problem und das ist schwierig sich dann eine gelassene Einstellung zuzulegen [...].	Ich bin frustriert darüber, dass mein Kind anders behandelt wird als Kinder im gleichen Alter z.B. aufgrund der geringen Körpergröße nicht ernst genommen wird.					
10		Es belastet mich, dass meinem Kind weniger zugetraut wird aufgrund seiner geringen Körpergröße.					
11	Meinem Sohn haben sie auf den Kopf gespuckt. Das ist natürlich irgendwie eine ganz üble Sache.	Mich belastet es zu sehen, dass mein Kind aufgrund seiner Körpergröße in der Schule/im Kindergarten gemobbt wird.					
12	Aber sonst so hat sie jetzt persönlich so mit ihrer Größe keine Probleme. Das bin wahrscheinlich mehr ich und mein Mann [...], und als Mama macht man sich da einfach immer etwas mehr Sorgen. Also ich bin da schon eher die, die immer eher pessimistisch ist [...].	Ich mache mir Sorgen um die finale Körpergröße meines Kindes.					

13	Wenn ich sehe, dass sie darunter leidet, wenn sie eben immer darauf angesprochen wird. Und man weiß irgendwann auch nicht mehr wie man ihr helfen kann. […].	Ich fühle mich hilflos im Umgang mit der Kleinwüchsigkeit meines Kindes z.B. weil mein Kind gemobbt wird.					
14	Die Schwiegereltern sind immer doppelt belastet als der Kleine, als sich das herauskristallisierte, dass er was hat. Dann haben sie gesagt: ,,Ihr übertreibt total und was ihr da alles macht mit dem Kind. Und was meinst du wieviele Kinder was ähnliches hatten und die sind auch alle groß geworden ohne den ganzen Schnickschnack." Also die haben uns da wirklich für belächelt und fanden das alles doof und haben das auch keinem so großartig erzählt.[...]. Es ist ganz ganz traurig sowas. Ist schade, aber ich glaube viele ältere Menschen denken einfach so.	Die Verwandtschaft bagatellisiert die Wachstumsproblematik meines Kindes.					
15		Verwandte werfen mir vor, dass ich die Wachstumsproblematik meines Kindes zu ernst nehme.					
	Falls Sie noch **keine** Diagnose haben:						
16	Und ich denke mittlerweile, wenn man eine eindeutige Behinderung hat, ist es sogar einfacher eine eindeutige Diagnose zu haben. [...]	Für mich ist es schwierig, keine genaue Diagnose für die Wachstumsproblematik meines Kindes zu haben.					

	Und das zermürbt auch ganz schön. Ich finde es teilweise, weil wir auch keine eindeutige Diagnose haben, dass es manchmal schwierig ist. [...].						
	Danach weiter bei Frage **19**						
	Falls Sie eine Diagnose haben:						
17	Aber das war echt eine ganze Zeit so lange für uns nicht klar war: ist eine Ursache dahinter beziehungsweise können wir etwas tun? Machen wir etwas?	Die Zeit vor der Diagnosestellung war belastend für mich.					
18	Also ich weiß nicht, wie es da anderen geht, da habe ich jetzt keine Erfahrung, aber für Luisa war das furchtbar. Für die ganze Familie war das halt sehr schrecklich.	Die endgültige Diagnose zu bekommen war für mich schlimm.					
19	Ich habe halt auch gedacht, das ist normal und das kann man auch nicht beschleunigen und er muss damit leben und je mehr das thematisiert wird, desto schlimmer wird das für ihn. Weil er sich dann auch seine Ausreden sucht, so von wegen er sei so klein. Und deswegen haben wir das dann auch eher ignoriert, bis es eben nicht mehr zu ignorieren ging.	Ich fühle mich schuldig, weil ich die Wachstumsproblematik meines Kindes lange ignoriert habe.					

20	[...] weil ich einfach Angst habe um ihn. Weil auf ihn stürzt man sich natürlich als allererstes. Er ist natürlich am leichtesten auch zu quälen. Er hat ja auch gewisse Geschichten schon gehabt […].	Ich mache mir Sorgen, dass mein Kind durch seine Kleinwüchsigkeit schneller Opfer von Gewalt wird.					
Alltag							
21	Große Unsicherheit bei Lehrern, man hat viel Aufklärungsbedarf.	Ich muss aufgrund der Kleinwüchsigkeit meines Kindes Erzieher:innen oder Lehrer:innen über die Wachstumsproblematik aufklären.					
22	Eva würde sich ja auch schon lieber ganz anders kleiden als wie es möglich ist von den Größen her. Wir gehen in irgendwelche Jugend-Boutiquen rein und das passt halt einfach noch nicht, das ist halt schwierig dann.	Ich habe Probleme beim Einkaufen von z.B. Kleidung oder Schuhen für mein kleinwüchsiges Kind.					
23	Aber ansonsten habe ich das voll und ganz in seine Hände übergeben und ich denke das ist auch völlig gut. Von daher habe ich das gar nicht mehr so auf dem Schirm.	Ich kann die Wachstumsproblematik meines Kindes gut in den Alltag integrieren.					

24	Oder ich lasse sie dann halt auch hinknien, das ist mir mittlerweile auch schon egal. Dann zieht man halt die Schuhe aus und dann lasse ich sie auf eine Bank knien. Aber es ist schon im Alltag schwierig…	Ich fühle mich durch die Kleinwüchsigkeit meines Kindes eingeschränkt bei der Planung von Freizeitaktivitäten z.B. bei dem Besuch von Freizeitparks.					
25	Und sie entdecken jetzt die Selbständigkeit, selber waschen, selber Zähne putzen. Was aber natürlich auch wieder mit ihren Größen mit Schwierigkeiten verbunden ist […]	Ich habe im Haushalt einen größeren Arbeitsaufwand aufgrund der Kleinwüchsigkeit meines Kindes, z.B. durch die Spezialanfertigung niedrigerer Arbeitsflächen.					
26	[…] wenn wir dann im Tiergarten sind und sie sagen nicht "ich will was sehen", sondern sie sagen dann einfach "mir tun die Beine weh", aber ich habe so Probleme mit meinem Rücken, also ich kann sie gar nicht tragen.	Aufgrund eigener körperlicher Einschränkungen kann ich mein kleinwüchsiges Kind nicht so unterstützen wie ich es gerne würde z.B. Probleme beim Hochheben.					
Wachstumshormontherapie							
	Falls Ihr Kind **keine** Wachstumshormonbehandlung bekommt, bitte weiter bei Frage **35**						
27	Also die Spritze ist bei uns überhaupt kein Problem, seit dem 2. Tag spritzt er für sich selbst beziehungsweise kommt er zu mir und sagt, dass ich es machen soll.	Ich empfinde die Wachstumshormonbehandlung als zusätzliche Belastung.					

28	Ja natürlich, das würde ich auch voll unterstützen. Das ist natürlich keine leichte Entscheidung. Das sind natürlich massive Eingriffe in den Körper.	Die Entscheidung für oder gegen eine Behandlung mit Wachstumshormonen ist mir schwergefallen.					
29	Gerade mit 1 Jahr macht man sich ja dann doch Sorgen, gibt es da dann irgendwelche anderen Verzögerungen.	Ich mache mir Sorgen um starke Nebenwirkungen der Wachstumshormontherapie.					
30	also er schießt unheimlich in die Höhe. Das ist schon prima. Ich bin schon dafür, dass das gemacht wurde und ich bin eigentlich auch zufrieden. […].	Ich bin zufrieden mit den Wachstumserfolgen meines Kindes durch die Wachstumshormontherapie.					
31	Absolut ja, also es ist Chaos pur. Also oft ist es so, dass er mir den Pen weghaut, sodass die Nadel verbogen war und alles. Also wollte sich dann auf keinen Fall spritzen lassen "Mama mach schnell!" Und schreit dabei […]	Das Spritzen der Wachstumshormone ist für mich belastend, weil mein Kind z.B. nicht gespritzt werden möchte und/oder sich wehrt.					
32	[…] Die sagen dann "also ich würde das nicht tun". Ich sage dann, ja ich bin aber ich. Man muss immer dagegen ankämpfen und sich rechtfertigen, warum ich meinem Kind Wachstumshormone gebe.	Ich muss mich gegenüber anderen Menschen bezüglich der Wachstumshormontherapie rechtfertigen.					

33	Das war bei uns ein großes Problem zum Beispiel, wenn wir am Wochenende fort waren. Da mussten wir immer schauen, dass wir einen Kühlschrank haben. […]	Durch die Wachstumshormontherapie habe ich einen erhöhten Organisationsaufwand, wenn wir z.B. in den Urlaub fahren oder mein Kind bei einem/r Freund/in übernachtet.					
34	Also für mich war das ein Problem mit der Behandung, weil ich bin alleinerziehend und wenn ich jetzt mal was machen wollte am Wochenende, dann konnte ich mir keinen Babysitter suchen, da habe ich aber immer eine Krankenschwester gebraucht, die die Spritze übernimmt.[...] aber am Anfang war das schon schlimm. [...] Dann musste ich das halt immer alles machen und ich konnte mich die ersten Jahre nicht fortbewegen.	Ich schränke mein Privatleben aufgrund der Wachstumshormontherapie ein.					
Gesundheitssystem							
35	Ja, ich war immer beunruhigt. Deshalb ärgere ich mich auch, dass wir immernoch in Behandlung sind…, wenn der Kinderarzt uns nicht immer davon abgeraten hätte, wäre ich schon viel früher hierher gekommen.	Der/die Kinderarzt/ärztin nimmt die Wachstumsproblematik meines Kindes nicht ernst.					

36	Kann man sich das überhaupt auch finanziell leisten, weil so eine Behandlung übers Jahr ja auch 60.000€ kostet, die sind dann ja auch weg.	Ich mache mir Sorgen, dass die Kosten der Wachstumshormontherapie nicht von der Krankenkasse übernommen werden.					
37	[...]. Ich habe mich sehr wohl gefühlt hier. Gut aufgehoben, gut aufgeklärt.[…]. Und meine Fragen werden darüber hinaus auch noch geklärt und von daher fühle ich mich gut aufgehoben.	Ich fühle mich von Ärzt:innen gut über das Thema Kleinwüchsigkeit aufgeklärt.					
38	[...] das waren so Themen, dass es allein die Gesetzgebung nicht hergibt, das dann selber zu entscheiden. Also diese Sache war für uns schon sehr problematisch, also damit umzugehen. Und letztendlich ist es dann ja über diese Studie gelungen. Aber anders...	Es ärgert mich, dass die Wachstumshormontherapie in Deutschland nur für spezielle Diagnosen zugelassen ist.					
Besondere Unterstützung							
39	Also sie tut sich immer behaupten und da lässt sie sich nicht drauf ein. Aber das ist anstrengend. Und das sind auch anstrengende Gespräche zuhause, weil sie dann mit viel Druck kommt.	Es kostet mich Kraft mein kleinwüchsiges Kind emotional aufzubauen z.B., weil es in der Schule gehänselt wurde.					

40	Ja eigentlich in dem Maße, dass man ihn ganz normal behandelt wie jeden anderen auch. Also nichts besonderes, das wäre ja schon wieder irgendwie auffällig. Ich denke mal das unterstützt ihn auch.	Ich behandle mein kleinwüchsiges Kind so normal wie möglich.					
41	Und Zuhause ist das also auch so, ich erwische mich selber dabei... die brauchen immer so lange, bis sie mal irgendwo raufkommen und dann macht man es eben schnell für sie.	Ich nehme meinem kleinwüchsigen Kind Dinge im Alltag ab, einfach weil es klein ist.					
42	[...] da hebt man sie eben schnell hoch und packt sie in den Sitz, wie bei einem Kleinkind eben. Man behandelt sie eben selber teilweise noch wie ein Kleinkind.	Ich bemerke, dass ich mein Kind manchmal nach seiner Größe und nicht nach seinem Alter behandle.					
Zukunftssorgen							
43	Ja also so 1,70 m sollte er schon werden. Aber das ist alles so unsicher…	Ich bin besorgt, dass mein Kind auch als Erwachsener noch klein sein wird.					
44	Und dadurch lösen sie eigentlich auch aus, dass sich das Kind im gewissen Sinne ja gar nicht so weiterentwickelt, weil es mit solchen Sachen ja gar nicht so konfrontiert wird.	Ich mache mir Sorgen, dass sich mein Kind aufgrund des Umgangs anderer nicht so gut entwickeln kann, z.B. Behandlung nach Größe und nicht nach Alter.					

45	Partnerwahl ist auch nicht einfach mit 1,66 m.	Ich mache mir aufgrund des Kleinwuchses Sorgen, dass mein Kind Schwierigkeiten hat eine/n Partner:in zu finden.					
46	Dann halt auch für Größere, wenn sie dann eben auch wieder sehr klein sind, ist das ja auch wieder ein Problem mit den Berufen. Ich merke es bei meinem Großen, der fängt jetzt an sich zu bewerben, der ist jetzt in der 9. Klasse und kommt in die 10. Klasse. Und da fragt man sich dann schon "Was macht er?" und "Wie wird er dann überhaupt angenommen von den Arbeitgebern?" [...]	Ich bin besorgt, dass mein Kind aufgrund der Kleinwüchsigkeit Nachteile in Kindergarten/Schule/Berufsleben haben wird.					
47	Aber inzwischen habe ich wirklich gelernt zu sagen: okay, es kommt wie es kommt, ich muss es nehmen wie es ist. Und wenn es gut ist, ist es gut, dann machen wir das Beste draus. Und wenn wir eine schlechte Phase haben, müssen wir auch das Beste draus machen. Aber ich habe lange dazu gebraucht, muss ich ehrlich sagen. Man braucht so seine Zeit, das geht nicht von heute auf morgen.	Ich blicke optimistisch in die Zukunft bezüglich der Kleinwüchsigkeit meines Kindes.					