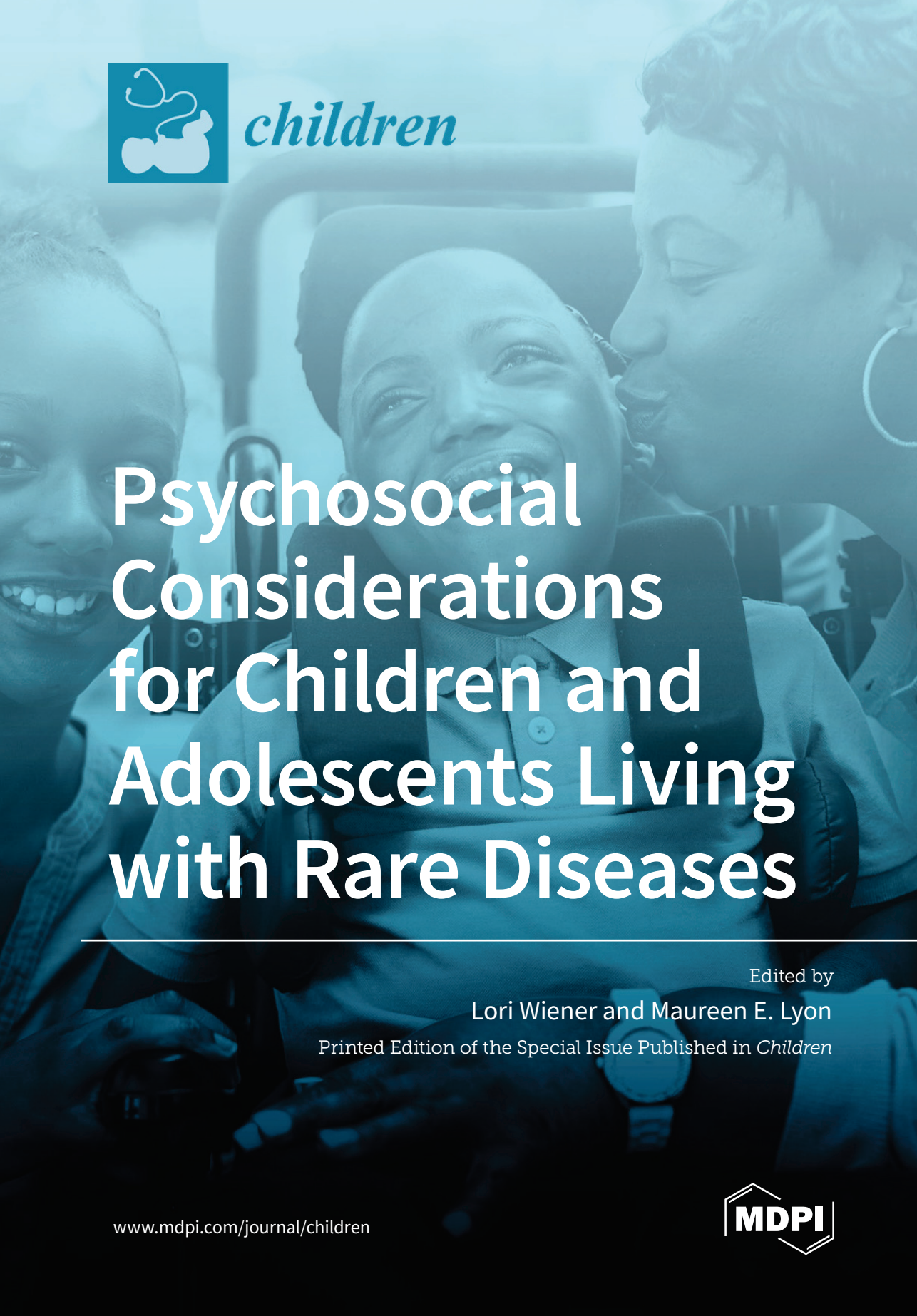

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Psychosocial Considerations for Children and Adolescents Living with Rare Diseases

Edited by
Lori Wiener and Maureen E. Lyon

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About the Editors

Lori Wiener

Lori Wiener is co-director of the Behavioral Science Core and Head of the Psychosocial Support and Research Program at the pediatric oncology branch of the National Cancer Institute. As both a clinician and behavioral scientist, Dr. Wiener has dedicated her career to the fields of oncology and pediatric HIV/AIDS. At NCI Pediatric Oncology Branch, she developed a robust clinical and research program that has focused on critical clinical issues such as parental coping, lone parenting, transnational parenting, emotional consequences of medically required isolation, sibling and sibling donor experiences, graph versus host disease, and end-of-life planning. Dr. Wiener has also dedicated a substantial part of her career to applying knowledge from her clinical experience and psychosocial studies to create innovative resources such as books, workbooks, therapeutic games and an advance care planning guide for children, adolescents, and young adults. Each of these resources are distributed worldwide and widely utilized in pediatric centers. Dr. Wiener has published extensively, co-edited the *Pediatric Psycho-Oncology: A Quick Reference on the Psychosocial Dimensions of Cancer Symptom Management*, New York, NY: Oxford University Press, 2015 and *Pediatric Psychosocial Oncology: Textbook for Multi-disciplinary Care*, Springer International Publishing, 2016. She has been part of the leadership team that has developed the first evidence-based psychosocial standards of care for children with cancer and their family members.

Maureen E. Lyon

Maureen E. Lyon is a Clinical Health Psychologist at Children's National Hospital and a Professor of Pediatrics at George Washington University School of Medicine and Health Sciences. As both a clinician and principal investigator, Dr. Lyon has focused her research on advance care planning interventions for persons living with serious illness, including HIV, cancer, and ultra-rare diseases. Dr. Lyon completed three National Institutes of Health 5-year clinical trials of FAmily CEntered (FACE) advance care planning; a 2-year pilot trial of FACE for family caregivers of children with ultra-rare diseases; and a study of gender effects on advance care planning outcomes. Dr. Lyon adapted the FACE protocol for Spanish speaking persons. She co-edited the book Teenagers, HIV, AIDS: Insights from Adolescents Living with the Virus in 2006 with Dr. Lawrence D'Angelo. Dr. Lyon led community based participatory research demonstrating the benefits of advance care planning.

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Editorial

Special Issue: Psychosocial Considerations for Children and Adolescents Living with a Rare Disease

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1. Introduction

This Special Issue of the journal *Children* constitutes an opportune moment to reflect on the psychosocial needs of children living with rare diseases and of their families. As medical advances, treatments, and developments have enabled many of these children to survive infancy and to live into adulthood, progress brings with it concerns and opportunities to enhance the psychosocial quality of life of children living with rare diseases, and of their families.

In August of 2021, we released a call for papers whereby healthcare providers could share their experience and research on the psychosocial needs of children living with rare diseases, and the needs of their families. Our call resulted in 13 accepted peer-reviewed submissions. The manuscripts covered a diverse range of topics and contributions from around the globe, including Asia (Taiwan), Australia, Europe (Germany, Italy, Sweden, and The Netherlands) and the United States.

We acknowledge that, as is often the case with Special Issues and their time constraints, the manuscripts within this Special Issue do not cover or represent all the potentially important contributions to the topic. However, as international perspectives are shared, we hope this Special Issue leads to future research collaborations. It is also our hope that the data presented in this Special Issue will ultimately reduce the systemic and structural inequities that place children with rare diseases at unfair, unjust, and avoidable disadvantages with respect to their quality of life and that of their families.

This Special Issue reflects the current state of psychosocial research, which is primarily qualitative in nature. There are no scientifically rigorous randomized clinical trials to create an evidence base of effective psychosocial interventions for the provision of care to children with rare diseases and to their families; nevertheless, the papers within this Special Issue provide a reflection on the state of the science, including ideas about future research and practice. In this next section we share observations about the contributions made by each of the 13 articles, which cover a diverse range of topics.

2. Contributions to the Special Issue

Belzer, Wright, Goodwin, Singh, and Carter provide a thorough, thoughtful, and comprehensive overview of psychosocial considerations for the child with a rare disease, including recommendations and a call to action [1]. Of particular importance, the authors note the experience of stigma and social isolation amidst the medicalization of homes and family lives, and the need for care coordination. The authors call for a focus on the intersectionality of identities (e.g., gender, race, and poverty), experiences, and care models. The impact of the social determinants of health, known to contribute to inequity outcomes, has not been fully characterized; this is, in part, because of small sample sizes. The importance of the child voice (when possible), of the family as part of the care and

research team, of gender differences in caregiving, of sibling caregiving, of access barriers in the community, of electronic health record functionality with documentation, and of the transition to adult healthcare is also reviewed here and further explicated in the articles within this Special Issue.

Each rare disease is unique with respect to the specific medical and psychosocial needs associated with the condition. Additionally, many studies only include the parent perspective because the child's rare disease involves communication and/or neurocognitive disorders that preclude the child's participation. Sharping and colleagues identify the unmet needs of the parents of children with urea-cycle disorders residing in Germany [2]. Using the validated Parental Need Scale for Rare Diseases Questionnaire, 59 parents reported on the needs of 24 children. Close to half of the parents reported a need for information on available services, and one-third on the need for additional information on the development of their children. More than two-thirds reported a need for additional support such as support groups or psychological counseling. The authors conclude that the findings underscore the importance of family-centered approaches to care. We concur that the template they used for their assessment of family burden could be used for children with other rare diseases, increasing the replicability of study findings, as children with rare diseases and their families share many commonalities in their need for knowledge about their or their children's conditions and desire for support.

Similarly, through data collected via a structured psychosocial interview and the Distress Thermometer/Problem Checklist, Lockridge and colleagues [3] found that patients (n = 63) with Multiple Endocrine Neoplasia 2 (MEN2B) and Medullary Thyroid Carcinoma (MTC) identified the need for information about available services and education about MTC as high-priority. MEN2 is a genetic cancer syndrome for which there are limited data pertaining to the quality of life and psychosocial experiences of persons affected. Over half of the pediatric patients reported experiencing attention challenges and difficulty concentrating. While pediatric and adult patients identified pain as interfering with their mood and daily activities, the parents of pediatric patients reported mood shifts as most concerning, thus highlighting the importance of both the child voice and parental perspectives. The children and parents agreed that they would want to meet others with this rare condition. The study suggests that the psychological impact of living with MEN2 and MTC extends beyond changes in physical attributes, daily life limitations, and pain and; therefore, it speaks to opportunities for educational and mental-health intervention and further research.

Beckwith-Wiedemann syndrome (BWS) is a rare overgrowth disease and is not usually associated with intellectual delay. In a cross-sectional exploratory study in Italy, assessing psychosocial difficulties in preschool-age children with BWS, Butti and colleagues [4] administered two standardized questionnaires to 30 parents—the Child Development Inventory and the Child Behavior Checklist. The authors found that overall, BWS was not associated with specific behavioral problems; however, at the individual level, almost a quarter of the sample had scores in the borderline range on the withdrawal scale, and half had scores within in the borderline or critical range in the social domain. Increasing age was associated with higher behavioral and developmental difficulties. Social withdrawal problems were independent of developmental difficulties in the social domains. The authors speculate that children with BWS might become more aware of their condition as they begin spending more time with their peers in social contexts outside the family. They recommend that children with BWS receive routine psychosocial assessment of emotional and psychosocial development as they enter kindergarten and elementary school. This could have beneficial effects on the national health system in Italy, reducing costs associated with the long-term consequences of neglected emotional–behavioral problems.

In a mixed-methods study, Chu and colleagues [5] explored gender differences in parenting stress, health outcomes, and illness perceptions among 100 family caregivers (42 men and 58 women) caring for children with genetic or rare diseases in Taiwan. Measures included the Pediatric Inventory for Parents (PIP) to assess caregiver distress, the

Center for Epidemiological Studies Depression Scale Short Form (CES-D Sort Form) to assess caregiver depression, and the Satisfaction with Life Scale (SWLS) to assess life satisfaction [5]. Open-ended questions were theoretically informed, using Leventhal's Common-Sense Model of Illness Representation. Consistent with prior research, most female caregivers served as the primary caregiver and provided more caregiving, while experiencing high levels of parenting distress and depressive symptoms compared with male caregivers. The authors identified a gender discrepancy in illness perception (negative consequences requiring disease control vs. quality of life), which may have contributed to the higher levels of stress and depressive symptoms in female caregivers than in males.

The standardized documentation of psychosocial concerns is the first step in improving the ability of healthcare providers to identify and intervene in psychosocial concerns and their risk factors. The documentation of psychosocial distress and its antecedents in children with rare diseases is often not captured in the medical record, as illustrated in McCarthy and colleagues' article [6]. The medical records of patients with rare or life-limiting chronic conditions (n = 60) being followed by a pediatric complex care coordination program in the United States were reviewed. The authors extracted both structured data elements and narrative text from the most recent visit with the clinician. Topics related to psychosocial distress were documented in notes, including child and parent emotional problems, parent social support, sibling emotional or physical problems, family structure, and financial concerns. However, 35% of the notes lacked any mention of psychosocial concerns and mention of parents' emotional health or concerns was largely absent. Risk factors and vulnerabilities of the family system (i.e., financial, sibling) were also rarely captured. The authors emphasized the need for universal psychosocial screening using structured, evidence-based tools, systematically entered into the medical record as a way to contribute to an integrated medical and behavioral service model.

Among nonhuman primates, siblings are "helpers at the nest." Therefore, it is not surprising that the siblings of children with rare diseases also function in this role, as demonstrated in the studies of Wawrzynski and colleagues [7] in the United States and Kreicbergs and colleagues in Sweden [8]. Their studies highlight the need for social support for the siblings as well as the patients. In semi-structured interviews of siblings aged 12–17 years, Wawrzynski and colleagues constructed ecomaps of support networks, including types of support and of support provider. Support networks ranged from 2–10 individuals, with mothers, fathers, close friends, and siblings, with and without cancer being major supports, in that order. We concur that this foundational knowledge of sibling networks will contribute to the design of interventions to improve support for the siblings of children with rare diseases, including cancer.

Little is known about the need for information and the involvement of the siblings of children with palliative care needs. Kreicbergs and colleagues, using four standardized communication tools (See–Hear–Do pictures, including the empty body as a separate element, Bear cards, and words originating from previous sibling research), conducted a conventional content analysis of the responses of nine siblings aged 6–14 years [8]. Most striking was that these siblings expressed an awareness that their brother or sister would die—"not if, but when". School was perceived as a place for leisure, friends, and learning. Relentless feelings of guilt and self-blame, as well as themes of loss and separation were elicited. Nevertheless, these siblings also felt they were part of a special, happy family.

Several other papers address palliative care needs for children and adolescents living with rare conditions. Aoun and colleagues assessed the support needs of 28 parents whose children were receiving pediatric palliative care (n = 20 with non-cancer diagnosis, n = 8 with cancer diagnosis) [9]. With the study conducted in Australia, the authors used structured telephone interviews upon parents' completion of an intervention using the Carer Support Needs Assessment Tool (CSNAT), a process for assessing the palliative care needs of children and their families. The interviews were audio-recorded and transcribed verbatim. The authors found that the parents appreciated a systematic approach in engaging them in conversations about both their needs and solutions to address them. Similar to

other studies, the interviews elicited the following themes: caregiving challenges; perceived gaps in psychosocial care and feelings of isolation; and validation and empowerment when participating in the CSNAT intervention, which helped them identify strategies and receive support in response to their needs. Nevertheless, parents were left wanting practical psychosocial and emotional support. Aoun and colleagues recommend that palliative care services build stronger partnerships with supportive community networks through compassionate community volunteer models of care to address the non-clinical needs of families whose children are receiving end-of-life palliative care.

The question of whether or not pediatric advance care planning (pACP) matters to the parents of children with rare diseases, particularly for those children who are unable to participate in decision making, is only beginning to be explored. Fratantoni and colleagues beta tested a pACP intervention with six families [10]. Their article describes a qualitative analysis of structured interviews examining what parents thought mattered most to their child and what they would want their doctor to know. Five themes emerged that might guide future interventions: getting out and moving freely; feeling included and engaged; managing symptoms and disease burden; coordinating care among the many care team members; and managing today and planning for the future. The parents strived to be effective advocates on their children's behalf.

Brunetta and colleagues conducted a systematic review of the literature on pACP, with a focus on how to operationally define age-appropriate pACP for children living with a life-limiting condition [11]. They identified 18 unique tools. These tools primarily assessed the preferences of the children and their families concerning their goals for care and end-of-life treatment preferences. In most studies, the children were adolescents who were able to participate in decision making. This article is well-organized, beginning with evidence from randomized control trials, observational studies, mixed-methods studies, qualitative studies, and descriptive studies. The authors identify six factors influencing age-appropriate care from the literature: willingness to participate; decision-making capacity; a child's understanding of their own medical process; cognitive impairment; the development of a social identity (defined as an awareness of self and others that influences children's preferences and goals in pACP); and legal responsibilities. The authors call for a more explicit explanation for the choice of age. For example, in adapting adult models for adolescents, it is important to address how the adaptations meet the developmental needs or capacities of the children studied. The authors also call for future studies to specify race and ethnicity.

Two studies addressed the needs of adolescents and young adults living with a chronic or rare condition. A quality-improvement study assessing the needs of adolescents and young adults (n = 89) with neurofibromatosis type 1, cancer, primary immunodeficiencies, or sickle cell disease, and of their caregivers (n = 37), was conducted by Allen and colleagues [12]. The subjects completed a survey developed for this study to identify a range of informational and service-related needs. Consistent with the other studies in this Special Issue, there was an overwhelming desire for information about their specific disease. The authors conclude that this is a critical and largely unmet component of care which requires the development and implementation of targeted educational and psychosocial interventions. Considering most adolescents and young adults have access to smartphone apps and web-based services, the authors suggest that future research should utilize digital technologies to expand services and address informational needs.

The transition to adulthood for youth living with chronic illnesses is complex. Sandquist and Lyon—in partnership with Davenport and Monaco, who are parents of children with rare diseases—provide a useful international review of the literature on challenges specific to the transition to adulthood for youth living with rare diseases [13]. Their review found that transitional support is lacking, particularly for maturing psychosocial needs. Many programs that do exist assume the young person can participate in decision making and live independently, which may not be the case for many young people with rare diseases. The parents of children with neurological conditions that impair decision making and/or inde-

pendent living are often surprised to discover that they need to establish legal guardianship over their children when their child becomes a legal adult and prove their competency as caregivers to the government. The barriers and challenges to transition to adult care are identified, including the need for programmatic support. The authors conclude that a large portion of children with rare diseases are underserved and experience health disparities in the transition.

While the papers published in this Special Issue provide important new knowledge, more work is required in several areas. Discovering effective approaches to improving the quality of life of children with rare diseases and of their families necessitates addressing the social determinants of health, which, in turn, should inform clinical practice and policy. We need to examine the systemic and structural problems that contribute to health disparities and consider ascertaining psychosocial needs through new systems and models of care. Macro-level interventions at the population or community-health level can help meet the psychosocial challenges that persistently affect children living with rare diseases and their families. Finally, we recognize that, along with the caveats of what is still needed, there are some wonderful programs available for children, adolescents, and young adults living with rare conditions. Unfortunately, it is not possible to list them all here.

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Article

The Social Networks and Social Support of Siblings of Children with Cancer

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Abstract: Siblings of children with cancer need support to ameliorate the challenges they encounter; however, little is known about what types and sources of support exist for siblings. This study addresses this gap in our understanding of the social networks and sources of support for adolescents with a brother or sister who has cancer. Additionally, we describe how the support siblings receive addresses what they feel are the hardest aspects of being a sibling of a child with cancer. During semi-structured interviews, siblings (ages 12–17) constructed ecomaps describing their support networks. Data were coded for support type (emotional, instrumental, informational, validation, companionship) and support provider (e.g., mother, teacher, friend). Network characteristics and patterns of support were explored. Support network size ranged from 3 to 10 individuals (M = 6 ± 1.9); siblings most frequently reported mothers as sources of support (n = 22, 91.7%), followed by fathers (n = 19, 79.2%), close friends (n = 19, 79.2%) and siblings (with or without cancer) (n = 17, 70.8%). Friends and brothers or sisters most often provided validation and companionship while instrumental and informational supports came from parents. This study provides foundational knowledge about siblings' support networks, which can be utilized to design interventions that improve support for siblings of children with cancer.

Keywords: cancer; childhood cancer; adaptation; psychological; neoplasm; oncology; sibling; social support; social adjustment

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1. Introduction

A pediatric cancer diagnosis causes disruptions within the family including shifting of roles, finances, and resources. The focus on the needs of the diagnosed child often leaves siblings feeling anxious, alone, and distracted [1,2]. Siblings may experience poor psychosocial adjustment, including poor school functioning, cancer-related traumatic stress, and poorer quality of life [3–5]. Due to distress and challenges with adjustment among siblings of children with cancer [4,6], supportive care, including providing education and psychological supports, for siblings is recommended as a standard of care in pediatric oncology [7].

Social support is broadly defined as the provision of assistance, comfort, or resources to individuals that alleviate stress and assist in coping [8]. The stress-buffering hypothesis of social support [9] has been extensively explored and suggests that social support offers resources and promotes coping to buffer stress. Social support is well established as a key factor in health outcomes and adjustment in children and adolescents [10–13].

Few studies have examined siblings' perspectives of their social support or associations between support and adjustment [14,15]. A recent scoping review suggested that social support is indeed helpful to siblings; however, the most important sources and types of helpful support for siblings of children with cancer remain unclear [16].

The purpose of this study was twofold. First, we aimed to advance our understanding of social support among siblings by identifying sources and types of support within their social networks. Second, we aimed to identify how support sources and types of support given to siblings alleviates the "hardest things" they have encountered since the cancer diagnosis of their brother or sister through their own narratives.

2. Materials and Methods

2.1. Participants

All study procedures were approved by the Institutional Review Board at the University of Utah (protocol #00124303). Eligible participants were healthy adolescent siblings (age 12–17) of children in active treatment for cancer or off treatment but diagnosed within the last two years. Our sampling was purposive to ensure representation of varied ages and genders of participants because developmental age and gender are known to influence perceptions of support [10,17]. Siblings were English-speaking, nonbereaved, and living in the home of the child with cancer at least 50% of the time. Table 1 provides participant, family, and cancer diagnosis demographics.

Table 1. Participant Demographics.

	Range	Mean (SD)	N	(%)
Age	12–17	14.2 (1.6)		
Gender	Female		12	50
	Male		12	50
Race	Asian		1	4.2
	Black		3	12.5
	White		20	83.3
Ethnicity	Hispanic or Latinx		6	25
Family Situation	Traditional		21	87.5
	Blended		3	12.5
Family Income [1]	Less than 500,000		6	25
	50,000–99,000		3	12.5
	150,000–199,999		7	29.2
	200,000–249,999		3	12.5
	250,000–299,999		2	8.3
	More than 300,000		1	4.2
Time since Diagnosis	0–3 months		2	8.3
	3–6 months		5	20.8
	6–12 months		5	20.8
	12–18 months		3	12.5
	18–24 months		4	16.7
	Over 2 years		5	20.8
Diagnosis	Leukemia		11	45.8
	Lymphoma		6	25
	Sarcoma		4	16.7
	Solid Organ		2	8.3
	Brain		1	4.2
Parent Education	Some College		5	20.8
	Vocational or Specialized Training		3	12.5
	Bachelor's Degree		11	45.8
	Master's Degree		4	16.7
	Doctoral Degree		1	4.2

[1] Two families did not wish to disclose income.

2.2. Screening and Recruitment

Two methods were used to recruit participants for this study. First, we used the electronic health records (EHR) at Primary Children's Hospital, a quaternary pediatric oncology center serving the Intermountain West of the United States, to identify pediatric patients diagnosed with cancer within the last two years. Second, we partnered with SuperSibs, a program of Alex's Lemonade Stand Foundation, to identify families with eligible siblings. SuperSibs is a free program providing comfort and care mailings to siblings of children with cancer. Parents identified through both sources received emails inviting participation in a study of sibling social networks and support. They were then contacted by phone to answer any questions and determine interest in participation. Interested caregivers completed a screening survey to confirm sibling eligibility. If eligible, parental permission and demographic information were collected via a Research Electronic Data Capture (REDCap) [18] link, along with contact information for the target sibling. Eligible siblings were then sent study information and invited to participate. Interviews were conducted after documentation of assent.

2.3. Data Collection

Participants completed audio-recorded interviews that lasted 20–47 (M = 30) minutes and took place via Zoom [19]. Participants worked with the researcher to build an ecomap [20], a visual representation of their social network, by identifying up to 10 people they perceived as a source of support throughout their brother or sister's cancer experience. Participants described characteristics of their social support networks (e.g., relationship, age, and closeness) and interactions with members (e.g., frequency, type of support) to complete the ecomap (see Appendix A, Table A1). Participants were asked about the kind of support each person provided to them using a set of terms and examples formulated in lay language developed and tested in previous work [21]. However, they were also allowed to freely describe specific or recent examples of the support received from each source they mentioned in their ecomap without using the terms provided.

Participants were also asked to describe what they felt was the "hardest thing" for them since their brother or sister's diagnosis along with any support they felt helped in dealing with or alleviating stress related to their identified "hardest thing".

2.4. Data Integration and Analysis

Demographic and ecomap data were summarized using descriptive statistics (mean, percentage) which were generated using SPSS version 26 [22]. Audio recordings of participant interviews were transcribed verbatim. Transcripts were then de-identified and imported into Dedoose [23] for management and coding. Participant demographic data were imported as case descriptors and linked with interview data.

To ensure theoretical and empirical coverage of the data, analysis took place in two stages of deductive and inductive coding. First, we used a deductive approach applying codes and definitions derived from theoretical constructs, interview questions, and review of the ecomap data (e.g., relationship and interaction characteristics, types of perceived support) [24]. This preliminary deductive coding scheme was refined by four members of our research team (SEW, WK, MA and KGC) by coding two interviews together. Primary coders (SEW and WK) then independently coded a series of interviews, discussing inconsistencies in coding and refining use of the code book after each one until reliability was established by achieving a Kappa within the "substantial" range [25], at 0.86 after four transcripts. Coders then independently coded the rest of the transcripts resolving discrepancies at weekly meetings.

Next, an inductive open coding approach with thematic analysis was undertaken to ensure novel content was captured and integrated into the coding [26]. Throughout the coding process, reflexive and analytic memos were recorded directly into Dedoose alongside the data to enhance the description and understanding of the data [27,28]. In the second phase of coding, the authors reviewed and discussed the codes and memos

to develop themes and summarize the data. Codes and subcodes were organized by conceptual similarity, subsuming the initial codes within emergent thematic categories.

3. Results

3.1. Sample Demographics

Twenty-four siblings between the ages of 12 and 17 were included in this study (Table 1). Half were male and half were female. Most siblings were white, but nearly one-third represented racial or ethnic minorities. All siblings came from traditional (mother, father, siblings) or blended (divorced and remarried or cohabitating adults and their children) two-parent homes; however, families varied regarding income, parental education, cancer diagnosis, and time since diagnosis.

3.2. Sources of Support

Ecomaps indicated that siblings' cancer social support networks ranged from 3 to 10 individuals. A total of 162 individuals were identified as sources of support in our sample's ecomaps, with each individual providing one to three types of support. Siblings reported an average closeness rating of each supporter at 4.5 (SD 0.78, range 1–5) with 5 indicating the greatest perceived closeness to the individual. On average, siblings' social networks were primarily made up of family members (71.6%, range 33–100%). Figure 1 shows the type of relationships included in each sibling's ecomap network by percent. Mothers were identified as a source of support by nearly all participants. The next most frequently mentioned sources of support were close friends and fathers, then a brother or sister in the home. One-third of siblings (33.3%) mentioned a teacher, school counselor, or coach, and 29.1% included their family pet in their support network. Several siblings mentioned a group of individuals as a single source of support in their ecomap, for example, a sports team, their local community, or a neighboring family who offered them important supports throughout the cancer journey (Figure 1).

3.3. Types of Social Support Received

Siblings identified support within all six deductively derived domains, including emotional, informational, instrumental, companionship, and validation support. Two additional types of support, appraisal support and indirect support, were identified via inductive coding. In total, N = 383 examples of support were identified across all interviews; what follows is a summary of the specific supports reported by siblings within each domain of support. Percent of support provided their most frequent sources are also included. Definitions for each type of support and exemplary quotes are noted in Table 2.

Emotional support was the most frequently identified type of support siblings reported (N = 144/383, 37.6%) receiving from their social network members. Examples of emotional support among siblings often related to encouragement and "check-ins" where the identified source of support would ask how the sibling was doing or make themselves available to the sibling to talk or answer questions. Some siblings had difficulty identifying a specific example of how emotional support had been given but articulated instead that the source was "just there for them", giving them a sense of presence and availability. Emotional support was provided across all types of sources of support; however, data matrices showed that emotional support was most frequently provided by friends (n = 35, 24.3%), mothers (n = 25, 17.4%), healthy siblings (n = 18, 12.5%), and fathers (n = 17, 11.8%).

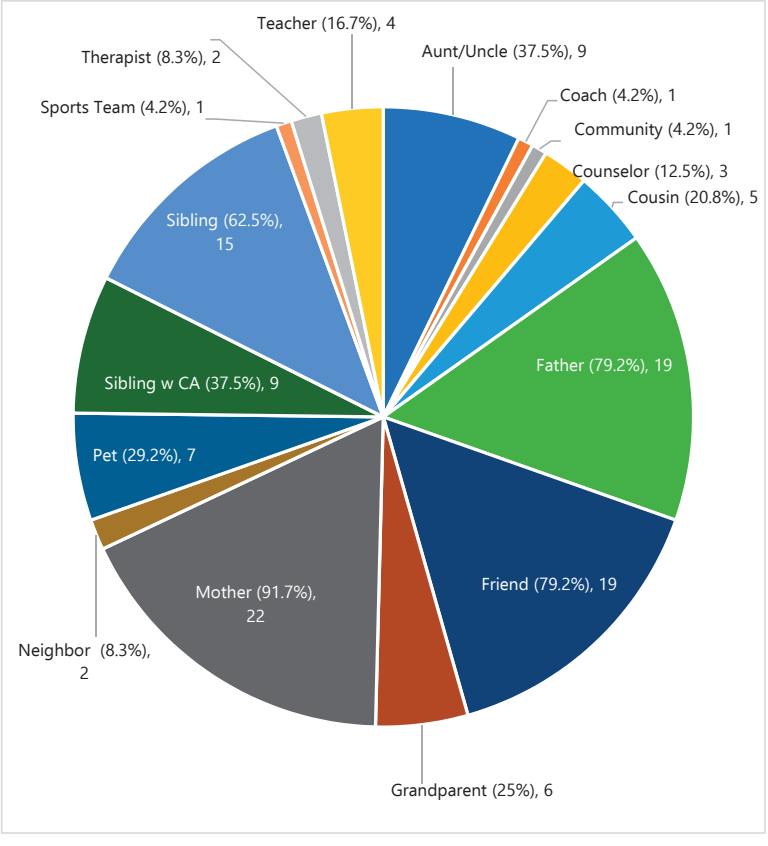

Figure 1. Percentage and number of siblings reporting each mentioned source of support.

Table 2. Social support examples from siblings by category of support.

Social Support	Codebook Definition	Example Quote
Emotional	Receive empathy, caring, reassurance, or encouragement. Knowing you have someone available who cares about you.	"She would ask questions about my feelings and stuff. Because, as a sibling,—it feels bad to think that you're going through something, rather than your sibling's going through something. So, like it was easy to talk to her." (16 y/F, talking about a cousin)
Informational	Receiving knowledge, recommendations, or advice.	"He was kind of like—it's going to be okay. He was the one—more than my mom, he was the one who kind of gave me the info on his cancer and he kind of like informed me what was going on and he did it in a nice way and everything." (15 y/F, talking about her dad)

Table 2. *Cont.*

Social Support	Codebook Definition	Example Quote
Instrumental	Receipt of services such as transportation, money, or help with household chores, homework, and skill building.	"She helped me by cooking for me and providing me meals." (13 y/M, talking about his grandmother) "yeah, and still helping me with homework even though he's busy." (12 y/M, talking about his dad)
Companionship	Spending time together for distraction an escape from cancer, offers reprieve and fun.	"I would say that he just like—he's so tiny that he doesn't really understand it fully yet. So, he just helps me just get my mind off of it and just like "Hey, [brother], you want to play Legos or something?" I'm like "Okay, sure." (14 y/M, talking about younger sibling)
Validation	A sense of belonging and shared world view, having someone who understands you.	"She understands, and she needs people to talk to just as much as I do" (12 y/F, talking about a sibling) "He has a relative, I think, who had cancer, and it's a different kind of cancer, of course, but he tells me all the time that he knows how hard it is, and he's there to help." (16 y/F, talking about a friend)
Appraisal	The provision of affirmation, or feedback for self-evaluation and social comparison.	"[brother w CA] was telling me about how for the past two years he was depressed because he was in and out of hospitals. He couldn't get to see us, and that really inspired me to try my best for him." (16 y/M talking about his older brother) "I was giving a speech to my prayer center, my mosque. And it went pretty well, and my dad gave me some feedback and told me how I could improve, what I did well, and he did it all in a very nice, friendly way." (14 y/M talking about his dad)
Indirect	Supports siblings report has helpful to them but are not directed at them specifically.	"People in my ward, they would bring us dinner,—they mowed our lawn, and they are constantly visiting us, trying to help with anything . . . it helps me feel like people care, and we have help if we need it, and that's comforting." (16 y/F talking about her neighbors)

Companionship was the second most frequently reported type of support among siblings (N = 80/383, 20.9%). Companionship primarily served the purpose of distraction for siblings. Companionship allowed siblings to feel normal, have fun and escape the cancer experience. This was in the form of sports activities, "hanging out" with friends, or a one-on-one trip to the store with a parent or older sibling. While parents and other sources of support were identified as providing companionship, friends (n = 22, 27.5%) and healthy siblings (n = 20, 25%) were the most frequently identified sources of companionship.

Siblings also identified instrumental support (N = 53/383, 13.8%) in a variety of forms. Several siblings mentioned receiving meals or having a place to stay while their parent(s) were at the hospital. Sometimes instrumental support was help with homework, sports, or facilitating sibling participation in their interests or activities. Instrumental support was

most frequently provided by fathers (n = 14, 26.4%), followed by mothers (n = 11, 20.8%) and aunts (n = 8, 15.1%). Instrumental support provided by parents also included acting as a link to other sources or types of support. For example, parents were able to connect siblings to teachers, therapists, or extended family in the sibling's social network who provided support.

Informational support was the next most identified support (N = 50/383, 13.1%). Informational support most often related to someone providing information about cancer, its treatment, or the effects of treatment. Several siblings mentioned someone providing information that supported them in dealing with specific challenges such as tips on interacting with the child with cancer or help with homework. Informational support was most frequently identified as being provided by mothers (n = 16, 32%), fathers (n = 13, 26%), and healthy siblings (n = 8, 16%). Teachers and aunts were also mentioned by some.

Validation was identified as having someone who understands you or your experience; this was typically related to the cancer experience (N = 32/383, 8.4%). Validation was most frequently provided by healthy siblings (n = 8, 25%) and friends (n = 7, 21.9%).

We also noted two additional types of support described by participants that did not fit our initial coding approach. First, appraisal support was identified, comprised of comments or behaviors from individuals in the siblings' network that assisted in the sibling's self-evaluation or their appraisal of their social situation. Appraisal support (N = 15/383, 3.9%) was occasionally related to cancer, but most often related to feedback or affirmation given to the sibling unrelated to cancer, such as praise for an accomplishment or help with typical adolescent interpersonal issues. Appraisal support was provided by fathers, healthy siblings, and the children with cancer with the same frequency (n = 3, 20%) followed similarly by mothers and friends (n = 2, 13.2%).

Second, indirect support occurring at the family level was identified (N = 9/383, 2.3%). This type of support was not directed at the sibling specifically but provided support targeted at alleviating family stressors, which provided siblings with the added benefit of feeling more secure in their situation. Examples of this included community fundraisers, GoFundMe campaigns, care of their family needs, or the care their brother or sister was receiving for their cancer. Siblings who identified these supports conveyed that these types of support helped them feel loved, watched over, or provided a sense of comfort regarding their worries about their brother or sister with cancer. Indirect support was identified as coming from medical professionals (n = 3, 33.3%), fathers (n = 2, 22.2%), and community (n = 2, 22.2%) most often. Frequencies of reported support by gender are noted in Table 3. Chi-square analysis on gender differences in reported support was significant, (X^2 (df = 6) = 15.21, p = 0.019; Cramer's V = 0.20) and appraisal support was noted to be the type of support contributing significance.

Table 3. Frequency of Social Supports Reported by Gender.

Social Support	Gender	
	Male	Female
Emotional	61	83
Informational	20	30
Instrumental	24	29
Companionship	30	50
Validation	7	25
Appraisal	12	3
Indirect	4	5

3.4. Hardest Things and Most Helpful Supports Reported by Siblings

Sibling reports of the "hardest thing" they had dealt with related to their brother's or sister's cancer aligned with their reports of the most helpful supports and the inductive themes identified in our analysis. In Table 4, we provide examples of what siblings identified as the hardest things, their most helpful supports, along with the overarching

themes noted in the data. Specifically, we identified involvement in family and care, distraction, creating connections and presence, and understanding as most relevant in addressing their identified challenges.

Table 4. Hardest and most helpful supports reported by siblings.

Hardest Things Since CA Dx	Overarching Themes	Most Helpful Supports
"When [brother w CA] is not feeling good, or when he starts feeling sick, during the chemo, or he's weak, and he's crying, like that's the hardest thing, because I don't like to see him in pain." (P22) "Probably mostly just feeling bad for him, like just all the hard things that he's had to go through." (P19) "Just accepting that things won't be the same for [sister w CA] . . . she is super tired and we can't joke around and she is getting super serious." (P14) "I think that's the hardest thing is just seeing my mom not take care of herself, and I think the hardest thing is just thinking into the future." (P1)	Involvement in Care and Family	"I try to like comfort him. Because usually, when he's like feeling like that, he'll ask for me. I'll come and just lay with him, watch a movie with him, and just try to comfort him as best as I can." (P22) "I think the thing that has helped me the most is that [my siblings] understand that like she's sick and stuff, and they'll help me make cards for her and things." (P11) "Just hanging out with [sister w CA] more maybe." (P14)
"A lot of the time my dad would be working and mom would take him to the hospital, so I'll be by myself." (P15) "I think probably feeling more alone because I was probably closer with my parents before my brother got diagnosed and obviously, my brother was in the hospital like a bunch of different times." (P11) "I would say probably the attention, like less attention." (P6)	Creating Connection and Presence	"When everybody's together." (P24) "[Aunt], she is just be there for us, to check up on us when we were down, and she was just there." (P22) "Well, it's always nice to like see people—see that people care and want to help you." (P19) "Probably just them being open to talk, being like "Hey, if you want to hang-out we can hang-out." (P15)
"Selfishly, the hardest thing has been just my mental health getting really bad since then. It kind of just downward spiraled since he was diagnosed." (P5) "Pretty much not being able to see people a lot and go places." (P12) "Losing friends" (P21) "Dad would be working, and my mom will have to take [brother w CA] to the hospital, and so I'll be by myself for a few weeks just at the house." (P15)	Distraction	"I'd just say like going to practice gets my mind off it, like my dad taking me to practice. I don't really think about it while I'm there." (P23) "I really like hanging out with my cousins and with some of my friends online." (P16) "You know, I could still do my music lessons . . . my theater classes. I had people to drive me to those. And I could do a show or something, because of that support that I had. Kept me feeling like, "Okay, my life is still going to go on. This just happened to my brother, but I can still live my life and do my things." (P5)

Table 4. *Cont.*

Hardest Things Since CA Dx	Overarching Themes	Most Helpful Supports
"When by brother first got diagnosed they were open to me asking questions . . . but I guess they got tired of it" (P21) "When I didn't know anything about it, I wasn't sure if he was going to be okay." (P17) "Well, I feel like if someone finds out that [my sister] has cancer, they'll be like, "Oh, I'm so sorry", and like feel all awkward if I tell them that like, "It's really not a big deal", and so I feel like that's hard and I never really understood it all the way." (P11) The hardest thing has probably been schoolwork . . . a result of distractions and stuff like that. You just don't know what's going to happen next, your mind is in a million different places. (P4)	Understanding	"I think the most helpful was knowing what was going on with my brother. I appreciate my mom the most for telling me straight-up what was going on with my brother. I felt like that kept me grounded the most." (P21) "I don't know, [my parents] gave me time and space and just like processing room. So, I feel like homework, I could have an extended amount of time or something or like with like different things, they'd be like "Oh, yeah, I understand." (P10) "Probably just like having a few people that understand." (P13)

Seeing their brother or sister sick or their parent's distress was most frequently reported as the "hardest thing". Siblings reported struggling with being treated differently by parents, friends, or others. Siblings felt more alone and limited in their interactions with friends or normal routines and their social networks provided a sense of security, integration, and normalcy that was important to the siblings in coping with their identified challenges.

Siblings identified their own ability to provide support to their family as important. Siblings took on caregiving activities out of a seeming desire to be a part of the family through the cancer trajectory. Siblings discussed the importance of spending time with their brother or sister with cancer, seeing improvements in their health, or even their joy however brief. Siblings also wanted to be a support to parents. One sibling even mentioned seeking to understand their mothers' challenges through an aunt in their social network. Overall, siblings conveyed that assisting with the care of other healthy siblings or their brother or sister with cancer provided siblings with a sense of integration, purpose, and visibility within their family.

Distraction, often occurring through companionship, allowed siblings to feel close to their family and gain a sense of normalcy while dealing with the distress and changes caused by cancer. Concurrently, instrumental support, such as transportation or money, was important to provide the means for siblings to spend time with friends and engage in extracurricular activities, which further supported distraction from cancer.

Most siblings reported that members of their social network were aware of their challenges and were available to them. This created meaningful connections and a presence felt by siblings. Checking in and knowing people were watching out for them were often expressed as important emotional supports. Even when discussing other forms of support, the emotional significance of the time or support an individual provided was simultaneously expressed by siblings.

Finally, siblings expressed understanding as important. This occurred in two ways. First, siblings wanted "real" information. Siblings could see the distress of their parents, siblings, and others. Information that helped siblings grasp the situation, gain perspective, and feel grounded and was identified as one of the most important supports in dealing with their brother or sister's cancer. Second, siblings felt understanding related to their feelings and challenges helped them feel seen. This type of understanding was identified in

things like having extra time to do a homework assignment and leeway in their emotions and processing of the situation.

4. Discussion

Previous work has identified that siblings of children with cancer are at risk for poor adaptation, difficulties in school, and altered relationships with members of their social networks [4,6]. Barriers to supporting siblings have also been identified [29,30], and structured support may not be available to many siblings. COVID-19 has further limited access to supportive services [31]. Notably, no siblings in our study mentioned receiving support or information from the oncology team or hospital for themselves, and when formal services from a therapist were obtained for siblings, it was reported as having occurred as a result of a parent or teacher concern and support.

In this study, we aimed to advance our understanding of social support among siblings and to fill a gap in the literature by characterizing sibling social support networks and identifying the sources and types of support they find helpful. We identified that existing, informal supports were most meaningful and helpful to siblings during their brother or sisters' cancer and that this support most often came from sources closest to them. Siblings identified specific examples of support across a variety of social support domains. The examples of support received from their networks were relatively typical for adolescents [32,33], contributed to the siblings' sense of security, and made them feel cared for during the stressful experience of cancer within the family. These findings are consistent with other research demonstrating siblings challenges [15] and their desire to be seen and involved when a brother or sister has cancer [1,2].

In this study, we also aimed to identify through narratives how the sources and types of support given to siblings alleviate the "hardest things" they have encountered since their brother or sister's cancer diagnosis. Sibling social networks were primarily made up of family members and close friends, highlighting the importance of support within close relationships. Unfortunately, lack of awareness of sibling support needs within the family is a recognized barrier to sibling support [30]. Based on our findings, siblings seem to benefit from meaningful connections formed when others regularly check in on their well-being and allow them space to express their specific needs. In turn, as others learn of siblings' needs, they may be better able to provide congruent support or seek out appropriate professional support when needed. Supports such as providing distraction activities, humor, and understanding of their experience help siblings in small ways to meet the challenges they face being a sibling of a child with cancer. In addition, while most support came from parents, others such as extended family or community can support siblings (and parents) by providing these types of support.

Siblings in our study expressed being acutely aware of the challenges that their diagnosed brother or sister and parents faced and the implications of this on themselves. Siblings also indicated that their parent and family members' well-being was important and contributed to their own sense of emotional security and coping. Previous research has documented similar findings noting that pre-existing family challenges, inadequate resources, or poor parental coping can contribute to poor adjustment to cancer in all family members including siblings [34,35]. Clinicians can routinely assess for these psychosocial issues within families, stratify risk, and improve health equity using tools like the Psychosocial Assessment Tool [36].

Important sibling supports were often related to being seen, involved, or part of the family. Our overarching theme of being "involved" may be more about siblings leveraging their own power to create or enhance cohesion and connection between themselves and their important supporters, rather than a desire for increased responsibility at home or in the care of the child with cancer. These findings align with family systems theory [37] and suggest that family focused interventions may be the most impactful for siblings because positive changes within their relationships with their most important social network members—family members—may enhance intervention effects.

Clinicians treating children with cancer can use our findings to offer additional evidence and guidance to parents about keeping adolescent siblings involved, supported, and connected as they navigate the cancer trajectory. Our findings point to helpful support coming from siblings' existing and informal social networks, available to siblings in their day-to-day activities, outside of structured hospital and community-based interventions. Previous research has demonstrated that siblings of children with other chronic illness experience similar emotional and psychological challenges [38,39] to those of children with cancer. Our reported findings should be compared to those reported by siblings of other childhood illnesses and may be applicable and useful in supporting other sibling groups.

This is among the first studies to report on the social networks of siblings, and our findings should be interpreted with caution. While participant selection was purposive, the sample was relatively small and under-represents the racial and ethnic diversity that is prevalent in the general population of adolescents in the United States [40]. In addition, many children who participated were recruited from SuperSibs, a program that recognizes the needs of siblings of children with cancer. These families may be more aware and in tune with sibling support needs. Finally, our sample was entirely composed of two parent families; the known challenges for single parent families [41] were not integrated into our findings. Our findings may in fact represent a "best case", as participants often expressed having adequate supportive resources.

It is important to note that siblings with supportive resources may still have unmet social support needs if the support they receive is mismatched to their specific challenges. These mismatches of support and need may play a role in poor or ineffective adjustment to the cancer experience. Furthermore, while emotional support was the most frequently reported type of support, it may not be the most needed; rather it may be the most easily offered or cognitively accessible to this age group. More work is needed to determine the specific support needs of individual siblings and how to leverage the supports available to them to promote their healthy adjustment. Future studies could undertake a more traditional social network analysis examining how support, cohesion, or the heterogeneity of their network influences sibling outcomes. Lastly, our research noted some differences in reports of appraisal support by gender, and other research suggests that cultural influences play a role in what supports are desired [42]. Additionally, this generation is the most diverse generation in US history [40] (race, ethnicity, orientation and gender identity), and that should be accounted for in research. Future research efforts should further examine and confirm if specific types of support are more relevant to specific demographic groups or socioeconomic aspects of families.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of University of Utah (protocol #00124303, 31 October 2019).

Informed Consent Statement: Parental permission and informed child assent and were obtained for all subjects involved in the study.

Data Availability Statement: The data presented in this study are available upon reasonable request from the corresponding author. The data are not publicly available due because participants of this study did not agree for their data to be shared publicly.

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Appendix A

Table A1. Interview Guide.

ECO-MAPPING INTERVIEW GUIDE
In this interview we are going to talk about the people in your life that provide you with support and help you. First, think about the people in your life who have supported you. This can be people that you see in person every day, or people that you text, talk or chat with online. We're going to make a list of people you feel have supported you the most throughout your sibling's cancer diagnosis and treatments. Together, we are going to make a diagram of your relationships with these people. Each circle will represent a person that you feel supports you. We are going to put your name in the center circle. Next let's add the names of the people and relationships you have been thinking about. We are going to talk about each person on your map here. I'm going to ask you a few questions about each person, including their relationship with you, and how they support you. As we go, you can make changes to the map, by adding or subtracting people from your map. *For each person identified in the siblings eco-map ask the following questions:* 1. What kinds of support does this person give you? 2. Can you give me a recent example of support that this person or interaction provided you? 3. On a scale from 1–5 how close do you feel to this person? (1 being not very close, an acquaintance that supports you and 5 being someone very close that you feel you could reach out to at any time for support) 4. Do you see or talk with this individual in-person? How often? (Multiple times a day, once a day, few times a week, few times a month) 5. Do you see or talk with this individual online or over the phone (texting, phone call, skype)? How often? (Multiple times a day, once a day, few times a week, few times a month) Now that you've thought about the people and support you have received, I am going to ask you a little bit more about your experiences as a sibling of someone with cancer. 6. What types of support do you think are the most helpful to you? Please describe how or why? 7. Do you ever use social media or the internet to get support? For example, to find information about cancer or to find other siblings like you who may be going through the same thing? 8. Does using social media [e.g., Instagram, YouTube, Snapchat] help you get the support you need? If yes, can you give me an example? 9. Do you think your SM or technology use has changed since your sibling was diagnosed with cancer? If so, how? 10. Can you talk about how confident you are in your ability to make friends online or seek out the help/support when you need it? 11. What has been the hardest thing for you since your [brother or sister] got sick with cancer? 12. Has there been anything in particular that you think has helped you deal with that? 13. *[Referring to their Ecomap]* How do you think these connections have changed since your sibling was diagnosed with cancer? [Alternative prompt: Do you think you would have made a different map before your [brother or sister] got cancer?] 14. How do you think things have changed or are different regarding your social support and connections with others since the COVID pandemic? Remember when schools closed, how have things changed with your friends or other people in your network here? Can you think of anything else that you think is important for us to know about your support system or what might be helpful to other siblings like you?

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Article

"It Is a Whole Different Life from the Life I Used to Live": Assessing Parents' Support Needs in Paediatric Palliative Care

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Abstract: Aims: This feasibility study aimed to systematically identify and address the support needs of parents of children with life-limiting illnesses and to assess whether the systematic approach was acceptable and relevant to parents. Methods: The CSNAT (Paediatric) intervention consisted of two assessment visits with the paediatric palliative care team, 2–8 weeks apart, comprising conversations about sources for support in a tertiary children hospital in Western Australia (2018–2019). Audio-recorded telephone interviews were conducted with parents, and inductive thematic analysis was undertaken. Results: All 28 parents who were involved in the intervention agreed to be interviewed. Five themes summarised their experience: caregiving challenges, perceived gaps and feelings of isolation; the usefulness and practicality of the systematic assessment; emotional responses to self-reflection; feelings of validation and empowerment; and received supports responsive to their needs. Conclusions: Parents appreciated the value of this systematic approach in engaging them in conversations about their needs and solutions to address them. While clinical service support was affirmed by parents, they were left wanting in other areas of practical, psychosocial, and emotional support. Palliative care services need to build stronger partnerships with supportive community networks through compassionate communities volunteer models of care to address the non-clinical needs of these families.

Keywords: palliative care; end-of-life care; equity; public health approach; compassionate communities; caregiving; parents; psychosocial support

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1. Background

Paediatric palliative care (PPC) begins with the diagnosis of a child's life-limiting illness and focuses on improving the quality of life for the child and their family [1–4]. PPC addresses physical, psychological, social, and spiritual needs for the child and their family. Families with seriously ill children face multiple and complex challenges that are individual to that family's circumstances. Receiving individualised supportive care from health professionals and the building of effective and trusting relationships have been reported to be essential components of PPC [5], yet there may be a gap between the identified ideal approach and the actual experiences of children and their families [6].

Families' support needs are not always adequately addressed by health professionals. Reported unmet needs include a lack of access to psychological support for parents and

siblings of the child with a life-limiting illness [6]. Other unmet needs include a lack of access to home support and to educational supports and resources [7]. Despite the known unmet needs, there have been very few reports of a systematic approach to assess and evaluate parent caregiver support needs [8,9] and no reports of using evidence-based tools to routinely help identify needs or review whether support needs were met [7].

The Carer Support Needs Assessment Tool (CSNAT) is a validated tool designed to identify and address the individual support needs of caregivers of adults with life-limiting conditions [10]. The CSNAT approach involves the creation of an action plan in response to the needs assessment, with ongoing further reviews and follow-ups. The 14-item CSNAT covers two domains that address enabling the caregiver to care as well as direct support for the caregiver. The adapted 16-item paediatric version, CSNAT (Paediatric) [11], was modified from the adult version for use with parent caregivers in the PPC setting.

While the benefits of implementing the assessment of caregiver needs into routine practice has been demonstrated in adult settings, this had not been shown in the paediatric setting. We undertook a pilot study to trial the use of the CSNAT (Paediatric) in an Australian PPC setting [12]. In designing the pilot study, we recognised that, in addition to testing initial CSNAT (Paediatric) implementation outcomes, it was also important to examine the feasibility to understand whether the CSNAT (Paediatric) was appropriate for further testing and whether it can be recommended for implementation into routine care [13].

Feasibility studies can address a number of focus areas and commonly include acceptability from the perspectives of individual recipients and from those involved in implementing the intervention [14,15].

2. Objectives

The objective of this qualitative study was to assess the acceptability of using the CSNAT (Paediatric), a systematic approach to caregiver needs assessment, from the perspective of parents in a paediatric palliative care setting in Western Australia.

3. Methods

A steering group guided the development and implementation of the project and included researchers, health professionals (HPs—palliative care consultants and specialist nurses), and two parents with lived experience of receiving paediatric palliative care services. A two-hour training session for HPs was conducted by the researchers and regular 8-weekly team meetings took place for the duration of the project to identify and discuss implementation and data collection issues. The project was approved by the Human Research Ethics Committee of the Child and Adolescent Health Service (RGS0000000772) and La Trobe University Research Ethics Committee. Participants provided written informed consent prior to the start of data collection. The standards for reporting qualitative research were followed [16].

3.1. Setting

Paediatric palliative care services in Western Australia are co-ordinated from the specialist children's hospital and provide care for children with life-limiting diseases and their families.

3.2. Participants

Parents of children aged 18 years and younger receiving palliative care who could speak, read, and understand English were invited to participate (2018–2019). Parents of children who were assessed to be within 6–8 weeks of dying were excluded.

Parents participated in semi-structured telephone interviews to obtain feedback regarding their experience using the CSNAT (Paediatric). The brief interview guide was developed and pre-tested with two parents to ensure clarity of the following questions: How easy or difficult was it for you completing the CSNAT (Paediatric)? Can you please describe in what ways completing this assessment approach was helpful in getting the

support you needed? In what ways did the experience of identifying your needs affect what you did yourself? In what ways did you feel that your needs as a caregiver were acknowledged and listened to in a way that was distinct from the needs of [child's name] for whom you provide care? What improvements if any could be made to this assessment approach?

3.3. Description of the Intervention

The adult version of CSNAT is a validated, evidence-based tool used to systematically identify family caregiver support needs during their relative's end-of-life care [17]. The tool is a caregiver-led, supportive intervention facilitated by the HP. The CSNAT uses a screening format and is structured around 14 broad domains. The domains fall into two distinct groups: those enabling the caregiver to care and those that enable more direct support for the caregiver. It is brief but comprehensive and enables caregivers to identify the domains in which they require further support, which can then be discussed with health professionals through an action plan that needs to be regularly reviewed. The CSNAT (Paediatric) has two additional domains, and its detailed description is reported in [12].

3.4. Recruitment and Data Collection

Eligible parents with a child known to paediatric palliative care services and attending a clinical appointment were identified by the HP, provided with information about the study, and invited to participate.

The CSNAT (Paediatric) was completed during a scheduled clinical appointment or over the telephone when deemed by the HP to be appropriate. Parents were given the option to complete the CSNAT (Paediatric) on their own or in the presence, and/or with the assistance, of the HP. Parents completed it for a second time 2–8 weeks later, either at a clinical appointment or over the telephone with the HP. Interviews took place approximately 2 weeks after the second assessment had been completed.

3.5. Data Analysis

Interviews were audio-recorded and transcribed verbatim. Transcripts were imported into NVivo version 12 software for data management (QSR International Pty Ltd., Melbourne, Australia). Inductive thematic analysis was undertaken using the six phases described by Braun and Clarke [18]. Initial coding was carried out independently by two co-authors, one being the interviewer. Transcriptions were read and re-read to identify key words and phrases that were then grouped into categories labelled with codes. To enhance the credibility of the findings, the interviewer participated in the analysis process so that consideration of the nonverbal context was assured. To further ensure the trustworthiness of our findings, transferability is established by our description of the study's setting and participants.

4. Results

4.1. Participant Characteristics

In total, 33 parents agreed to be enrolled in the project, and 28 of them completed the intervention: there were 8 parents of children with cancer (code C in quotes) and 20 with non-cancer diagnoses (code NC in quotes). Most parent caregivers were female (93%) and aged from 27 to 55 years old, with a mean of 41.7 years (SD = 8.4). In addition, 82% of parents were married/de facto married and 14% were separated/divorced, and 75% of parents had an Australian background, of which one was of Aboriginal descent. Approximately 80% of parents lived with their child in the metropolitan area. Children's ages ranged from under one to 18 years, with a median of 10 years. The median time from diagnosis was 64 months, the median time since the child first became unwell was 94 months, and the median time interval following referral to palliative care was 23 months. Other characteristics are described in more detail in [12].

Reasons for declining to participate or not completing the study were due to the child rapidly deteriorating or because the parent was feeling overwhelmed.

4.2. Parents' Feedback

The interviews explored parents' experiences using the CSNAT (Paediatric), its usefulness to them, and the support they received. All participating 28 parents agreed to be interviewed by the research officer over the telephone. The median length of interview was 16 min (range 6–45) with a mean duration of 17.6 min (SD = 7.92).

Five themes were identified: (1) caregiving challenges, gaps, and feelings of isolation elicited by the assessment process, (2) the practicality and usefulness of systematic assessment, (3) the self-reflection evoking emotional responses, (4) the validation and empowerment experienced by being asked about their needs, (5) receiving support responsive to their needs. Table 1 summarises the five themes and their sub-themes.

Table 1. Summary of themes and subthemes.

Theme	Subthemes
Theme 1. Caregiving challenges, perceived gaps, and feelings of isolation	Mental impact on parents and perceived gaps in support
	Feelings that parents come last
	Frustration with inadequacies of external providers
	Care lacking a psychosocial focus and feelings of isolation
Theme 2. Practicality and usefulness of the systematic assessment	Straightforward form and approach—structured and comprehensive
	Improved communication
	Raised awareness on issues including the family unit
Theme 3. Emotional responses to self-reflection	Prompted self-reflection in a positive way
	Elicited feelings of confrontation
	Allowed a different perspective
	Helped with a sense of meaning
Theme 4. Validation and empowerment	Validation of parent caregiver's needs and role
	Established own strategies
	Felt reassured to ask for support
	Engaged in advocacy
Theme 5. Receiving support responsive to their needs	Felt better informed and prepared
	Increased confidence and coping
	Felt received support addressed needs

Theme 1. ***Caregiving challenges and gaps in support elicited by the assessment process.***

- Subtheme 1.1: Mental impact on parents and perceived gaps in support

Feedback on the assessment process triggered parents to describe their long, challenging journey through the course of the disease and the impact it had on them mentally and the perceived lack of support for their own needs.

> *I actually ended up, I had a major breakdown, about 18 months into this. My marriage had already broken down and there were issues at work, a stressful job. So, with this, with [child name] I think once we went through the process of him having the surgery, chemo, radiation, more chemo, when it was sort of getting to the end of that and I realised, "oh gosh" and I recognised the fact that I was falling into a deep hole despite having, you know, medication and gone to a psychologist.* (P07-C)

> *So, there is none of that is, none of that care services are free [for parents]. You have to go and do it externally. But sometimes you even wonder if it actually would be helpful if it was done as part of the overall care for the child, because it's really if the parents are not coping the child is not going to get what they need either.* (P27-NC)

- Subtheme 1.2: Feelings that parents come last

As parents, they were putting themselves last *"Because I felt it wouldn't be fair for the focus be on me when my child is so ill"* (P10-C), although for them major life changes happened: *"It's changed my life, it is a whole different life from the life I used to live"* (P19-NC); *"That side of the whole caring role, the parent's role, their life stops"* (P13-NC). Therefore, some

assessment questions did not seem relevant to them when internal or external support was not forthcoming:

> *When it comes to the questions where you are getting time for yourself and looking after your own needs etcetera. Obviously, we don't really get to do that because we are parents at the same time.* (P4-NC)

> *Like at the moment I have absolutely no time for doing things for myself or socialising or anything. So, you know, there is just nothing. I tried to go out the other night and [child name] had a really bad night and I had to come home. And it was the first time in six months, I think, I am gone out. So, this was just, you know, it was a bit of a disaster. Yeah. It's a bit disappointing.* (P14-NC)

- Subtheme 1.3: Frustration with inadequacies of external providers

A number of parents of children with complex needs commented that the assessment process would not be useful because of entrenched systematic inadequacies:

> *So, I would say, no it hasn't helped. But that has nothing to do with the survey. Because of outside providers I am struggling with. Because my thing is the whole transition . . . I am still fighting the same fights with the same people. And getting the same frustration.* (P25-NC)

> *Sometimes a lack of understanding of the day-to-day needs that we have and it's almost like it's so much red tape you have to get through and it is almost like there is no common sense at the other end. You know, our child is in a wheelchair, we are having to lift him in, you know, we've hurt our backs doing it. So, frustration, you know, when it appears black and white to us.* (P28-NC)

- Subtheme 1.4: Care lacking a psychosocial focus and feelings of isolation

The perceived lack of guidance, information, and feelings of isolation with no one to turn to for other types of support compounded negative feelings, *"The focus is much more there on the clinical side, rather than the psychological and social side"* (P11-C):

> *Yeah, big gaps in, I am going to say in care. Because the child gets medical support which is amazing. There is absolutely no fault there. but there is no guidance for parents, like, you know, especially in the early days of a diagnosis.* (P27-NC)

> *Yeah, parent struggle because there is no one in your current circle to talk to. So, when you often become friends with other families in a similar situation which is great. But those families can't really deal with your problems either because they've got their own. You don't want to burden other family with your worries because they are feeling the same.* (P30-NC)

> *You do need lots of hands on, lots of people to come in, you know, such as the OT, the social worker, the doctor, the nurse, whether it's physio required as well. I think we just sort of find out various other things just by chance, sometimes by stumbling across something, or another parent, perhaps in the waiting room talking about a particular thing.* (P10-C)

Theme 2. ***Practicality and usefulness of the systematic assessment.***

- Subtheme 2.1: Straightforward form and approach, structured and comprehensive

Parents described that the CSNAT (Paediatric) and its structured format comprehensively acknowledged their support needs. They experienced the assessment as straightforward and relevant. The systematic assessment also highlighted issues that might otherwise have been forgotten, especially in a stressful situation. Parents expressed this with various comments, such as:

> *This really ticks all the boxes that need to be discussed. Because, obviously sometimes you can only think of one thing or the first thing that is most pertinent to you, you and your family, and the person you are caring for and other things get forgotten.* (P23-NC)

- *Subtheme 2.2: Improved communication*

The CSNAT (Paediatric) improved communication between parent and the palliative care service providers or team. Parents described that the assessment opened a discussion between them and the HPs and enabled the parents to identify their needs and to articulate them.

> *It was helpful because it did open up discussions with the team and highlighted some of the areas that I have been struggling with.* (P14-NC)

- *Subtheme 2.3: Raised awareness on issues including the family unit*

Parents acknowledged the impact of their child's illness and the parental caring role on the family unit, as well as the necessary solutions.

> *It highlighted the fact that I probably need to look at him going into respite care maybe once a month. And that is something I always not wanted to do up until now. But it probably highlighted the fact that for my other children it's a necessity, so they can have some breathing room as well . . . So, it helped me to recognise that is something that we need to do.* (P14-NC)

Theme 3. ***Emotional responses to self-reflection.***

- *Subtheme 3.1: Prompted self-reflection in a positive way*

The systematic assessment prompted the parent to pause and reflect; *"it made me stop and think"* (P25-NC) was a common experience. The questions offered the opportunity for a pause in the daily routine and for them to re-assess the caring situation. Parents commented positively on how this experience affected them.

> *I think it was helpful because it just made me think more about [child name]'s needs, my needs and if they are being addressed and how they are being addressed. So, sometimes we just don't stop to think about all these questions or issues that are raised through this program. And I think it's a good process. So especially beneficial for me as a caregiver and a parent.* (P22-NC)

- *Subtheme 3.2: Elicited feelings of confrontation*

For other parents, this triggered a sense of confrontation, and they admitted that *"it's hard and when you're reading the questions you have to try and think honestly about how you feel inside"* (P09-C). The parent explained that the avoidance of this confrontation represented a way of coping with the necessary daily life tasks.

> *Well, it's just the whole thing. When you read the questions, it's not like you are trying to blank out the illness, it's just, just hard dealing with your feelings and worries, I suppose. I am no different to everybody else, you try to bury your feelings and worries because you still have to go on with other things.* (P09-C)

- *Subtheme 3.3: Enabled a different perspective*

Reflecting on their needs enabled the parents to take a different perspective, which was expressed as *"just made you think outside the box"* (P12-NC). This process helped them to analyse and understand their thoughts and feelings.

> *the questions open up different pathways for your thoughts as well. I think. So, you know it helps you to sort of break down your own thoughts and to, you know, go more into depths of why you are thinking the way you are thinking.* (P08-C)

- *Subtheme 3.4: Helped themselves and others*

One parent felt that the process of reflection helped in her search for meaning in the serious illness of her child and spoke of positive feelings that emerged despite the sadness.

> *At the end of the day I actually realised that even though I am in that situation I actually still feel blessed and that there is actually a lot more that's positive that's coming out of this. And it's not all just bad and sad and so and so. No, I really think it was good for me, personally for me, myself.* (P02-C)

Likewise, participating in the research was seen as an opportunity to help other parents in a similar situation and comforted the parents that their situation and care experience contributed to something meaningful.

> *I see that as a positive in providing information to you. So, that hopefully that feeds back and it provides help to others. And that's my ultimate goal. I know in the end, that, we might not be able to help [child name]. But, you know, the end goal for me is, if I can, if something good comes out of this it is going to be that we've helped inform others about our situation and about what areas are lacking and what can be improved.* (P08-C)

Theme 4. ***Validation and empowerment.***

- Subtheme 4.1: Validation of parents' needs and role

Parents appreciated the added comprehensiveness of the assessment and found that it allowed for a different level of acknowledgement and validation of their needs, including their caregiver role:

> *This is on a completely different level. And this is about acknowledging and diving deeper and getting me to do some self-reflection. And, and knowing and acknowledging the issues that I've got. I think it's been invaluable; I think it is fantastic and very different.* (P24-NC)

- Subtheme 4.2: Established own strategies

This systematic assessment also encouraged the parents to develop their own strategies, and they adhered to the mutual action plan they had discussed during the assessment.

> *But I did start one thing that we discussed on there, which was the meditation. So, I definitely started doing that after the assessment.* (P21-NC)

> *I haven't seen this psychologist for three months. And I thought I didn't need to. And then when I went and saw her, I realised how much I had to talk about. So, I can't leave it that long I have to definitely check in with her every now and again.* (P21-NC)

- Subtheme 4.3: Felt reassured to ask for support

The acknowledgment received during the conversation with the HPs not only made parents' needs visible, but also legitimised their own needs. Parents' self-confidence to ask for help increased as they described that they felt reassured to ask, for instance, *"for more respite under the new NDIS [National Disability Insurance Scheme] rollover thing. I have asked for that. So, I put my needs forward with them. And asked for more respite"* (P05-NC).

In addition to taking time for themselves, parents also intended to take care of their own medical needs: *"Just made me realise that some parts like her care I might need to find some support with, just like with time for myself and my medical needs and things like that"* (P31-NC).

- Subtheme 4.4: Engaged in advocacy

Some parents mentioned how they engaged in advocacy and that this had been reinforced by the CSNAT (Paediatric) experience. They turned to politicians to raise awareness of their support needs and to increase support for themselves and other families caring for a child with a life-limiting illness.

> *I think we just try and look at other avenues to see if we could get things ourselves to speed up the process. I've even tried to ring members of parliament and the radio station just to, yeah things like that, just to bring to light the issues what we have. Because sometimes I think if we don't speak people don't understand.* (P28-NC)

Theme 5. ***Received supports responsive to their needs.***

- Subtheme 5.1: Parent felt better informed and prepared

The information and assistance they received from the HPs alleviated parents' concerns and created a sense of empowerment. They felt better prepared:

> *It's sort of prepared me for what's going to come and had a plan in place.* (P07-C)

> *having talked to [HP name] and the doctor we know we have plans in action if we need it. So, I feel a little bit more comfort with that.* (P11-C)

> *I guess by having gone through the process and being able to talk to [HP name] about some of my concerns around transition allowed me to have a conversation about what is a clear plan. Who can I turn to in between the process? It helped me to put some steps into place, I guess. Just through having those conversations.* (P15-NC)

- *Subtheme 5.2: Increased confidence and coping*

The improved confidence increased parents' sense of coping and managing *"I actually do feel stronger about most of the things that I thought I would fail in"* (P02-C) and *"It made me realise that I do a lot and I am taking on a lot and I am managing it quite well"* (P07-C).

- *Subtheme 5.3: Support addressed needs*

The HPs answered parents' questions, liaised with other services, provided advocacy, and arranged required referrals according to what was identified and discussed in the CSNAT (Paediatric) conversation and action plan. Parents found the provided support to be very helpful:

> *She has been able to answer a lot of the questions I had and find the answers that I needed, by going through that form. So, it's been very helpful. And I am very thankful that you've done it.* (P11-C)

> *Obviously, [HP name] and [HP name], anything that I had issues with or that is, you know, I needed help through what we've worked out from the questionnaire that they have been able to help, which has been amazing.* (P23-NC)

The following comment seems to sum it all by reflecting on the uniqueness of this approach, which is truly centred on caregivers:

> *Well, I just want to say, thank you very much, really. Because I think that's something that is, all the year that we had, so many things, we got bombarded with people who want to do surveys and from the health department or, you know, I get calls all the time. But this one seems to be the one right for us and that made it, again, reassuring that somebody is out there trying to understand, or trying to find out where we are coming from.* (P08-C)

5. Discussion

This study examined the feasibility of using the CSNAT (Paediatric) in the paediatric palliative care setting from the perspectives of parent caregivers of children with life-limiting illnesses. All study participants agreed to be interviewed, and it is apparent that parents appreciated the value of this systematic approach in engaging them in conversations about their needs, priorities, and solutions. They felt it gave them the opportunity to consider and express needs and identify what is important to them in a timely manner where possible. Parents welcomed the focus on their individual situation and hoped that this research would increase the awareness of service providers and policy makers to create a positive change.

The use of the CSNAT (Paediatric) facilitated the identification of the parents' support needs, where over 60% reported the following needs: having time for yourself in the day (direct support for the caregiver); practical help in the home (direct support for the caregiver); knowing what to expect in the future when caring for your child (enabling support for patient); financial, legal, or work issues (direct support for the caregiver); knowing who to contact if you are concerned about your child (enabling support for patient); looking after your own health (direct support for caregiver) [12]. It is worth noting that parents needing direct support for themselves featured high on this list, as is supported by the quotes in this article.

5.1. Gaps in Supportive Networks

While clinical services and the support they can offer was affirmed by parents, these parents were left wanting in other areas of practical, psychosocial, and emotional support. This is echoed by a recent independent review of adult palliative care services in WA that used a cross-sectional consumer survey of quality indicators to respond to the six priorities of the WA End of Life for developing and improving palliative care services across WA. Of the six priorities, quality indicators for Priority Four (families and carers are supported) lagged behind the others [19]. Family carers reported not being well supported before and after bereavement by palliative care services. Emotional support and the ability to discuss worries and fears were not adequate, and 40% felt that they did not receive as much support as they wanted from palliative care services during the patient's illness, and 50% did not after the patient's death [20]. By way of contrast, responses to Priority Six (the community is aware and able to care) gave high ratings to the care provided by informal networks. Over 90% of respondents relied on the community (family/friends/neighbours/community organisations) to support them before and after bereavement and reported that this informal support was helpful in attending to practical, social, emotional, and spiritual support needs [20].

Another key finding of the independent review was the lower standard of care for non-cancer conditions across all six priorities, dubbed as one of the 'loser' groups in palliative care service delivery, thus highlighting the inequity in care [20]. This finding was also echoed in this paediatric study, where there were higher levels of unmet needs for the non-cancer group, as reported in our first article from this study [12].

While the independent review focused on adult palliative care, it is worth replicating the consumer survey on quality indicators for the paediatric population. In fact, the more recent Western Australian Paediatric Strategy for End-of-Life and Palliative Care (2021–2028) has reiterated the need to consolidate the two priorities related to family carers and the community for the paediatric population [21]. Building blocks that will help to achieve Priority Four include the use of standardised assessment tools, ensuring the child's family has equitable access to support and respite, and services are urged to look at ways to improve opportunities for consumers to support consumers. Priority Six has building blocks around engaging the community to care, including volunteer models and the development of compassionate communities.

Hence, where our study group was left wanting is within the realm of support from their naturally occurring social informal networks or circles of care [22]. If these informal networks or the inner circles of care are not operational or activated, as expressed in parents' quotes, then compassionate communities models of end-of-life care need to be bolstered (as recommended by the Paediatric Strategy). This can be achieved by training volunteers from the community to seek the practical and social support the family needs to care for the dying from any age group [23]. Volunteers help families tap into the outer circles of care in their community to enhance their social networks in a sustainable way. A local example is the Compassionate Connectors program, a partnership between the South West Compassionate Communities Network and the WA Country Health Services, where the program has been translated into routine practice by the health service: this is a case of a successful partnership between formal and informal networks [23].

Compassionate communities, as part of the public health approach to end-of-life care, offer the possibility of solving the inequity in the difference in the provision of care by enhancing the naturally occurring supportive networks surrounding the patient and family and through palliative care services building stronger partnerships with supportive networks to transform end-of-life care at home [24,25]. Experts in the field have lamented the reality that, *"although palliative care looks beyond the patient to the family, it rarely looks beyond the family to the community or sees the whole person as an individual-in-community"* [26] (p. 133).

5.2. Limitations

We acknowledge the lack of diversity in the study sample where parents were primarily Caucasian women from a metropolitan area.

6. Conclusions

Assessing needs is a first step in acknowledging areas where parents need support. Formal and informal networks need to work together to provide a platform of psychosocial, emotional, and existential support that is sustainable in people's own communities. Given that equity in end-of-life care provision is a goal of government policy [27], inequity arising from disease type should be addressed within the health system. Inequity arising from inadequate social support must be addressed by local communities. Both aspects are taken into account by a public health approach to palliative and end-of-life care. Hence, the distinctive focus of this public health approach is that it views the community as an equal partner in the long and complex task of providing quality healthcare at the end of life [20].

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Data Availability Statement: Ethical approval precludes the data being used for another purpose or being provided to researchers who have not signed the appropriate confidentiality agreement. Specifically, the ethical approval specifies that all results are in aggregate form to maintain confidentiality and privacy and precludes individual level data being made publicly available. All aggregate data for this study are freely available and included in the paper. Interested and qualified researchers may send requests for additional data to Samar Aoun at samar.aoun@perron.uwa.edu.au.

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Article

Family-Centered Advance Care Planning: What Matters Most for Parents of Children with Rare Diseases

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Abstract: Few studies have described the goals and wishes of parents caring for their children with rare diseases, specifically when children are unable to communicate their preferences directly. The purpose of this study was to describe the parent's understanding of their child's illness, goals of care, and what mattered most to their child from the parent's perspective. Six families completed a feasibility study of the FAmily CEntered (FACE)-Rare pACP intervention. Qualitative content analysis was performed on transcripts of videotaped responses to the Respecting Choices Next Steps pACP Conversation facilitated conversation guide about the goals of care. Codes were grouped into themes, with direct participant quotations representing the themes. Five themes emerged: getting out and moving freely; feeling included and engaged; managing symptoms and disease burden; coordinating care among many care team members; and managing today and planning for the future. In the context of pACP, families reported that what mattered most to their children included the freedom of movement and human connection and engagement, while parents strived to be effective caregivers and advocates for their child with a rare and severely disabling disease.

Keywords: rare disease; advance care planning; decision-making; family caregiver; palliative care; psychosocial care; communication; pediatric

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1. Introduction

Children with rare, life-limiting diseases face challenges to their physical and psychosocial health. A child diagnosed with a rare disease may require total life-long care, and a parent often provides that care for the duration of their child's life. If a child cannot communicate, a parent must also try to determine their desires. There is no roadmap for this journey, leaving parents often feeling stressed or isolated [1]. Even though the parent is usually the most involved in the child's care, there is a lack of literature on a parent's experience caring for their child with a rare disease [2]. Few studies have described the goals and wishes of parents caring for their children with rare diseases, especially when children are unable to communicate their preferences directly.

There is a need for more research regarding parents' experiences and desires when caring for children with rare diseases. In addition, specific information about their children's medical conditions is often lacking, making it difficult to manage symptoms [3,4]. Often, little is known about future care needs [5–7]. General knowledge about the disease and its consequences is lacking [7], which may result in inadequate care [8]. There is also a gap in research focused on parents' experience with the healthcare system [9], although recent

studies focus on pathways to psychosocial care at a system level [10,11]. Overall, parents of children with rare diseases report that there is a lack of coordination of care [2]. In a survey administered toward 46 families of children with rare diseases in Australia, parents felt that the care of their children could be improved if there was better coordination of care and interaction between multiple providers [3].

Pediatric Advance Care Planning (pACP) is a process that facilitates discussions with parents and potentially with children about future medical treatment, care, and decisions if the child's condition becomes life-threatening. It also helps families prepare for situations that may occur, and it can improve the family's understanding of the child's prognosis. Pediatric ACP is a core component of palliative care for children living with chronic conditions [12], and it should be offered to all parents of and children living with rare diseases.

The FACE-Rare intervention integrated two evidence-based processes: the Carer Support Needs Assessment Tool (CSNAT-Paediatric) Approach [13,14] and Respecting Choices® Next Steps pACP conversation [15]. Quantitative outcomes of both aims were reported previously [16].

The aim of this article is to highlight the qualitative findings from the Respecting Choices® Next Steps pACP session during which parents engaged in facilitated conversations about their understanding of their child's illness, goals for their child, and what mattered to their children from parental perspectives.

2. Methods

From October 2017 to January 2018, we recruited and enrolled parents of nonverbal children with rare diseases to participate in a feasibility study of a 4-session needs assessment and pACP intervention. Complete methodological details of the FACE-Rare intervention have been previously described [16]. Parents who were ≥18 years old, had a child with a rare disease, and spoke English were invited to participate. Participants' children were between the ages of 1 and 24 years old, had a diagnosed rare disease, were not admitted to an intensive care unit during the study, were unable to participate in medical decision making due to age or disability, were not in foster care, and did not have an active Do Not Resuscitate Order. Children with the primary diagnoses of autism, rare cancers, HIV, sickle cell, cystic fibrosis, down syndrome, lupus, and muscular dystrophy were excluded, as previously published studies have investigated their disease-specific needs. Written informed consent was obtained from the parents, along with a signed waiver of assent for their child. The study was approved by the Institutional Review Board of Children's National Hospital in Washington, DC, which is a quaternary hospital and the study site.

2.1. Interviews

Table 1 illustrates the FACE-Rare study protocol timeline, which provides the context for the study results. The 4-session intervention was administered in person at the study site or by telemedicine. This study only reports on the qualitative data that emerged from Sessions 3 and 4, which consisted of structured goals of care conversation using the Respecting Choices Next Steps pACP conversation guide and a pACP document [15]. The structured conversation guide and pediatric Advance Care Plan are proprietary and are made available upon the completion of training and certification by Respecting Choices, a Division of C-TAC Innovations [15].

Table 1. FACE-Rare Study Protocol Timeline.

Intervention	Session 1 Week 2	Session 2 Week 3	Session 3 Week 4	Session 4 Week 5
FACE-Rare	CSNAT	CSNAT	Respecting Choices Next Steps Conversation	Respecting Choices Next Steps pediatric Advance Care Plan

Respecting Choices is designed to be culturally sensitive to persons with disabilities [17]. This session was facilitated by two trainers from Respecting Choices, including one of the authors (SS). Interviews were videotaped, transcribed verbatim, and deidentified (using pseudonyms). A psychology graduate student/research volunteer transcribed and deidentified the videotapes. Transcriptions were then verified by the last author (ML). This study reports on the data that emerged from Sessions 3 and 4, which comprised responses to the Respecting Choices Next Steps pACP conversation guide and pACP care plan.

2.2. Data Analysis

The authors (K.F., J.L., and S.E.S.) performed conventional content analysis [18] on the transcribed Respecting Choices conversations using an iterative process. Four iterations occurred over a 4-month period from 4 March 2019 to 2 June 2019. For researcher characteristics, please refer to Biographies at the end of this article.

J.L. and K.F. individually read the transcripts and assigned codes to transcripts. Codes were then jointly reviewed with S.E.S. and grouped into code families. Similar code families were combined into themes. Disagreements were resolved by consensus during monthly conference calls (K.F., J.L., S.E.S., and M.E.L.). Representative quotations illustrate key themes. Data were managed using hardcopy files. We used the Standards for Reporting Qualitative Research (SRQR) to guide our report [19].

3. Results

Eight parents were approached: One declined participation, and one was lost to follow-up after Session 1. Six parents completed Sessions 1, 2, 3, and 4. All participants were female, mean age 40 years (standard deviation = 7.7 years), 57% Caucasian, 29% black or African American, and 14% biracial. Two fathers participated with the mothers in Session 4 for the creation of an advanced care plan. The children ranged in age from 2 to 12 years with a mean age of 7 years. Five children had seizure related comorbidities, and all were technology dependent. Five used a wheelchair and feeding tube/pump, and one had a home ventilator.

4. Key Themes

Five themes emerged throughout the structured interview, which not only followed specific questions. See Tables 2–6. The five themes about what matters most for parents of children with rare diseases were as follows: (1) getting out and moving freely; (2) feeling included and engaged; (3) managing symptoms and disease burden; (4) optimizing coordinated care among many team members; and (5) planning for the future. See Tables 2–6 for subthemes and illustrative quotations.

Table 2. Theme 1 Getting Out and Moving Freely.

Theme 1 Illustrative Quotations
Supporting and Encouraging Independence
P1: "She has to be able to do some things that she wants to do . . . allow her to be as independent as possible"
Creating a supportive environment
P1: " . . . create an environment so that she can still be active as she can be or do what she would like to do."
Optimizing mobility
P1: "Being able to be on the move. Just not being limited. When she's in the activity chair, she's in the feeding chair, she's in the wheelchair, she's not happy. She wants to explore. And so being able to move and being able to engage to the extent that she's able to, is huge for her."
P1: "So, moving through a good day would be being active, exploring, not being limited and engaging . . . "
Ensuring safety during exploration
P2: "We come to the beach a lot because it's, you know, peaceful and quiet. And it's one-on-one attention with his grandparents when they come. And he gets the vacation experience in a safe way that we can control."
Offering new experiences
P5: "Good quality of life is her being happy . . . exposing her to as much as we can, to give her the opportunity to experience . . . she can do a lot more than people expect."

Table 2. *Cont.*

Theme 1 Illustrative Quotations
P7: "He loves to get out of the house and go places. He really likes it if he's in his wheelchair so that he can explore the new place. But not too loud."
Disabilities can impede full inclusion
P5: "Hope . . . a world that is more inclusive. When leaving the house, because we do not have a child that is ambulatory, [it's] hard to find a place that we can change a diaper because changing tables are only for infants and at 100 pounds, I can't put her up on the changing table and yet if I put her on the floor, I can't get her up from the floor. So, we're limited between or changing her in the back seat of the car, and she's an 11-year-old little girl, and so it limits her being included in a world the way we want her to be, and from us being in the world that we want."

Table 3. Theme 2 Feeling Included and Engaged.

Theme 2 Illustrative Quotations
Interact with others
P1: "She needs to be able to have some form of communication. She needs to have her sisters."
P5: " . . . being able to be with her peers but making accommodations to make it happen."
Engaged in enjoyable activities
P1: "Being engaged. She loves her tablet; she'll play her little computer games. She likes the swiping aspect. She can swipe and kind of navigate her way around."
P6: "Being held by someone and a massage"

Table 4. Theme 3 Managing Symptoms and Disease Burden.

Theme 3 Illustrative Quotations
Limit unnecessary interactions with the healthcare system
P1: "Stay away from some of the orthopedic surgeries that she needs. I'm trying to hold off as long as I can."
P1: "Stays healthy . . . I need her to not have the cold or flu because things kind of snowball . . . keep her healthy and out of the healthcare system."
Limit the progression of disease
P3: "Eliminate the chronic eye issue."
P7: "Worry about there being more issues . . . he had an ASD [Atrial Septal Defect] that was repaired a few years ago. But he started getting followed by a cardio myopathy clinic so, I get worried that something may turn up . . . like a new condition."
Seizure control
P1: "So, my ultimate hope is much better seizure management . . . when we get better seizure management, then we're better able to maximize speech therapy and receptive expression."
P3: "I'd love it if we'd reduce a lot of his seizure medication one day. Yeah, they sedate him . . . we've seen alertness change with medication, so it sure would be nice if we could reduce it someday."
Optimize Quality of Life
P1: " . . . be as comfortable as possible. Her comfort would be of utmost concern"
P7: "Address those baseline needs . . . I think he has a lot of little things where, very seemingly little things, that bother him and so he's not comfortable. And that affects his ability to kind of grow and progress and learn."
Minimize medications
P3: "Minimize how many medications he's on and how we give them to him, so it maximizes his abilities and alertness."
Self-Injuries
P7: "He's banging his head on things. We're worried about getting him too strong. You know, getting too big and too strong for me to be able to take care of everything . . . unintentional injuries, him injuring himself, something that will injure him."

Table 5. Theme 4 Optimizing Coordinated Care among Many Team Members.

Theme 4 Illustrative Quotations
Optimal communication and coordination among team members
P1: "That there's better communication among our healthcare providers . . . nice if doctors got together once or twice a month to discuss . . . so they can get a good snapshot of where you are."

Table 5. *Cont.*

Theme 4 Illustrative Quotations
P6: "And this idea of, we'll do the procedure, and we'll work out the home care and the nursing after . . . that's not going to work for us because there's not going to be a place for us after. And those are the types of things that every thought, thoughts, you really have to forecast, way down the road. And that's a lot of the concern, who's going to do that? Who's going to be willing to own that and am I going to get team members that are really going to work with us?"
Preparing for transition
P3: "I guess looking ahead with [his] age, parents like us have a discussion with the transition to adult care so I brought that up to his physicians periodically, and they assured me, don't worry about him, especially with a rare disease, you know. He's, he's not going to be sent away and he's at a children's hospital, I mean I know but he's not your typical patient that can go anywhere. A huge concern for when we are away and we've had to seek medical care, we seek help, other hospitals are just not equipped for him and we've had doctors tell us, we're just not equipped to helping [him]. And so, that just makes your heart sink and you always want him to be in the hands of someone who knows him best and have already done such good already in managing him."

Table 6. Theme 5 Planning for the Future.

Theme 5 Illustrative Quotations
Hopes for the future
P2: "So, I want him to thrive as much as he can, for as long as he can, but I don't want him to hang on just for me or for my husband or parents. I want his life to be his life and that for him, to leave hopefully or a little more peacefully."
P6: "I hope that we're able to try to be able to give her the best possible life possible and that she knows that we do our best to make that happen and that she feels loved and she feels acknowledged as an individual and that she knows, despite all of it, that we think she is a wonderful, miraculous little girl. And that she lives the best life and that we're able to support that."
P7: " . . . stability and being able to be happy and enjoy each other . . . not stressed out worrying about who will take care of him or working or money or things like that."
Fears
P5: "If that day comes . . . . I kind of like want to be there and to hold her hand and to let her know it's okay. I don't want [her] to go through that alone and I think for me, that's my biggest fear, is her having to go through that alone and suffer."
P7: "When I'm not here anymore, who's going to take care of him?"
Uncertainty of what might happen next-that the family may not be able to handle
P2: "Every ED visit is more like-fear oriented . . . I fear every hospitalization is one step closer to something horrible and disease progressing out of what we can manage right now."
P3: " . . . we have everything so well managed and so there's always there's that little concern with, what if a new challenge arises and the current method of treatment doesn't meet the needs, can't take care of the challenges. So, whole team is very proactive with keeping that under control. Just you know, his medical needs never outweigh the available treatment."

4.1. Theme 1: Getting out and Moving Freely

As illustrated in Table 2, parents emphasized the importance of encouraging independence for their children and providing opportunities to participate in activities. Physical exploration, optimizing mobility, and offering new experiences were all essential while simultaneously ensuring their safety. Creating and being a part of a supportive and inclusive environment were necessary to accomplish this goal, yet families were often reminded of the barriers to full inclusion.

4.2. Theme 2: Feeling Included and Engaged

As illustrated in Table 3, parents want their children to feel connected to the outside world beyond their diagnosis and medical care. They desire meaningful interaction with others and opportunities to engage in enjoyable activities.

4.3. Theme 3: Managing Symptoms and Disease Burden

As illustrated in Table 4, parents wanted to limit unnecessary interactions with the healthcare system, recognizing that their children with rare diseases have regular and frequent medical appointments, hospitalizations, and emergency department visits. Slowing the progression of disease and controlling symptoms are integral to a good quality of life. Many families mentioned the desire for seizure control, as seizures were disrup-

tive to daily life and occupy attention that could be directed to other impactful therapies and interventions.

4.4. Theme 4: Optimizing Coordinated Care among Many Care Team Members

As illustrated in Table 5, parents wanted to optimize good care team communication means better care for children with rare diseases, especially at times of transition.

4.5. Theme 5: Managing Today and Planning for the Future

As illustrated in Table 6, parents expressed their hopes for the future: for their children to feel complete, whole, not a burden, thrive, and experience life to its fullest. Parents shared their fears about what the future may bring and their uncertainties about their ability to handle the challenges.

5. Discussion

To the best of our knowledge, this is the first study to examine parents' goals, values, and hopes for their child with a rare disease in the context of a structured family-centered pACP intervention. After completing the goals of care conversations with a trained/certified facilitator, all parents returned to complete an advanced care plan document [16]. Five themes emerged. With respect to living well, parents reported that their severely disabled children enjoyed getting out and moving freely, even though all but one of the children were wheelchair bound. Moreover, interactions with others so that they could feel included and engaged were also important to their children. Parents highlighted their caregiving role in managing symptoms and disease burden, coordinating care among many team members, and coping one day at a time by balancing their hopes and fears for their medically fragile child. Seizures were a common symptom associated with rare diseases [20], which caused significant distress.

These findings are consistent with a scoping review that identified five themes with respect to the support needs of parent caregivers of children with a life-limiting illness [21]. The themes identified were support for communication; choice; information; practical information; and social, psychological, emotional, and physical needs. Unmet needs included support for siblings; respite care; out-of-hours care; and psychological, home, and educational support [21]. A focus group with adults living with a rare diagnosis also highlighted the value of participation in society [7].

Our family-centered approach, which included parents in the development phase of the protocol, is consistent with calls for a family-centered framework relative to pACP for children with medical complexities [22]. There is also agreement that pACP should be an ongoing process from the time of diagnosis for seriously ill children [23–25], which is especially important for children living with prognostic uncertainty. In our clinical experience, long-term relationships and trust develop between patients and families and their providers. As the medical condition progresses, a disconnect may develop between a parents' beliefs, values, hopes, goals, and their child's quality of life and developing a holistic treatment plan. The FACE-Rare intervention did not require the pACP facilitator to be well-known to the parents, as has been recently recommended [22,25]. Our findings are consistent with our previous trials of a three-session FACE pACP model, which demonstrated that the initial pACP conversations about the goals of care with parents of seriously ill children and the completion of an initial advance care plan can be successfully conducted by trained/certified facilitators that are not known to the parents, who are referred by their treatment team [16,26,27]. A summary of these conversations and the documents were then emailed by the facilitator to the treating clinician, and the facilitator places the documents in the medical record, laying the groundwork for future pACP conversations with their health care provider. Thus, FACE-Rare demonstrated families' willingness to engage in goals of care conversations with a trained/certified nurse facilitator who was unknown to them.

The FACE-Rare intervention is consistent with findings from focus groups with parents of children with medical complexities and their health care providers (HCPs) [22]. HCPs and parents expressed the desire that the patient and family be at the center of pACP discussions. HCPs noted the importance of taking time to recognize, understand, and support diversity and individuality between families. Parents also explained that the best pACP conversations were the ones in which they felt involved, respected, and accepted, which is similar to our findings. Parents identified topics that they felt should be included in pACP discussions, which were included in the FACE-Rare model: (1) quality of life, (2) beliefs and values, and (3) hopes and goals. In our study, the parents noted that their child's quality of life was often underestimated by HCPs, thus highlighting the importance of asking parents about their child's quality of life at baseline rather than making inferences based on their clinical status when admitted to the hospital, which is consistent with findings from a focus group with parents of children with medical complexities [22]. The focus groups with parents and HCP also thought a family's values and belief system was foundational to pACP discussions, allowing HCP to better tailor care to each individual family [22], as was accomplished in the FACE-Rare intervention. Focus group parents and HCP also indicated that pACP discussions should include conversations surrounding their hopes and goals for their child because this process provided opportunities to collaboratively work toward and/or reframe hopes and goals [22]. Thus, study findings highlight the importance of incorporating parents' hopes and values for what it means for their child to live well, prior to the completion of an advanced care plan. Understanding a parent's focus on what is most important is possible with the FACE-Rare intervention. This approach may improve a parents' ability to advocate on their child's behalf and assist care team members to provide a person-centered care approach that matches the goals and values, with the needed care and resources as their child's condition changes.

6. Limitations

Research participants were selected to beta test the study protocol and to gain preliminary information on feasibility. Thus, we did not use sampling saturation as a criterion for our sampling strategy. This means that other themes might have emerged if we had continued sampling, which may limit generalizability. The cohort was small and from a single site. A larger pilot trial is ongoing to test the initial efficacy of FACE-Rare with 30 parents of children with ultra-rare diseases who are unable to participate in medical decision making [28].

The sex of the parent may have introduced bias. The primary caregiver in the home may depend on multiple factors, including parental employment; medical insurance; and the size, gender, and weight of the child. Clinically, many fathers have reported discomfort when caring for their female children with rare diseases once their child reach puberty age.

Moreover, information that was not reported is also important. No parents reported service providers' negative responses as a barrier for accessing services or assistance for their children, as has been reported in two small qualitative studies [5,6].

7. Conclusions

This study begins to close a gap in our knowledge [29] of parents' goals of care for their children living with a serious illness who, in aggregate, constitute a significant proportion of pediatric inpatients with life-limiting conditions in tertiary and quaternary pediatric hospitals [30]. Children with rare diseases are part of a heterogeneous group and are often excluded from research [31], thereby creating a health disparities. Collecting qualitative data on patient and family member goals and wishes is a pivotal part of quality care. With information about the goals and wishes of the patients and families being discussed, accurate and appropriate recommendations for palliative and end-of-life care from the care team can be provided. Ongoing research will determine if the FACE-Rare pACP process of decision making for parents [27] adds benefits to clinical care and family well-being [32],

as has been true with the FACE pACP model with adolescents with cancer and HIV and their families [26,27].

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The Needs of Adolescents and Young Adults with Chronic Illness: Results of a Quality Improvement Survey

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Abstract: Adolescent and young adults (AYAs) with chronic illnesses cope with complex issues that require unique psychological support and healthcare services to reduce psychosocial difficulties, improve disease management, and facilitate positive transitions to adult care. Engaging patients and caregivers can help providers understand the specific needs of this population and identify the perceived areas of support. The purpose of this quality improvement initiative is to assess the needs of AYAs with chronic medical conditions at a large government research hospital. Eighty-nine AYA patients (age = 23.5 years; range 13–34) with neurofibromatosis type 1, cancer, primary immunodeficiencies, or sickle cell disease, and a sample of caregivers (n = 37, age = 52 years; range: 41–65), completed an anonymized survey that assessed their preferences for a wide range of informational and service-related needs. The results indicate an overwhelming desire for information about general health and wellbeing and disease-specific medical knowledge. The most endorsed item was the need for more information about an individual's medical condition (72%), which was a primary concern across disease, racial, and gender groups. Demographic and disease-specific needs were also identified. Thus, providing information to AYA patients and caregivers is a critical and largely unmet component of care, which requires the development and implementation of targeted educational and psychosocial interventions.

Keywords: adolescents and young adults; healthcare needs; chronic illness; AYA transition

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1. Introduction

Large numbers of adolescents and young adults (AYAs) live with chronic medical conditions [1]. The vast majority (90%) of AYAs with chronic illness will survive into older adulthood [2,3] and this percentage will continue to increase, given the continued medical advances and improvements in survival rates [4,5]. Unfortunately, relatively less attention has been focused on AYAs with chronic health conditions, compared to children and adults; thus, the needs of patients within this age band may be less well understood and, as a result, less well addressed by the broader healthcare system.

Among the AYAs with medical conditions, the developmental period is marked by unique physical and psychosocial experiences that co-occur with chronic health needs. Under healthy circumstances, there is a normative increase in social and school or work responsibilities, and AYAs begin to differentiate themselves from caregivers and move closer to their peer group [6]. In addition, adolescence and young adulthood are associated with identity development and substantial physical change. Many of these developmental experiences can be impacted by a chronic illness. For example, on a social level, AYAs with chronic health conditions may need to rely on parents/caregivers to help manage disease morbidities, provide financial support, or handle logistical/pragmatic challenges [7,8], which constrains their level of independence. Further, disease morbidities (e.g., pain and disfigurement), adverse treatment side effects, physician visits, and/or inpatient

hospitalizations impede typical social endeavors, such as extracurricular activities, routine socializing, or dating [9,10]. In addition, the developing adolescent brain [11], as well as disease- and treatment-related cognitive impairments, may limit the ability of AYAs to function independently and manage their complex healthcare needs [12]. The disruption caused by chronic health challenges during the AYA period directly impacts developmental processes and creates vulnerability into adulthood [13].

Given the challenges faced by AYAs with chronic illnesses, it is not surprising that research reports lower levels of socioemotional health compared to same-aged individuals without chronic health needs. Poorer social-emotional functioning is evident across AYA populations, including high rates of anxiety and depression in youths with sickle cell disease (SCD) [14] and increased feelings of self-consciousness in youths with lupus [15]. In addition, AYAs with neurofibromatosis type 1 (NF1) have higher rates of emotional and behavioral problems, as well as a diminished quality of life, compared to the AYAs of the general population [16]. Taken together, these examples suggest that AYAs with chronic illness face significant burdens, which make it that much more important that this population receive targeted support during the transitional period.

Current Research on the Unmet Needs of the AYAs with Chronic Illness

There is a clear need to provide tailored support and services to AYAs with chronic health conditions. Unfortunately, designated support and services for this population are often unavailable [17,18]. Unmet healthcare needs among AYAs with chronic medical conditions are associated with reduced quality of life [19] and put them at risk of negative behavioral health outcomes, such as nonadherence to medication, missed medical appointments, and poor health outcomes [20–22]. However, quality of life may be improved both during treatment and after discharge with the addition of specific, tailored informative processes and social services [23]. These services aid the transition from being an AYA who is fully dependent on others for their medical care to an independent adult who manages their own healthcare needs.

Specifically, studies suggest that AYAs want wide-ranging information and guidance from their providers on major life concerns, ranging from brain fog to fertility to finances [19,24]. An equally important unmet need is social support. Studies show that these patients would like to make social connections early on in their care and that many of them report loneliness and disconnection from the AYA community [24,25]. Further, the provision of developmentally appropriate information and activities that enhance social connections within care systems are important needs that remain unmet [26]. Despite the identification of these problems and potential solutions, gaps in AYA services persist.

To best plan for the growing AYA population at our institution, we engaged patients and caregivers in the process to determine the programmatic services that are needed for this age group at the National Institutes of Health through an anonymous survey. Gathering stakeholder input early on is critical for understanding the relevant concerns and will aid in decision-making about the development and implementation of programs and services. Thus, the first aim of this quality assurance study was to examine the needs and services of AYAs with chronic illnesses (i.e., cancer, SCD, NF1, and primary immunodeficiencies) and their caregivers. The secondary aims were to explore the differences between AYAs with different diagnoses as well as among AYAs of different demographic groups, including age, sex, and race. Moreover, this paper aims to highlight the key areas for improving transitional care and services and provides recommendations for those who treat AYAs with chronic illnesses.

2. Materials and Methods

2.1. Survey Development

A quality improvement and needs assessment survey was developed to evaluate the gaps in services for AYA patients (ages 13 to 34 years) and their caregivers (of pediatric and young adult patients) at a large clinical research hospital in the United States. We solicited

expert input from psychologists, social workers, and physicians in the development of the surveys to iteratively generate the domains to assess, determine the response format, and draft the items. The survey spanned topic areas typically encompassed by the construct of health-related quality of life (HRQOL; e.g., physical health, emotional wellbeing, school/work, and social wellbeing), alongside practical healthcare concerns. In addition, the surveys were developed to be brief (approximately 5 min) and were administered via paper and pencil or electronically on an iPad.

The final surveys contained 43 items, and asked patients and caregivers about a broad range of informational needs (i.e., a desire to have more information or knowledge in a specific domain) and service needs (i.e., the desire to have access to specific services of interest). The informational needs section included the following categories: (1) physical/medical health, (2) emotional wellbeing, (3) social and interpersonal wellbeing, (4) school and/or work, (5) general adjustment issues, (6) and practical/legal issues. The service needs section inquired about services of interest, including (1) counseling, (2) recreational services, and (3) social groups or events hosted or organized by the hospital. Slightly different surveys were developed for adolescents versus young adults (e.g., slight wording changes, such as a reference to school *or work* for young adults). Caregivers were asked to rate their own informational and service-related needs as well as their thoughts about the needs of their child. Respondents also were asked to provide basic demographic and medical data (e.g., whole year age, primary medical condition, race, and gender), but no personally identifiable information (PII) was collected. Please see the Supplementary Materials for a copy of the patient and caregiver surveys. For the purposes of this paper, only patient-reported needs and caregiver perception of patient needs are reported.

2.2. Procedures

The survey and methods were sent to the Office of Human Subjects Research Protections (OHSRP) at the National Institutes of Health (NIH) to determine whether the IRB review was necessary. Because the survey was deemed a quality improvement/needs assessment survey and did not collect PII, this project was granted an IRB exemption.

Patients between the ages of 13 and 34 years who attended a visit to the National Institutes of Health (NIH) between 2017 and 2019 and had a diagnosis of a chronic or relapse/refractory cancer, SCD, a primary immunodeficiency, or NF1, and/or their caregivers were eligible to participate in this survey. The NIH is a large clinical research hospital, in which patients participate in natural history studies, clinical trials (mostly phases 1 and II), and brief clinical assessments, among other types of studies. Patients who enroll in research at the NIH, typically maintain a home-based physician/hospital with whom they seek regular clinical care for their health condition.

A convenience sampling method was used for this needs assessment. A member of the clinical staff known to them (e.g., a patient's nurse, social worker, psychologist, and physician) approached the patients and caregivers in the clinic about completing the survey. The staff member provided patients and caregivers with a written description of the project, and verbal consent/assent by the patient and/or caregiver was granted prior to administering the survey. The survey took approximately five minutes to complete and consisted of a list of needs and services that could be endorsed, if it was an area of interest or need (a blank response was coded as a no). Patients and caregivers could be approached separately, so that not all caregivers had a child who participated and vice versa.

2.3. Statistical Methods

All statistical analyses were performed using SPSS version 24. Descriptive statistics were used to examine the demographic and medical characteristics of the sample. In addition, the frequency of positive endorsements (i.e., a "yes" response) to each item on the survey was obtained. Pearson's chi-squared tests were used to examine differences between the groups based on medical condition, demographic variables, including race, gender, and age, and between patients and caregivers. If an omnibus test was significant for medical

condition or race, the data was partitioned [27], so that a series of 2 × 2 chi-squared tests could further evaluate the specific groups that diverged in their item response frequency.

In the context of medical condition, the following post hoc comparisons were made: Cancer by SCD; cancer by NF1; cancer by primary immunodeficiencies; SCD by NF1; SCD by primary immunodeficiencies; and NF1 by primary immunodeficiencies. In the context of racial categories, the following post hoc comparisons were made: Caucasian by Black; Caucasian by Asian; Caucasian by multirace; Black by Asian; Black by multirace; Asian by multirace. Of note: in addition to the Caucasian, Black, Asian and multirace participants, there were three individuals who identified as Native American or Alaskan Native in our sample. A decision was made to exclude this group from racial group comparisons, due to the nonrepresentative nature of such a small subsample. In addition, five individuals did not disclose a race and were also excluded from chi-squared tests involving race. Because the purpose of this project is to ascertain patient needs and inform program development better, we did not correct for multiple post hoc comparisons as would be indicated for hypothesis-driven research.

3. Results

3.1. Descriptive Statistics

In total, 89 patients and 37 caregivers completed the survey. Two individuals who were approached declined to complete the survey; they opted not to provide a specific reason for non-participation. The mean patient age was 23.49 years (SD = 5.9; range 13–34 years), with the overwhelming majority of patient respondents being young adults (≥18 years old; $n = 75$; 84.3%). The majority of patients were male (60.2%) and less than half were Caucasian (41.6%). The primary medical diagnosis of patients surveyed included NF1 (36.9%), cancer (22.6%), SCD (22.5%) and a primary immunodeficiency (16.7%).

Among the caregivers, the majority were female (77.1%) and Caucasian (70.3%). Caregivers ranged in age from 41 to 65 years (M = 52.05, SD = 6.267). Almost half of the caregivers had a child with NF1 (48.6%), followed by a primary immunodeficiency (25.7%), cancer (20%), and then SCD (5.7%). Table 1 shows the demographic characteristics of the patient and caregiver samples.

Table 1. Sociodemographic characteristics of survey respondents.

Variable	Patients M ± SD	Patients *n* (%)	Caregivers M ± SD	Caregivers *n* (%)
Age (years)	23.5 ± 5.9		52.1 ± 6.3	
Gender				
Male		53 (59.6)		8 (21.6)
Female		35 (39.3)		27 (73.0)
Not disclosed		1 (1.1)		2 (5.4)
Race				
White		37 (41.6)		26 (70.3)
Black		27 (30.3)		3 (8.1)
Asian		9 (10.1)		5 (13.5
American Indian or Alaska Native		3 (3.4)		1 (2.7)
Multiracial		8 (9.0)		1 (2.7)
Not disclosed		5 (5.6)		1 (2.7)

3.2. Results from the Total Sample of Patients (All Medical Conditions)

Regarding the informational needs, the patients' top three most endorsed items fell within the general health and wellness category. Specifically, these items included a need for more information about their primary medical condition (71.9%), nutrition and healthy eating (66.7%), as well as physical activity (66.7%) and pain management (66.7%). The three least endorsed items overall included information regarding attention problems (35.7%), keeping and making friends (33.3%), and spiritual and religious wellbeing and coping (23.6%). As far as service and program needs, just under two-thirds of patients

endorsed a desire to connect with others who have a similar health condition via social media (63.10%), although there was much less of a desire for a structured online support group for AYAs with similar health conditions (38.1%). The least endorsed service need overall was teletherapy sessions at home with a therapist at our institution, although there was still a notable proportion of respondents who endorsed this need (33.3%). The item-by-item results of the patient survey are presented in Table 2, which includes the overall sample and a breakdown of responses for each medical condition.

Table 2. A: Informational needs endorsed by AYAs with chronic health conditions. B: Service-related needs endorsed by AYAs with chronic health conditions.

Item	Cancer		NF1		SCD		Autoimmune		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
My health condition	12	63.2	22	71.0	17	85.0	9	64.3	60	71.4
Nutrition/healthy eating	14	73.7	18	58.1	18	90.0	6	42.9	56	66.7
Physical activity and exercise	13	68.4	17	54.8	17	85.0	9	64.3	56	66.7
Pain	12	63.2	19	61.3	18	90.0	7	50.0	56	66.7
Treatment side effects	9	47.4	21	67.7	15	75.0	8	57.1	53	63.1
Stress management	12	63.2	18	58.1	13	65.0	9	64.3	52	61.9
Complementary healthcare	11	57.9	16	51.6	16	80.0	8	57.1	51	60.7
Impact of condition on school or work	13	68.4	13	41.9	15	75.0	10	71.4	51	60.7
Financial assistance	10	66.7	12	48.0	13	65.0	8	66.7	43	59.7
Medical insurance	11	57.9	19	61.3	13	65.0	7	50.0	50	59.5
Sleep difficulties	9	47.4	15	48.4	16	80.0	9	64.3	49	58.3
Eating and/or weight	13	68.4	15	48.4	13	65.0	6	42.9	47	56.0
Uncertainty about the future	12	63.2	13	41.9	14	70.0	8	57.1	47	56.0
Returning to school/work	14	73.7	8	25.8	18	90.0	7	50.0	47	56.0
Transitioning to adult care	11	57.9	17	54.8	11	55.0	8	57.1	47	56.0
Academic support in college	10	66.7	13	52.0	13	65.0	3	25.0	39	54.2
Fertility	12	63.2	14	45.2	12	60.0	7	50.0	45	53.6
Coping with condition/tx	9	47.4	15	48.4	14	70.0	7	50.0	45	53.6
Physical limitations	9	47.4	15	48.4	13	65.0	7	50.0	44	52.4
Jobs/careers	9	47.4	16	51.6	14	70.0	5	35.7	44	52.4
Adjust to life post-treatment	11	57.9	9	29.0	16	80.0	7	50.0	43	51.2
Anxiety/depression	9	47.4	16	51.6	10	50.0	7	50.0	42	50.0
Legal and practical services	12	63.2	12	38.7	10	50.0	6	42.9	40	47.6
Appearance	8	42.1	13	41.9	9	45.0	8	57.1	38	45.2
Dating, sexuality	9	47.4	13	41.9	11	55.0	5	35.7	38	45.2
Communicating w/med team	8	42.1	13	41.9	10	50.0	7	50.0	38	45.2
Difficult conversations	11	57.9	11	35.5	10	50.0	6	42.9	38	45.2
Adjusting to dx/tx	12	63.2	8	25.8	11	55.0	5	35.7	36	42.9
Discussing medical condition	9	47.4	11	35.5	7	35.0	5	35.7	32	38.1
Attaining social support	7	36.8	11	35.5	7	35.0	6	42.9	31	36.9
Learning difficulties	6	31.6	13	41.9	8	40.0	4	28.6	31	36.9
Attention problems	6	31.6	12	38.7	7	35.0	5	35.7	30	35.7
Keeping and making friends	7	36.8	11	35.5	5	25.0	5	35.7	28	33.3
Transitioning to college	2	50.0	1	16.7	0	0.0	1	50.0	4	33.3
Spiritual/religious coping	2	13.3	10	40.0	3	15.0	2	16.7	17	23.6
Connecting with others with a similar health condition on social media	13	68.4	19	61.3	15	75.0	6	42.9	53	63.1
A hang-out space for AYAs	11	57.9	14	45.2	15	75.0	8	57.1	48	57.1
An NIH event where experts would address AYA issues related to condition	11	57.9	16	51.6	13	65.0	6	42.9	46	54.8
Scheduled daytime recreational activities for AYAs	12	63.2	11	35.5	11	55.0	9	64.3	43	51.2
Website with information related to my health condition	10	52.6	13	41.9	13	65.0	6	42.9	42	50.0
Recreational weekend programs with other AYAs with my condition	11	57.9	10	32.3	13	65.0	8	57.1	42	50.0
Willing to make an extra visit to NIH for patient events	7	36.8	16	51.6	10	50.0	7	50.0	40	47.6
Electronic newsletter	9	47.4	13	41.9	12	60.0	5	35.7	39	46.4
Supportive counseling for patient at NIH	11	57.9	11	35.5	10	50.0	4	28.6	36	42.9
In person support group for AYAs with my condition	9	47.4	11	35.5	9	45.0	7	50.0	36	42.9
Supportive counseling for my family at NIH	8	42.1	10	32.3	9	45.0	5	35.7	32	38.1
Online support group for AYAs with my condition	10	52.6	9	29.0	9	45.0	4	28.6	32	38.1
Video chat sessions at home with therapist between visits	5	26.3	9	29.0	11	55.0	3	21.4	28	33.3

Note: the table lists informational needs first, ordered from the most to the least endorsed item, followed by service-related needs, ordered from most to the least endorsed item; abbreviations: tx = treatment; dx = diagnosis; SCD = sickle cell disease; NF1 = neurofibromatosis type 1; AYAs = adolescent and young adults; NIH = national institutes of health.

3.3. Results from the Patient Sample: Between-Group Differences by Medical Condition

When comparing the responses between different medical conditions, the omnibus chi-squared tests indicated significant differences among the respondents' interest in information about (a) nutrition and healthy eating (X^2 (3) = 9.93, $p < 0.05$); (b) adjustment to diagnosis and treatment (X^2 (3) = 8.37, $p < 0.05$); (c) adjustment to life post-treatment

(X^2 (3) = 13.09, $p < 0.01$); and (d) returning to school and/or work (X^2 (3) = 23.46, $p < 0.001$). See Table 3 for results.

Table 3. Significant differences in endorsements among medical condition.

	Percent of Respondents Who Responded "Yes"				
	Cancer (%)	**NF1 (%)**	**SCD (%)**	**PI (%)**	**X^2 Statistic**
Information re: returning to school/work	73.7	25.8	90	50	23.5 **
Information re: adjusting to life post-treatment	57.9	29.0	80	50	13.1 **
Information re: adjusting to diagnosis and treatment	63.2	25.8	55	35.7	8.4 *
Information re: nutrition and healthy eating	73.7	58.1	90	42.9	9.9 *

* $p \leq 0.05$; ** $p \leq 0.01$. Abbreviations: NF1 = neurofibromatosis type 1; SCD = Sickle cell disease; PI = Primary immunodeficiency.

Post hoc partitioning of the data clarified where these differences occurred between the four medical conditions represented in this sample. For simplicity, only significant differences are reported herein. Regarding the desire for information about nutrition and healthy eating, individuals with SCD were significantly more likely to endorse this item than individuals with NF1 (X^2 (1) = 4.90, $p < 0.05$) and primary immunodeficiency (X^2 (1) = 7.36, $p < 0.01$). This same pattern was observed regarding the need for information about how to adjust to life post-treatment, as individuals with SCD were significantly more likely to endorse this need than individuals with NF1 (X^2 (1) = 11.98, $p < 0.02$) and primary immunodeficiencies (X^2 (1) = 5.97, $p < 0.05$). Individuals with SCD and cancer were much more likely to endorse a need for information about adjusting to their illness/treatment, compared to individuals with NF1 (X^2 (1) = 4.52, $p < 0.05$ and X^2 (1) = 5.76, $p < 0.05$, respectively). In addition, the need for more information about returning to school or work post-treatment was more commonly endorsed by individuals with SCD than those with NF1 (X^2 (1) = 16.15, $p < 0.001$) and primary immunodeficiencies (X^2 (1) = 8.67, $p < 0.01$). Individuals with cancer also were more likely to endorse a need for information about returning to school or work relative to those with NF1 (X^2 (1) = 16.54, $p < 0.001$).

3.4. Results from the Patient Sample: Differences by Demographic Characteristics

3.4.1. Patient Differences by Race

When comparing the responses to survey items among racial groups, several differences emerged. There were significant differences between respondents of different races on several items within the general health and wellness category. This section included the patients' interest in learning more about (a) their medical condition (X^2 (3) = 13.479, $p < 0.01$); (b) physical activity (X^2 (3) = 11.32, $p = 0.01$); (c) interventions for sleep (X^2 (3) = X^2 (1) = 9.45, $p < 0.05$); and (d) treatment side effects (X^2 (3) = 8.00, $p < 0.05$). Prior to discussing the post hoc comparisons, it is important to note that individuals with SCD represented 70% of Black respondents in this sample, reflecting a potentially meaningful confound. This finding should be taken into consideration when interpreting differences by race. See Table 4 for results.

Table 4. Significant differences in endorsements among racial groups.

	Percent of Respondents Who Responded "Yes"				
	White (%)	**Black (%)**	**Asian (%)**	**Multirace (%)**	**X^2 Statistic**
Information re: primary medical condition	64.9	92.6	77.8	37.5	15.2 **
Information re: physical activity	46.9	81.5	88.9	87.5	15.1 **
Information about treatment for sleep	43.2	70.4	88.9	75	12.6 *
Information re: treatment side effects	56.8	77.8	88.9	37.5	13.8 *

* $p \leq 0.05$; ** $p \leq 0.01$.

Post hoc partitioning of significant findings indicated that Black respondents reported significantly more interest in learning about their medical condition compared to Caucasian (X^2 (1) = 8.57, $p < 0.005$) and multiracial respondents (X^2 (1) = 12.86, $p < 0.001$). In addition, compared to Caucasian participants, Black and multiracial respondents more commonly endorsed a desire for information about physical activity (X^2 (1) = 9.08, $p < 0.005$ and X^2 (1) = 4.25, $p < 0.05$, respectively) compared with all other races. Regarding an interest in learning about treatment side effects, Asian respondents endorsed this item more frequently than multiracial respondents (X^2 (1) = 4.00, $p < 0.05$), while Black respondents had a greater endorsement rate relative to Caucasian respondents (X^2 (1) = 4.06, $p < 0.05$). Finally, regarding interest in treatments for sleep difficulties, the only difference that emerged suggested greater endorsement by Asian respondents compared to Caucasian respondents (X^2 (1) = 5.09, $p < 0.05$).

There were varying rates of endorsement among races on several other items throughout the needs survey. This included differences in the need for assistance/information regarding returning to school and/or work (X^2 (3) = 14.50, $p < 0.01$), with Black and multiracial participants endorsing this item more frequently than Caucasian participants (X^2 (1) = 11.32, $p < 0.005$ and X^2 (1) = 6.70, $p = 0.01$, respectively). There was also a significant difference in respondents' interest in teletherapy sessions (X^2 (3) = 9.39, $p < 0.05$). Specifically, Black and Asian respondents had greater interest relative to the Caucasian respondents (X^2 (1) = 8.73, $p < 0.005$ and X^2 (1) = 4.10, $p < 0.05$, respectively). Furthermore, there was a significant difference in respondents' interest in an AYA "hang out" space at the hospital (X^2 (3) = 9.78, $p < 0.05$), with Black and multiracial respondents indicating a higher degree of interest (>70% endorsement), than Asian and Caucasian respondents (falling between 33–43%). Finally, there were differences among those needing help coping with uncertainty about the future (X^2 (3) = 8.15, $p < 0.05$). Specifically, Black respondents endorsed this item more frequently than Caucasian respondents (X^2 (1) = 5.12, $p < 0.05$).

3.4.2. Patient Differences by Sex

There were several differences between the needs endorsed by male versus female respondents. Specifically, males endorsed significantly more interest in obtaining help to transition to an adult doctor (68.3%) compared to females (39.4%; X^2 (1) = 6.18, $p < 0.05$). In contrast, females were more likely to endorse an interest in psychosocial therapeutic supports than males. This difference was significant for one-on-one counseling at the hospital (X^2 (1) = 3.87, $p < 0.05$), teletherapy sessions while at home (X^2 (1) = 5.17, $p < 0.05$), and web-based support groups for other AYAs with a similar health condition (X^2 (1) = 6.00, $p < 0.05$). In addition, females more frequently endorsed a desire for an AYA "hang out" space at the hospital compared to males (X^2 (1) = 4.33, $p < 0.05$). See Table 5 for results by gender.

Table 5. Significant differences in endorsements by gender.

	Percent of Respondents Who Responded "Yes"		
	Males (%)	**Females (%)**	**X^2 Statistic**
Information re: transitioning to an adult provider	64.2	42.9	3.9 *
One-on-one counseling at hospital	35.9	57.1	3.9 *
Teletherapy sessions	22.6	45.7	5.2 *
Web-based support group	28.3	54.3	6.0 *
Interest in an AYA hang-out space	49.1	71.4	4.3 *

* $p \leq 0.05$.

3.4.3. Patient Differences between Adolescent and Young Adult Respondents

Adolescent and young adult respondents were generally consistent in their endorsement of needs. The only significant difference pertained to the need for information about dating and love life (X^2 (1) = 4.06 $p < 0.05$), with young adults endorsing this item more

often than adolescents. Of note, these items had somewhat different wording, with the adolescent form referring to an interest in information about sexual identity and relationships and the young adult form referred to an interest in information about sexuality and intimacy. See Table 6 for results pertaining to age differences.

Table 6. Significant differences in endorsements by age.

	Percent of Respondents Who Responded "Yes"		
	Adolescents (%)	**Young Adults (%)**	**X^2 Statistic**
Transitioning to an adult provider	21.4	50.1	4.1 *

* $p \leq 0.05$.

3.5. Caregivers' Perspectives on Patient Needs

When caregivers were asked about their perception of their child's needs, they most frequently endorsed interest in their child receiving more information about treatment side effects (70.3%). This was followed closely by a desire for information about their child's primary medical condition (67.6%), nutrition/healthy eating (67.6%), impact of the diagnosis on their child's school/work (67.6%), and transitioning from a pediatric to adult doctor (67.6%).

Among the 43 items included in both the caregiver and patient questionnaires, there was general consistency in their endorsements, suggesting that they have similar perceptions of the patients' needs. Indeed, there were only three items for which caregivers and patients expressed significant differences. Specifically, caregivers less frequently endorsed that their child would have a need for information about health insurance (X^2 (1) = 5.49, $p < 0.05$) or returning to school/work after treatment (X^2 (1) = 8.91, $p < 0.01$). On the other hand, compared to the patients, caregivers more frequently endorsed that their child would benefit from web-based support groups ($X^2(1) = 6.06$, $p < 0.05$). See Table 7 for results.

Table 7. Significant differences in endorsements between patients and caregivers.

	Percent of Respondents Who Responded "Yes"		
	Patient (%)	**Caregiver (%)**	**X^2 Statistic**
Information re: returning to school/work post-treatment	56.2	27.0	8.9 **
Information about health insurance	60.7	37.8	5.5 *
Interest in web-based support groups	38.2	62.2	6.1 *

* $p \leq 0.05$, ** $p \leq 0.01$.

3.6. Open-Ended Perspectives of Patients and Caregivers

Patients and caregivers had the opportunity to provide open-ended comments at the end of the survey. Among the 19 AYA patients who provided comments, 13 individuals made comments about creating a social space in which they could pursue enjoyable, relaxing activities, and/or connect better with others who have health conditions. For example, one respondent shared that "(I would like) anything social, that's not too overly intrusive . . . an opt-in social environment." Another person explained, "Maybe have teen nights and games for young adults to meet and hang out." Two AYAs reiterated the desire for more information about their health condition, and one person expressed a desire for better communication. Other comments were complimentary in nature.

Caregivers made several additional comments about enhancing social connections among AYAs with health conditions, and also among caregivers themselves. Out of 13 caregiver comments, 6 comments referenced a social space or opportunities for patients and caregivers to relax and connect with others. Four comments were complimentary in nature, and two regarded a need for more information about their child's health condition and how they could best support their child's wellbeing.

4. Discussion

The results of this needs assessment provide new insights into AYAs with chronic health conditions, including NF1, chronic or refractory cancer, primary immunodeficiencies, and SCD participating in clinical research. Overall, the survey suggested that there was an overwhelming need for general health and medical information from the respondents. Indeed, the most commonly endorsed item was the need for information about an individual's primary health condition. This topic remained a significant concern when we examined the endorsement rates by disease groups, racial groups, and male and female sexes, which suggests that its importance cuts across medical and demographic variables.

While it may seem counterintuitive that AYA patients with longstanding health conditions would need more information about their disease, this particular finding is consistent with the extant literature and has been reported. For example, a systematic literature review of adolescent oncology patients suggested there is an unmet need for more information about a range of illness-related issues throughout the disease trajectory, including the illness itself, available medical therapies, and long-term effects of treatment [28]. This need is echoed in the SCD literature, in which adolescent patients with SCD reported a desire for self-management tools that included disease-based education [29].

Notably, 90% of Black respondents expressed a particular interest/need for information about the health condition, which was significantly greater than other racial groups surveyed. This finding is important because the U.S. healthcare system has an unfortunate history of disenfranchising Black and Brown patients [30]. As a healthcare community, it is important to recognize this historical context and make a concerted effort to equip minority patients with the knowledge and information to heed medical recommendations and promote wellbeing. More generally speaking, it is important to maintain awareness that AYA patients with different ethnic and racial background may maintain different healthcare needs. This pattern was observed in the current study and is important to consider when working with patients in different hospital and community settings.

Alongside the need for more information about an individual's health condition, the results suggest a strong need for more information about physical activity and nutrition. These needs are nonspecific to having a chronic health condition, and are common issues raised in the context of primary care more generally. However, it is possible that individuals with rare and chronic health conditions are less likely to receive this information during their visits, because there are numerous other items to address. Further, despite the advantages of multidisciplinary care and efforts to promote a more integrated care system, symptom management has the potential to become siloed when so many providers are involved [31]. This may create a gap in the information communicated about overall wellbeing.

It is important that AYA patients feel they have a solid understanding of their specific health condition and healthy behavior in general. In fact, research suggests that an awareness of physical symptoms, disease risks, and health-promotion behaviors can help patients self-monitor their health and promote wellbeing [32]. In addition, health knowledge underlies compliance with treatments and recommendations made by medical providers [33,34]. Despite the well-known benefits of this information, interventions that promote disease knowledge and physical wellness are not universally integrated into AYA care. Addressing the need for disease knowledge entails relatively simple and cost-effective efforts, including nurse or physician directed education during appointments. It is, however, notable that information must be developmentally appropriate, and easily comprehendible [35]. In other words, information needs to be digestible in order to have an impact.

4.1. Least-Endorsed Items

Surprisingly, the results of the current survey suggested less desire for mental health or psychosocial services by patients. There may be several explanations that account for this finding. In particular, the hospital at which this survey was administered has a national and international catchment of patients. Respondents were asked if they would like to receive mental health services through our institution (in-person or virtually), and it is

possible that these services are better accessed through their local hospital or communities. In fact, we do not know how many respondents already were receiving therapeutic services in their local area. Another possibility is that respondents are simply less interested in individual or family therapy as a traditional service. This result begs the question as to whether behavioral health clinicians should broaden how they think about best serving the chronically ill AYA community. Perhaps, some patients may be in greater need of assistance implementing health behaviors rather than addressing acute mental health conditions.

4.2. Differences by Sex

While there was generally modest interest in psychosocial supports (as explained above), it is notable that more females than males endorsed interest in these types of services. This is consistent with rates of engagement with the mental-health field more generally, in which females are more likely to seek behavioral health support compared to males [36]. In contrast, males expressed a greater need for support as they seek out an adult doctor. Historically, women tend to have higher healthcare utilization than men, so it is possible this finding reflects greater comfort by women in obtaining care or identifying a doctor [37].

4.3. Differences between Caregiver and Patient Respondents

The results of this study indicate strong convergence between caregiver and patient perceptions of need, suggesting that caregivers of individuals with chronic health conditions likely have a solid sense of what their child is seeking. This was further evidenced by convergence in open-ended comments made by caregivers and patients on the survey. Thus, providers would benefit from seeking parental input when trying to assess AYA patient needs. However, there were a few exceptions to these findings, such as parents (compared to AYAs) reporting less need for information about insurance and support to return to school/work, and a greater need for internet support groups for their child.

4.4. Limitations

The results of the current study should be viewed in the context of several limitations. In particular, we were limited by our sample in multiple ways. While the overall sample size was reasonable, it was far more limited when we parsed the sample into smaller groups, such as by racial group, age, or health condition. Comparisons between these subgroups were offered, but they have limited generalizability. In addition, the current sample included limited health conditions, including cancer, NF1, SCD, and a primary immunodeficiency. Thus, results cannot speak to the needs of AYAs with other chronic conditions. Further, the current survey was anonymized, which constrained additional analyses that would deepen our understanding of how patient characteristics relate to specific needs. This includes associations between how a patient's point in the disease trajectory, or treatments, for example, may relate to their needs. These factors should be explored by future research. Finally, this study's findings are limited by the somewhat unique setting in which the information was obtained. Specifically, our institution is typically a secondary site of medical care, as visiting patients have a provider or hospital nearer to their home community. Furthermore, all patients at our institution are enrolled on a clinical research protocol and many are undergoing experimental treatments. Thus, this patient population may reflect a slightly different set of needs than would be observed in a primary healthcare setting. It also bears noting that the current survey was administered prior to the COVID-19 pandemic. Therefore, the needs expressed by respondents in the current survey may be different, had the survey been administered following the onset of the pandemic.

4.5. Future Directions and Conclusions

There are several future directions based on this research. First, it would be beneficial for additional data to be collected pertaining to needs of AYAs with chronic health condi-

tions across healthcare settings to compare the differences between the findings. While the current QI survey was developed to improve services at our institution, it can be easily administered and adapted across settings, which is encouraged. Future research and clinical initiatives also should focus on developing services that can better meet the needs of AYA patients. A particularly feasible target is disseminating information during routine visits. Such information can be delivered through verbal education, written materials, or a combination of approaches, and should be available virtually and in a hard-copy format. Moreover, research that utilizes digital technologies to expand services and address informational needs is particularly compelling, as 91% of AYAs have access to smartphone apps and web-based services [38]. Ultimately, with a more thorough assessment of needs and with the development of supports and services, we can make significant strides in improving the quality of life for vulnerable AYA patients with chronic health conditions.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/children9040500/s1, Survey S1: Young Adult Needs Survey; Survey S2: Adolescent Needs Survey; and Survey S3: Caregiver Needs Survey.

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Institutional Review Board Statement: Ethical review and approval were waived for this study by our institution's committee on human subjects research (review number 17-NCI-00175). The rationale for waiver included the fact that the survey was an anonymous quality improvement needs assessment to inform the development of clinical programs and services for adolescent and young adult (AYA) patients and their caregivers at the National Institutes of Health. The information obtained from the survey also may be used to better generalize to the psychosocial needs of vulnerable AYA populations more broadly (outside of the National Institutes of Health).

Informed Consent Statement: Written patient consent was waived due to the anonymous needs survey being primarily for the purpose of quality improvement of clinical programs and services. However, a consent document was provided in writing to participants prior to completing the surveys; the research team offered to read it aloud to prospective participants. Contact information was provided for the lead investigator and associate investigators. Subjects were not asked to sign a hard copy of the consent.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Psychosocial Difficulties in Preschool-Age Children with Beckwith–Wiedemann Syndrome: An Exploratory Study

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Abstract: Beckwith–Wiedemann syndrome (BWS) is a rare overgrowth disease and is not usually associated with intellectual delay. Living with a chronic illness condition such as BWS, however, might affect emotional-behavioral functioning and psychosocial development. To investigate this issue, parents of 30 children with BWS between 1.5 and 6 years old compiled standardized questionnaires assessing the presence of emotional-behavioral and developmental problems. The group mean scores in each scale of behavioral problems fell within the average range. Nevertheless, 23% of the sample presented scores beyond the risk threshold for social withdrawal. As regards psychomotor development, a lower mean score was reliable in the social domain compared to other developmental scales, and in the gross-motor compared to fine-motor functions. Moreover, scores in the at-risk band were reliable in almost half of the children for social development. Notably, older age was overall associated with higher emotional-behavioral and developmental difficulties, while no other socio-demographic or clinical variables accounted for the scores obtained in the questionnaires. These findings ask for a wider consideration by health and educational professionals of the psychosocial functioning of children with BWS, so as to early detect at-risk conditions and eventually promote adequate interventions.

Keywords: Beckwith–Wiedemann syndrome; emotional-behavioral problems; psychosocial difficulties; psychomotor development; preschool-age children; pediatric chronic illness; rare diseases

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1. Introduction

First described in the 1960s by the parallel work of Bruce Beckwith and Hans Rudolf Wiedemann, Beckwith–Wiedemann syndrome (BWS) is an overgrowth disorder, with an estimated prevalence of 1 in 10,500 newborns [1]. The clinical manifestation is very varied and often includes macroglossia, abdominal wall defects, lateralized overgrowth, enlarged abdominal organs and a heightened risk of developing embryonal tumors. Despite the diagnosis of BWS mainly relying on physician's clinical assessment and a new scoring system that has been proposed [2], more than three out of four cases of BWS can be ascribed to altered expression of imprinted genes in two functionally independent domains of the chromosome 11p15.5. In detail, approximately 60% of BWS patients present altered expression of the growth suppressor gene *CDKN1C*, mostly due to loss of methylation of the *KCNQ1OT1*:transcriptional start site differentially methylated region (DMR) (also known as IC2) on the maternal allele of the centromeric domain. Less frequent causes are known to be a gain in methylation in the *H19/IGF2*:intergenic differentially methylated region (also known as IC1), associated with increased expression in the growth promoter gene *IGF2* on the paternal allele of the telomeric domain and Uniparental Paternal Disomy (UPD) of 11p15.5 [3].

The complex clinical picture and the presence of different (epi)genetic variants have led research to focus on medical and etiopathogenic aspects of the syndrome [4], while

the psychosocial consequences of BWS are not yet fully investigated. The few previous studies documented that risk conditions often presented by children with BWS, such as hypoglycemia and prematurity, could result in behavioral problems and developmental delay [5–7]. More recently, impairments in the areas of emotional-behavioral functioning and social relationships, assessed through a parent-compiled questionnaire, were described in 87 children with BWS [8]. However, the study of Kent and colleagues did not consider any developmental difficulties presented by children with BWS, which could affect their emotional-behavioral and social functioning.

Even though the prognosis is essentially favorable, BWS can be considered as a chronic illness since it is a life-long condition that requires ongoing medical attention [4,9]. Especially in the first years of life, children with BWS are frequently subjected to invasive diagnostic procedures and surgical interventions (e.g., tongue reduction) [10]. As in other chronic pediatric diseases, in BWS, frequent hospitalizations, restrictions in daily activity and concerns about physical appearance might increase the risk for emotional-behavioral difficulties [11] and affect diverse areas of development, such as motor abilities, language acquisition and social adjustment [12,13]. Accordingly, sequelae on psychosocial functioning in the first years of life have been reported for some main features of BWS, namely, macroglossia [14] and abdominal wall defects [15,16]. These findings suggest that, even in absence of a diagnosis of neurodevelopmental disorder, preschool children with BWS may present psychosocial difficulties. Nevertheless, it is still lacking a detailed investigation of emotional-behavioral difficulties and of psychomotor and social development in this population.

Examining these aspects would be particularly important in preschool age. This stage of development represents, indeed, a critical period for identifying possible at-risk conditions that have not yet become structured and eventually programming psychological interventions and supports [17]. Moreover, in this development phase, parents are privileged observers with respect to later periods of growth, so that questionnaires and checklist could be considered as reliable instruments to assess behavioral difficulties and specific areas of child development [18].

In the light of these premises, the current exploratory study investigated the presence of psychosocial difficulties in preschool children with BWS without documented neurological and psychiatric diseases. Parents were asked to fill out two standardized questionnaires assessing emotional-behavioral problems and the developmental level in different domains, from social to motor skills, with the aim to describe the behavioral and developmental profile of BWS in preschool age.

2. Materials and Methods

2.1. Participants

Thirty participants were recruited in collaboration with the Italian Association of Beckwith–Wiedemann Syndrome (AIBWS). Inclusion criteria were: (i) confirmed clinical and/or genetic diagnosis of BWS, (ii) age > 1.5 years and < 6 years and (iii) absence of documented neurological and psychiatric conditions (e.g., epilepsy, autism spectrum disorder). This latter criterion allowed us to verify whether preschool children with BWS presented psychosocial difficulties that were not secondary to the presence of a neurodevelopmental disorders. In total, 7 participants were excluded, corresponding to 19% of the sample. This percentage is in line with recent literature documenting the prevalence of neurodevelopmental disorders in children younger than eight years old in the USA [19].

Recruitment was country-wide, and was conducted in two different time windows (2012–2013, 2016–2017).

2.2. Procedure

The families enrolled in the AIBWS received a letter from the president of the Association informing them of the possibility of participating to the study. All interested families

were then sent an envelope containing: (a) an informed consent form; (b) an ad-hoc information form to collect socio-demographic and clinical variables; and (c) the two questionnaires assessing emotional-behavioral problems and different developmental areas. Parents were asked to sign the informed consent form and fulfill all the documents before sending them back via mail. All procedures of the study were in accordance with the Declaration of Helsinki and were approved by the Ethical Committee of the Scientific Institute, IRCCS E. Medea. Please note that the study was carried out before the COVID-19 pandemic.

2.3. Behavioral and Emotional Problems

Parents filled out the Child Behavior Checklist (CBCL 1.5–5), an internationally adopted, standardized questionnaire designed to assess various types of behavioral and emotional problems in children aged 1.5 to 5 years [18]. The CBCL 1.5–5 provides the following 7 syndrome scales: Emotional Reactivity; Anxiety/Depression; Somatic Complaints; Withdrawal; Sleep Problems; Attention Problems; and Aggressive Behaviors. Raw scores of each scale were summed up and then transformed into T-scores (mean = 50, SD = 10) according to the normative values, so as a higher score indicated higher behavioral problems in that scale. Moreover, the CBCL 1.5–5 provides cutoff scores according to percentile distribution so as to determine children scoring in the borderline and in the clinical range. The term clinical is used here as being synonymous with problematic, thus referring to children who show consistent problems in their behavior, without any psychopathological evaluation of these problems having been made.

2.4. Child's Development

The child's development was assessed using the Child Development Inventory (CDI [20]), a parent-report questionnaire that describes children's abilities from 15 months to 6 years of age. To obtain a profile of the child's development, the items are summed up into the following scales: Social development; Self-help; Gross-motor; Fine-motor; Expressive language; Language comprehension; Letters knowledge; and Numbers knowledge. Raw scores obtained by summing the items of each scale were converted into T-scores according to the mean expected for each age group reported in the original manual. This way, the lower was the T-score, the lower the developmental level was in that scale. According to the normative manual, scores $\leq$1.5 SD and $\leq$2 SD were considered, respectively, as falling within the borderline and the clinical range. Similarly to the CBCL 1.5–5, the term clinical adopted here does not reflect a diagnosis of developmental delay; rather, it helps to identify those children whose development is questionable and who could show less expected age-related competences in each specific area.

2.5. Socio-Economic Status (SES)

SES was coded according to the information provided by caregivers on the basis of Hollingshead's [21] classification for parental occupation. Scores ranging from 70 to 90 correspond to the upper status, while scores ranging from 40 to 65 correspond to the middle status and scores ranging from 10 to 35 correspond to the lower status.

2.6. Statistical Analyses

Preliminarily, descriptive statistics and the percentage of children exceeding the borderline and clinical thresholds were calculated for each scale of the two questionnaires. For the scales in which the number of children exceeding the borderline threshold was >20%, we adopted chi-squared tests among dummy variables of the two questionnaires to verify whether the same individuals had behavioral problems and difficulties in specific developmental domains.

Then, for each scale of the two questionnaires, we ran Spearman's r correlations and Student's t-tests with selected, background continuous variables and categorical factors, respectively. Specifically, to control for socio-demographic variables, we inserted gender, age and SES into analyses. In line with previous literature [1,14,15], we also considered

clinical variables that have been pointed as risk-factors for psychosocial development, namely, prematurity, neonatal hypoglycemia, abdominal wall defects and macroglossia, and the clinical score obtained by each child according to the Consensus statement [2].

For each test, a false-discovery rate analysis (FDR) was conducted to control for multiple testing, thus correcting the accepted *p*-value according to the number of comparisons [22]. Eventually, significant background variables were inserted as covariates into repeated-measure analyses of covariance (ANCOVAs) separately for the two questionnaires, with scale as within-subject variable. Significant interaction effects were further examined with Tukey HSD post-hoc tests. The α value was set at $p < 0.05$ for all statistical tests. Effect sizes for the ANCOVAs were reported as partial Eta squared ($\eta 2p$), adopting conventional cut-offs of $\eta 2p = 0.01$, 0.06 and 0.14 for small, medium and large effect sizes, respectively [23]. Data were reported as mean and standard error of the mean (SEM). All analyses were performed by means of the Statistica software version 8 (Statsoft, Tulsa, OK, USA).

3. Results

3.1. Socio-Demograsphic and Clinical Variables

A description of the socio-demographic and clinical variables of the sample is reported in Table 1.

Table 1. Socio-demographic and clinical variables of the sample.

	Mean (SD)/N (%)	**Notes**
Demographic variables		
Sex (males)	8 (27%)	
Age (years)	3.3 (1.4)	
Familiar variables		
Maternal age (years)	37.7 (4.6)	
Maternal education (years)	13.7 (3.3)	
Paternal age (years)	41.2 (5.8)	
Paternal education (years)	13.3 (3.2)	
Socio-economic status	57 (19)	Corresponding to a medium–high level according to Hollingshead (1975)
Siblings	0.9 (0.7)	
Perinatal variables		
Birth Weight (g)	3427 (643)	
Birth Length (cm)	51 (4)	
Prematurity	13 (43%)	13 moderate-to-late preterm (32 to 37 weeks)
Genetic diagnosis		
Altered expression of *IGF2*	2 (7%)	
Altered expression of *CDKN1C*	21 (70%)	
Paternal Uniparental Disomy	5 (16%)	
Other	2 (7%)	1 altered methylation of both IC1 and IC2, 1 unknown
Main clinical features		
Macroglossia	24 (80%)	
Omphalocele /abdominal wall defects	12 (40%)	
Birthweight/Length > 2 ds above the mean	10 (33%)	
Neonatal hypoglycemia	10 (33%)	
Lateralized overgrowth	13 (43%)	
Tumor onset	1 (3%)	1 hemangioendothelioma
Clinical index according to the Consensus statement (2018)	5.1 (1.8)	

IGF2: Insulin Like Growth Factor 2; *CDKN1C*: Cyclin Dependent Kinase Inhibitor 1C; IC1: Imprinting Center 1; IC2: Imprinting Center 2.

For the CBCL 1.5–5, significant correlations emerged between age and both the Emotional reactivity (r = 0.45, p = 0.012) and Anxiety/Depression scales (r = 0.61, p < 0.001), while all other findings for either continuous or categorical variables were non-significant (all r < |0.39|, all t < 2.65, all $p \geq 0.013$).

In a similar vein, for the CDI, age was significantly correlated with the Social development (r = −0.79, p < 0.001), Self-help (r = −0.45, p = 0.013), Gross-motor (r = −0.45, p = 0.014) and Letters knowledge scales (r = −0.47, p = 0.009). Moreover, a significant association emerged between familial SES and the Numbers knowledge scale (r = 0.53, p = 0.003), while all other correlations and t-test analyses were non-significant after controlling for multiple testing (all r < |0.42|, all t < 2.26, all p > 0.020).

3.2. ANCOVA

For the CBCL 1.5–5, the ANCOVA confirmed the significant effect of the covariate age (F1,28 = 9.98, p < 0.001, η2p = 0.26), indicating that the older the age was, the higher the obtained scores were at the CBCL/1.5–5 (r = 0.51, p = 0.004). All other effects were non-significant (all F < 1.62, all p > 0.144), thus highlighting no differences between the scales (Figure 1).

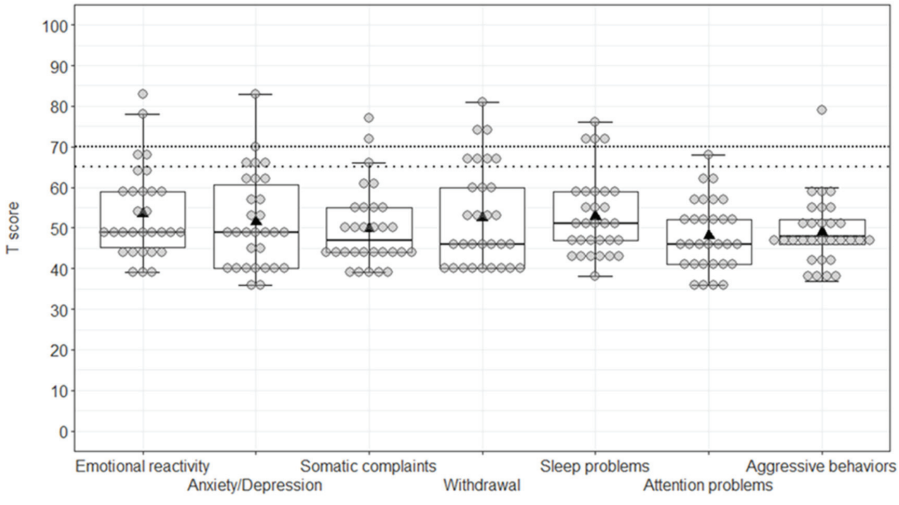

Figure 1. Boxplot of T-scores at the CBCL/1.5–5. Grey circles (●) represent individual scores, black triangles (▲) indicate group mean scores; lines with wide and dense dots show, respectively, the borderline and clinical thresholds.

For the CDI, the ANCOVA confirmed a significant age effect (F1,27 = 17.22, p < 0.001, η2p = 0.39), with a decrease in T-scores in older children across the scales (r = −0.64, p < 0.001). Furthermore, the interaction scale × age was significant (F7,189 = 3.32, p = 0.002, η2p = 0.11). The Tukey HSD post-hoc comparisons indicated lower scores at the Social development scale than at the Fine-motor (p = 0.001) and Language comprehension (p = 0.036) scales. Moreover, lower T-scores were reliable at the Gross-motor compared to the Fine-motor scale (p = 0.026). All other effects were non-significant (all F < 1.191, all p > 0.178) (Figure 2).

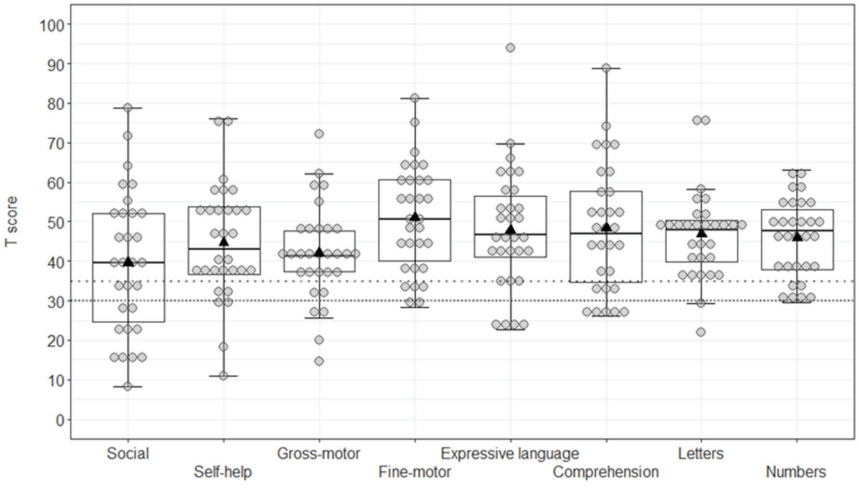

Figure 2. Boxplot of T-scores at the CDI. Grey circles (●) represent individual scores, black triangles (▲) indicate group mean scores; lines with wide and dense dots show, respectively, the borderline and clinical thresholds.

3.3. Associations between the Two Questionnaires

As regards the possible associations between behavioral problems and specific developmental difficulties, the chi-squared tests did not highlight significant results (all chi-squared < 0.72, all $p > 0.398$).

4. Discussion

In the current study, we examined the presence of emotional-behavioral problems and of difficulties in specific developmental domains, from motor to social functioning, in preschool children with BWS through two standardized parent-report questionnaires. The results indicated that overall BWS was not associated with specific behavioral problems, but, at the individual level, almost a quarter of the children in the sample presented scores beyond the borderline threshold for the Withdrawal scale. As concerns specific areas of development, a lower group mean score emerged in the Social development scale compared to others, and almost half of the sample obtained individual scores within the borderline or the clinical range in the social domain. Lower scores also emerged for the Gross-motor compared to the Fine-motor scale. Moreover, in the Gross-motor and Language comprehension scales 23% and 27% of the sample presented scores within the borderline or clinical bands, respectively. Of note, older ages were associated with higher behavioral problems and lower developmental scores across the scales of both the questionnaires, while no other socio-demographic or clinical variables accounted for the scores obtained in the two questionnaires.

Partially in contrast with the study of Kent and colleagues [8], our results regarding the emotional-behavioral problems highlighted neither a group score lower than the expected mean nor significant differences between the scales. This inconsistency might depend on the age range of the samples, since we limited them to preschool children, while Kent and colleagues recruited children from preschool age to adolescence. On the other hand, as also shown by our results, higher behavioral problems could arise as age increases.

Moreover, almost 7% of the children in the study of Kent and colleagues had a diagnosis of autism while, here, the presence of documented neuropsychiatric diagnosis was considered as an exclusion criterion. Nevertheless, when we look at the individual performance, 7 out of 30 children presented problems of social withdrawal. Previous research documented that children with different chronic diseases tend to show less prosocial

behavior and could present emotional problems such as anxiety and depression symptoms [12,24]. Interestingly, here, we also found that increasing age was associated with higher emotional reactivity and anxiety/depression problems. Overall, despite the fact that these results do not highlight a specific behavioral profile, they suggest that, even in the absence of neurodevelopmental disorders, preschool children with BWS could present problems in their emotional experience and in participating in the social context, and these difficulties could increase in older ages.

Regarding the psychomotor and social development, the results highlighted reliable differences between the scales, with developmental difficulties in the social domain, which became more pronounced in older children. Moreover, the 43% of children obtained scores exceeding the borderline threshold for social development, with even 10 out of 30 children scoring within the clinical range. Thus, according to previous findings suggesting that children with chronic illness exhibit difficulties in social interaction [25,26], our study corroborated that, already at preschool age, children with BWS showed reduced interpersonal skills, which could become more pronounced in older children [8].

It is worth noting that out of seven children with withdrawal problems, four had scores in the borderline (N = 1) or clinical (N = 3) ranges for the Social development scale, two were in the borderline (N = 1) or clinical (N = 1) ranges for the Gross-motor scale and one fell in the borderline range for the Language comprehension scale. The analyses, however, indicate that social withdrawal problems were independent from developmental difficulties in the social domain or in other scales. This suggests that despite problems of withdrawal and delays in acquiring age-appropriate social skills potentially affecting the social functioning of children with BWS, it is quite possible that there is not a direct association between these variables. As an example, a child may have adequate social skills but appear as withdrawn and, vice versa, he/she could not show problems of social withdraw despite having fewer social competences compared to peers. As a consequence, our findings highlight that both these aspects are worthy to be monitored by caregivers, clinicians, and educational professionals.

For the CDI, a significant difference was also reliable between gross-motor and fine-motor skills, with lower scores obtained at the former scale. This result might depend by overgrowth conditions typical of the syndrome [1], which would mainly affect gross-motor abilities, such as walking, running or climbing. This discrepancy, however, should be taken into account for screening and assessment in the first years of life, even considering that 7 out of 30 children scored beyond the borderline threshold. Moreover, for the Language comprehension scale, a high percentage (27%) of children were in the borderline (N = 3) or in the clinical range (N = 5). Given the critical importance of comprehension abilities in the preschool period for the general cognitive functioning [27], it would be useful to monitor difficulties in this area during routine pediatric evaluation.

Importantly, increasing age was overall associated with higher behavioral and developmental difficulties. Previous research on children with typical development documented that, across diverse countries and cultures, problems in emotional reactivity, social withdrawn, anxiety and depression increase with age [28]. In a similar vein, a study regarding another pediatric rare disease, that is congenital central hypoventilation syndrome, reported that problems in diverse areas of development, and particularly social functioning, were reliable across different age groups with the exception of children younger than 3 years old [29]. In this light, we would speculate that children with BWS might become more aware of their condition as age increases and also because they spend more time in social contexts outside the family so that they could experience being different from peers [12,24,25]. In line with this speculation, it would be helpful to monitor emotional and psychosocial difficulties of children with BWS when entering at the kindergarten and, later, at school [30].

Notably, no other socio-demographic and clinical variables were associated with emotional-behavioral and developmental problems. This finding suggests that, beyond the presence of risk factors such as prematurity or neonatal hypoglycemia, preschool-age

children with BWS could present psychosocial difficulties, which might depend on their experience of living with a rare disorder that requires complex medical assistance since the first years of life.

The results of this study should be discussed considering several limitations. First, even though BWS is a rare syndrome, the sample size is relatively small and includes a higher number of female than male participants. Preliminary t-tests, however, did not highlight significant differences in both the questionnaires between boys and girls. Moreover, despite the adoption of validated, standardized questionnaires provides reliable results, the lack of an age-matched, control group asks for caution in generalizing our findings. While we controlled for possible effects of background demographic and clinical variables, our sample size prevented us from investigating the role of other familiar conditions and parental psychological variables as well as of each genotype. Since Paternal Uniparental Disomy was reported to be frequently associated with neurodevelopmental problems [3,8], future studies on wider samples should investigate whether specific (epi)genotype-phenotype could be associated with behavioral and developmental problems [31]. Lastly, we decided to include children without neurodevelopmental disorders, a criterion that could have biased our sample. On the other hand, this choice ensured us that the social and emotional-behavioral difficulties reported here were not secondary to other neurological or psychiatric conditions.

Despite these limitations, this study provides first evidence that preschool-age children with BWS could present psychosocial difficulties, sustaining that standardized assessments of these aspects should be included in routine follow-up evaluations, even when there are no previous diagnoses of neurological or psychiatric disorders [10]. This way, it would be possible to detect children that require rehabilitative/educational interventions and psychological support early before possible emotional-behavioral disorders become structured [17]. An early psychological assessment would also have potential beneficial outcomes for the national health system, as it would reduce the costs associated with long-term consequences of neglected emotional-behavioral problems [11]. In sum, even if further research on BWS is required, this study would be a first step for a further consideration of the psychosocial sequelae associated with this rare syndrome.

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Gender Differences in Caring for Children with Genetic or Rare Diseases: A Mixed-Methods Study

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Abstract: As a factor in parenting stress, gender differences in caring for children with genetic or rare diseases warrant research attention; therefore, this study explored gender differences in parenting stress, health outcomes, and illness perceptions among caregivers of pediatric genetic or rare disease populations to improve the understanding of such gender differences. Applying a concurrent triangulation mixed-methods design, we conducted a questionnaire survey to assess study measures for 100 family caregivers (42 men and 58 women), which included a free-text response item to probe caregivers' subjective perceptions of the children's illness. The gender differences hypothesis was tested with statistics and the qualitative data about illness perception was analyzed by directed content analysis. Most female caregivers served as the primary caregivers and provided more caregiving, while they experienced significantly increased levels of parenting stress and depressive symptoms compared with male caregivers. Female caregivers perceived the conditions of their children's diseases to be highly symptomatic, with negative consequences and requiring disease control. By contrast, male caregivers had stronger perceptions regarding the negative effects of the disease on the children's quality of life. The gender discrepancy in viewpoints of illness perception sequence may contribute to female caregivers' higher levels of stress and depressive symptoms than males.

Keywords: family caregivers; gender differences; genetic or rare diseases; health outcomes; illness perception; parenting stress

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1. Introduction

Genetic diseases are a group of disorders caused by complete or partial abnormal change in DNA sequences, one or multiple gene mutations, a combination of gene mutations and environmental factors, or chromosomal damage [1]. Rare diseases, by contrast, are characterized by their infrequent occurrence and are differently defined across countries (e.g., as diseases with a prevalence of less than 1 in 200,000 in the United States; of 5 in 10,000 in European countries; and of 1 in 10,000 in Taiwan) [2–4]. Most rare diseases are genetic disorders [5]. Because of the inheritability of genetic and rare diseases, these disorders, such as congenital hypothyroidism and congenital adrenal hyperplasia, may present in an individual prenatally or after birth, and can be detected through prenatal genetic examination or newborn screening with appropriate medical care [6–8]. However, some cases of genetic or rare diseases may have gradual onset, delayed diagnosis, receive no effective treatment, or entail chronically comorbid conditions, which can lead to delayed development, intellectual disability, and maladaptive emotional or behavioral responses or can become life threatening. This can affect the quality of life of the children with such

diseases and their families [9–11]. Studies have indicated that family caregivers who serve as the primary caregivers face higher medical care burdens and are often psychosocially or financially affected by this role [12,13]. However, such caregivers generally receive little information or support from health-care providers [14]. Family caregivers also experience emotional burdens, such as feelings of isolation or illness-related distress [15,16], and perceive themselves to be stigmatized in academic, medical, community, and family settings [17].

However, few studies have investigated how gender influences caregiving for children with genetic or rare diseases. According to traditional gender roles, women are socially and morally expected to serve as primary informal care providers for family members with illnesses [18], and consequently face higher levels of caregiving burdens and psychological distress [19]. A quantitative study revealed that such differences in gender expectations are present when caring for children with rare diseases, with mothers being reported to experience higher levels of parenting stress and distress than fathers [20]. Another quantitative study found that the quality of life of mothers was significantly lower than that of fathers after a child with a disability obtained a genetic diagnosis [9]. Another qualitative interview study revealed that, although both parents' lives were influenced by their child's diagnosis to a similar degree, cultural expectations for gender roles led to some caregiving tasks being viewed as gender specific [21]. For example, fathers reportedly became more focused on their jobs and financial matters, whereas mothers often left or changed their jobs to focus on caring for their child's everyday needs and to maintain their family relationships.

Although studies have reported gender differences with respect to parenting stress and caregiving tasks, how gender affects illness perception is unknown. Illness perception involves an individual's knowledge and beliefs about symptoms, illnesses, medical conditions, and health systems [22]. It also involves individuals' subjective understanding or lay beliefs regarding illness and health, which are entrenched in the self and in sociocultural systems. Leventhal, Brissette, and Leventhal proposed that lay people's thoughts on the threat of an illness could be organized into five dimensions: identity, timeline, causes, consequences, and cure and control [23]. According to Leventhal's common-sense model (CSM) of self-regulation, each of an individual's cognitive representations guides their selection of coping behaviors for controlling an illness, which in turn can determine their health or emotional outcomes [24]. Because illness occurs within the family, every component of the self-regulation process can affect family members [25]. For example, perceptions of the severity of the consequences and the chronicity of a child's disease were reported to be associated with parental depressive symptoms [26] and caregiver burdens [27]. In addition, discrepancies in illness perceptions among family members were reported, with one study indicating that mothers focused more on the negative aspects of their children's chronic illnesses than fathers did [28].

This study explored gender differences in parenting stress, health outcomes, and illness perceptions among family caregivers of children with genetic or rare diseases. Using a concurrent triangulation mixed-methods design [29,30], this study converged both quantitative and qualitative data to enable a holistic evaluation of the gender differences in caregiving. A questionnaire survey was designed to assess caregiving tasks, parenting stress, and health outcomes according to Lazarus's view on stress [31]. In addition, a free-text response item was included to inquire about family caregivers' perceptions of their child's illness situation according to Leventhal's CSM [23,24]. This study hypothesized that male and female family caregivers would differ significantly with respect to caregiving tasks, parenting stress, and health outcomes. In addition, this study explored the illness perceptions of family caregivers and how gender discrepancy in illness perception may explain the phenomenon of gender differences.

2. Materials and Methods

2.1. Participants

Participation in this study was open to the family caregivers of children affected by genetic or rare diseases who attended a regularly scheduled outpatient genetic counseling clinic of a medical center in eastern Taiwan. Family caregivers whose level of Chinese was insufficient to complete a questionnaire survey were excluded. Recruitment announcement was implemented by the first author, a senior attending pediatrician at the clinic, and lasted for one year. A total of 297 attendants diagnosed with 84 types of genetic or rare diseases visited the genetic counseling clinic during the study period. The family caregivers of 99 patients were contacted. Informed consents were finally obtained from 100 family caregivers of 77 patients, of which 50 family caregivers are couples. Each participant was assisted by the third author, a genetic counselor, to ensure the questionnaires were completed after the clinical encounter.

As indicated in Table 1, the 100 family caregivers (42 men and 58 women) were on average 43.4 years old (standard deviation (*SD*) = 11.6), mostly senior high school educated (47%), married (84%), and had served as caregivers for an average of 8.7 years (*SD* = 5.8). Significant gender differences were identified with respect to participants' occupations (χ^2 [4] = 32.48, $p < 0.01$, Cramer's $V = 0.57$) and their familial relationships with their children (χ^2 [3] = 100.00, $p < 0.01$, Cramer's $V = 1.00$). For the male caregivers, 90.5% were employed. For the female caregivers, 50.0% were employed and 41.4% were housewives. In addition, 95.2% of male caregivers were biological fathers and 86.2% of female caregivers were biological mothers.

Table 1. Gender comparisons of family caregivers on demographics and measure variables.

Variables	Total (*N* = 100)	Males (*n* = 42)	Females (*n* = 58)	*t* or $\chi 2$ [1]	Cohen's *d* or Cramer's *V*
Age (y) (mean ± *SD*)	43.4 ± 11.6	44.9 ± 11.0	42.4 ± 12.2	1.09	
Education, *n* (%)				3.95	
No school enrollment	2 (2.0)	0 (0.0)	2 (3.4)		
Elementary school	7 (7.0)	3 (7.1)	4 (6.9)		
Junior high school	14 (14.0)	6 (14.3)	8 (13.8)		
Senior high school	47 (47.0)	22 (52.2)	25 (43.1)		
Undergraduate	29 (29.0)	10 (23.8)	19 (32.8)		
Graduate	1 (1.0)	1 (2.4)	0 (0.0)		
Marital status, *n* (%)				2.97	
Married	84 (84.0)	37 (88.1)	47 (81.0)		
Partnered	1 (1.0)	1 (1.0)	0 (0.0)		
Single	15 (15.0)	4 (9.5)	11 (20.3)		
Occupation, *n* (%)				32.48 **	0.57
Employee	67 (67.0)	38 (90.5)	29 (50.0)		
House husband/Housewife	24 (24.0)	0 (0.0)	24 (41.4)		
Unemployed	4 (4.0)	0 (9.5)	4 (6.9)		
Part-time worker	4 (4.0)	4 (0.0)	0 (0.0)		
Student	1 (1.0)	0 (0.0)	1 (1.7)		
Familial relationship with children, *n* (%)				100.00 **	1.00
Parents	90 (90.0)	40 (95.2)	50 (86.2)		
Grandparents	10 (10.0)	2 (4.8)	8 (13.8)		
Years in caregiver role (y) (mean ± *SD*)	8.7 ± 5.8	8.7 ± 5.6	8.8 ± 6.0	−0.15	
Hours of care in per day (h) (mean ± *SD*)	10.2 ± 8.7	7.0 ± 6.9	12.5 ± 9.1	−3.33 **	−0.67
No. of caregiving tasks per day (mean ± *SD*)	4.0 ± 2.5	3.2 ± 2.3	4.6 ± 2.5	−2.92 **	−0.59
PIP Total– Frequency (mean ± *SD*)	86.5 ± 28.6	75.8 ± 23.4	94.2 ± 30.0	−3.34 **	−0.68
Communication	17.2 ± 5.7	14.9 ± 4.5	18.8 ± 6.0	−3.53 **	−0.71
Emotional distress	32.3 ± 11.3	28.5 ± 9.6	35.1 ± 11.7	−3.00 **	−0.61
Medical care	17.7 ± 6.7	15.3 ± 5.6	19.5 ± 7.0	−3.21 **	−0.65
Role constraints	19.4 ± 7.0	17.2 ± 5.6	20.9 ± 7.6	−2.72 **	−0.55

Table 1. *Cont.*

Variables	Total (N = 100)	Males (n = 42)	Females (n = 58)	t or $\chi 2$ [1]	Cohen's d or Cramer's V
PIP Total–Difficulty (mean ± *SD*)	71.12 ± 24.7	63.8 ± 18.1	76.4 ± 27.4	−2.60 *	−0.53
Communication	14.1 ± 5.1	12.6 ± 3.6	15.3 ± 5.7	−2.72 **	−0.55
Emotional distress	30.0 ± 10.2	25.0 ± 8.0	30.1 ± 11.1	−2.57 *	−0.52
Medical care	12.6 ± 4.8	11.4 ± 3.6	13.0 ± 5.4	−1.69	
Role constraints	16.7 ± 6.5	14.9 ± 4.9	18.0 ± 7.2	−2.43 *	−0.49
Psychological health					
SWLS	20.7 ± 6.2	21.8 ± 5.9	20.0 ± 6.3	1.50	
CES-D (short form)	7.8 ± 6.2	5.4 ± 4.6	9.5 ± 6.7	−3.44 **	−0.70
Recent suffering from illness, *n* (%)				0.09	
No	82 (82.0)	47 (81.0)	35 (83.3)		
Yes	18 (18.0)	11 (19.0)	7 (16.7)		

[1] t or $\chi 2$ denotes the differences of demographics and measure variables between male and female caregivers. p-values are for 2-tailed tests. * $p < 0.05$ ** $p < 0.01$

As presented in Table 2, the 77 children (49 men and 28 women) that the caregivers were caring for were, on average, 9.9 years old (*SD* = 5.9) and had received a diagnosis (rare diseases, n = 33; genetic diseases, n = 44) an average of 8.4 years prior (*SD* = 5.6). Few patients demonstrated high heterogeneity in their diagnoses (16 rare disease types and 16 genetic disease types). These diseases were widely categorized into 10 disorders (e.g., congenital metabolic disorders, brain/nervous system disorders, kidney and urinary system disorders, skin disorders, muscle disorders, bone and cartilage disorders, endocrine disorders, congenital malformation syndromes, chromosomal abnormalities, and other unclassified or unknown causes) according to the ICD-10-CM code.

Table 2. Demographic and disease profile of children.

Characteristics of Children (N = 77)			
Age (y) (mean ± *SD*)		9.9 ± 5.9	
Years after diagnosed (y) (mean ± *SD*)		8.4 ± 5.6	
Male/female (*n*)		49/28	
Children's disease conditions			
Rare Diseases, *N (%)*	33 (43.0)	Genetic Diseases, *N (%)*	44 (57.0)
Diagnosis	*n*	Diagnosis	*n*
Glycogen Storage Disease Type II	1	VACTERL Syndrome	1
Robinow Syndrome	1	Hemifacial Microsomia	1
Tuberous Sclerosis Complex	1	Protein S Deficiency	1
Mucopolysaccharidoses type IIIB	1	Sever Intellectual Disability	1
Mucolipidosis type II	1	Intellectual Disability, R/O Mitochondrial Disease	1
3-Hydroxy-3-Methyl-Glutaric Acidemia	2	R/O Neonatal Intrahepatic Cholestasis caused by Citrin Deficiency	2
Lowe Syndrome	2	Congenital Adrenal Hyperplasia	2
Hereditary Epidermolysis Bullosa	2	Hereditary Blistering Disorder	2
Homozygous Familial Hypercholesterolemia	2	Multiple Disabilities	2
Crouzon Syndrome	2	Chromosomal Abnormality	2
Williams Syndrome	2	Marfan Syndrome	2
Maple Syrup Urine Disease	2	Turner Syndrome	3
Duchenne Muscular Dystrophy	2	Noonan Syndrome	4
WAGR Syndrome	3	Down Syndrome	9
Rubinstein-Taybi Syndrome	4	Congenital Hypothyroidism	10
Prader-Willi Syndrome	5	Congenital Hypothyroidism comorbid with Growth Hormone Deficiency	1

2.2. Design and Procedures

A concurrent triangulation mixed-methods design was used [29,30]. Quantitative and qualitative data were collected at the same time in a questionnaire survey, but were analyzed and presented separately. The study related the qualitative results to the quantitative findings through a discussion to find the overall interpretation of gender differences in caring. The study protocol was approved by the institutional review board of Buddhist Tzu Chi General Hospital (IRB103-127-B).

2.3. Materials

Quantitative data. Two open questions were used to evaluate caregivers' caregiving experiences, namely "How many average hours of care do you provide each day?" and "How many disease-related caregiving tasks do you perform each day (for example, taking the child to the doctor, administering medicine, providing the child with physical exercise, cleaning phlegm, and feeding)?". Caregivers' parenting stress was evaluated by the Pediatric Inventory for Parents (PIP), which is a 42-item tool for evaluating the frequency and difficulty of caring events for children with serious illnesses over the preceding week, with items in four domains (communication, medical care, emotional functioning, and role constraints) that are scored using a 5-point scale [32]. The PIP demonstrated strong internal consistency (α = 0.80–0.96) and construct validity among parents of children with cancer [32] and is a commonly used assessment of parenting stress among caregivers of children with chronic illness [33].

Caregivers' physical health was evaluated with a yes–no question: "Have you experienced any serious diseases in the past 2 years?". Caregivers' mental health was evaluated by two measures. The Center for Epidemiological Studies Depression Scale Short Form (CES-D Short Form) is a 10-item revised version of the CES-D, a widely used measure to assess depressive symptoms occurring over the preceding week by a 4-point scale in the general population [34]. The CES-D Short Form showed satisfactory internal consistency (α = 0.78–0.87) and construct validity [35]. The Satisfaction with Life Scale (SWLS) is a 5-item tool to assess, using a 7-point scale, individuals' global cognitive judgments of their life satisfaction [36]. The SWLS demonstrated a single factor, and high internal consistency is appropriated for a wide range of groups [37].

Qualitative data. According to Leventhal's CSM [23,24], an illness representation is guided by current experience with the illness. A free-text response question "What are your illness-related concerns for your child?" was designed to probe the illness perceptions of caregivers in caring their children.

2.4. Data Analysis

Quantitative data were analyzed using descriptive statistics to define the caregivers' demographics, caregiving experiences, and measurement tool variables. In addition, an independent t test with Cohen's d for continuous variables and a chi-square test with Cramer's V for categorical variables were used to analyze gender differences and effect sizes. The differences between the groups were considered significant if p was smaller than 0.01 or 0.05 (two-tailed). All data were analyzed using SPSS Statistics 20.0 (IBM, Armonk, NY, USA).

Content analysis is a qualitative research technique used to extract desired and specific information from a body of qualitative materials (usually written or transcribed verbal) through the systematical classification procedure of coding and identifying themes or patterns by coders or raters [38]. In addition, qualitative information may be transformed into quantitative information, such as category frequencies or ratings for differentiating experiences or perspectives between individuals or groups [39].

In the present study, the qualitative data were analyzed using a directed content analysis to explore gender discrepancy in the illness perceptions of family caregivers. Directed content analysis is one of the content analysis approaches for which analysis starts with a theory or relevant research findings as guidance for initial coding category [40]. The

coding strategies of this study were as follows. First, the male and female text responses were separately coded, and the first and corresponding authors read the text responses and highlighted all instances indicating children's illness-related concerns (e.g., unable to walk or sit, poor learning ability, and negative impressions from others), determined based on the authors' impressions. Second, all instances were compared and divided into named topics according to their similarities and differences (e.g., physical development, learning, and stigma). The frequencies of the instances of each topic were separately counted. Finally, the topics and related instances were identified and categorized into the following five dimensions of cognitive illness perception: (1) identity—the symptoms attributed to the illness; (2) timeline—expected duration of the illness; (3) causes—the origin of the illness; (4) consequences—the overall evaluation of the seriousness and impacts of the illness in daily life; and (5) cure and control—the extent to which treatment could cure or control the illness [23]. Discrepancies in the coding were discussed until a consensus was reached.

3. Results

3.1. Quantitative Results

As presented in Table 1, significant gender differences with medium effect sizes were identified for hours of care per day (t (98) = −3.33, $p < 0.01$, $d = -0.67$), the number of caregiving tasks performed per day (t (98) = −2.92, $p < 0.01$, $d = -0.59$), levels of parenting stress, cognitively appraised through PIP–total frequency (t (98) = −3.34, $p < 0.01$, $d = -0.68$) and PIP–total difficulty (t (98) = −2.60, $p < 0.05$, $d = -0.53$), and depressive symptoms (t (98) = −3.34, $p < 0.01$, $d = -0.70$). No significant gender differences were observed in life satisfaction and physical health. Female caregivers provided more hours of care and performed more caregiving tasks per day (mean = 12.5 and 4.6, respectively) than male caregivers (mean = 7.0 and 3.2, respectively), and experienced more parenting stress and depression (mean = 94.2 and 76.4, respectively) than male caregivers (mean = 75.8 and 63.8, respectively).

3.2. Qualitative Results

Of the 100 participants, two female and six male caregivers indicated no illness-related concerns about their children. However, 92 participants (36 men and 56 women) provided responses with 142 instances of illness-related concerns (men n = 51, women n = 91; Table 3). All instances were grouped into 15 topics that were further categorized into three dimensions of cognitive illness perception: identity (N = 64); consequences (N = 58); and control (N = 20).

3.2.1. Identity

As presented in Table 3, identity-related cognitive illness perception was most frequently identified by caregivers. The caregiver responses included 64 instances of identity (men n = 18, women n = 46), which were organized into five topics that were used to represent the main symptoms of the diseases the caregivers' children experienced: emotional and behavioral problems, physical development, language and communication, eating and weight, and intelligence.

Identity was the most frequently perceived dimension among female caregivers (n = 46). Female caregivers described the emotional and behavioral problems of their children as manifesting in various ways (e.g., stubbornness, bad temper, dependence, no patience, irritability, always crying when sick, hyperactivity, sleeplessness, running around and too strong to control, and adolescent emotional instability). Although both male and female caregivers were concerned about delays in their children's physical and language and communication development (e.g., not tall, unable to walk, unable to speak, and unclear speech), the female caregivers provided more detailed descriptions of the developmental problems (e.g., walking on tiptoes, unequal leg length, osteoporosis, abnormal articulation, and stubbornness). Female caregivers also reported more problems regarding eating (e.g.,

picky when eating, and overeating) and intellectual deficiencies (e.g., poor memory and no concept of danger or right or wrong).

Table 3. Frequencies and percentages of reported instances of each topic and three dimensions of illness perception provided by 92 family caregivers.

Dimension/Topics		**Male, *n* (%)**	**Female, *n* (%)**	**Total, *N* (%)**
Identity	Instances	18	46	64
Emotion/behavior	• Stubbornness, bad temper • No patience, irritability, always crying, dependent, emotional instability • Hyperactivity, running around and too strong to control, disobedient, not sleeping at night, Internet addiction	4 (22.2)	14 (30.4)	18 (28.1)
Physical development	• Short stature, delayed physical development, thin, little subcutaneous fat • Unable to walk or sit, slow movement, walking on tiptoes • Scoliosis, osteoporosis	5 (27.8)	11 (23.9)	16 (25.0)
Language/ communication	• No language, slurred speech, impaired articulation • Poorly verbalizing their needs, not responding, stubbornness, poor communication skills • Delayed linguistic and cognitive development	6 (33.3)	7 (15.2)	13 (20.3)
Eating/weight	• Overweight, underweight, poor appetite • Poor appetite, picky eating, overeating, enjoyment of eating, choking easily • Dietary problems	3 (16.7)	8 (17.4)	11 (17.2)
Intellect	• Intellectual disability • Poor memory, no concept of danger or left or wrong	0 (00.0)	6 (13.0)	6 (9.4)
Consequences		25	33	58
Good health	• Health, physical health, poor physical healthy, physical illness • Physical and mental growth	6 (24.0)	4 (12.1)	10 (17.2)
Illness and medical cares	• Often ill and requiring clinic visits or hospitalization, experiencing sudden illness, life is threatened when ill • Concern regarding accidents when going out, difficulty sleeping due to wearing medical respirator • Long-term medicine use, experiencing side effects	6 (24.0)	5 (15.2)	6 (10.3)
Learning	• Education, study, and learning problems • Insufficient or poor learning ability, unable to keep up with classmates, requiring special education or postponed enrollment for a year	5 (20.0)	6 (18.2)	11 (19.0)

Table 3. *Cont.*

Dimension/Topics		Male, *n* (%)	Female, *n* (%)	Total, *N* (%)
Relationships	• Peer relationships, poor peer relationships, no opposite-sex friends, friends are a negative influence • Few friends due to differences in appearance and a bad temper, self-consciousness • Verbally or physically bullying peers, being bullied by peers • Reject or defense by classmates and teachers	2 (8.0)	9 (27.3)	11 (19.0)
Adaptation	• Maladaptation to a new school or city • Differences in appearance or caring problems after attending school, growing up and handling social perceptions • Failed engagement with society, interaction with negative members of society	3 (12.0)	3 (9.1)	6 (10.3)
Employment	• Future employment, lack of internship opportunities, early independence and employment, adaptation to employment	2 (8.0)	4 (12.1)	6 (10.3)
Stigma	• Negative perceptions or impressions from others • Being misunderstood due to behavioral problems of hitting people or scratching and touching things	1 (4.0)	2 (6.1)	3 (5.2)
Control		8	12	20
Children's control	• No ability to self-care, have an independent life, or handle menstruation • Noncompliance in taking medicine or receiving injections	5 (62.5)	4 (33.3)	9 (45.0)
Long-term care	• Follow-up medical treatments and education • Caring problems or placement after parents grow old	2 (25.0)	3 (25.0)	5 (25.0)
Caregivers' control	• Difficulty in life due to caring for three children, unemployment, seeking financial subsidies for low-income households, and seeking early interventions • Lack of control in feeding, second-hand smoke from the husband's family members, mother discovering the child was left at home unattended when she returned to give the child their medicine	1 (12.5)	5 (41.7)	6 (30.0)
Total instances, *N*		51	91	142

3.2.2. Consequences

As presented in Table 3, the caregiver responses included 58 instances (men $n = 25$, women $n = 33$) of consequence-related cognitive illness perception, which were organized into seven topics that were used to represent how the diseases affected the caregivers' children's lives: good health, illness and medical care, learning, relationships, adaptation, employment, and stigmas.

Consequences was the most frequently perceived dimension among male caregivers (n = 25). Male caregivers more likely to perceive the diseases as negatively affecting their children's good health (e.g., health, physical health, physical unhealthiness, physical illness, and normal physical and mental development) and show concern about the illness-related consequences and medical care for their children (e.g., life being threatened when ill, experiencing sleeping difficulties from medical respirators, potential accidents when going out, and experiencing side effects).

In comparison, the female caregivers provided more details regarding their children's difficulties in forming relationships with their peers (e.g., few friends due to differences in appearance and bad temper, rejection by or wariness from classmates and teachers, verbally or physically bullying peers, or being bullied by peers), and learning problems in school (e.g., educational and learning problems, insufficient learning ability, and requiring postponed enrollment for a year).

3.2.3. Control

As presented in Table 3, the caregiver responses included 20 instances (men n = 8, women n = 12) of control-related cognitive illness perception. Both types of caregivers indicated that their children had no ability to self-care (e.g., handling menstruation, taking medicine, or self-administering injections) or to live an independent life (N = 9). The caregivers further expressed concerns regarding the children's follow-up medical treatments, education, and long-term care (e.g., child's placement after the parents grow old) (N = 5).

Female caregivers reported more concerns regarding their control as caregivers (n = 5), including their economic burdens (e.g., unemployment, obtaining financial subsidies for low-income households, and early interventions) and daily care problems (e.g., feeding, second-hand smoke from the husband's family members, the mother discovering the child was left unattended at home when she returned to administer the child's medicine).

4. Discussion

This study applied a triangulation mixed-methods design to investigate the gender differences in caretakers caring for children with genetic or rare diseases. The 100 participants (42 men and 58 women, average 43.4 years old, and 84% married) of this study served as family caregivers, having provided care for 77 total children (average 9.9 years old) for an average of 8.7 years. Analysis of the quantitative data revealed significant gender differences in daily caregiving hours and performance of caregiving tasks, parenting stress, and depressive symptoms. These gender differences were clinically significant, with medium effect sizes. As reported in other studies [20,41,42], female caregivers performed more daily care tasks, were more likely to be exposed to parenting stress from communication, medical caregiving, emotional functioning, and role constraints, and were more likely to have recently experienced depressive symptoms. This study also revealed a clear gender-influenced difference in the division of labor in the family, with 90.5% of male caregivers being employed and 50.0% and 41.4% of female caregivers being employed or housewives, respectively. This suggests that women are more likely to adopt the role of stay-at-home parents when their child experiences a chronic medical condition according to traditional gender role expectations in Taiwanese families. It is possible that female caregivers could be what has been termed "lone parents". Lone parents are those who feel alone when it comes to caring for their child with cancer, regardless of marital/partnership status. In previous published data, lone parents were found to have significantly greater distress. They also reported greater difficulty in meeting the needs of their child with cancer and their other children, and less financial or emotional support than non-lone parents [43,44].

Analysis of the qualitative data revealed that 92 family caregivers had provided responses detailing 142 instances of illness-related concerns regarding their children. Content analysis according to the CSM revealed that both male and female caregivers perceived the same dimensions of their children's illnesses (i.e., identity, consequence, and control). This indicates that the family caregivers perceived their children's illnesses to have led to

various physical and psychological symptoms, negative impacts on several aspects of the children's lives, and illness control problems when reflecting on the course of the children's diseases. This finding was partially congruent with those regarding parental illness perceptions reported in other studies [26,27,45]. The family caregivers of children with genetic or rare diseases perceive the negative consequences of their children's diseases and their problems with control similarly to how parents of children with mental illnesses do. The caregivers of children with such diseases believed the diseases affected many aspects of their children's lives, leading to problems regarding the child's good health, illness and medical care, learning problems, problems regarding peer relationships, stigmatization, and likely problems in future adaptability and employability. The caregivers also indicated that their children had no ability to self-care or to achieve independence, and would rely on lifetime support from caregivers, educational institutions, medical institutions, and long-term care facilities. In this study, we discovered that family caregivers reported the most concern in the identity dimension, with their concerns mostly involving the five main symptoms their children experienced: emotional and behavioral problems, delayed physical development, language and communication problems, intellectual development problems, and eating and weight problems. This may be because perceived dimensions of an illness can differ with the type of disease. Most genetic or rare diseases caused by gene or chromosome mutations affect the brain and nervous (e.g., tuberous sclerosis complex and Rett syndrome), musculoskeletal (e.g., Duchenne muscular dystrophy, mucolipidosis, VACTERL syndrome, and Down syndrome), respiratory (e.g., Rubinstein–Taybi syndrome), and digestive systems (e.g., maple syrup urine disease) [2,4]. Caregivers perceived that multiple body and organ dysfunctions significantly impaired their children's physical and mental development. This finding is in line with those of other studies [9–11].

The quantitative results revealed gender differences in caregiving, parenting stress, and depressive symptoms, and the qualitative results revealed a gender discrepancy in viewpoints about the sequence of three dimensions of cognitive illness perceptions. Female caregivers were more concerned about symptoms than about negative consequences and control, whereas male caregivers were more concerned about negative consequences than about symptoms and control. This suggests that, in female caregivers, perceptions of their children's illnesses as being highly symptomatic or having a strong illness identity were negatively associated with parenting stress and depressive symptoms, according to Leventhal's CSM of self-regulation [24]. A possible explanation for this is gendered caregiving influencing the perceived degree of the child's symptoms. The literature has indicated that mothers of children with rare diseases usually serve as primary caregivers and perform intensive and time-consuming physician-prescribed treatments and home care tasks [46,47]. Mothers are also, generally, the first to recognize symptoms of a disease in children by comparing the child's behaviors with their caring experiences with other children [48]. However, mothers also often lack information regarding the disease, medical services, and symptom-management strategies [14]. Another explanation may be that the negative affective responses of female caregivers potentially intensify their perceptions of symptoms. Studies have indicated that fathers of children with rare diseases were less emotionally affected by and more accepting of their children's diseases [47]. By contrast, most mothers had more illness-related distress, including feelings of guilt, worry, sorrow, and anger, long-term uncertainty, and fewer emotional resources [15].

These findings suggest that the psychosocial conditions of female caregivers of children with genetic or rare diseases should be addressed. Psychosocial support should be offered that assists female caregivers in exploring the identity of their children's diseases, develops their illness perceptions through medical information, offers effective caring and rehabilitation strategies, and teaches caregivers emotional regulation techniques to control their illness-related distress. The female caregivers' spouses should be invited to consider the gendered discrepancies in caregiving and illness perception related to parenting stress to balance the load of parenting tasks.

The limitations of this study were related to the data collection methods. First, the generalization of the present study results should be approached with caution because of the limited sample size (N = 100) recruited from an outpatient genetic counseling center of a medical center in eastern Taiwan. The results regarding the gender segregation of labor in Taiwanese families and gender differences in parenting stress and illness perception might be representative, but cannot be representative of all genetic or rare diseases. The characteristics of rare and genetic diseases with quite low incidence have low prevalence, and are highly heterogeneous. Each disease with different clinical presentations manifests different problems encountered by patients and their caregivers. Secondly, this study applied a free-text response item (What are your illness-related concerns for your child?) to probe caregivers' illness perceptions regarding their children's illnesses. Because only a few text responses were obtained, the quantitative content analysis regarding gender discrepancies of illness perceptions and the understanding of caregivers' representations for their children's illnesses may have been limited.

Future research may further investigate potential associations between gender discrepancies regarding illness perception and parenting stress and psychological adjustment by administering a questionnaire in larger samples. The illness perception questionnaire is recommended as being specifically applicable to pediatric genetic or rare disease populations [49]. Open or semi-structured interviews guided by Leventhal's CSM of self-regulation may provide qualitative information regarding gender discrepancies of caregivers' illness perceptions. Future research should also investigate how family caregivers perceive parenting their ill child, and whether an association exists between the perception of lone parenting and illness perception in Taiwanese families.

5. Conclusions

The findings of this study support the existence of gender differences in caregiving, parenting stress, and depressive symptoms in family caregivers of children with genetic or rare diseases. In addition, a gender discrepancy in viewpoints about the sequence of three dimensions of cognitive illness perception was found. Identity may be the key domain of illness perception, leading female caregivers to experience higher levels of parenting stress and depression than male caregivers.

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Article

Using Communication Tools to Explore Young Siblings' Experiences of Having a Brother or Sister with Pediatric Palliative Care Needs

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Abstract: Siblings of children with palliative care needs often suffer feelings of being neglected, and their needs for information and involvement are frequently unmet. This study aims to explore the experiences and feelings of siblings of children with palliative care needs, and to determine what is important to them. Nine siblings, aged 6–14 years, were interviewed using four different communication tools: See-Hear-Do pictures, including the empty body as a separate element, Bear cards, and words originating from previous sibling research. Data were analyzed using conventional content analysis. Five categories emerged concerning aspects that the siblings described about their situation and things that they found important: being part of a special family; school—a place for leisure, friends, and learning; relentless feelings of guilt and self-blame; losses and separations; and awareness of death—not if, but when. Siblings of children with rare diseases expressed an awareness that their brother or sister would die, although still felt they were part of a special, happy family. Siblings of children with palliative care needs due to an accident described relentless feelings of self-blame and guilt. The needs of siblings may vary depending on the condition that resulted in the ill sibling's palliative care needs.

Keywords: siblings; bereavement; palliative care; communication; emotions

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1. Introduction

Living with severe illness in the family is known to be stressful for all family members, and being a sibling living in the shadow of a severely ill brother or sister is no exception. Previous research has found that these siblings differ significantly from their peers in the general population, both socially and in terms of their quality of life [1]. Much of the sibling research has been performed in a pediatric oncology context, while the perspectives of those living with a brother or sister with another disease or disability are relatively unexplored. In a review of experiences among siblings with a chronically ill brother or sister, only 6 of 28 studies were based on siblings of a brother or sister with an illness other than cancer. It was found that siblings experienced negative psychological and emotional symptoms and post-traumatic stress, and that these symptoms interfered with their school functioning [2]. Problems in school have also been reported by Malkolm and co-workers, who studied siblings of children with rare life-limiting conditions and found that bullying was a problem they experienced. Two of the eight siblings interviewed reported that they had been teased by peers in school because of their ill brother's or sister's condition, and

that teachers or other adults had not intervened. This may reflect a social attitude towards disabilities in society [3].

Winger, Kvarme, Løyland, Kristiansen, Helseth, and Ravn [4] examined families' experiences of pediatric palliative home care; in 3 of the 23 articles reviewed the sibling's voice was heard while in others it was their parents, mainly the mothers, who gave reports. It was found that families wanted respite care in order to be able to maintain a normal life. The authors stressed the need to include siblings' perspectives in future studies. Family communication and family cohesion are known protective factors for psychosocial distress in families who have a child with severe illness or who has died [5,6]. Conversely, poor communication and lack of family cohesion are known risk factors for long-term psychosocial distress [7,8]. Jaaniste and co-workers recently published a paper focusing on parent–sibling communication. Thirty families with a severely ill child participated; 28 mothers, 2 fathers, and 46 siblings were studied as dyads and close to half of the siblings never or rarely initiated a conversation about their brother's or sister's illness or death [9]. Lack of information about the brother's or sister's prognosis can lead to siblings being absent at the time of death and can result in later regrets and ineffective grieving [7,10]. Siblings' grief has been found to take considerable time. It has been reported that even two to nine years after the loss, most siblings report unfinished grief [11]. Cancer-bereaved siblings also describe lower self-esteem and maturity as compared with non-bereaved peers. A negative impact on schooling has also been reported among bereaved siblings together with poor adult socioeconomic outcomes [12]. Even higher mortality rates have been noted [13].

Little is known about the situations of siblings of a brother or sister with palliative care needs for a severe illness other than cancer. The aim of this study was, therefore, to use communication tools to explore their experiences and feelings, and further understand what is important to them in their situation. The study results may help healthcare professionals and families tailor the support given to siblings of children with palliative care needs and act accordingly.

2. Materials and Methods

2.1. Design and Population

This interview study involved siblings of children in need of round-the-clock palliative care services. Each participant took part in an individual semi-structured interview where they were asked to describe their experiences and feelings by using various communication tools. Inclusion criteria were that the siblings were non-bereaved, could speak Swedish, were aged 5–18 years, and had a brother or sister who was receiving or had received respite care at Sweden's hospice for children and young people for a diagnosis other than cancer. The siblings were identified by the sibling supporter at the hospice who then informed the researcher so that they could contact the parents to invite the sibling to participate. Both parents and siblings received age-adapted written information about the aim of the study and the structure of the interviews. Nine siblings were willing to participate in interviews, which were conducted in their homes or at the researchers' workplace during April to November 2019 (Table 1).

Table 1. Siblings included in the study.

Number	Age of the Sibling (Years)	Sex of the Sibling	The Brother's or Sister's Illness/Disability
1	10	Female	Rare disease
2	6	Female	Brain injury due to trauma
3	8	Female	Brain injury due to trauma
4	10	Female	Brain injury due to trauma
5	14	Female	Rare disease
6	14	Male	Rare disease
7	8	Female	Rare disease
8	7	Male	Rare disease
9	14	Female	Rare disease

Written informed consent was obtained from the parents if the sibling was younger than 15 years, which was the case for all the siblings involved in this study. The study was conducted in accordance with the guidelines of the Declaration of Helsinki and approved by the Regional Ethical Review Board, Dnr. 1091-17, 19 April 2018.

2.2. Data Collection

The first and last authors conducted the interviews with the children. The interviews followed a guide that included four communication tools in order to build a dialogue about the siblings' experiences and life situation. Four user-friendly, non-computer-based tools were used to ensure suitable options for siblings of all ages. The See-Hear-Do pictures developed for and often used in Swedish pediatric oncology were the first choice. In order to capture the emotional aspects more fully, Bear cards were used, along with 27 words often used in research to describe siblings' situations. The blank body from the See-Hear-Do pictures was used so that siblings could draw and describe certain aspects of their situation. The siblings were asked to think about what it is like to be a sibling of a child with palliative care needs and what is important for them in their own life. Follow-up questions were asked throughout the interviews using the different communication tools so we could deepen our understanding, for example, "would you like to tell us more about these pictures/cards/words"?

The following communication tools were used in the following order:

1. Each sibling selected an unlimited number of pictures from a selection of See-Hear-Do pictures [14]; these are part of a pedagogical teaching tool for children with cancer. The pictures illustrate illness-related subjects, treatment, and the daily environment around the child (Figure 1). The siblings were asked to choose pictures to describe what they value in their life. These pictures have been developed by healthcare professionals in pediatric oncology in Sweden and have been used for many years when talking to siblings in that context.

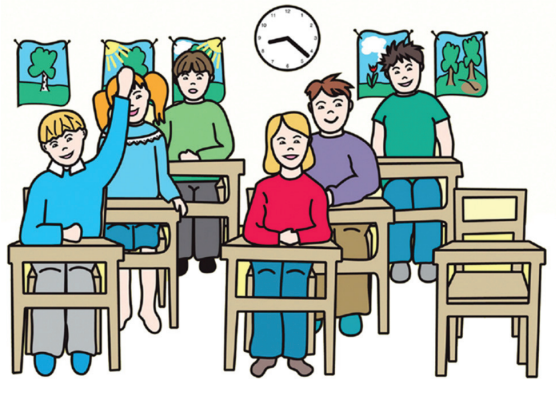

Figure 1. An illustration from among the See-Hear-Do pictures [14].

2. The siblings selected an unlimited number of images from the Bear cards. This tool was developed in Australia and consists of cards illustrating different emotions, e.g., anger, sadness, happiness, etc. [15] (Figure 2). The Bear cards were used to describe the siblings' feelings about being a sibling of a child with palliative care needs or about any special event in their life. They were asked to choose images that either mirrored how they usually feel or help them talk about a particular moment; this was up to the sibling.

Figure 2. An example of a Bear card [15].

3. In the next step, from a range of words the siblings were asked to choose the words that described their experiences of being a sibling of a brother or sister with palliative care needs. The number of words they could choose was not fixed and the siblings were asked to talk more about the words chosen. The range of words presented was derived from previous research about siblings and their experiences of living with an ill brother or sister [16–18].
4. Lastly, the siblings were asked to draw and describe how they usually feel using a blank body outline (Figure 3).

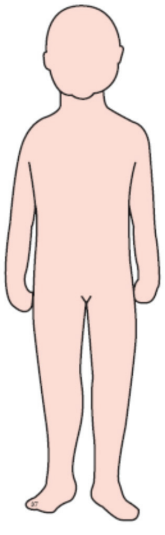

Figure 3. The blank body outline [14].

After this, we asked if there was anything else that the siblings wanted to tell us.

All interviews were audio-recorded and transcribed verbatim. The interviews each took around 30 min (16–48 min) and were most often conducted with the sibling on their own. One or both parents were present at two interviews; in one case this was the choice of the sibling and in the other of the parent.

2.3. Data Analysis

Data were analyzed using conventional content analysis in accordance with Hsieh and Shannon [19]. Conventional content analysis is a method often used when there is a shortage of theories and literature concerning the studied phenomenon. Analysis began with a naïve reading of the transcribed interviews by all authors to gain a sense of the entirety of the data. Thereafter, meaning units were selected and sorted into codes based on similarities and differences in areas of special meaning that emerged from the different tools used in the sibling's stories (first and last author). This work was data-driven rather than based on preconceptions and was conducted by the two authors independently. Thereafter, the codes were grouped into categories (first and last author) based on similarities in content. Examples of codes included the importance of school, friends, family, pets, medication, care, caring, daily life, feelings (good and bad), fear of change, relations, and normality. Initially, seven categories were formed: 1. school, leisure time and friends; 2. family life, including pets; 3. awareness of sibling's death—when rather than if; 4. connectedness to many feelings and thoughts; 5. knowledge about brother's or sister's disease; 6. not being seen and feeling unacknowledged; and 7. losing part of oneself and one's life. However, after discussions with all investigators, consensus decisions were made to rearrange some of the codes and to collapse two of the categories based on their connection and relationship; these were "5. Knowledge about brother's or sister's disease" and "6. Not being seen and feeling unacknowledged". Many of the codes that had been placed in these two categories were then merged into either a category describing being part of a special family or a category describing school as a place for learning and friends. Ultimately, this resulted in five categories.

3. Results

Participating siblings, aged 6 to 14 years, all belonged to families with a child with palliative care needs due to a rare disease or sequelae of a trauma. Two sibling pairs participated, each pair belonging to a different family. All families were nuclear families and the ill children had been in need of palliative care for a year or more. The five categories were: being part of a special family; school—a place for leisure, friends, and learning; relentless feelings of guilt and self-blame; losses and separations; and awareness of death—not if, but when.

3.1. Being Part of a Special Family

Family, including grandparents and sometimes pets, meant a lot to all the siblings. They described their mother, father, brothers, and sisters with love. Some of the siblings who had a brother or sister with a rare disease mentioned that they were part of a happy family. Their particular circumstance had added another dimension to their life and the siblings reported perceiving themselves as having a positive attitude or feeling towards life—more so than their peers. This positive attitude was grounded in their family and usually passed on from their mother. The siblings often described themselves as happy, joyful, and funny. Almost all siblings reported being eager to learn, both in general and also more specifically about philosophical views on life. One of the siblings told us that they wanted to learn more about their ill sibling's illness. This child had never seen their ill sibling healthy.

Grandparents played a big role in the siblings' lives, since they felt that their grandparents always saw and acknowledged them. A feeling of being invisible was expressed by several of the siblings, most often related to situations at home.

All siblings described themselves as having a broad spectrum of feelings and emotions, ranging from anger to joy and happiness. They reported that they could express their feelings openly, both at home and with friends. Anger was often related to events happening within the family and directed towards their parents or healthy brothers or sisters. No sibling expressed any anger towards their ill brother or sister.

"And then, I don't get angry very often at home, but when I do, I get very angry and annoyed too."

"Sometimes you can be annoyed with . . . or kind of irritated with your parents or your friends or when something is unfair."

The siblings mentioned medication as something that was essential for their ill brother or sister. They hoped for new, better drugs for them, especially if the ill sibling had a progressive disease. Siblings said that having a severely ill brother or sister made their family special. This was described in a positive way—it had given them a different perspective on life and meant that they found life precious. This was often stated in particular by siblings of children with rare diseases.

"That, like that . . . . yeah, but that we are maybe not a normal family, that . . . because not all families are alike, but there are some that are a bit more unusual."

"Yeah, I think that I can be, actually, because it is a . . . like, it's my everyday life, but at the same time, it's a much harder everyday life for me, and then you should be . . . and then you learn, you quickly learn to be happy and satisfied with what you have."

"Well, our entire family is made up of happy, positive people."

3.2. School—A Place for Leisure, Friends, and Learning

The siblings highlighted the value of school, both as a place for learning but also for leisure and friends. They emphasized the importance of education and several siblings had ambitious goals for their future working life, such as becoming an author, a teacher, or a physician. Siblings also mentioned that their parents helped and supported them in their schoolwork. School gave them a break from illness and time with friends. Friends helped to ease their sadness, as it could be shared with them. One sibling mentioned that they were comforted by hugs from friends, and how much they liked being hugged when they were sad. At school, some siblings had not revealed that they had a severely ill brother or sister, which made them feel ordinary. One sibling, who had recently changed school, said that they longed for the fact that they had a brother or sister with a severe illness to be revealed so that they could be themself. Not being known as "the one" with a severely ill brother/sister could feel awkward. This illustrates the value of being a "special" sibling, as well as losing part of oneself (see first quote below).

"When they knew, it felt good."

"Because I've always dreamed of becoming a writer, so I've started writing stories and that kind of thing a lot in school. And I . . . and always when we get . . . and I . . . think I'm good at writing because every time there is a test in writing, I always have . . . I've always got everything right."

"I see a child and then I kind of see a school and then I think that school is quite important, because you learn things then, yeah, you grow up and then you become something, or yeah, you start working, and then it's kind of good that you have an education."

3.3. Relentless Feelings of Guilt and Self-Blame

Feelings of guilt and self-blame were described by siblings of children who had palliative care needs as the result of an accident. These siblings described in detail what had happened to their brother or sister and their role in it. One sibling was themself physically affected for a long time. An effect of feeling guilt and self-blame was crying, although not always out loud—described as a silent cry on the inside, without anyone else knowing.

"You always feel a bit of guilt about what happened, but that's just life. Instead of just waiting, you have to . . . instead of just thinking that 'What were you doing? Why didn't you do that?' or 'Why didn't you realize that someone was missing?' or 'Why, why, why?' you think in your head, but if I think like that all the time . . . I mean, nothing happens. You can never change it back, so it's better to just leave it be."

"Yes, I don't feel like . . . I don't have the same feeling all the time, so . . . I'll draw onehalf of the body happy and the other half sad Figure 4."

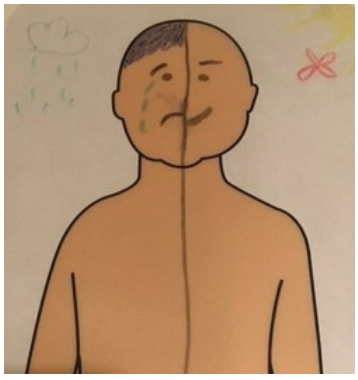

Figure 4. Relentless Feelings of Guilt and Self-Blame.

3.4. Losses and Separations

The siblings talked about losses and separations; the loss of the healthy brother or sister they once had, separation from friends and family, and the death of loved ones are all included in the category of losses and separations. Loss is so much more than just death. For example, losing the opportunity to be the one who can teach a brother or sister and be their role model was described as a great loss by some of the siblings. They referred to this as losing a part of themselves, a loss of normality. In the past, they could play with their brother or sister—now they could not. Separation, both direct and indirect, was also mentioned. One sibling expressed concern about his/her mother and father divorcing, though most losses were related to friends and friendships. Some children had lost friends because of their new circumstances of having a brother or sister with a severe illness; their families could not travel as much as they used to or live abroad. This was particularly true for siblings of children who had been injured in accidents and now had palliative care needs. The siblings experienced a loss of normality, but found a new normal.

Siblings of children affected by accidents also expressed an awareness that things that change family dynamics can happen at any time. One sibling expressed a wish for normality, without illness, and that they wanted to live "a normal life." Access to "24/7 support" at home was vital for the ill child, the sibling, and the family as a whole; when such support was suddenly withdrawn it changed life for the family once again.

"So, in one way you lose your regular life. But now this has become my regular life, so in one way I haven't lost it. They've taken away our support, so we can't do things."

"No, when we were little or . . . I was three when he was born, so I remember that he . . . we could sit and play ball and stuff before he . . . like lost everything, so he could sit and so."

"Yeah, like talking to him and so. You can't really do that now, because you don't know if he hears or understands. Yeah, and then to have someone to play with and so. That would have been fun too."

3.5. Awareness of Death—Not If, but When

Death was described as natural, although thinking about it made the siblings sad. Siblings of children with rare diseases told us that their brother or sister would die soon. Some said it should have happened already. This topic came naturally to the siblings, and it was not a matter of whether the brother or sister would die, but when. One sibling opened our meeting by saying: *"Yeah, I've been thinking a lot about what will happen when X has died,*

will we be happy again? Will we ever be able to laugh? Yeah, I've been thinking a lot about it." Siblings of children with palliative care needs due to an accident did not mention death. Their worries were connected to living with uncertainty—that anything could happen at any time, which could change life entirely.

> *"You don't really know what is going to happen either. Yeah, maybe a bit helpless, because there is no real antidote or anything like that yet. I don't know, I think there's research being done on this, but they've not come up with that much. So it will be difficult to help X, but it may be possible to help others. So it's like that, a bit helpless."*

> *"I don't know, but I think I learned a lot from my mum, because in the beginning when I was younger I didn't really understand that my big sister was ill. But then I've lived with the fact that she's become more and more ill and just from that I think I've learned a lot, but then mum and dad have talked to me a lot about it and then I've also learned a lot. I think that's also why I'm a positive person."*

4. Discussion

Using the four different communication tools, siblings presented stories about what is important in their lives when living with a brother or sister with palliative care needs. Observations from this study are novel. To our knowledge, this is the first study to report that siblings of children with rare diseases expect the death of their brother or sister while at the same time reporting that they are part of a happy, special family. These siblings felt that they viewed life as more precious than their peers. In contrast, siblings of children with palliative care needs due to accidents described relentless feelings of self-blame and guilt. Our observations were limited due to the number of siblings participating, but their narratives differed depending on the cause of the ill brother's or sister's palliative care needs. Overall, the siblings described having active lives, with friends and activities, but had an internal sense of insecurity, knowing that life could change at any time. This reflects the human ability to adjust to certain situations—in this case as a young sibling and part of a larger system, the family.

The siblings were aware that their brother or sister could die at any time, especially if the brother or sister had a rare disease. This seemed not to be age-dependent among the siblings we spoke with, who were 6–14 years of age. Younger children may understand the permanence of death without truly realizing that it is forever, something that older children are more likely to comprehend [20]. Our findings are in line with those of Gaab and co-workers who, based on interviews with bereaved siblings whose brother or sister had palliative care needs before dying, reported that death is a companion to these siblings. Most of them wanted to be informed about the imminent death, to be able to be involved. This is something that we have also seen in our previous work among siblings of children with cancer, although death had not been talked about in this way [10]. It may be that, because cancer is often curable, there is more hope among those affected than for many siblings of children with rare diseases or sequelae of trauma, where the hopes of cure or improvement are limited. The study by Gaab, Owens, and MacLeod [21] was not able to identify the difference that we observed in the current study. Jaaniste and co-workers recently reported that siblings never or rarely talk about a severely ill brother's or sister's illness or death [9]. Not surprisingly, siblings' satisfaction with family communication was significantly associated with family cohesion.

The impact of the severe illness on the family was considerable; however, the siblings stated that they were part of happy families. This happiness and positive view of life was particularly emphasized by those whose brother or sister had a rare disease. Siblings of children who had suffered an accident did not express such joy or happiness. They spoke instead about uncertainty and living with the knowledge that everything could change in an instant. Losses and separation were also mentioned more often by these siblings. This could be in reference to personal losses or losses for the entire family that implicitly affected the sibling's life. Most of the losses were not related to death; the siblings instead referred to the loss of friends or the normal life they once had. Much of the above, i.e., the

impact of illness on the family, uncertainty, losses, and separations, has been reported by parents, but it is rare to hear this from young siblings [22].

The difference in the experiences and feelings described by this small sample of siblings in relation to the cause of their brother's or sisters' palliative care needs was novel. We have not previously encountered this in either clinical work or research. The rapid change from a normal life to a life with constant uncertainty may explain the feelings and concerns expressed by siblings of a child with palliative care needs due to trauma. Living with such uncertainty and self-blame at a young age may have a long-term impact on their development and wellbeing. Further knowledge is needed to find ways for healthcare professionals and social systems to support these children and help them cope with such feelings.

The healthcare and social systems around the ill child and family should not be taken for granted. All these families had been given the chance to receive respite care at the hospice. Respite care has been shown to be of value for the whole family [4,23]. However, the siblings in our study did not talk much about the "good side" of it. Instead, they emphasized that rapid changes in the healthcare services provided could impact the whole family in a negative way. The family, as a system, is vulnerable to changes [24].

Communication tools are used worldwide in pediatric cancer care to help affected children find ways to express themselves and have their voice heard [14,25–27]. This led us to believe that siblings of a brother or sister with palliative care needs due to other causes than cancer might also benefit from using communication tools to express their experiences and feelings. A strength in this study was the use of four different tools in the conversations, since some siblings preferred letters and words rather than pictures and vice versa. We believe the variety of tools helped the siblings, some as young as six years old, express what was important to them.

A limitation of this study was the small and homogeneous sample of only Swedish-speaking siblings, and that the participants were mostly girls. Given the small sample and the wide age range (6–14 years), it is not possible to study to what extent additional factors, such as age, gender, deaths within the family, bullying, coping style, and health status, may impact the siblings' daily lives. Nor can our findings relating to the brother's or sister's cause of palliative care needs, i.e., being part of a special happy family or being aware of one's brother or sister's imminent death, be explained. Larger studies need to be performed to confirm such findings. Some might also consider the use of a selection of communication tools that lack a theory to be a limitation, although the tools that were used have their origin in both clinical work and research. In addition, conventional content analysis was used to explore the siblings' narratives because of the lack of theory, as is recommended. The presence of parents during two of the interviews could be viewed as both a strength and a limitation. A parent's presence can be a source of security but may also hinder children in being able to express themselves [28]. In one case, the parent's presence helped the child feel secure and able to talk freely; the sibling in this case was a seven-year-old boy. Although he did not thank his parent verbally, his body language indicated that his parent's presence made him feel secure. In the other case, the sibling was a 14-year-old girl, and, in contrast, the parent exploited the conversation, and it became obvious that parent and daughter viewed things differently.

In this study, we noted that siblings living with children with rare diseases seemed to have internalized thoughts that their brother or sister would die. Further, they felt that they belonged to a special and happy family. Siblings of children with palliative care needs due to an accident expressed relentless feelings of self-blame and guilt. Communication tools, such as those used in this study, may be useful for healthcare professionals to initiate communication and further understand and support each sibling's needs. Healthcare professionals may also introduce some of the tools to parents and teach them how to use them, for example Bear cards, since they may help open up family communication and give siblings a voice for the undisclosed feelings they carry, thereby reducing the risk for poor long-term health outcomes for siblings.

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children

MDPI

Article

Documentation of Psychosocial Distress and Its Antecedents in Children with Rare or Life-Limiting Chronic Conditions

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Abstract: Children with rare or life-limiting chronic conditions and their families are at high risk of psychosocial distress. However, despite its impact on patient and family health and functioning, psychosocial distress and its antecedents may not routinely be captured in medical records. The purpose of this study was to characterize current medical record documentation practices around psychosocial distress among children with rare or life-limiting chronic conditions and their families. Medical records for patients with rare or life-limiting chronic conditions (n = 60) followed by a pediatric complex care program were reviewed. Study team members extracted both structured data elements (e.g., diagnoses, demographic information) and note narratives from the most recent visit with a clinician in the program. Psychosocial topics were analyzed using a mixed quantitative (i.e., frequency counts of topics) and qualitative approach. Topics related to psychosocial distress that were documented in notes included child and parent emotional problems, parent social support, sibling emotional or physical problems, family structure (e.g., whether parents were together), and financial concerns. However, 35% of notes lacked any mention of psychosocial concerns. Although examples of psychosocial concerns were included in some notes, none were present in over one-third of this sample. For both patients with rare or life-limiting chronic conditions and their caregivers, more active elicitation and standard documentation of psychosocial concerns may improve the ability of healthcare providers to identify and intervene on psychosocial concerns and their risk factors.

Keywords: psychosocial distress; pediatrics; complex chronic conditions; rare diseases

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1. Introduction

Over the past 50 years, medical advances have reduced overall childhood morbidity and mortality, allowing children with rare or life-limiting chronic conditions to survive and live longer [1–5]. Rare or life-limiting chronic conditions include congenital abnormalities, neurodegenerative diseases, metabolic disorders, the sequelae of extreme prematurity, and other disorders that are often serious and incurable but may be managed with ongoing medical intervention and lifestyle adaptations. However, despite medical and scientific advances, children with rare or life-limiting chronic conditions and their families often face significant challenges to their quality of life as a result of long-term, complex medical regimens [6], frequent provider visits and hospitalizations [3], gaps in care coordination [7,8],

and functional limitations that are typically severe and may include reliance on technology [8–10]. In addition to healthcare and functional challenges, children with rare or life-limiting chronic conditions are at increased risk for the development of social [11], behavioral [12], and emotional problems [13], which, if not detected and treated, can impact the child's adherence to medical recommendations [14,15], exacerbate physical illness [16], and increase healthcare utilization [17].

The struggles associated with childhood rare or life-limiting chronic conditions are not limited to the patients themselves, as parents and other family caregivers assume tremendous responsibility on behalf of these vulnerable patients [18]. Collectively, caregivers for children with rare or life-limiting chronic conditions have been described as a "shadow" healthcare system for children with medical complexity [19], forced to act as patient advocates, care coordinators, and home health aides, resulting in significant disruptions to work and family function [20–22]. Not surprisingly, parents of children with rare or life-limiting chronic conditions frequently report problems related to mood [23], physical function [24], marital discord [25], social isolation [22], and unmet needs [26]. Many parents of children with rare or life-limiting chronic conditions experience disruption to their careers [27,28] and financial insecurity [29]. High levels of parental distress, in turn, can impact a child's medication adherence [30] and has been linked to greater emotional distress and reduced quality of life in the child [31,32]; highlighting the importance of attention to parental emotional functioning in the context of the child's care [33].

Together, these behavioral, emotional, social, and financial challenges to children with rare or life-limiting chronic conditions and their families can be termed *psychosocial distress*. Pediatric psychosocial distress in this clinical context has been conceptualized in a variety of ways. Kazak et al. developed the widely used Pediatric Psychosocial Preventative Health Model (PPPHM), which employs a public health framework to match family psychosocial risk with appropriate interventions. The Psychosocial Assessment Tool (PAT) is a parent-reported screening tool based on the PPPHM that operationalizes psychosocial risk into the following domains: family structure/resources, family problems, social support, stress reactions, family beliefs, child problems, and sibling problems. Additional approaches to categorizing psychosocial risk among families with children who have rare or life-limiting chronic conditions include the Distress Thermometer, which screens for distress in domains related to practical, familial, emotional, and physical problems, as well as spiritual and religious concerns. Although no single definition exists for psychosocial distress among children with rare or life-limiting conditions, current approaches all take a broad, social-ecological approach that includes not only the psychological wellbeing of the patient but that of their caregivers and siblings, as well as their socio-economic circumstances, family structure, and social function.

While it is clear that children with rare or life-limiting chronic conditions and their families are at increased risk for psychosocial distress, the extent to which this phenomenon and its antecedents are documented during routine medical appointments is unknown. Without adequate or standardized documentation of psychosocial concerns, families who would likely benefit from further assessment, targeted referrals, and service linkages may be at risk of slipping through the cracks. Therefore, the goal of the current study was to characterize the current medical record documentation practices around child and family psychosocial distress and risk factors for distress. Specifically, this work sought to answer the following research questions: (1) What information about patient and family psychosocial distress is extractable from the narrative text of clinical notes? (2) How frequently is psychosocial distress or its antecedents mentioned in routine outpatient clinical notes? and (3) How is psychosocial distress characterized by providers in the medical record?

2. Materials and Methods

Eligible patients were children and adolescents (<20 years old) followed by a pediatric complex care coordination program at Mayo Clinic in Rochester, MN, USA (henceforth

referred to as "the program"). The program is not a medical home but rather a consultative service that serves as the primary point of contact for patients and their families while receiving care from multiple specialty groups within Mayo Clinic. Approximately half of enrolled patients have at least one disease considered to be rare (i.e., affecting less than 200,000 Americans). The goal of the program is to improve communication among specialists at Mayo Clinic with local primary care providers and families to ensure a unified and holistic view of treatment plans and goals. Children who are followed by the program typically have significant chronic conditions in three or more body systems, need ongoing subspecialty care (longer than one year), and receive most of their subspecialty care at Mayo Clinic.

The program maintains a list of active patients (n = 166 at time of study), which was shared with the study team. Using a random number generator, 60 eligible patients from this list of active patients were identified for inclusion in our chart review. The most recent clinic visit with one of the program pediatricians or nurse practitioners was identified and the associated note was extracted for each patient in our sample. Two co-authors (EG and DG) each independently extracted five randomly selected patients to pilot test the extraction form and ensure consistency, which was deemed satisfactory after comparing responses and reaching consensus through discussion as a team. The remaining charts were divided between EG and DG and extracted individually. The following data elements were extracted from each patient's chart using a REDCap [34] electronic data capture form: visit date and provider; demographic information, including patient age, gender, race, city and state of residence, preferred language, and health insurance; problem list; and the full narrative text of the note. Analysis proceeded according to a mixed methods explanatory sequential design (Figure 1).

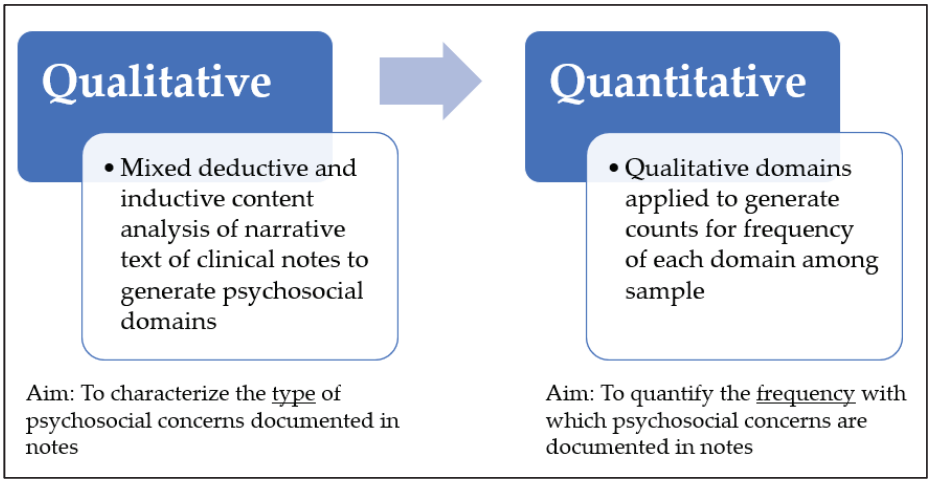

Figure 1. Mixed methods explanatory sequential design.

2.1. Qualitative Analysis

Qualitative analysis was performed using NVivo qualitative data analysis software, Version 12. All clinical notes in the sample (n = 60) were coded on a line-by-line basis for narrative sections of the note (e.g., "History of Present Illness", "Assessment"). The narrative text of the extracted encounter notes was coded using a mixed deductive (i.e., identified a priori based on existing literature on psychosocial distress in this population) and inductive (i.e., developing emergent codes that arose through review of the notes) approach. Key sources for deductive coding included domains from Kazak's Psychosocial Assessment Tool (PAT) and the pediatric Distress Thermometer. An initial coding scheme was outlined

based on previously described domains of psychosocial risk for children with serious medical illnesses and their families [35–41]. Authors then read through the narrative text of each note to further develop and refine the initial coding scheme, including determining which specific topics of discussion would be included in each broader coding category. After the development of the coding scheme, coding was performed on five notes in triplicate (SM, EG, and DG), using consensus to arrive at final code assignments for each note. Disagreements were taken as an indicator that the coding scheme required further clarification and the codebook was expanded and clarified as needed, eventually resulting in a final coding scheme organized into the following higher-order domains: Child Psychosocial Health, Family Adjustment and Support, and Family Structure and Resources. The final domains and subdomains reported on in this manuscript are detailed in Table 1 below. Each note was coded independently by two authors (DG, JC, EG). Any discrepancies between coding decisions were discussed as a team, with the third coder responsible for making final decisions in cases where disagreements could not be resolved. Quotes are used within the results section for illustrative purposes.

Table 1. Psychosocial domains developed during qualitative coding, their descriptions, and their prevalence in the study sample of clinical notes (n = 60).

Psychosocial Domains	Description	Frequency (%)
Child Psychosocial Health		
Developmental	Status of age-specific milestones (i.e., behavioral and/or physical skills associated with normal development).	18 (30.0)
Emotional function	References to child's ability to regulate emotional expression and identify emotional expressions of others. Includes references to mood, behavioral, or attention problems, exposure to trauma, aggression, past or current therapy, and past or current psychiatric medication.	30 (50.0)
School	Mentions of school attendance, homebound, homeschool, grade; types of classes (e.g., special education); services received (e.g., PT, OT, speech therapy); Individualized Education Program (IEP) or 504 plan; academic performance or behavioral issues related to school.	49 (81.7)
Social Interaction	Opportunities for interaction with same-age peers; presence of friends, peer relationships, involvement in activities.	12 (20.0)
Family Adjustment and Support		
Intra-Family Conflict	Patient not getting along with family; parents not getting along; other members of the household not getting along; parents have conflicting ideas about parenting or conflict around medical decision making.	5 (8.3)
Parent Emotional Function	References to parent ability to cope; mood issues (e.g., worry, anxiety, depression, sadness); excessive substance use; avoidance, hypervigilance, a disabling parent health concern, current or past therapy.	10 (16.7)
Parent Social Support	References to social support and resources available to or used by parents (e.g., community resources, friends, family).	7 (11.7)
Sibling Emotional and Physical Function	Descriptions of anxiety or other mood concerns; disruptive behavior; current or past medical conditions; presence of sibling rivalry or conflict.	3 (5.0)

Table 1. *Cont.*

Psychosocial Domains	Description	Frequency (%)
Family Structure and Resources		
Family Structure	Descriptions of individuals who live in the patient's home (e.g., one parent only, grandparents, siblings) and/or the individuals involved in the patient's care.	47 (78.3)
Financial Concerns	Issues related to money problems (e.g., trouble paying bills), obtaining transportation, maintaining adequate health insurance, parent's ability to work, government assistance, and housing quality (e.g., evidence of overcrowding, frequent moves/evictions, or health hazards).	7 (11.7)
Parent Ability to Navigate Health System	References to parent's ability to take time off to attend medical appointments, arrange child care, and follow through on medical treatment plan.	18 (30.0)
Parent Work-Family Conflict	References to issues with parent's work situation, including having difficult hours/shifts, being under-employed, or interaction between caregivers' work and subsequent stress or inability to care for child.	5 (8.3)

2.2. Quantitative Analysis

After the authors completed the coding of all 60 notes, descriptive statistics were generated for demographic information and visit diagnosis counts. Additionally, the number of notes in which each code appeared was counted. These counts acted as a proxy for the frequency in which discussion and documentation occurred around the respective topics in our sample of 60 patients.

3. Results

3.1. Sample Characteristics

Demographic information is shown in Table 2. Patients included in this study had a mean age of 7.3 years (ranging from 10 months to 18 years). Slightly over half (56.7%) of patients were male. Most of the sample (91.7%) was white. All patients' preferred language was listed as English. Twenty-five percent of patients had private insurance, 40.0% had Medicaid, and 35.0% percent had a combination of the two. Patients' average drive time to receive care at Mayo Clinic was 187.6 min. The most common visit-related diagnosis categories were neurologic/neuromuscular (63.3% of visits), gastrointestinal (53.3%), and respiratory (41.7%).

Table 2. Characteristics of the patient sample (n = 60).

Variable	*n* (%)	Mean (SD)
Age		7.3 (4.4)
Gender		
Male	34 (56.7)	
Female	26 (43.3)	
Race		
White	55 (91.7)	
Asian	3 (5.0)	
American Indian or Alaska Native	1 (1.5)	
Other	1 (1.5)	

Table 2. *Cont.*

Variable	*n* (%)	Mean (SD)
Insurance		
Private	15 (25.0)	
Medicaid	24 (40.0)	
Private and Medicaid	21 (35.0)	
Driving minutes from home to Mayo Clinic		187.6 (154.6)
Visit diagnoses per patient (Median (Range))		4.0 (1–13)
Visit diagnosis categories		
Neurological or neuromuscular	38 (63.3)	
Gastrointestinal	32 (53.3)	
Respiratory	25 (41.7)	
Congenital or genetic	23 (38.3)	
ENT	18 (30.0)	
Endocrine	14 (23.3)	
Cardiovascular	11 (18.3)	
Orthopedic	10 (16.7)	
Psychiatric	9 (15.0)	
Renal or genitourinary	9 (15.0)	
Hematologic/immunologic	5 (8.3)	
Dermatology	2 (3.3)	
Ophthalmic	2 (3.3)	

3.2. Child Psychosocial Health

Problems or concerns specifically regarding the patient's emotional function were mentioned in 30 of the 60 medical notes (50%). While some notes described specific behaviors (e.g., "She does not listen to what her parents ask her to do") others were vaguer (e.g., "[patient] has been struggling with social media interactions"). Difficulties with the patient's behavior (n = 9) and anxiety (n = 4) were discussed most frequently. Treatment for these concerns was discussed in seven notes, usually by referencing ongoing treatment (e.g., "he is followed locally by a psychiatrist to manage his ADHD and anxiety and is scheduled to see a local counselor for his anxiety" and "she has benefited from her ABA program") or the discussion of a referral for further evaluation and treatment (n = 1). The child's school situation was mentioned in a majority of notes (n = 49; 81.7% of notes), with providers typically noting the patient's current grade level at a minimum. However, many notes contained additional context on the child's school function (e.g., "School is not going well due to fatigue"; "has attended 4 days of school this year due to Make A Wish, illness and appointments"). Concerns related to development were less common (n = 18; 30%) but still present in nearly one-third of notes in our sample. Finally, remarks about social interaction were coded in one-fifth of notes (n = 12; 20%) and included references to both positive experiences related to patient extracurricular activities, hobbies, and friendships, as well as difficulties related to participating in activities and socializing (e.g., "She is having a lot of urinary incontinence. This is making it difficult socially for her.").

3.3. Family Adjustment and Support

Although 10 notes (16.7%) referred to parental emotional function, none of them identified specific concerns regarding a parent's emotional health (e.g., parent mental health diagnosis; parent mental health treatment). Five notes referenced how the child's medical illness and caregiving responsibilities were a source of significant stress on the parent ("[Parent] feels she is 'hanging on by a thread"). Respite care was the only potential intervention mentioned in response to these stressors. It is interesting to note, some of the notes had a family history section which included parental mental health history; however, whether this section was included depended on the template the author used, and we were not able to ascertain who had entered these data into the medical record, or when it was entered. Therefore, this information was not included in our analyses.

Seven of the 60 notes (11.7%) referenced the provision of social and material support to the parents or family. Examples of this included grandparents being trained to provide care for a patient, a patient's mother who expressed feeling well-supported by resources being provided from the county, and another mother who was receiving extra supplies from a friend. A small number of notes (n = 5; 8.3%) mentioned instances of intra-family conflict (e.g., "Family has been under some stress as father is no longer involved with [child's] care"). Finally, concerns regarding sibling emotional function were mentioned in 3 of the 60 notes (5%). In one case, a sibling's diagnosis of autism was mentioned, and their aggression towards the patient was discussed as an ongoing stressor. In other cases, siblings were described as also having chronic health conditions, sometimes similar to those of the patient (e.g., "The family has been incredibly busy with managing three children (two with chronic health conditions)".

3.4. Family Structure and Resources

Information about family structure was included in 47 of the 60 notes (78.3%). The most common descriptor was who the child lived with (n = 43), although specific information about risk factors, such as the age of these family members, was rarely included. Notes frequently mentioned the parents' occupation (n = 29) if they were employed but did not include additional information about unemployment or underemployment. If the parents were not married, or were going through a divorce, this was also mentioned in some of the notes (n = 9). Nearly one-third of notes (n = 18) referenced barriers or facilitators to obtaining medical care and following treatment plans (e.g., " . . . as travelling to Rochester is a challenge for the family, they would like to limit medical appointments). However, financial concerns were specifically mentioned in only seven notes (11.7%). Most of these referenced struggles with obtaining insurance authorization or appealing denials for coverage of specific tests (e.g., genome sequencing), medications (e.g., injections), or services (e.g., increased nursing hours). Information regarding the impact of the child's medical illness on parental employment (e.g., mother left the workforce to care for the child; stress taking care of the child and the family business simultaneously) were included explicitly in five notes (8.3%).

4. Discussion

In this chart review and analysis of pediatric outpatient encounter notes, we found that psychosocial distress and/or risk factors for distress were not consistently documented. Only one-third of notes in our sample documented discussion of the child's emotional health, while mention of parent's emotional concerns was largely absent—despite recent national data indicating that almost 20% of parents of children with rare or life-limiting chronic conditions report poor or fair mental health [23]. In addition, most notes in our sample did not capture risk factors and vulnerabilities of the broader family system (i.e., financial, parent and sibling adjustment). Although financial concerns were discussed in 12% of visits in our sample, survey data indicate much higher rates of financial hardship among this population [20], as well as high rates of unmet healthcare needs due to cost [42].

It is important to note that we do not intend for these findings to be critical of individual clinicians, as the reasons for lack of documentation are multifactorial and, in most cases, cultural and institutional. First, one key limitation of medical record data in the absence of validation methods (e.g., recording or observation of the clinical visit) is the inability to shed light on discussions that occurred but were not explicitly documented. Providers may be discussing psychosocial concerns to some degree during appointments but may feel reluctant to incorporate this information into medical notes for many reasons, including ambiguity about which problems rise to the level of clinical significance and which are a function of temporary stressors [43]. In addition, providers may also work under the assumption that psychosocial information is better covered in notes by social work or psychology. However, given the direct association between patient and caregiver psychosocial distress and medical outcomes, we argue that this information should also

be included in medical provider documentation. Finally, psychosocial concerns in this population are often not limited to patients but are linked to family circumstances or parental factors. Providers may feel that questions about—let alone, formal documentation of—parental mental health or stressors are perceived as intrusive. However, the importance of including parents and caregivers in psychosocial assessments needs to be stressed, since these concerns are inextricably linked to the child's well-being [44].

For both patients and their caregivers, universal psychosocial screening offers an opportunity to normalize the psychosocial impact of a child's illness on the child and the family, and proactively identify children and families who may be experiencing current psychosocial distress or who are at risk for distress during the course of medical care [40,45,46]. Feedback about psychosocial concerns provided to clinicians through screening tools has been found to systematically increase discussion of emotional and psychosocial functioning [47]. Evidence suggests both pediatric clinicians and the parents of their patients support the practice of documenting psychosocial and mental health information in the patient's health record [43].

There are several evidence-based tools available for screening for psychosocial risks and concerns in pediatric populations. These include the Distress Thermometer [39,40,48], the Psychosocial Assessment Tool 3.0 [37] and Checking In [49]. Research in pediatric oncology [37,39,49] (e.g., Kazak et al., 2018; Patel et al., 2019; Wiener 2021), organ transplant [50] and other life-threatening conditions [41] has demonstrated that psychosocial screening is feasible and acceptable to patients, caregivers, and medical providers. Systematic and routine psychosocial screening provides the opportunity to match the psychosocial care to the specific needs of the child and family, including providing further assessment, preventative interventions, and more specific evidenced-based care [46], with the goal of improving overall quality of life for the patient and their family [51]. The implementation of psychosocial screening increases the number of performed and accepted referrals to psychosocial providers [52], and vastly improves documentation of psychosocial concerns [53]. Screening tools also provide a starting point for clinicians, patients, and families to ease into what may be difficult or awkward conversations. In addition, several of these existing tools include instruments tailored for pediatric patients themselves to answer, allowing older children and adolescents an opportunity to actively participate in these discussions. However, further research is needed to inform best practices around implementation of pediatric psychosocial screening programs as well as the long-term impacts of screening on process and outcome metrics related to how effectively this information is integrated into clinical care [44,54,55]. It is important to note that psychosocial screening in the absence of appropriate referral or intervention strategies will not be sufficient to improve outcomes.

There are several limitations of our study. Our findings are a function of provider documentation in a single clinical note at one academic institution, which may limit the generalizability of these results. Additionally, the clinic notes assessed were from a complex care program which is not designated as a primary care medical home because the majority of patients do not live in the clinic's immediate vicinity. Therefore, it is certainly possible that patients and families may be receiving social services in their local communities. However, even if psychosocial concerns are being discussed at a higher frequency than our study would imply, or if a patient and their family are receiving social support locally, we argue that documentation of these issues in the medical records of children with rare or life-limiting chronic conditions are critical to ensure surveillance, follow-up, and care coordination.

Another limitation of our study is that data are from patients at a single academic medical center, limiting the generalizability of these results to other settings. In addition, only a single note from a medical provider at our institution was evaluated for this study, leaving the possibility that other notes could have mentioned topics related to psychosocial distress. However, we argue that these discussions should be occurring frequently, if not during each visit. Patients and their families may also be receiving social services outside our hospital system, especially given that many patients in the program do not live in the immediate vicinity of Mayo Clinic.

5. Conclusions

Children with rare or life-limiting chronic conditions and members of their families are at increased risk for the development of psychosocial distress, which, if left unidentified and untreated, can negatively impact the child and the family. The purpose of this research was to identify which elements of psychosocial distress and its antecedents are documented in the medical record, as well as their frequency and nature. While information related to family structure and patient school status was widely documented in our sample, many other important psychosocial domains (namely, child and family emotional function) were not routinely documented within medical provider notes. As these children continue to survive and live longer, they and their families may benefit from universal psychosocial screening, and an integrated medical and behavioral service model which could provide an evidence-based system of care encompassing more of the patient's lived experience (Appendix A).

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Appendix A

Table A1. Coding Categories.

Code	Definition
Emotional Function	Ability to regulate their emotional expression and identify emotional expressions of others. Trauma, mood problems, anxiety, depression, sadness, behavior problems, attention problems, ADHD, fear, aggression, past or current therapy, past or current psychiatric medication
Family Structure	Who lives in the home Single-parent home Who is involved in care

Table A1. *Cont.*

Code	Definition
Financial Concerns	Transportation Insurance Parent's ability to work Government assistance for food Money problems (phone, heat, light bills, rent/mortgage, medical bills, child care) Housing quality (evidence of overcrowding, frequent moves/evictions, health hazards e.g., mold)
Parent Ability to Navigate the Health System	Take time off to attend medical appointments, arrange child care, follow through on medical treatment plan
Parent Emotional Function	Coping, worry/anxiety, mood problems, depression/sadness, alcohol/drug abuse, avoidance, jumpy hypervigilance, disabling parent health concern, current therapy, past therapy
Parents' Work Family Conflict	Difficult hours/shifts Part-time/full-time/unemployed Caregiver occupation/employment Mention of the interaction of caregivers' work and subsequent stress or inability to care for child
Parent Social Support	Community, friends, partner, family
Sibling Emotional and Physical Function	Anxiety, mood concerns, disruptive behavior, current or past medical condition Sibling rivalry or conflict

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children

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Review

The Transition to Adulthood for Youth Living with Rare Diseases

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Abstract: More children with rare diseases survive into adulthood. The transition period to adult healthcare presents many challenges for pediatric rare diseases. Few adolescents or their families receive any transitional support for the transition to adult healthcare or for their maturing psychosocial needs. Understanding the challenges in the transition process is critical to ensure that interventions designed to improve the transition are holistic and meet the needs of the youth and their families. Few transition programs are in place to meet the needs of those youth with rare diseases who cannot participate in medical decision making or who live independently because of severe disabilities and comorbidities. We searched the literature on preparation and outcomes for youth living with rare diseases in PubMed, CINAHL, and PsychInfo, excluding publications before 2010. The results revealed seven studies specific to rare diseases, special needs, or chronic conditions. Next, we discussed transition with experts in the field, GotTransition.org, and citation chaining, yielding a total of 14 sources. The barriers and challenges to transition were identified. Articles discussing solutions and interventions for transition in medically complex children were categorized care coordination or transition readiness. A large portion of children with rare disease are underserved and experience health disparities in transition.

Keywords: pediatric to adult transition; rare disease; special needs; interventions; care coordination; transition readiness

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1. Introduction

As modern medical practices improve, an increasing number of children with rare diseases are surviving into adulthood [1–3]. A 2018 study conducted in Italy estimated that 9.2% of adults in the healthcare registry were transitioned with rare diseases from pediatric institutions. The transition period presents a challenge to many young adults with diseases that are widely considered a pediatric concern [2]. Many receive inadequate care or are lost completely in the gap between pediatric and adult care providers. The National Survey of Children's Health found that only 18.4% of adolescents in 2019 received any transitional support [4].

TjaMeika Davenport, a Parent Navigator at Children's National Hospital and a community advisory board member for Got Transition, described the transition for children with complex care needs as one of the most difficult challenges to navigate as a young adult in the US healthcare system. She explained that the transition is uniquely difficult to counter because it is driven by a variety of factors, including the complexity of their care, differing specialist recommendations, and the adult providers' lack of experience

with rare pediatric diseases, among other factors. She detailed several efforts she and her team make to improve transition for adolescent patients and their families at Children's National, including the parent navigator program and the Got Transition National Resource Center. One such support was a "warm-handoff" strategy, in which patients met with both pediatric primary care or specialty providers they were transitioning away from and the adult specialist they were transitioning towards, creating a support network for both patients and providers. While largely effective, the warm hand-off strategy is expensive and unlikely to be covered by insurance companies without proof of concept, which makes widespread implementation nearly impossible in a privatized healthcare system, such as that in the United States [5,6]. This process also does not address the needs of young adults who may need Emergency Department services that are unable to meet their special needs nor the loss of a pediatrician before finding an adult provider or practice to transition into. Parents, such as Jana Monaco whose young adult son has a rare genetic metabolic disorder, are left with the case management role of facilitating this transition to adult healthcare with little professional support. As efforts to improve transitional healthcare increase, the need for transitional care research is also increasing. This literature review will outline the current state of transition literature on the barriers and solutions faced by adolescents and young adults with rare diseases who require complex care and who have special needs.

2. Materials and Methods

The initial search of literature was conducted in PubMed, CINAHL, and PsychInfo. As seen in Figure 1, the keywords "pediatric to adult transitions," "rare disease," and "special needs" returned 39 peer-reviewed journal articles. These keywords were selected to define a specific research goal: transition of care in children with non-specific, ultra-rare disease resulting in special needs and/or complex care. The National Organization for Rare Disorders lists over 1200 rare diseases. There are transition models for specific rare conditions, such as whole organ transplant or Cystic Fibrosis [5,6]. While specific rare disease transition models address specific and general transition challenges, including the literature on the transition of each disease is not feasible at this time. For this reason, the literature review was limited to non-specific rare disease and special needs transition.

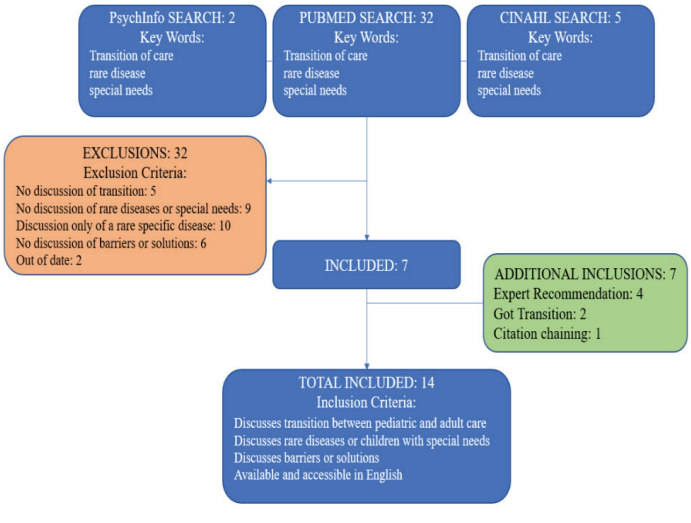

Figure 1. Flow diagram of literature search methods, inclusion, and exclusion criteria.

After the exclusion of articles written before 2010 and in languages other than English, there were 29 results. The results were further refined by including only articles that discuss the transition between pediatric and adult care for children with rare diseases,

special needs, or chronic conditions, and excluding articles that were not accessible in the United States. The final number of results was seven. Due to the limited results, we looked to other means of identifying relevant articles. A total of seven additional journal articles were identified through discussion with experts in the field, GotTransition.org, and citation chaining, including 1 unpublished manuscript. In total, 14 sources were selected. The included articles were then identified as contributing to the literature on the barriers to transition and possible solutions to transition barriers.

3. Results

3.1. Barriers and Challenges to Transition

An article published in *Pediatrics* details a number of barriers adolescents, young adults, and their families face during healthcare transition and why transition care is so necessary [2]. The authors defined transition as more than the simple physical transfer of a patient from one practice or hospital to another, but instead as the designed effort to ensure healthcare independence, preparation, and the completion of this transfer. Barriers to the transition include the loss of ancillary staff common in pediatric settings, healthcare culture differences, and even simply the work involved in transferring medical records. This is exacerbated in countries such as the US where the transfer of insurance coverage is yet another concern [2].

A 2018 systematic review of barriers to transitional care discovered four overarching themes [7]. The most prominent of which was relationships: Patients were reluctant to leave the providers and staff at their pediatric institutions and were slow to build new ones in the adult care setting. Access, trust, and knowledge issues also pervade the transition process [7]. Patients struggle to find adult specialists willing and capable of treating their conditions, and once they do, they have troubling beliefs and expectations of those providers—yet another barrier to successful care. The authors note that while different illness groups experience these challenges at different rates, the themes are common across most patient types [7].

Similar barriers were identified by adult providers engaging in transitional care [2,4]. A 2021 focus group of interdisciplinary adult providers conducted by the same research group found that providers struggle to perform post-transitional care when a patient or family's beliefs and expectations of adult care do not align with that of the provider, causing distrust and resistance to change. The providers also explained a lack of communication with the patient's pediatrician limits their ability to treat the patient, especially when they do not have access to medical records and histories [4]. The final theme identified by the focus group was issues related to access and insurance; interdisciplinary care coordination and social work are largely inaccessible in an adult care setting compared to the interconnectedness of pediatric care, a problem that may be better addressed by payor- and system-level intervention.

A qualitative cross-sectional survey of providers who care for young adults with chronic diseases and complex healthcare needs was conducted in 2015 [8]. Researchers coded responses into 5 themes: size of the medical team, access to medical records, time constraints and administrative burden, lack of training and experience in pediatric diseases, and financial constraints [8]. Although it has a more robust study design than a focus group, the paper has its limitations. Similarly, to the focus group, this study has a small sample size. Only 22 providers responded to the survey, limiting its power and generalizability. It is difficult to say if these providers' perspectives represent the average transitional adult provider.

3.2. Solutions

The articles that discuss solutions and interventions for transition of care in medically complex children can be split into two categories: care coordination and transition readiness. This section also includes examples of generalized transition models in Europe.

3.2.1. Care Coordination

The results of a randomized control trial in young adults with chronic illnesses showed that healthcare transition care coordination was effective in improving patients' perceptions of care in a transitional period [9]. Those who received the care coordination were more than two times as likely to report receiving the care they thought they needed and speak to their providers about their future care than patients in the control group. Although the study design is strong and these results are promising, the study is limited by its use of self-reported measures. Because the authors were not able to use a more empirical measure of care, only the difference in patients' perceptions can be confirmed.

Another multidisciplinary transition team was designed and implemented at the Children's Hospital of Philadelphia [10]. The team consulted on 80 cases over a 2-year period. The team identified appropriate referrals for over 70% of these cases and created health summaries for 90%. In a program evaluation, 78% of referring pediatricians felt the program helped them identify adult providers for their patients, and 90% planned to use a Multidisciplinary Intervention Navigation Team (MINT) for future transitions. The evaluators concluded that MINT was a worthwhile program and recommended further funding and implementation of the team. The Adult Care and Transition Team (ACTT), formerly known as MINT, is now an established interdisciplinary consulting service that requires a referral by a provider. The team helps with: (1) creating a transition care plan that includes an updated medical summary; (2) finding adult doctors and nurse practitioners; (3) answering health insurance questions; (4) coordinating care across pediatric and adult hospitals; (5) transferring the medical records to the new provider; (6) finding services and support in the community.

A 2018 review of healthcare transition frameworks found that while there are many aspects to a smooth transition, cooperation between the patient's pediatric and adult physicians is the most impactful solution [3]. They emphasize that transition preparation should begin long before the transition and that the issues faced by patients are better mitigated by a team of providers who may offer different perspectives and solutions.

3.2.2. Transition Readiness

A cross sectional study of 17,114 adolescents and young adults on transition readiness in 2013 found healthcare systems lacking [11]. While providers are encouraging patients to take charge of their own health, approximately 56% of participants never had a conversation about transition with their providers. In addition, only 35% reported discussions about health insurance. While these statistics are somewhat improved for patients in a medical home (46.3 and 46.5, respectively), improvements are still necessary [11]. The authors recommend implementing transition preparation on a system-wide level, specifically with payor systems. They reference adult care to nursing home transition programs in Medicare that may be adapted and improved upon for the younger generation covered by public insurance [11]. Monetary investments may increase transition preparedness outcomes in and out of the medical home. This review did not address the transition needs of families of children with severe cognitive or motor limitations who will never be able to take charge of their own health.

A first step to improving transition readiness is consistent measurement. A 2014 review of transition preparedness measures found 10 widely used measures with published validity date, 6 of which were disease-specific [12]. While each measure was found to be a valid benchmark of transition preparedness, the measures that included patient and family participation were most likely to identify patients in need of intervention. The authors caution that although seemingly effective, the measures were created for and tested in specific populations and are, therefore, not necessarily generalizable to a larger population [12]. Further evaluations of and improvements upon these measures are necessary to create standardized readiness measures. Standardized measures may help to identify disparities in transition readiness by decreasing misclassification when comparing readiness across demographic groups.

In 2014, data from the National Survey of Children with Special Healthcare Needs and the Survey of Adult Transition of Health were analyzed to discover if young adults with a healthcare plan were more likely to use dental services [13]. Dental care is an important, if often overlooked, aspect of healthcare and an important aspect of a smooth transition. The researchers found that having a healthcare plan before transition was significantly associated (OR 1.11, 95% CI 1.04 to 1.18) with increased utilization of dental service in young adults with special healthcare needs but no functional limitations [13]. As a retrospective cohort study, the results are subject to some minor information bias. The study was also limited by lack of data on the type of dental care sought. Whether the patient was seen at a pediatric or adult dentist may determine the effectiveness of their transition. Patients who had been seeing a general dentist since childhood and required no transition may have also swayed the results. While it is a relatively small magnitude, an 11% increase in the likelihood of dental care suggests that a healthcare plan is an effective strategy for improving outcomes during transition [13].

A Vermont health system designed and piloted a chatbot that strived to encourage teenage patients with special needs to engage in their medical care [14]. The intended improvements included increasing personal knowledge about their conditions, medications, and medical history as well as preparing for appointments, contacting their providers, and understanding their insurance systems. There are technical and medical difficulties in the transition of care in rare diseases. Adult experts in rare diseases frequently do not know the adolescent specific needs of young adults, as is also the case in transitioning healthy adolescents [15]. Thus, transitioning patients may benefit from personal knowledge of their own conditions and complex care needs, especially when consulting with their pediatric provider is not feasible. The small sample of patients had a 97% engagement profile and showed improvements in many of categories, especially taking control of their medication and pharmacy refills [14]. Due to the study's status as a pilot program, the sample size was small (n = 16), severely limiting its power. The use of testing technology also required all participants to not only own a cell phone but be relatively tech literate. This may introduce selection bias. Another limitation of note was the study's compensation structure. A total of USD 100 was given to participants who completed the entire study, which may have swayed the engagement statistics, particularly in the young adolescents. The authors conclude that the pilot study showed the chatbot has serious potential to improve transition readiness in youth with special needs but caution against using similar technologies in a vacuum: transition is a complex hurdle that requires multiple solutions [14].

3.2.3. European Models

Two notable transition interventions in Europe include the United Kingdom's Ready-Steady-Go and Germany's Medizinische Behandlungszentren für Erwachsene mit geistiger Behinderung oder schweren Mehrfachbehinderungen (MZEB) programs. An analysis of transition interventions in a nationalized healthcare setting may help in differentiating the effectiveness of an intervention from the financial barriers to healthcare transition seen in privatized insurance systems.

The Ready-Steady-Go program is a generalized transition approach that starts with patients at 11 years old in the UK [16]. Patients work with their providers to develop a transition plan where both parties are comfortable. This allows the transition to proceed at an individualized pace specific to the needs of the patient. It empowers young patients to have confidence and control over their own healthcare. The wide implementation and success of this program suggests that care coordination and early transition preparation are effective in an environment with fewer financial barriers to be concerned with.

Across Germany, adults with intellectual disabilities are cared for in MZEBs. There are specialized clinics designed to serve adult patients with complex intellectual needs [17]. Their success in treating adult patients with complex pediatric disorders supports evidence that specified care centers are effective in bridging the gap between pediatric and adult care in nationalized health systems.

3.3. Gaps in Research

A single article, published in 2010, addressed race- and ethnicity-based disparities in transition care and support [18]. The authors of this systematic review concluded that there were significant differences between racial and ethnic groups, and further intervention should be applied to help fill gaps in transition care. Despite a publishing date of more than a decade ago, this study is the most recent research on the topic, and there is little reason to believe the disparity has been resolved. Although race and ethnic disparities are primarily limited to the United States, further research in outcome and transitional support disparities is required to develop appropriate solutions and interventions.

We identified no research that addressed sexual health in transition care for individuals living with rare diseases. Challenges for those with severe intellectual and motor limitations include sexual and reproductive health. Ethical and legal challenges surround issues such as hormonal suppression or birth control for persons with rare diseases who are unable to give consent. Moreover, we did not identify any research that addressed the impact on health of guardianship at the age of 18, living at home versus in the community or long-term care setting, or contingency planning as families age and can no longer provide care. One question rarely asked in this context is "What does a good life look like for your child as an adult?" Programs or interventions that address additional transition challenges are likely implemented in the US and Europe without publication as transition research is both time and resource intensive.

Countries such as the United States and Italy [19] have no national transition model for individuals living with rare diseases. Similarly, there is no current consensus on safe and equitable healthcare transition for patients with rare diseases in resource-limited countries [20]. Although programs such as Got Transition® [21] have identified the six core elements of health care transition, many countries still lack adequate resources to address these elements. In Canada [22], France [23], and Ireland [24], progress has been made towards developing such models and guidelines for transition programs.

4. Discussion

The transition from pediatric to adult healthcare is difficult, especially for families of young adults with ultra-rare diseases who are unable to participate in healthcare decision making because of severe disabilities and/or medical comorbidities with unique treatments. Young adults and their providers face a variety of barriers, including knowledge and skill-based challenges, distrust and low expectations, and access and financial concerns. The specifics of each rare disease or group of rare diseases contributes to unique transition issues. Furthermore, the rarity of experts in these rare pediatric and genetic diseases among adult healthcare professionals is a barrier to successful transition. Creative solutions have yet to be identified to overcome these barriers, most prominently in care coordination and transition readiness. System-based interventions of care coordination seem to be most effective in ensuring that patients are successfully transferred from one practice to another while transition preparation programs help improve patient skills necessary for success in an adult care setting, such as medical knowledge and self-advocacy. Both angles of support would be beneficial to adolescents and young adults with rare diseases attempting to transition to adult care and should recognized as a necessary part of medical care.

Additionally, although not addressed in any of the research or quality improvement studies, family caregivers could benefit from guidance through the process of establishing guardianship. Family caregivers need to be educated about this process as their severely disabled child reaches adulthood (age 18 years in the United States), for those children unable to live independently and/or unable to participate in medical decision making. There should be a better way to support these families so they do not experience shock, fear, or intimidation that they might lose custody of their adult child as they proceed through the legal process of establishing guardianship in the United States. Alternatively, as children transition to adult healthcare, family caregivers may also decide to explore relinquishing guardianship. Referrals to social work resources should link family caregivers

with available resources to provide support for transitioning to group homes or creative alternative living situations.

There is a concerning gap in knowledge about the disparities of transition care by race and ethnicity. A large portion of children with rare diseases are members of marginalized groups that regularly experience healthcare disparities [1]. Research is necessary to identify, understand, and combat gaps in transitional care for children living with rare diseases. A recently completed National Institutes of Health Workshop further identified gaps in healthcare systems and payment models that require an evidence base to support reimbursement models for healthcare transition services that work [25].

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children

MDPI

Article

Unmet Needs of Parents of Children with Urea Cycle Disorders

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Abstract: (1) Background: Phenotypic diversity and long-term health outcomes of individuals with urea cycle disorders (UCDs) have been described in detail. However, there is limited information on the burden on affected families. (2) Methods: To evaluate the family burden in parents with children suffering from UCDs, we used validated questionnaires. Socio-demographic characteristics were evaluated, and an adapted version of the Parental Need Scale for Rare Diseases questionnaire was used. The survey was conducted in families of UCD patients cared for at the University Children's Hospital Heidelberg. (3) Results: From April to November 2021, 59 participants were interviewed (mothers n = 34, fathers n = 25). The affected patients most frequently suffered from ornithine transcarbamylase deficiency (OTC-D) (female n = 12, male n = 12), followed by argininosuccinate synthetase deficiency (ASS-D, n = 13) and argininosuccinate lyase deficiency (ASL-D, n = 8). About one-third of the participants were "dissatisfied" or "extremely dissatisfied" with health professionals' disease knowledge. In addition, 30% of the participants reported a medium or high need for "additional information on the development of their children", and 44% reported a medium or high need "for information on available services". A majority of 68% reported a need for additional support regarding services such as support groups (42%) or psychological counseling (29%). (4) Conclusions: Our study indicates that there is an unmet need for sufficient information about the development of children with UCDs, as well as for information about available support services for families with UCD patients. Furthermore, the results highlight the importance of establishing or improving family-centered care approaches. This pilot study may serve as a template for the assessment of the family burden associated with other inherited metabolic diseases.

Keywords: family burden; parental need; urea cycle disorders; E-IMD; inherited metabolic diseases

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1. Introduction

Inherited metabolic diseases (IMDs) comprise more than 1600 disorders, which are classified into 130 groups based on defects of the respective biochemical metabolic pathways [1]. Most IMDs are rare diseases with low incidences. In the European Union, a disease with an incidence of <1:2000 is considered rare. Patients with rare diseases such as urea cycle disorders (UCD) are cared for in a variety of clinics, most of which are local. The medical expertise and experience of the specific center can vary widely [2]. There can be significant differences in infrastructure, diagnostic procedures, time to diagnosis, strategies and outcomes, and these differences can have a negative impact on health outcomes. In the European Union and other industrialized countries, the care of patients with rare diseases has received special attention in recent years [3]. The newly established

European Reference Networks (ERNs) for rare diseases provide a platform for the harmonization of patient care and knowledge exchange across different European countries. Urea cycle disorders comprise a group of IMDs of ureagenesis, which is required for the irreversible elimination of excess nitrogen through the formation of dialyzable urea from ammonium and bicarbonate in periportal hepatocytes. The overall prevalence of UCDs ranges between 1 in 35,000 and 1 in 52,000 in Germany, Austria, and Switzerland, with OTC deficiency (OTC-D) being the most frequent subtype (>50%) [4,5]. Other UCD subtypes are argininosuccinate synthetase deficiency (ASS-D) as the second most frequent disease subtype (19%), followed by argininosuccinate lyase deficiency (ASL-D, 11.5%) and carbamoylphosphate synthetase 1 deficiency (CPS1-D, 4.5%) [5,6]. UCDs are caused by pathogenic variants in genes encoding enzymes or transporters of the urea cycle [7]. The majority of individuals with an UCD manifests with recurrent hyperammonemic episodes precipitated by catabolism, protein-rich meals, medications such as valproic acid, and other trigger factors [8]. The first symptoms may occur during the newborn period or later in life, reflecting the high phenotypic diversity of UCDs [6,9,10]. The degree of enzymatic dysfunction determines the metabolic disease course and its phenotypic severity, i.e., individuals with lower residual enzymatic activity are confronted with higher peak plasma ammonium concentrations at initial presentation and develop more often hyperammonemic decompensations during their disease course [11,12]. Importantly, the level of plasma ammonium at disease manifestation is associated with the neurocognitive outcome, which is most pronounced for mitochondrial UCDs [4,10,13]. Hyperglutaminergic hyperammonemia is the biochemical hallmark of most UCDs. Without immediate therapy, it induces a cascade of synergistically acting mechanisms, such as excitotoxicity, bioenergetic impairment and astrocytic swelling that often results in life-threatening encephalopathy, brain edema, irreversible brain damage and can cause a severe neurodevelopment disorder [14,15]. Hyperammonemia-associated symptoms range from somnolence, nausea, vomiting, liver failure, to seizures, multiorgan failure, acute encephalopathy, and death [16]. The prognosis of UCDs is strongly influenced by the duration of coma and peak ammonia levels in the setting of the initial decompensation [11,12]. In addition, metabolic decompensation can contribute to a worsening neurologic outcome and is therefore a particular burden for parents and caregivers [13,16,17].International recommendations, currently in their second version, have been published for the treatment of UCDs [18]. The long-term management of patients with UCD consists of a low-protein diet, which must be balanced and supplemented to avoid deficiencies of essential amino acids, trace elements or vitamins, and the use of nitrogen scavengers [18]. The acute treatment includes detoxification of ammonia, which often requires extracorporeal hemodialysis, and the use of intravenous drugs that act as nitrogen scavengers [18–21]. Liver transplantation may be another option [18]. The majority of UCDs are inherited in an autosomal recessive manner [22]. OTC-D is inherited in an X-linked manner [23,24], which leads to severe courses in hemizygous male individuals, while the clinical course in females is extremely variable [23]. So far, UCDs are not part of the German newborn screening program [18]. Currently, the first pilot studies are ongoing to evaluate newborn screening for ASS and ASL deficiency [15,25].

The European registry and network for Intoxication-Type Metabolic Diseases ("E-IMD") (https://www.eimd-registry.com (accessed on 23 March 2022) gathers comprehensive information on the clinical and biochemical natural history and outcome of UCDs. The goals of the E-IMD include the achievement of a better understanding of the natural history, diagnosis, and treatment options of the diseases, as well as the establishment of guidelines to reduce inequalities in care [2]. However, there is limited information on the psychosocial burden of affected families and their need for support.

Previous studies focused on patients and their challenges associated with a UCD. Specifically, it has been shown that a child's disease has often an impact on the entire family, as it affects the dynamics of the family and can result in a significant parental burden [26–30]. The time-consuming care for a patient with a UCD requires adjustments for parents, such as a strict dietary control [18], frequent appointments with specialists,

and a constant risk of metabolic decompensation. It is assumed that the genetic origin as well as the associated uncertain physical, cognitive, and psychological functioning of the child puts an additional burden on parents [31]. Furthermore, the parental burden can in turn have a negative impact on the affected children and siblings [29]. The difficulties experienced by the parents of children with rare diseases can involve emotional aspects, the relationship with the partner, the own behavior, as well as the process of diagnostics and the challenges of the health care system [32,33]. By understanding the support needs of families with affected children, needs-adapted concepts can be established and further improved, harboring the chance to reduce the family burden in the future [34]. The aim of this work was to evaluate the family burden in parents of children with UCDs in Germany and to assess the parental needs for specific support. Furthermore, we investigated the impact of gender, age, UCD subtype, and income on family burden.

2. Materials and Methods

2.1. Study Population

The study was conducted as a prospective single-center pilot study at the University Children's Hospital Heidelberg and as an amendment to the E-IMD study protocol, approved by the Ethics Committee of the University Heidelberg (S-525/2010, approval date is 31 January 2011). All E-IMD UCD patients were identified, duplications caused by siblings or mothers with diagnosed OTC-D were excluded.

In total, 54 E-IMD families including 108 parents were eligible to participate. In addition, one family including 2 parents of a patient with lysinuric protein intolerance (LPI) treated at the University Children's Hospital Heidelberg and not registered with E-IMD declared interest to participate. Signed consent of all parents to participate in the study was obtained. From April to November 2021, parents were contacted and interviewed by phone or during outpatient visits. All parents were interviewed individually and independently of each other. Out of the 110 eligible parents, 59 (from 46 families) answered the questionnaire (response rate = 53.6%); 22 of the 110 parents screened could not be reached during the data collection period. Other reasons for excluding screened participants were lack of consent (n = 15), lack of German language skills (n = 10) or death (n = 4).

2.2. Questionnaire

The study questionnaire used was derived from validated questionnaires: the Parental Needs Survey (PNS) [35] and items for the survey of sociodemographic characteristics "About you being a parent of a child with a rare disease". In the first part, we collected the sociodemographic data of all participants. For the second part, an adapted version of the PNS was translated into German and used for the interviews. The selection of items from the 108-item PNS questionnaire was conducted by two independent experts with experience in family psychology and therapeutic care of families (MWH/BW). Subsequently, a shortened 28-item version of the PNS was consented. The shortened questionnaire was translated into German by two independent translators (MWH/BW). After backward translation into English by a native Speaker, a German version was compiled. The final version (Supplementary File S1) included 28 items, divided into 6 sections: (1) Understanding the disease (4 items), (2) Working with health professionals (4 items), (3) Financial needs (3 items), (4) Information needs and social, physical, spiritual, and psychological needs (15 items), (5) Need for further support, as well as (6) a free text answer option. The items of the first four categories were answered using a 5-point Likert scale where 1 represented no need for support/full satisfaction, while 5 represented a high need for support/complete dissatisfaction. The need for additional support services was assessed by a list of options to choose from and a free-text field. The questionnaire was implemented using the online survey tool LimeSurvey to ensure correct data entry during the interview and facilitate data extraction.

2.3. Statistical Analysis

All survey responses were recorded using LimeSurvey. The complete data were exported as a single csv file. Statistical analyses were performed using R (Version 4.1.0.). Due to the exploratory character of this pilot study, the items were grouped by several categorical variables to reveal potential associations or group-wise differences. For the analysis of gender (mother/father), income (Questionnaire—Item 8: "How do you manage on your available income from all sources?") and disease subtype (female OTC-D, male OTC-D, ASS-D, ASL-D, CPS1-D, hyperornithinemia–hyperammonemia–homocitrullinuria syndrome (HHH), LPI) specific burden, the results were stratified by subgroups and compared with a X^2 test. The subgroups female OTC-D and male OTC-D were additionally compared separately due to the X-linked inheritance of this disorder. For the analysis of age-specific differences, we divided the study population into four groups (0–6 y, 6–12 y, 12–18 y, >18 y) according to the age of the patients. The results were then stratified according to these age groups, and a X^2 test was applied. No a priory hypotheses were tested; therefore, the *p*-values should be regarded as descriptive values. Due to the explanatory approach of our analyses, we omitted controlling the family-wise error rate.

3. Results

3.1. Sociodemographic Data

Fifty-nine parents (mothers $n = 34$, fathers $n = 25$) of 50 patients with UCDs participated in this study. OTC-D was the most frequent disease subtype, with $n = 12$ male and $n = 12$ female patients, followed by argininosuccinate synthetase deficiency (ASS-D, $n = 13$) and argininosuccinate lyase deficiency (ASL-D, $n = 8$). The frequency of the subtypes was representative of the affected population [5]. The mean age of the parents was 46.1 years (SD = 12.0, range 24–71 years), the mean age of the patients was 15.7 years (SD = 9.9, range 0–47 years). Most parents reported being married ($n = 44$). The most frequently reported highest educational qualification was lower secondary education ("Hauptschulabschluss") ($n = 18$), followed by high school ("Realschulabschluss") ($n = 16$) and high school graduate ("Abitur") ($n = 13$). Most participants reported being in permanent employment ($n = 38$) or homekeeper/retired ($n = 17$). In addition, 73% of the participants stated that they could "easily" manage on their available income, 24% reported "not bad", and 3% reported "difficulties some of the time". On median, 2–3 people lived in one household ($n = 54$) with $\leq$2 children ($n = 52$). Most of the participants described their own health as good ($n = 38$) or fair ($n = 11$). About a quarter of the participants reported being consanguineous ($n = 16$ out of 14 families), with 43% being first-grade cousins, and 57% being second-grade cousins.

3.2. Parental Needs Survey

Most parents reported feeling very confident or confident about understanding the disease and explaining it to others (Part 1, Items 1–4). The majority of parents were extremely satisfied or satisfied with working with health professionals and the overall support (Part 2, Items 1–3). About half of the parents reported to feel extremely satisfied (37%, $n = 22$) or satisfied (12%, $n = 7$) with the health professionals' knowledge about their child's disease, while about one-fourth reported dissatisfaction (14%, $n = 8$) or extreme dissatisfaction (14%, $n = 8$). This included health professionals from the university hospital as well as from non-specialized institutions.

Most participants indicated that they could easily afford paying for medical care/therapy (75%, $n = 44$) or paying for babysitting/short-term care (76%, $n = 45$). Approximately half of the parents (53%, $n = 31$) reported that they could easily pay for special equipment or clothing, while only few of the participants stated that they had difficulties (14%, $n = 8$) or could not afford special equipment or clothing (12%, $n = 7$). Despite expressed confidence about understanding the disease, about one-third reported a medium (22%, $n = 13$) or high (8%, $n = 5$) need for additional information on the growth and development of their child. Furthermore, the participants reported a medium (22%, $n = 13$) or high (22%, $n = 13$) need for information on current or future services available for their child.

The parents also shared a need for additional supporting services. In fact, 14% (n = 8) of them indicated a medium, and 19% (n = 11) a high need for support in finding a suitable caretaker; 69% (n = 41) of the participants requested no additional need for support regarding the reconciliation of work and family life, while 22% (n = 13) reported a high need. About one-third indicated a need (medium = 15%, n = 9; high need = 17%, n = 10) to talk to other affected families. Most parents reported satisfaction or no additional need for support regarding the relationship with their partners or the siblings of the affected child (Part 4, Item 8 + 9). Only a few participants stated a high need of support for their insomnia (12%, n = 7), fatigue (5%, n = 3), loss of appetite (2%, n = 1) or in finding meaning in the situation (3%, n = 2). In contrast, about one-third indicated a medium (15%, n = 9) or high (14%, n = 8) need of support for their feeling of physical exhaustion.

Moreover, the participants shared a need for support (medium = 15%, n = 9; high = 15%, n = 9) with feeling useless, powerless, and helpless. Most parents explained no need of support for their communication with health professionals (does not apply = 14%, n = 8; satisfied = 59%, n = 35). When asked whether they had needs for any further services, 42% (n = 25) of the participants reported a need for additional support groups, and 29% (n = 17) indicated a need for additional psychological support. Less required additional services were financial counseling (22%, n = 13), marriage counseling (20%, n = 12), genetic counseling (19%, n = 11) and social work (12%, n = 7). Overall, 68% (n = 40) of the participants reported an unmet need regarding one or more of the listed services.

3.3. Gender and Income

Stratification of the data set by participant gender showed a difference ($X^2(4) = 10.9$; $p \leq 0.05$) in terms of satisfaction with "having a consistent team of health professionals who take responsibility for the overall health of my child": overall, mothers reported to be more satisfied than fathers.

Item 8 of the sociodemographic data collection asks participants to self-assess their ability to manage their situation with the financial income available to them. Looking at the data after stratification, differences were found in three sections: "Financial needs" revealed differences in the need of support with paying for medical care/therapy ($X^2(8) = 16.4$; $p \leq 0.05$) and with paying for special equipment/clothing ($X^2(8) = 15.7$; $p \leq 0.05$). Both items revealed that participants who indicated to have difficulties managing their available household income more often reported a high need for support. The section "Information needs and social, physical, spiritual and psychological needs" showed differences in the need for support regarding the physical and psychological needs. For physical needs such as "feeling of physical exhaustion" ($X^2(8) = 19.0$; $p \leq 0.01$), "insomnia" ($X^2(8) = 25.3$; $p \leq 0.001$) and "loss of appetite" ($X^2(8) = 35.9$; $p \leq 0.001$) and psychological needs like "the need to speak to other parents" ($X^2(8) = 16.5$; $p \leq 0.05$), "finding meaning in the situation" ($X^2(8) = 19.9$; $p \leq 0.01$) and "feeling useless, powerless and helpless" ($X^2(8) = 18.3$; $p \leq 0.05$), our data showed that parents with difficulties managing their available household income more often reported high needs for support. Further, we studied whether there was a difference in the need for additional supporting services. Respondents with higher financial needs more often reported a need for marriage counseling ($X^2(2) = 7.5$; $p \leq 0.05$), financial counseling ($X^2(2) = 15.0$; $p \leq 0.001$), and support groups ($X^2(2) = 10.2$; $p \leq 0.01$); the reported overall need of support for the listed services was also higher ($X^2(2) = 6.8$; $p \leq 0.05$).

3.4. Disease Subtypes

The results revealed some differences in all sections, for the data stratified by disease subtype. In the first section, the results showed a difference in the understanding of the disease in items 1 "Teach my child about the disease" ($X^2(18) = 29.5$; $p \leq 0.05$) and 4 "Explain my child's disease to my parents or relatives" ($X^2(24) = 51.5$; $p \leq 0.001$). Parents of patients with CPS1-D, HHH syndrome or LPI stated more often that they did not feel confident. Parents of patients with HHH syndrome more often reported dissatisfaction regarding "Feeling that you are part of a health care team looking after your child" ($X^2(24) = 37.7$;

$p \leq 0.05$). Furthermore, parents of patients with HHH syndrome or LPI more often reported a high need for financial support with "Paying for special equipment or special clothes" ($X^2(24) = 36.6$; $p \leq 0.05$). In the fourth section, the data showed a difference in support needs for item 8, "Relationship with my child's siblings" ($X^2(18) = 29.2$; $p \leq 0.05$), with parents of patients with ASL-D more often reporting high support needs. There was a difference in the need for support for items 13, "Finding meaning in the situation" ($X^2(24) = 66.0$; $p \leq 0.001$), and 15, "Feeling useless, powerless and helpless" ($X^2(24) = 42.2$; $p \leq 0.01$). Parents of patients with CPS1-D, HHH syndrome or LPI reported a high need more often. The results also showed a difference in the need for additional support services, especially for marriage counseling ($X^2(6) = 13.4$; $p \leq 0.05$), psychological counseling ($X^2(6) = 13.1$; $p \leq 0.05$), support groups ($X^2(6) = 15.9$; $p \leq 0.01$), genetic counseling ($X^2(6) = 15.6$; $p \leq 0.05$) and social work ($X^2(6) = 16.8$; $p \leq 0.01$). The comparison within the OTC group between parents of male OTC-D and female OTC-D patients showed a difference in the need for additional genetic counseling ($X^2(1) = 4.5$; $p \leq 0.05$). Parents of female OTC-D patients indicated a need for genetic counseling more often than parents of male OTC-D patients.

3.5. Age of the Patients

For age stratification, the study population was divided into four age groups, each spanning 6 years, based on the age of the patients. The groups of parents interviewed were distributed as follows: 1 (0–6 years): 10 individuals; 2 (6–12 years): 19 individuals; 3 (12–18 years): 12 individuals; 4 (>18 years): 18 individuals. Group 1 represented parents of young patients, group 2 parents of primary school patients, group 3 parents of adolescents, and group 4 parents of adult patients. The results showed, when stratified by age group, differences in the need of support. Parents of younger patients (Group 1 + 3) reported a higher need regarding "Speaking to health professionals" ($X^2(12) = 23.3$; $p \leq 0.05$). In addition, the data revealed a difference in the need for additional services such as marriage counseling ($X^2(3) = 10.1$; $p \leq .05$), psychological counseling ($X^2(3) = 17.6$; $p \leq 0.001$) and genetic counseling ($X^2(3) = 12.0$; $p \leq 0.01$). Also in this case, the parents of patients of a younger age (group 1–3) reported more often a need for support. Furthermore, the parents of older patients (group 4) more often indicated no further need for support ($X^2(3) = 10.5$; $p \leq 0.05$).

4. Discussion

The aim of this observational, single-center pilot study was the assessment of family burden and need for support in parents of patients with UCDs. The study revealed a consistent need for additional support and information, mainly in the fields of working with healthcare professionals, information, supporting services, and an income-/disease subtype-specific burden.

Our data did show that needs pertaining to understanding the disease were actually met. Previous studies on the support needs of parents with chronically ill children showed a gender difference and a higher burden among women [33], but the results of the present study did not show any difference in this respect (Section 3.3). In addition, the majority of respondents to surveys asking about burden and coping with sick children are usually mothers, as they often share the greater share of parenting responsibilities [29,36]. In our study, about half of the respondents were male (Table 1).

Table 1. Sociodemographic Characteristics.

Participants	***n***	**%**
Mothers	34	57.6
Fathers	25	42.4
Total	59	100.0
Patients	50	
UCD Subtypes		
ASL-D	8	16.0
ASS-D	13	26.0
CPS1-D	2	4.0
HHH Syndrome	2	4.0
LPI	1	2.0
OTC-D	24	48.0
Female OTC-D	12	24.0
Male OTC-D	12	24.0
Marital Status		
Divorced	4	6.8
Separated	4	6.8
Member of an unmarried couple	4	6.8
Married	44	74.6
Widowed	3	5.0
Highest Educational Status		
Never attended school or kindergarten	1	1.7
Lower secondary education	18	30.5
High school	16	27.1
High school graduate	13	22.0
College (≤3 Years)	2	3.4
College (>3 Years)	7	11.9
I do not know/Not sure	2	3.4
Employment Status		
Employed for wages	38	64.4
Homekeeper/Retired	17	28.8
Self-employed	4	6.8
How do you manage on your available household income from all sources?	*n*	%
Easily	43	72.9
Not Bad	14	23.7
Difficult some of the times	2	3.4
How many people live in your household?		
<18		
0	16	27.1
1	16	27.1
2	20	33.9
3	5	8.5
4	0	0.0
5	2	3.4
>18		
1	1	1.7
2	41	69.5
3	13	22.0
4	4	6.8

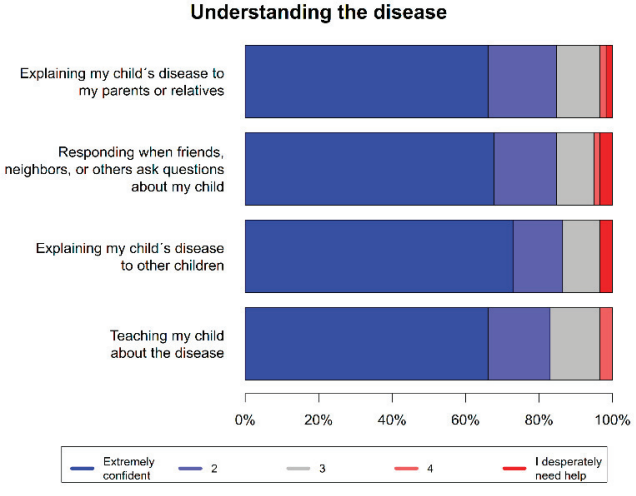
Table 1. *Cont.*

Participants	*n*	%
Would you say that in general your health is . . .		
Excellent	3	5.1
Very Good	4	6.8
Good	38	64.4
Fair	11	18.6
Bad	3	5.1
How many of your children are affected by a rare disease?		
1	51	86.4
2	7	6.8
3	1	1.7
How many biological siblings does your affected child have?		
0	19	32.2
1	25	42.4
2	12	20.3
3	1	1.7
4	2	3.4
Are you and the other parent of the affected child related? If yes, please indicate the degree.		
Yes	16	27.1
First	6	10.2
Second	8	13.6
>Second	2	3.4
No	42	71.2
Do not know	1	1.7

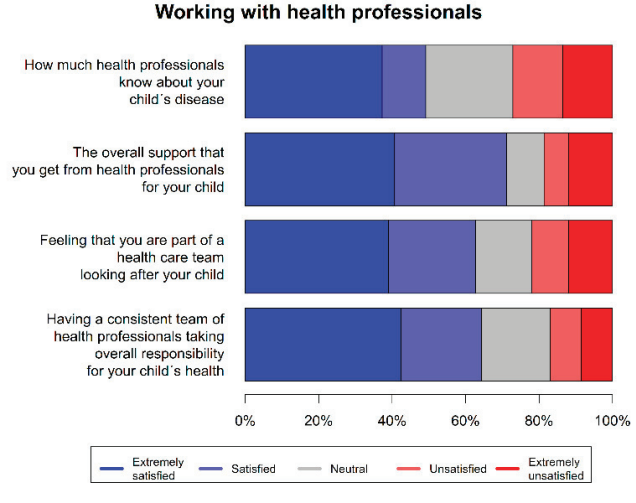
List of abbreviations: OTC-D (ornithine transcarbamylase deficiency) with subgroups *female/male* OTC-D, ASS-D (argininosuccinate synthetase deficiency), ASL-D (argininosuccinate lyase deficiency), CPS1-D (carbamoylphosphate synthetase 1 deficiency), HHH (hyperornithinemia–hyperammonemia–homocitrullinuria syndrome), LPI (lysinuric protein intolerance).

4.1. Working with Health Professionals

The complexity of IMDs often requires treatment by specialized multidisciplinary teams [37,38]. It has been shown before that medical care for IMDs outside of specialized centers can be unsatisfactory, especially in emergency situations [37]. On the one hand, our results revealed that most parents were extremely satisfied or satisfied with working with health professionals and the overall support (Figure 1b). In this context, it is important to consider that the participants in this single-center pilot study were cared for by the Department of Pediatric Neurology and Metabolic Medicine at the Centre for Child and Adolescent Medicine University of Heidelberg, which employs IMD specialists. On the other hand, about one-third indicated a dissatisfaction with the health professionals' knowledge about their child's disease (Figure 1b). This dissatisfaction might be related to the lack of information on the disease and therapeutic options, as difficulties caused by a lack of knowledge about the disease and a lack of disease-specific support services are common for rare diseases [34]. At the same time, low awareness on rare diseases is often associated with delays in diagnosis and treatment, which in turn leads to an increased burden [33]. In particular, non-specialized health professionals often lack the necessary experience and knowledge [39]. Therefore, there is a need to raise awareness of rare metabolic disorders such as UCDs and improve the medical care outside of specialized facilities. For this, low-threshold collaborations within specialized networks on a national or even international level can be helpful. Patient representatives should be included in these networks. Further studies following this pilot study should further analyze the conclusions mentioned above and the differences between different health care institutions through specific surveys.

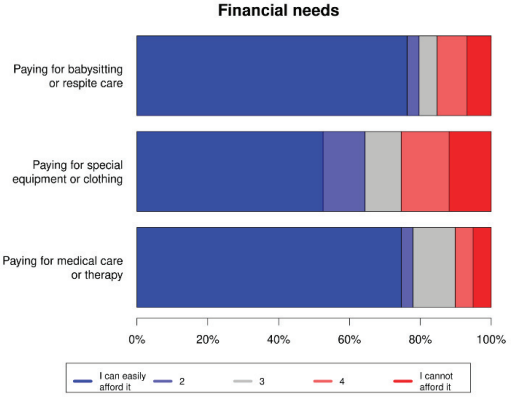


(**a**)

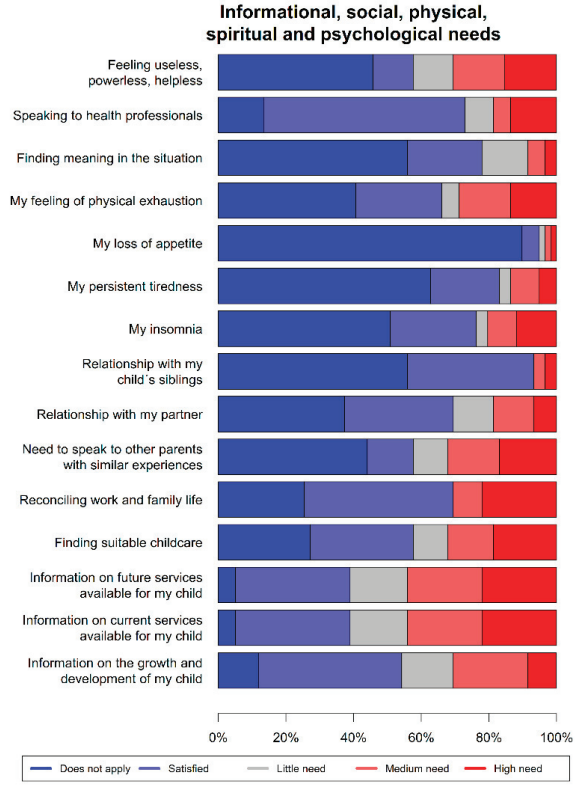


(**b**)

Figure 1. *Cont.*



(**c**)



(**d**)

Figure 1. (**a**) Part 1: Understanding of the disease, (**b**) Part 2: Working with health professionals, (**c**) Part 3: Financial needs, (**d**) Part 4: Informational, social, physical, spiritual and psychological needs. (The answer option "does not apply" in Section 4 is to be understood as "no need" (neither satisfaction with existing services nor need for additional support).

4.2. Disease-Specific Information Needs

Although most participants reported to feel very confident or confident about the understanding of the disease, about one-third reported a medium or high need for additional information on the growth and development of their child, and nearly half reported a medium or high need for information on current or future services available for their child (Figure 1a). This need might be related to the difficulty of arising questions about the disease that cannot be clearly answered, mostly because of a lack of evidence-based information [40]. The need for information, expressed by the parents, underscores the importance of regular appointments and assessments at specialized facilities for the whole family to keep the families informed of the latest developments in their IMD, answer their questions, and respond to emerging needs [36]. At the same time, parents' needs highlight the importance of the scientific support of medical care through the establishment of natural history studies and deep phenotyping approaches. For rare diseases, patient registries are thought to be key instruments to achieve a sufficient sample size for the evaluation of the clinical course as well as of diagnostic and therapeutic interventions. In addition, the information supply could be improved through the development of quality-controlled web-based databases and information systems accessible through websites or apps, which could facilitate the accessibility to easy-to-understand knowledge for affected families.

4.3. Supporting Services

The need for psychological support among parents of children with IMDs is high, while few reported sufficient availability [36]. It has been shown before that, regardless of the type of condition, the parents of chronically ill children are more likely to have limited health-related Quality of Life (QoL) compared to the parents of healthy children [30,31]. In this study, 68% of the participants indicated an unmet need for one or more of the proposed services, especially the need for support groups and psychological counseling. These findings underscore the importance of support services such as parent advocacy groups and strongly suggest their promotion. Due to the rarity of the diseases and their geographical distribution, the parents of affected children often lack contact with a peer group with similar experiences [34]. In recent years, however, the possibilities for networking via the internet have become more popular and versatile and offer opportunities for affected families to connect. This contact can be beneficial through emotional support and additional information, which could support the parents in dealing with the disease [33,39].

4.4. Income-/Disease Subtype-Specific Burden

The results showed differences in the support needs when stratified by the disease subtype of the affected patients or the subjective satisfaction with the participants' income (Section 3.3). A weakness of our study is the small sample size and, particularly, the uneven distribution within the subgroups. Nevertheless, trends can be derived regarding the need for support. Overall, the reported need for financial support was low (Figure 1c). This is presumably due to the fact that in Germany, medical expenses are in most cases completely covered by the national health care system [36]. In contrast, about a quarter of the respondents indicated an additional need for financial counseling. Furthermore, it could be shown that parents who indicated difficulties with managing their income more often indicated a high need for support in the following sections of the questionnaire (Section 3.3). This is in line with previous studies, which showed a financial burden on the parents of children with an IMD, especially those with a required dietary treatment [26,28]. The analysis of the data according to the diagnosis subtype also showed differences (Section 3.4), whereby the unequal and sometimes very small group size of the subgroups must also be considered here. However, a tendency can be shown that the parents of patients with HHH syndrome, CPS1-D or LPI, disorders that have a very low incidence in common (approx. < 1:2,000,000 [5]), more often indicated a high need for support. This may be related to the lack of evidence-based information and peer support [34,40], which may be even more pronounced for these very rare diseases. Stratification by sex of the patients revealed

a difference in burden among the parents of patients with OTC-D, as the parents of female patients with OTC-D more frequently reported a need for genetic counseling (Section 3.4). Apart from this, no specific burden was found among the parents of male patients with OTC-D compared with those of female patients with OTC-D, which is surprising, considering the higher severity of the disease course in male patients.

4.5. Age-Specific Burden

Due to advances in the diagnosis and therapy options of IMDs, more and more affected children are reaching adulthood, which presents new challenges [27,41,42]. UCD patients usually require lifelong therapy, which is why appropriate care is also necessary in adulthood [41–43]. Such transitions are challenging for the health care system, as well as for patients and caregivers [38], and the access to services that promote the transition to an independent adult life of patients with IMDs is limited [36]. This suggests that depending on the age of the patient, varying difficulties and burdens for the parents could be in focus. When stratified by the age groups of the patients, the results showed some differences in the need for additional support services (Section 3.5). Overall, the evaluation showed that parents of older patients in group 3 (12–18 years) and 4 (>18 years) more often had no need for additional support services. Those results are in line with previous studies on the psychological adjustment of parents of chronically ill children, which suggest that good adjustment is possible, but still the risk of poor adjustment is significantly higher than in the general population [29,30,44].

4.6. Study Limitations and Strengths

This study is subject to certain limitations. First, the study was planned and conducted as a pilot study and includes patients treated only in one university center in Germany. This consideration neglects possible differences between care in different sectors of the health care system. Furthermore, national differences in care and support, e.g., due to different health care systems, must be assumed, so follow-up studies should include an international perspective. The European collaboration of the E-IMD network may be helpful for this. In addition, because of the rarity of UCD-associated diseases, only single families could be studied for some enzyme defects. Therefore, confirmation of the results in a larger collective would be desirable. Another limitation is the partly deficient language skills and e-health competence, which may have influenced the accuracy of the responses of the respective participants. Furthermore, it must be considered that the study was conducted during the COVID-19 pandemic. The effects of the pandemic and changes in the daily lives as well as in the healthcare systems may have put an additional burden on the families during the study period [45] and biased the results of this study.

A strength of this study is found in the fact that despite being single-center study on a rare disease, a high number of participants, especially of male responders, was achieved. The study population covered a wide age range of UCD subtypes. Despite an overall small study group, trends could be identified. Through the multidisciplinary team of contributors, versatile views and interpretations of the results could be achieved. The use and adaptation of validated questionnaires and the online implementation makes the survey easily applicable to other disorders in multi-center studies.

5. Conclusions

In conclusion, the results of this study demonstrate the importance of developing and piloting family-centered care approaches. The burden situation and support requirements of families with affected patients still do not seem to be fully assessed by medical professionals and should therefore be regularly and thoroughly reviewed. Knowledge of the disease process and the latest information about it should be regularly shared with families. This pilot study can serve as a template for assessing the family burden of inherited metabolic diseases. In a future study, a multicenter approach could be taken to increase the number of participants to also identify site-specific gaps in care to capture regional differences. A

structured international comparison of different health care systems, e.g., in the context of the European reference network MetabERN, could also be considered.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/children9050712/s1, Supplementary File S1: Questionaires_Englisch_Scharping_Supplement_S1.

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Institutional Review Board Statement: The study was approved by the local ethics committee of the University Hospital Heidelberg. All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent with regard to being included in the study was obtained from all patients or their legal guardians prior to being included in the study in countries where this was needed by law.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: All data supporting the findings described in this manuscript are not publicly available due to existing data protection laws but are available from the corresponding author (T.O.) upon reasonable request and within the limitations of the informed consent.

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Article

Psychosocial Characteristics and Experiences in Patients with Multiple Endocrine Neoplasia Type 2 (MEN2) and Medullary Thyroid Carcinoma (MTC)

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Abstract: Multiple Endocrine Neoplasia type 2 (MEN2) is a genetic cancer syndrome for which there are limited data pertaining to the quality of life and psychosocial experiences of persons affected. Medullary thyroid carcinoma (MTC) is a rare disease of the thyroid gland often associated with MEN2. MTC often progresses slowly and may present with a myriad of physical symptoms including hair loss, sleep disturbance, fatigue, weight changes, heart palpitations, and constipation or diarrhea. Like other cancers or rare, inheritable illnesses, patients with MEN2 and MTC may be at risk for psychosocial stressors. The current, cross-sectional study administered a structured psychosocial interview and The Distress Thermometer/Problem Checklist to 63 patients with MEN2 and MTC and their caregivers. Despite reports of overall good health, 46% of adults and 44% of youth reported that pain interferes with their daily life; 53% of adults and 59% of youth reported that pain interferes with their mood. Pediatric patients frequently reported experiencing attention challenges (50%) and difficulty concentrating (65%). Parents reported that mood shifts and becoming upset easily were the most prevalent concerns for their children. The most frequent need for services included education about MTC, treatment and research participation, and the opportunity to meet others with MTC.

Keywords: medullary thyroid carcinoma; psychosocial; pediatrics; young adults

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1. Introduction

Multiple Endocrine Neoplasia (MEN) 2A and 2B are rare cancer predisposition syndromes resulting from germline mutations of the Rearranged during Transfection (RET) oncogene [1]. In children and young adults, MEN 2A and 2B is frequently associated with Medullary thyroid carcinoma (MTC), a rare malignancy derived from neural crest-derived parafollicular C cells of the thyroid gland. It accounts for 3–10% of all thyroid carcinomas [2,3]. Sporadic MTC (in the absence of germline RET alteration) is typically seen in middle-aged adults [4–7]. MEN 2A is characterized by hereditary MTC in almost all affected individuals. Additionally, around half of affected individuals also develop pheochromocytoma, and approximately 15% may also develop hyperparathyroidism. Patients can present as early as five years of age, but typically present between the ages of 15–20, and age of disease onset and symptom phenotype is influenced by the type of RET mutation [8,9]. MEN 2B is less common than MEN 2A, but is a clinically more aggressive form, and it also presents in the earlier years of life. MTC develops in virtually all patients with MEN 2B and is the leading cause of death in these patients. Patients with MEN 2B may also have gastrointestinal (GI) dysmotility and abnormal dilation of the GI tract such as megacolon or megaesophagus. Skeletal deformities such as slipped capital femoral

epiphysis (SCFE), scoliosis, pectus, and foot abnormalities may also be associated with MEN 2B [4,5,10–12].

MTC is the most common cause of death in patients with MEN 2A and MEN 2B, as there are limited treatment options for advanced or metastatic disease and the tumor is relatively unresponsive to conventional doses of radiation therapy and to standard chemotherapeutic regimens [2,13–21]. Tyrosine kinase inhibitors that block RET activity are effective in treating patients with MTC, but resistant disease can develop [22]. Thyroidectomy performed at an early age when the tumor is confined to the thyroid gland is the only curative treatment for patients with MTC. In patients with known family history, early recognition through genetic screening and detection of one of the characteristic mutations followed by prophylactic thyroidectomy has become the standard of care [23–25]. However, in many instances, particularly in patients with MEN2B, there is no known family history, and patients are diagnosed with more advanced disease that cannot be cured by surgery alone [26].

MTC is often described as having a chronic and indolent disease process because it progresses slowly, over years or decades, with or without symptoms. Like other cancers, over time MTC has the potential to significantly impact the physical as well as emotional, social, and financial well-being of diagnosed individuals and their loved ones. Patients may suffer from symptoms related to iatrogenic hypothyroidism such as hair loss, sleep disturbance, fatigue, weight changes, heart palpitations, temperature sensitivity, and constipation or diarrhea. Psychological symptoms may include inability to concentrate, depression, or anxiety. As MTC in association with MEN 2 is an inheritable disease, unique psychosocial stresses associated with this disease have been noted as important to investigate [27,28].

Studies have examined the psychosocial aspects associated with genetic testing [27,29] and the impact of being at risk of MTC on patients' quality of life [28,30]. Additionally, psychological distress, coping, and quality of life have been assessed in patients with MEN2 [28,31–33]. However, few studies have explored whether there are unique parental concerns and family stresses associated with MTC compared to those for parents of children with other pediatric cancers. Similarly, there are no data to examine whether the stresses for youth living with MTC and their family members change over time, or if concerns differ across the lifespan. This is an area of particular concern given the potential impact on fertility and risk of passing on MEN in future children.

As part of a larger NIH IRB approved study designed to develop a better understanding of the biology and natural history of MEN 2 with or without MTC in children and young adults, we aimed to learn about the psychosocial experiences of this patient cohort.

2. Materials and Methods

2.1. Participants

Pediatric and adult patients with histologically or cytologically confirmed MTC, or those with known MEN2 syndrome (with or without MTC) who were able to travel to the NIH and undergo evaluations, were eligible for the natural history study. Exclusion criteria included not being able to return for follow-up visits, obtain required follow-up studies, or sign a written informed consent document.

All patients enrolled in the natural history study were invited to participate in the collection of psychosocial measures. A psychosocial provider (L.W., S.B.) met with each patient during their visit, during which time the measures were completed. Pediatric and young adult patients ($\geq$12 years) completed self-report measures and parents/caregivers (referred to as parents from here on) of children or young adults of all ages completed proxy measures. However, for this sample, parent responses were only included for patients under 18 years of age. Notably, responses were collected and included from one parent only. All participants provided consent or assent, when applicable, or consent was obtained from their parent or legal guardian.

2.2. Measures

Structured Psychosocial Assessment Interview: As no specific standardized instrument assessing how MTC impacts quality of life was available, a structured self-report assessment was designed for the overall study. A version of the structured psychosocial assessment was developed for the NIH Gastrointestinal Stromal Tumor (GIST) Clinic in order to identify specific psychosocial areas of concern and self-identified patient-related needs [34]. The assessment was adapted for the MTC cohort after conducting a literature review related to MTC and psychosocial functioning. It contains items covering demographic factors, family stressors, general health, psychosocial concerns, psychiatric history, self-identified needs, expectations regarding disease outcome and positive events that might have occurred since diagnosis, and interest in a range of possible psychosocial services [34]. To enhance the face validity of the data, the questions were checked by medical and nursing staff experienced in the care of persons living with MTC. Three versions of the assessment were created: one for adult patients (age $\geq$ 18 years), one for parents of children with MTC to complete about their child, and a third, shorter assessment for adolescent patients (ages 12–17 years).

Distress Thermometer: The Distress Thermometer (NCCN, 2008) is a brief screening tool endorsed by the National Comprehensive Cancer Network (NCCN) to assess for distress in adult cancer patients. The Distress Thermometer (DT) is a visual-analog scale similar to those used to assess pain. The scale ranges from 0 (No Distress) to 10 (High Distress) and includes a "problem list" where patients can identify the specific reasons for their distress. The DT has been widely validated in adult ($\geq$18 years) cancer patients, recognized as a good alternative to many of the longer measures commonly used to screen for distress in cancer patients [35], and has been adapted and validated in pediatric patients with cancer and other serious conditions [36–38]. The DT was further adapted for this protocol to include some of the specific issues thought to potentially cause distress in patients living with MTC, including body image, pain, weight gain or loss, and gastrointestinal concerns. Two versions of the DT have been developed for this protocol, one for parents of children to complete about their child, and a second for adolescent and young adult patients. As the questions contained in both the psychosocial assessment and on the DT problem list are not developmentally appropriate for children under the age of 12, data for children younger than 12 years were obtained though parent report only.

2.3. Statistical Analysis

Data were analyzed using IMB SPSS 27 statistical software. Unless otherwise indicated, when items contained missing responses, the valid percent was reported.

Qualitative analyses were conducted on open-ended, free-text narrative responses. These responses were analyzed by two authors (R.L., S.B.) to identify common themes. The authors met to refine themes and develop codes for analysis (Macqueen et al., 1998). Free-text responses were then coded in parallel (R.L., S.B.) with differences resolved through consensus discussion. Responses that were judged to fall under one or more thematic categories were coded under all applicable themes.

3. Results

3.1. Characteristics of the Total Sample

3.1.1. Demographic Characteristics

Sixty-three patients participated in this study; 77.8% (n = 49) were diagnosed with MEN2B and 22.2% (n = 14) were diagnosed with MEN2A. Additionally, 82.5% (n = 52) had also been diagnosed with MTC at the time of this study. As shown in Table 1, the total patient sample was largely pediatric (73%) and predominantly white (71.4%). The sample was comprised of 31 males and 32 females. Over half of adult participants had graduated high school or received an equivalent degree (28.6%), completed some college or vocational school (21.4%), or graduated college or vocational school (28.6%). Parents of pediatric patients (n = 46) were predominantly mothers (71.1%), married (80%), and highly

educated, with 28.9% having graduated from college or vocational school and 20% having completed a professional or graduate degree.

Table 1. Demographic characteristics of pediatric and adult patients with Medullary Thyroid Carcinoma (MTC).

	Total Sample		**Pediatric (<12 Years)**		**Pediatric (12–17 Years)**		**Adult Sample (≥18 Years)**	
Characteristic	*n*	%	*n*	%	*n*	%	*n*	%
Total N	63	100	15	23.8	31	49.2	17	26.9
Diagnosis								
MEN2B	49	77.8	10	66.7	27	87.1	12	70.6
MEN2A	14	22.2	5	33.3	4	12.9	5	29.4
MTC Diagnosis								
Yes	52	82.5	10	66.7	28	90.3	14	82.4
No	11	17.5	5	33.3	3	9.7	3	17.6
Age								
Mean (M)	16.4		8.5		14.9		26.0	
Standard Deviation (SD)	8.2		2.4		1.4		9.5	
Range	2.7–49.1		2.7–11.9		12.1–17.9		18.2–49.1	
Gender								
n	63		15		31		17	
% Male	31	49.2	8	53.3	14	45.2	9	52.9
% Female	32	50.8	7	46.7	17	54.8	8	47.1
Race								
n	63		15		31		17	
% White	45	71.4	12	80.0	22	71.0	11	64.7
% Black/African American	5	7.9	0	0	3	9.7	2	11.8
% Latino/a	8	12.7	1	6.7	4	12.9	3	17.6
% Asian/Pacific Islander	3	4.8	2	13.3	0	0	1	5.9
% Other	2	3.2	0	0	2	6.5	0	0
Received Special Education								
n	59		14		30		15	
% Yes	15	25.4	4	28.6	7	23.3	4	26.7
% No	44	74.6	10	71.4	23	76.7	11	73.3
Highest Education Completed *								
n							14	
% Less than high school							1	7.1
% Graduated high school/GED **							4	28.6
% Some college/vocational							3	21.4
% Graduated college/vocational							4	28.6
% Some professional/graduate							0	0
% Graduate/professional degree							2	14.3

* Adult participants only. ** General Educational Development.

3.1.2. Clinical and Mental Health Characteristics

Parents and adult and pediatric patients were asked to indicate whether they or their child had experienced any mood, psychological, or social difficulties over the past month. As shown in Table 2, the most frequently reported areas of concern indicated by adult patients ($n = 15$) with MEN2 or MTC were a tendency to "cry or become upset easily" (40%), "feeling sad or depressed" (33.3%), "difficulty concentrating" (33.3%), and "anxiety or panic attacks" (26.7%). As shown in Table 3, 3 of 17 adults reported currently being under the care of a mental health provider for therapeutic or prescription-based treatment. However, despite reporting very few symptoms on the psychosocial assessment, of adult patients that provided responses ($n = 15$), over half (66.6%) indicated moderate to severe distress over the past month on the DT scale. The average overall distress rating was 5.0 (SD: 2.8,

Range 0–10). Of those reporting moderate to severe distress (n =10), the predominant areas of concern were "feeling worried or anxious"(80%), "pain" (70%), and fatigue or lack of energy (80%).

Table 2. Adult self-report of psychosocial symptoms.

Symptom	Adult Self Report [1] ≥18 Years (n = 15)	
	n	%
Mood shifts	3	20.0
Attention difficulties	3	20.0
Cries or upset easily	6	40.0
Difficulty concentrating	5	33.3
Anxiety or panic attacks	4	26.7
Sad/Depressed	5	33.3
Loss of interest or pleasure in activities	2	13.3
Feeling hopeless	1	6.7
Difficulty making friends	1	6.7
Difficulty keeping friends	3	20.0

[1] Valid percentage reported.

Table 3. Mental health treatment characteristics.

	Pediatric (n = 46) [1]		Adult (n = 17)	
	n	% [2]	n	%
Receiving mental health treatment	10	21.7	3	17.6
Taking medication for anxiety	5	10.9	2	11.8
Taking medication for depression	3	6.5	3	17.6
Taking medication for attention difficulties	2	4.3	2	11.8

[1] Based on parent/caregiver responses for pediatric patients < 18 years. [2] Percentage of the total pediatric sample (n = 46).

Psychosocial symptoms were reported more frequently amongst pediatric patients and their parents. "Difficulty concentrating" (65.4%) and "attention challenges" (50.0%) were among the most prevalent symptoms identified by pediatric participants. In contrast, as shown in Table 4, parents across pediatric age groups reported that "mood shifts" and a tendency to "cry or become upset easily" were the most frequent challenges for their children. Despite the increase in symptom reporting, the pediatric population remained similar to adults in that a much smaller proportion of those reporting symptoms were receiving any form of therapeutic treatment for their psychosocial concerns at the time of the study. Twenty-six adolescent patients (ages 12–17) provided responses to the DT scale; the average distress rating was 4.27 (SD: 2.6, Range: 0–10). Half reported scores within the moderate to severe range. Among those patients (n = 13), "feeling worried or anxious" (76.9%) and "schoolwork" (69.2%) were the most frequently reported sources of distress. Doctor/hospital visits, pain, and difficulty concentrating were also reported by just over half of the pediatric sample (53.8%). Parents of adolescent patients with MTC were also asked to indicate their child's distress over the past month and they reported an average distress rating of 4.48 (SD:2.5; Range 0–10). Sixty-one percent endorsed scores within the moderate to severe range. Within this subgroup of parents, "worry and anxiety" (63.0%), "fatigue" (55.6%), "frequency of doctor and hospital visits" (59.3%), and "parental stress" (59.3%) were among the most distressing experiences for their child.

Table 4. Pediatric and parent report of psychosocial symptoms.

Symptom	Pediatric Self Report [1] 12–17 Years (n = 26)		Parents of [1] Child 12–17 (n = 30)		Parents of Child <12 Years (n = 15)	
	n	%	*n*	%	*n*	%
Mood shifts	7	26.9	17	56.7	7	46.7
Attention difficulties	13	50.0	9	30.0	3	20.0
Cries or upset easily	10	38.5	12	40.0	6	40.0
Difficulty concentrating	17	65.4	10	33.3	3	20.0
Anxiety or panic attacks	8	30.8	8	26.7	3	20.0
Sad/Depressed	8	30.8	6	20.0	5	33.3
Loss of interest or pleasure in activities	7	26.9	4	13.3	0	0
Feeling hopeless	2	7.7	4	13.3	3	20.0
Difficulty making friends	3	11.5	8	26.7	5	33.3
Difficulty keeping friends	5	19.2	6	20.0	4	26.7

[1] Valid percentage reported.

3.2. Perceptions of Physical Health and Pain

Most adults living with MTC reported that their overall physical health was in 'good' (40%) 'very good' (26.7%), or 'excellent' (6.7%) condition. Twenty-three percent of adults that provided responses (n = 15) reported their overall health was 'fair.' Over half of adults reported experiencing pain at least once per week (Figure 1). Forty-six percent reported that pain interfered with their daily lives and fifty-three percent reported that pain interfered with their mood.

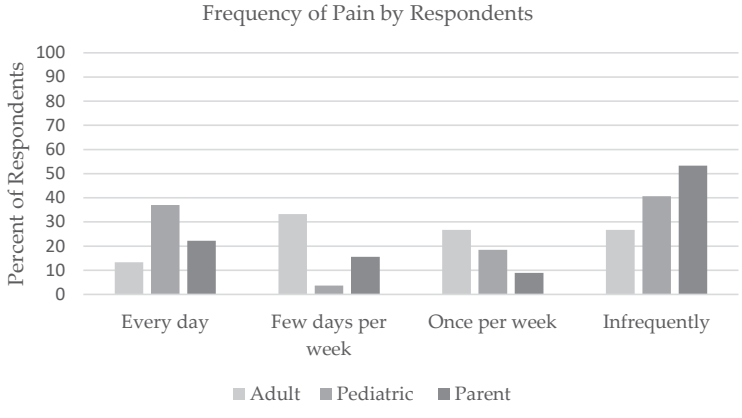

Figure 1. Ratings of pain frequency as reported by adult and pediatric self-report population, and parents of pediatric MTC patients of all ages. Pediatric self-report n = 27; parent report n = 45 Adult self-report n = 15.

The majority of pediatric participants living with MTC reported to be in 'good' (37%), 'very good' (33.3%), or 'excellent' (14.8%) physical health, while 14.8% reported their physical health as 'fair.' Although 40.7 percent of the pediatric cohort reported experiencing pain 'infrequently,' a similar proportion (37%) reported experiencing pain everyday (Figure 1). Forty-four percent of youth reported that pain interferes with their daily life, and 59.3 percent reported that pain interfered with their mood. Fifty-three percent of parents reported their child experienced pain 'infrequently' and that pain did not interfere with their lives. However, 46.7% of parents reported that pain interfered with their child's life, and just over half (51.1%) reported that pain did interfere with their child's mood.

3.3. Qualitative Data and Interest in Supportive Resources

In an open-ended question, patients with MTC and their parents were asked to identify the three most difficult parts of living with MTC. Forty-four patients (adult and pediatric) and forty-four parents provided at least one response. Three consistent themes emerged: (1) disease-related experiences and challenges, (2) internalized experiences of living with MTC, and (3) external impact of living with MTC, under which nine codes were developed. Example responses can be found in Table 5.

Table 5. Patient and parent samples of thematic codes.

Theme	Code	Sample
Disease related experiences and challenges	Diagnosis specific concerns	"general sense of illness" (parent) "he will never be cured" (parent) "stress of knowing I have a rare disease" (patient 12–17)
	Treatment Impact	"needles, iv, doctors' visits all the time" (parent) "keeping my medicine organized" (patient 18+) "all the tests, especially needles" (patient 12–17)
	Symptom Impact	"the constant pain" (parent) "physical issues of colon/urinary problems" (parent) "sleep (not sleeping well)" (patient 12–17)
	Physical Limitations	"unable to do things—physical weakness" (parent) "not able to follow the rhythm of peers of my age (physical activity)" (patient 18+) "Not as physically strong as I'd like to be" (patient 12–17)
Internalized experiences of living with MTC (e.g., sadness, depression)	Mental Health Impact	"sadness" (parent) "social/emotional wellbeing" (parent) "overthinking, stress" (patient 18+) "constant worries" (patient 12–17)
	Coping with Uncertainty	"wondering what's going to happen" (parent) "not knowing what will happen from scan to scan" (parent) "doubt with testing and what comes next" (patient 18+) "don't know what the future will bring" (patient 12–17)
	Being and feeling different	inside his mouth that its visible, teeth difference" (parent) "noticing that he is different (physically)" (parent) "people looking and staring" (patient 12–17)
External experiences and challenges of living with MTC (e.g., relationships and school/work environment)	Social Impact	"he has to deal with bedwetting with his friends" (parent) "embarrassment of gas" (parent) "sacrificing a lot of time with friends and family" (patient 18+) "I hate people feeling sorry for me" (patient 12–17)
	Family Impact	"worries about how it affects parents" (parent) "feel guilty for having more attention than my brothers-take up my parents time" (patient 18+) "stress on my family (siblings)" (patient 12–17)
	School/Work-Related Impact	" struggling with ADHD * and school" (parent) "maintaining school alongside doctor visits" (patient 18+) "miss school- make up work, if I miss too many classes I have to repeat 9th grade" (patient 12–17)

* Attention-deficit/hyperactivity disorder.

Diagnosis specific concerns Patients with MTC and their parents described the learning of and presence of the illness itself, rarity of the disease, and limited treatment options as particular challenges related to their diagnosis.

Treatment Related Impact One of the most prevalent codes was related to treatment-related experiences. This code highlighted patient experiences and difficulties with numerous hospital and doctor visits, surgeries, medication management, and medical tests.

Symptom Impact Physical symptoms and the impact of physical symptoms were recurring concerns identified by patients. These frequently included pain, gastrointestinal (GI) symptoms, and sleep disturbance.

Physical Limitations Strength, mobility, and difficulty engaging in physical activities were notable areas of concern for participants. Participants often remarked about feelings of weakness and difficulty keeping pace with their same-aged peers.

Mental Health Impact Participants described feelings of sadness, anxiety, stress, and general decline in social-emotional wellbeing as a result of diagnosis, treatment, or ongoing management.

Coping with Uncertainty Patients and parents often referred to their discomfort surrounding the uncertainty of the future and how the presence of MTC and potential for disease progression would continue to impact their lives and future plans. Participants also described feelings of uncertainty as they waited for results from diagnostic scans. Parents reported uncertainty or feelings of guilt surrounding their genetic mutation and specifically, the impact on their child's health and future.

Being Different Participants noted the difficulty of having to cope with feeling and appearing different than their peers. Differences were attributed to both physical attributes (e.g., mucosal neuromas, bumps on the lips or tongue) as well as the inherent difference of living with MTC, a rare disease, that is not present in the lives of their peer groups.

Social Impact The impact of living with MTC on social interactions was identified as an area of difficulty. Participants described embarrassment surrounding the presence of symptoms, including challenges participating in social activities due to symptom management or medical care appointments. Participants also reported concerns that others would feel sorry for them.

Family Impact Participants described several areas within their families that have been impacted by their MTC diagnosis. Worries about parental and sibling stress, finances, and equally dividing attention amongst affected and unaffected siblings were described.

School/Work Impact Difficulty attending or completing and managing school or work assignments alongside multiple hospital visits or doctor appointments were reported as consistent hardships.

Amongst parents of children with MTC, the most frequently endorsed needs for services were education about MTC, MEN 2, treatment options or current research (92.7%), the opportunity to meet other patients with MTC or MEN 2 (76.9%), and a support group for themselves or other family members (60.0%). Pediatric and adult patients also reported interest in opportunities to meet others with MTC or MEN 2 (Pediatric: 76.0%, Adult: 53.3%) and additional education about MTC, MEN 2, and treatment options (Pediatric: 57.7%, Adult: 73.3%).

4. Discussion

Although the current sample largely reported good to excellent physical health, several interesting results emerged surrounding the utility of supportive services, the impact of pain, and patients' own description of their unique daily challenges. Despite reporting moderate to severe distress in the last month, adult participants generally reported very few mental health symptoms, which was consistent with their current utilization of mental health treatment services. Our results are in contrast with data from adults living with MEN2, which found frequent symptoms of anxiety and depression and indicated that psychological distress is a chronic symptom for adults with MEN2 and is likely due to a number of MEN2-related factors [31]. It is possible that our sample has developed effective

coping strategies over time and that the stress they are reporting is intermittent and not atypical. Conversely, access to mental health support due to financial or other resource barriers may be limited. These results are only a snapshot of the patient experience at one timepoint. In order to evaluate whether effective coping strategies among MTC patients improves with age, it will be important to continue to collect and analyze longitudinal data.

Pediatric patients reported more functional symptoms (inattention and difficulty concentrating) while their parents noticed more mood concerns (e.g., crying, mood shifts). It is well-known that anxiety and worry can present as inattention or difficulty concentrating, which suggests that the pediatric group's symptom endorsements are consistent with some of their most frequent sources of stress in the past month. Despite the apparent prevalence of these challenges in their daily lives, it is quite notable that very few participants had received any current mental health treatment. Pediatric patients did report receiving special education support at a proportion that is higher than the current United States (U.S.) national average [39]; however, the extent of supportive services (e.g., pull-out services, reduced assignments) and the specific learning domains impacted remain unclear. This, coupled with the potential impact that various treatment regimens can have on learning, suggests that objective assessments of attention and anxiety and broad cognitive domains may be warranted in this group. Similarly, it is unclear if parental reporting of mood concerns within their children is potentially a result of their child's frustration with schoolwork, disease-specific worries, the parents' own stress, or a combination of factors.

As anticipated, pain emerged as a frequent area of difficulty for both adult and pediatric patients, with many reporting that pain interfered with their mood and daily lives. Currently, there is no cure for locally advanced or metastatic MTC; thus, patients must manage living with this disease, often for many years. This concept of balancing medical and social-emotional needs with the desire to maintain a sense of normalcy was echoed by patients and parents in their responses to qualitative probes. Particularly revealing were the ways the participants described the burden of multiple hospital visits, uncertainty regarding their futures, and the impact of physical symptoms. In this context, increased support (e.g., pain management, access to therapeutic services) is an important consideration for practitioners across disciplines and their efforts to improve patient functionality and overall quality of life. A critical element to providing this increased support is accurate and consistent measurement of symptoms, quality of life, and psychological distress over time through patient- and observer-reported outcome measures [40,41]. Our sample's qualitative responses are consistent with the current literature surrounding MEN2 patients' reports of psychological distress related to genetic testing and treatment. Specifically, MEN2 patients have reported that initial diagnosis-related stressors lessen over time; however, fear of recurrence and guilt of transmission to children appears to persist [32].

We acknowledge several limitations present in this study. First, there is the potential that this sample population is biased towards patients who felt well enough or had the capacity and means to visit NIH and participate in this study; we may not be fully capturing the range of disease progression and status in this population. Similarly, while this study provides valuable insights into patients' experiences at a single point in time, there is a need for prospective, longitudinal studies to show how psychosocial strengths and vulnerabilities may change over time [42]. Next, our patient sample was not comprised of a diverse racial and ethnic population, which could influence the generalizability of these results. For future studies, we also recognize the need to collect and evaluate relevant disease and treatment variables. This should include the number of surgeries, chemotherapy, and targeted therapies which may be impactful to cognitive, functional, and social-emotional factors and in determining which symptoms could be biological in nature. We only collected self-reported data for children over the age of 12. How children feel and function is critical to understanding their experience of the illness, and future studies should attempt to capture the self-reported experiences of younger children. Finally, collaboration across treatment centers and harmonization of measures used to assess psychosocial and cognitive impacts are also important next steps.

5. Conclusions

MEN2-associated MTC is a rare disease that presents with a number of physical symptoms including changes in physical attributes, limitations, and pain. The present study clearly indicates that the psychological impact of living with MEN2 and MTC extends far beyond these areas. Patients with MTC must balance the burden of their medical and educational needs, unique psychosocial concerns, and uncertainty of the future living with a rare and hereditary syndrome. The challenges described by patients in this study are opportunities for clinical providers. Ongoing, patient-centered education about MTC and symptom management, access to mental health resources, and continued research are paramount in the continued improvement of quality of life for those living with MTC.

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children

MDPI

Systematic Review

Age-Appropriate Advance Care Planning in Children Diagnosed with a Life-Limiting Condition: A Systematic Review

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Abstract: Pediatric advance care planning (pACP) is an important strategy to support patient-centered care. It is known to be difficult, yet paramount, to involve the child in pACP while adjusting treatment to age and the corresponding stage of development. This systematic review was aimed to evaluate the age appropriateness of pACP interventions by assessing their characteristics, content, and evidence. CINAHL, Embase and MEDLINE were searched from 1 January 1998 to 31 August 2020 in order to identify peer-reviewed articles containing strategies and tools to facilitate pACP in both children (0–18 years) with life-limiting conditions and their families. An assessment of quality was performed using Cochrane tools and COREQ. The full protocol is available as PROSPERO CRD42020152243. Thirty-one articles describing 18 unique pACP tools were included. Most tools were developed for adolescents and young adults. In most cases, the interventions tried to assess the child's and family's preferences concerning their current and future hopes, wishes, and goals of the care. This was aimed to enhance communication about these preferences between children, their families, and health-care providers and to improve engagement in pACP. The relevance of an age-appropriate approach was mentioned in most articles, but this was mainly implicit. Seven articles implemented age-appropriate elements. Six factors influencing age appropriateness were identified. Tools to support pACP integrated age-appropriate elements to a very limited extent. They mainly focused on adolescents. The involvement of children of all ages may need a more comprehensive approach.

Keywords: palliative care; life-limiting conditions; pediatrics; adolescents; advance care planning; age-appropriate; development; cognitive functions; young adults; interventions

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1. Introduction

Children with life-limiting conditions often receive highly complex care over a long period of time. This care may include high-risk treatments with severe side effects and palliative care services. The medical conditions and care needs of these children often interfere with their daily life, including their social activities [1]. These children live with the burden of invasive treatment procedures, hospital admissions, and (often) side-effects from therapies [2,3]. However, these children are not routinely asked about their experiences regarding living with illness [3]. In addition, the child's voice is not systematically included in decision making or when discussing treatment preferences [3]. The involvement of parents and children, in a way appropriate for both age and level of development [4],

in decision making is considered obligatory in family-centered health care. However, involving children and families is challenging in practice. Uncertainty about prognoses, fears of disrupting coping strategies, intercultural differences, and the changing demands of developing children make clinicians feel reluctant to initiate conversations about future care with children and their families [5–7]. Furthermore, tools to support the participation of children in decision making regarding their own health care are scarce. However, these tools are needed if the child's perspective when discussing goals and preferences for care and treatment is to be included [8]. In the literature, reports of pediatric advance care planning (pACP) interventions are increasing [9–13]. They are intended to connect the expertise of the child and family with that of the medical team in order to define the shared goals of their care and to better communicate these to all caregivers involved in the child's treatment [14–16]. Advance care planning includes considering the voice of the child, either by listening to the child itself or by identifying the child's perspective through the parents or other involved caregivers. An age-appropriate approach is needed to identify the child's perspective in an adequate way. The child's age, with their corresponding cognitive development, will influence their ability to participate in conversations [4]. The development age of children was divided by Piaget into four stages based on the level of development adequate for the calendar age. These stages are: the sensorimotor stage (from zero to two years old), the pre-operational stage (from two to seven years old), the concrete operational stage (from seven to 11 years old), and the formal operation stage (12 years and above) [5,17]. These stages were based on the idea that different age groups correspond with different levels of cognitive development. However, due to multiple factors, including illness, development age can differ from calendar age. We refer to age appropriateness for a certain development age. Clinicians experience difficulties in incorporating age-appropriate communication strategies tailored to individual needs of children [5]. Even when a child is not too young or cognitively impaired and is able to participate in a conversation, clinicians still tend to focus on the parents when discussing the child's illness [18]. While parents will act as advocates for their child's health, their needs, interests, and coping strategies may interfere with the child's perspective and best interests. This limits the parents' ability to discuss or represent the voice of their child, particularly during the palliative phase [19,20]. Although the outcomes of pACP interventions are promising, it is unknown to what extent interventions elicit the voice of the child in a manner appropriate to their age. The adequate participation of children in ACP can therefore be achieved by using strategies that consider the development ages of children. An overview of pACP interventions appropriate to different ages would be helpful in order to gain insight into strategies for adequately involving children with life-limiting conditions in their own health-care decisions. To our knowledge, an overview of such pACP interventions is still lacking. Therefore, this review was aimed to identify if and how pACP interventions incorporate elements appropriate to the child's age.

2. Materials and Methods

2.1. Data Sources and Searches

This review was structured using The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist and the Palliative Care Literature Review Iterative Method (PALETTE) [21,22]. A structured computerized literature search was conducted in three databases: CINAHL, Embase, and MEDLINE. The search strategy was developed in collaboration with an information specialist and included terms describing the following domains: advance care planning, critical illness, and pediatrics (Table 1). These terms were searched for in all fields, with synonyms and truncations added. Three reviewers independently screened all abstracts in order to select papers reporting on pACP tools in children (0–18 years old) with life-limiting conditions [23]. We resolved questions about whether to include some papers through discussion. The reference lists of studies we included were hand-searched for additional relevant articles.

Table 1. Search string for Medline. Search date: 31 August 2020.

(critical illness[MeSH Terms] OR critical illness*[tiab] OR "critically ill"[tiab] OR life limiting condition*[tiab] OR life-limiting disease*[tiab] OR life threatening illness*[tiab] OR life limiting illness*[tiab] OR life threatening condition*[tiab] OR serious illness*[tiab] OR palliative care[MeSH] OR terminal care[MeSH] OR "palliative care"[tiab] OR "palliative medicine"[tiab] OR "palliative nursing"[tiab] OR "palliative period"[tiab] OR "palliative phase"[tiab] OR "palliative therapy"[tiab] OR palliative treatment*[tiab] OR "palliative supportive care"[tiab] OR "terminal care"[tiab] OR "terminal medicine"[tiab] OR "terminal period"[tiab] OR "terminal phase"[tiab] OR EOL[tiab] OR end of life*[tiab])
And
("advance care planning"[MeSH] OR "advance directives"[MeSH] OR "decision making"[MeSH] OR "living wills"[MeSH] OR "patient participation"[MeSH] OR advance care plan*[tiab] OR ACP[tiab] OR pACP[tiab] OR advance decision*[tiab] OR advance directive*[tiab] OR advance medical directive*[tiab] OR advance healthcare planning*[tiab] OR advance medical planning*[tiab] OR advance statement*[tiab] OR "do not hospitalize"[tiab] OR "do not hospitalise"[tiab] OR "do not resuscitate"[tiab] OR "do not attempt cardiopulmonary resuscitation"[tiab] OR "DNR order"[tiab] OR DNACPR[tiab] OR "planning ahead"[tiab] OR "refusal of treatment"[tiab] OR treatment limitation*[tiab] OR conversation guide*[tiab] OR guide*[tiab] OR program*[tiab] OR procedure*[tiab] OR practice*[tiab] OR treatment limiting*[tiab] OR shared decision*[tiab] OR "patient participation"[tiab] OR "patient involvement"[tiab] OR "child centered care"[tiab] OR "person centered care"[tiab] OR "patient centered care"[tiab])
And
(Infan*[tiab] OR toddler*[tiab] OR minor[tiab] OR minors*[tiab] OR boy[tiab] OR boys[tiab] OR boyfriend[tiab] OR boyfriends[tiab] OR boyhood[tiab] OR girl[tiab] OR girls[tiab] OR girlfriend[tiab] OR girlfriends[tiab] OR kid[tiab] OR kids[tiab] OR child[tiab] OR children*[tiab] OR schoolchild*[tiab] OR school child*[tiab] OR adolescen*[tiab] OR juvenil*[tiab] OR youth*[tiab] OR teen*[tiab] OR underage*[tiab] OR pubescen*[tiab] OR puberty[tiab] OR pediatrics[MESH] OR pediatric[tiab] OR pediatrics[tiab] OR paediatric[tiab] OR paediatrics[tiab] OR school[tiab] OR school*[tiab] OR prematur*[tiab] OR preterm*[tiab] OR youth[tiab] OR youths[tiab] OR teen[tiab] OR teens[tiab] OR teenager[tiab] OR youngster*[tiab] OR child[MeSH] OR neonat*[tiab] OR baby[tiab] OR babies[tiab] OR toddler*[tiab] OR newborn*[tiab] OR postneonat*[tiab] OR postnat*[tiab] OR perinat*[tiab] OR preschool*[tiab] OR suckling*[tiab] OR picu[tiab] OR nicu[tiab] OR neo-nat*[tiab] OR neonat*[tiab] OR premature*[tiab] OR postmature*[tiab] OR pre-mature*[tiab] OR post-mature*[tiab] OR preterm*[tiab] OR pre-term*[tiab] OR playgroup*[tiab] OR play-group*[tiab] OR playschool*[tiab] OR prepube*[tiab] OR preadolescen*[tiab] OR junior high*[tiab] OR highschool*[tiab] OR senior high[tiab] OR young people*[tiab])

* Truncations were added.

2.2. Study Selection

Articles published in English in peer-reviewed journals between 1 January 1998 and 31 August 2020 were eligible for inclusion if they reported on a well-described strategy or tool for supporting pACP. pACP was defined as a strategy to identify preferences and goals for future care and treatment [24] by connecting the expertise of the child and family with the expertise of the medical team [14–16]. Exclusion criteria were systematic reviews, articles published before 1998, and articles reporting on prenatal advance care planning. The full texts of potentially eligible studies were independently assessed by three reviewers. Disagreements were resolved in discussion with members of the research team. If an article did not provide a comprehensive description of the tool, then more detailed information was requested from the first author by email.

2.3. Data Extraction and Quality Assessment

Data extraction was conducted by two authors using a predesigned form [25]. Data regarding the content of the tool, the person conducting the conversation about ACP, its target population, and the items and outcomes related to age appropriateness were extracted. Two authors independently evaluated the studies' methodological rigor by using the appropriate tool. Disagreements were resolved through discussion. We used the Cochrane Collaboration's risk of bias tool for randomized controlled trials [26]. This

enabled us to evaluate the following: random sequence generation, allocation concealment, the blinding of participants, the blinding of outcome assessments, incomplete outcome data, and selective reporting. One or zero points were allocated when there was a low or high bias risk, respectively. An unclear risk of bias was noted with a question mark, resulting in zero points. A total score of six was achievable. Observational studies were evaluated with an adapted version of the Cochrane bias tool. This enabled us to appraise the selection of study population, the comparability of study groups, the standardization of intervention protocols, the standardization of outcome measurements, any missing data, any confounders, and any selective outcome reporting [26]. Points were assigned as mentioned above. A total score ranging from zero to seven was counted. Qualitative studies were evaluated using the COmprehensive consolidated criteria for REporting Qualitative research (COREQ), assessing 32 criteria concerning three domains: the research team and reflexivity, the study design, and the analysis and findings [27]. Scores of one, 0.5, and zero points were assigned when the score was, respectively, properly described in the manuscript, incomplete, and not described. Assessments of both the risk of bias and the quality of reporting were conducted for mixed-method study designs. A few articles were not critically appraised due to their narrative, non-empirical study design. This review was exploratory in nature, so inclusion was not affected by the quality of selected papers [28].

2.4. Data Synthesis and Analysis

The researchers listed the characteristics and content of the pACP tools and their reported empirical outcomes. A narrative synthesis was provided to summarize the results [29]. Any age-appropriate elements and related theoretical groundings were identified by using a qualitative approach. Age-appropriate elements were defined as components of the tool that were adapted to a specific age and corresponding stage of cognitive development. It was reported whether elements were adapted on the basis of age groups in general or, specifically, on the development capacities that matched a specific stage of development. Fragments of articles related to age appropriateness were extracted. The open coding of these fragments resulted in a list of codes related to age appropriateness. Overarching concepts that describe factors influencing age appropriateness in the context of pACP were identified [30]. The protocol of this review is registered in the public registry PROSPERO, with registration number CRD42020152243.

3. Results

The search identified 11,685 unique hits, resulting in 62 articles eligible for full-text screening. Thirty-four articles were excluded after full-text screening. Twenty-seven had no description of a pACP tool, one article reported on adults, and six articles were excluded based on their study design (systematic review, prenatal pACP or published before 1998). Thirty-one articles, reporting on 18 unique pACP tools, met the inclusion criteria (Figure 1). Twenty-one articles were original empirical studies reporting outcome data, including six trials [31–36], six observational studies [37–42], four qualitative studies [11,43–45], and five studies that used mixed methods (observational and qualitative study design) [46–50]. Ten articles described a tool or intervention without reporting any empirical data [51–60]. Most studies (n = 24) were conducted and published in the USA [31–43,46–49,51–53,56,58–60], five were published and conducted in the UK [44,45,50,54,55], one was published and conducted in the Netherlands [11], and one was published and conducted in Canada [57].

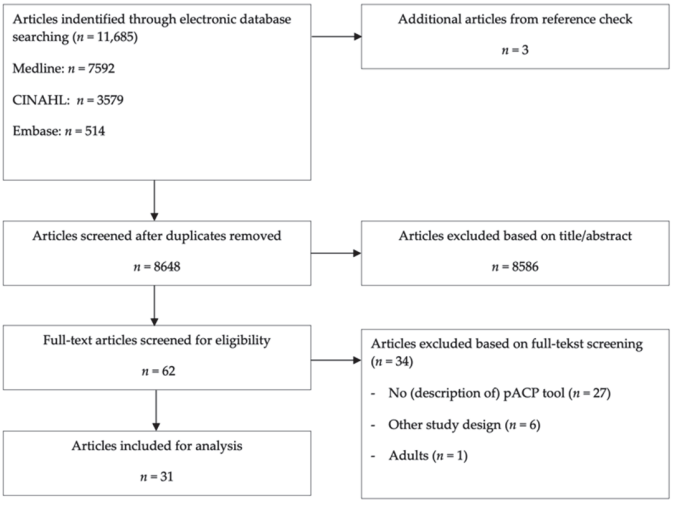

Figure 1. PRISMA flow diagram of the literature review process.

3.1. Risk of Bias and Quality of Reporting

Tables A1–A3 of Appendix A show an overview of the scores per article, with regard to the risk of bias and an assessment of the quality of reporting. The total scores per study are presented below (Tables 2–6: Article Characteristics). The six randomized controlled trials had a median total score of 4 out of 6 (range: 3–5). All six articles could not blind their participants and therefore did not meet this criterion. For observational studies (n = 6) and the quantitative parts of mixed-method studies (n = 5), the median scores were 3 (range: 2–5) and 4 (range: 2–5), respectively. The qualitative studies (n = 4) had a median total score of 10 out of 32 (range: 4–18). For mixed-method studies (n = 5), the median total score of the qualitative part was 8.5 (range: 4.5–12).

Table 2. Evidence from randomized controlled trials.

Author, Year, Country *	Aim	Population (Age in Years), *n*	Outcome Parameters	Risk of Bias Total Score (6)
Dallas, 2016, USA [31]	FACE (FAmily/Adolescent-CEntered Advance Care Planning) vs. Healthy Living Control Condition	Adolescents with HIV (14–21) and their family decision maker, dyads *n* = 97 (I: 48, C: 49)	FACE: 1. Participant enrollment and attendance 2. Satisfaction based on positive and negative experienced emotions (Satisfaction Questionnaire) 3. Serious adverse event	5
Lyon, 2009, USA [32]	FACE vs. Healthy Living Control Condition	Adolescents with HIV/AIDS (14–21) and surrogate, dyads *n* = 38 (I: 20, C: 18)	FACE: 1. Participant enrollment, attendance, and retention 2. Data completeness 3. Satisfaction based on positive and negative experienced emotions (Satisfaction Questionnaire)	3
Lyon, 2009, USA [33]	FACE vs. Healthy Living Control Condition	Adolescents with HIV/AIDS (14–21) and surrogate, dyads *n* = 38 (I: 18, C: 17)	FACE: 1. Family congruence 2. Adolescent decisional conflict 3. Quality of communication	3

Table 2. *Cont.*

Author, Year, Country *	Aim	Population (Age in Years), *n*	Outcome Parameters	Risk of Bias Total Score (6)
Lyon, 2010, USA [34]	FACE vs. Healthy Living Control Condition	Adolescents with HIV (14–21) and legal guardian, dyads *n* = 38 (I: 18, C: 17)	FACE: 1. Data completeness 2. Psychological effects (based on anxiety and depression scales) 3. Quality of life 4. Physical effects on HIV symptoms	4
Lyon, 2013, USA [35]	FACE vs. Treatment as Usual	Adolescent with cancer (14–21) and their Surrogate, dyads *n* = 30 (I: 17, C: 13)	FACE: 1. Family congruence 2. Adolescents decisional conflict 3. Quality of communication	3
Lyon, 2014, USA [36]	FACE vs. Treatment as Usual	Adolescent with cancer (14–21) and their surrogate, dyads *n* = 30 (I: 17, C: 13)	FACE-TC (Family/Adolescent-Centered Advance Care Planning for Teens with Cancer): 1. Satisfaction based on positive and negative experienced emotions (Satisfaction Questionnaire) 2. Quality of life 3. Emotional effects based on anxiety and depression scales 4. Spiritual well-being 5. Participant enrollment, attendance, and retention 6. Data completeness	4

AIDS: acquired immunodeficiency syndrome; HIV: human immunodeficiency virus; * Country where study was conducted.

Table 3. Evidence from observational studies.

Author, Year, Country *	Aim (A), Design (D)	Population (Age in Years), *n*	Outcomes	Risk of Bias Total Score (6)
Friebert, 2020, USA [42]	A: To assess adolescents' EOL needs and family congruence D: Survey study from intervention arm FACE-TC (FAmily/Adolescent-CEntered Advance Care Planning for Teens with Cancer) (session 1) RCT	Adolescents with cancer (14–21) and their legal or chosen guardian, dyads *n* = 80	FACE-TC 1. Adolescent's EOL values and needs 2. Family congruence	6
Hays, 2006, USA [37]	A: To assess the effects of DMT (Decision-Making Tool) on family satisfaction and QOL non-experimental pre-test and post-test D: Nonexperimental pre-test, post-test comparison study	Children and adolescents with potentially life-limiting illness (0–22) and their parents, dyads *n* = 41	DMT: 1. Effects on quality of life on four domains (physical, emotional, social, and school functioning) 2. Family satisfaction	4
Hendricks, 2017, USA [38]	A: To evaluate COMPLETE (Communication Plan: Early through End of Life intervention) on the parent and provider levels and to describe the given parental responses. D: Prospective, longitudinal, single-group pilot study	Parents of children (0–18) with a brain tumor and a poor prognosis, mostly mothers; parents *n* = 13 and children *n* = 11	COMPLETE: 1. Parents: emotional well-being (needs, hopes, decision regret, resources, distress, and uncertainty), satisfaction with provider communication and symptom management, and perception of information provided 2. Provider: satisfaction and communication competence	5

Table 3. *Cont.*

Author, Year, Country *	Aim (A), Design (D)	Population (Age in Years), *n*	Outcomes	Risk of Bias Total Score (6)
Jacobs, 2015, USA [39]	A: To examine EOL family congruence D: Survey study from intervention arm RCT provider post-hoc survey	Adolescents with cancer (14–21) and their legal or chosen guardian, dyads $n = 17$ and clinicians $n = 30$	FACE-TC: 1. Adolescent's EOL preferences 2. Family congruence 3. Provider survey on three sections: career, FACE-TC interactions, and EOL care experiences	5
Kazmerski, 2016, USA [40]	A: To assess patient and provider attitudes and preferences towards VMC (Voicing My Choices) D: Pre–post-test training survey quality improvement study	Patients with advanced CF (≤22); patients $n = 12$, providers (pre-training) $n = 6$, and providers (post-training) $n = 7$	Patient and provider (pre- and post-training): 1. ACP: positive and negative associations, preferences in CF care 2. VMC: thoughts on VMC and age appropriateness	2
Moody, 2020, USA [41]	A: To assess effects of COMPLETE on EOL outcomes D: Two-phase, single-arm, two-center prospective pre–post-intervention pilot study	Phase I: Parents of children with newly diagnosed cancer (1–<18 months), parents $n = 21$ and children $n = 18$ Phase II: Parents of children with any prognosis, parents $n = 20$ and children $n = 17$	COMPLETE: 1. Parent and child: time of hospice enrollment, pain, EOL interventions, and location of death 2. Parent: negative emotions	4

ACP: advance care planning; CF: cystic fibrosis; EOL: end of life; QOL: quality of life; RCT: randomized controlled trial; * Country where study was conducted.

Table 4. Evidence from mixed-method studies.

Author, Year, Country *	Aim (A), Design (D)	Population (Age in Years), *n*	Outcome Parameters		Risk of Bias Total Score (6)	Quality of Reporting Total Score (32)
			Quantitative	Qualitative		
Kline, 2012, USA [46]	A: To assess family satisfaction and preferences with their palliative care program and its DMT tool (Decision-Making Tool) D: Supportive care survey and open-ended questions interview study	Guardians of high-risk hemato-oncology pediatric patients (mean of 9.7), $n = 20$ (quantitative outcomes) and $n = 6$ (qualitative outcomes)	1. Understanding treatment options 2. Factors, people and services guiding treatment decisions 3. Effectiveness of the decision-making conference, the palliative care program and DMT	Open-ended questions on the palliative care program and DMT; questions NS	4	6
Lyon, 2019, USA [47]	A: To assess the feasibility and acceptability of FACE-Rare (FAmily-CEntered pediatric Advance Care Planning-Rare) D: Pre–post-test questionnaire study	Pediatric patients with rare diseases (≥1–≤21) and their legal guardians or family caregivers (all mothers), dyads $n = 6$	FACE-Rare 1. Caregiver appraisal 2. Family satisfaction based on positive and negative experienced emotions 3. Families' quality of communication with providers	Questions NS	5	8.5

Table 4. *Cont.*

Author, Year, Country *	Aim (A), Design (D)	Population (Age in Years), *n*	Outcome Parameters		Risk of Bias Total Score (6)	Quality of Reporting Total Score (32)
			Quantitative	Qualitative		
Noyes, 2013, UK [50]	A: To evaluate 'My Choices' and enhance future care planning D: Pre–post-test questionnaire (quantitative) and semi-structured interview (qualitative) study	Children and young people (0–≥16) with complex health and palliative care needs, as well as their parents and health-care providers, children *n* = 11 parents *n* = 12, bereaved parents *n* = 3, professionals *n* = 13 (qualitative outcomes), professionals (pre-study) *n* = 27, and professionals (post-study) *n* = 20 (quantitative outcomes)	Professionals evaluating My Choices on preferred: 1. Location of care 2. Diverse aspects in palliative care	Views of parents, children, and professionals on the My Choices booklets; questions/themes NS	2	12
Wiener, 2008, USA [49]	A: To assess the acceptability of Five Wishes, helpfulness, and defining important EOL concerns D: Descriptive study data and closed- and open-response interviews	Adolescents and young adults with HIV-1 or metastatic/recurrent cancer (16–28), *n* = 20	Five Wishes: 1. Age appropriateness for someone their age 2. Helpful for someone of the participant's age 3. Helpful or stressful to the participant	Adjustments to the Five Wishes document	4	11
Wiener, 2012, USA [48]	A: To assess and compare the usefulness, helpfulness, and stressfulness of the MTMWMV (My Thoughts, My Wishes, My Voice) with the Five Wishes D: Descriptive study data and closed- and open-response interviews	AYAs with metastatic or recurrent cancer or HIV infection (16–28), *n* = 52	Evaluating both tools regarding: 1. Age appropriateness for someone their age 2. Helpful for someone of the participant's age 3. Helpful or stressful to the participant 4. Perceived legality of the document	Adjustments to the MTMWMV document	4	4.5

AYAs: adolescents and young adults; EOL: end of life, HIV: human immunodeficiency virus; NS: not specified; * Country where study was conducted.

Table 5. Evidence from qualitative studies.

Author, Year, Country *	Aim (A), Design (D)	Population (Age in Years), *n*	Outcomes	Quality of Reporting Total Score
Fahner, 2020, the Netherlands [11]	A: To evaluate the acceptability of content of IMPACT (Implementing Pediatric Advance Care Planning Toolkit) D: Qualitative pilot study	Children with life-limiting diseases (0–<18), children *n* = 27, parents *n* = 41, physicians *n* = 11, and nurses *n* = 7	1. Acceptability of materials 2. Adjustment of tool	8.5
Feraco, 2018, USA [43]	A: To address and ameliorate existing communication gaps in cancer care and to incorporate resulting knowledge in the development of the D100 (the Day 100 talk) D: Qualitative semi-structured interview study	Children, adolescents, and young adults undergoing cancer treatment for from 1 to <7 months (≥13), as well as their parents and oncology providers, adolescents *n* = 5, parents *n* = 6, and providers *n* = 11	Perceived communication gaps in cancer care	18

Table 5. *Cont.*

Author, Year, Country *	Aim (A), Design (D)	Population (Age in Years), *n*	Outcomes	Quality of Reporting Total Score
Finlay, 2008, UK [45]	A: To enhance family engagement in EOL planning through incorporating the results in their 3 × 3 framework D: Documentary analysis study	Children with non-malignant life-limiting illnesses (2–16·months), *n* = 8	Content of EOL plans	4
Hartley, 2016, UK [44]	A: To evaluate the assessment of family needs and concerns by the HNA tool (Holistic Needs Assessment) D: Qualitative analysis study and qualitative pilot study	Care managers employed by Anglia's Children's Hospices, *n* = 7	1. Hopes and reservations 2. Impact on clinical practice 3. Family effect and experiences using the tool 4. Training experiences	10.5

EOL: end of life; * Country where study was conducted.

Table 6. Evidence from descriptive studies.

Author, Year, Country *	Aim (A), Design (D)	Population (Age in Years), *n*	Outcomes	Quality Appraisal
Baker, 2008, USA [58]	A: To assess clinical gaps in pediatric cancer care and to enhance this by integrating these aspects in the tool D: Narrative review study	Children with cancer (NS) and their parents, *n* = NA	The development of the Individualized Care Coordination Plan	NA
Christenson, 2010, USA [51]	A: To present communication gaps in palliative care of adolescents and to improve this by using the CCCT (Comfort Care Communication Tool) D: Case report study	Woman with CF (18), *n* = 1	One case study	NA
Curtin, 2017, USA [52]	A: To assess FACE-TC (FAmily-CEntered pediatric Advance Care Planning-Rare) efficacy on family congruence, quality of life and early ACP document completion D: Study protocol of a dyadic, longitudinal RCT	AYAs (14–20) with cancer and their family decision maker), dyads *n* = 130	Design of dyadic, longitudinal RCT	NA
Dallas, 2012, USA [53]	A: To assess long-term FACE (FAmily/Adolescent-CEntered Advance Care Planning) efficacy on EOL care and tries to enhance physical, psychological, spiritual well-being D: Study protocol of a dyadic, longitudinal RCT	Adolescents with HIV (14–21) and their family decision makers (>21), *n* = 130	Design of dyadic, longitudinal RCT	NA
Fraser, 2010, UK [54]	A: To present the importance of sensitive pediatric EOL planning and to describe the history and format of the Wishes document D: Narrative review study	NA (NS)	The importance of EOL planning The development of the Wishes document	NA
Gallagher, 2018, UK [55]	A: To highlight the importance of knowledge and skills required to engage with children with learning disabilities in their EOL planning D: Narrative review study	NA (NS)	The importance of and challenges in EOL planning ADVANCE toolkit content	NA

Table 6. *Cont.*

Author, Year, Country *	Aim (A), Design (D)	Population (Age in Years), *n*	Outcomes	Quality Appraisal
Snaman, 2019, USA [59]	A: To identify high-priority factors in cancer treatment decisions and incorporating this in a new tool D: Descriptive study of tool development	AYAs with newly diagnosed high-risk cancers (NS), their parents, and HCPs, dyads *n* = 5 and HCP *n* = 2	Development of MyPref	NA
Toce, 2003, USA [60]	A: To develop a tool that improves the pediatric quality at the EOL D: Descriptive study of tool development	Children with life-threatening conditions (6–>12 months), children *n* = 83 and continuity providers *n* = 105	Development of Footprints	NA
Van Breemen, 2020, Canada [57]	A: To describe the steps in the SICG-peds (Serious illness conversations in pediatrics) using one case as an example D: Case report study	Child diagnosed with osteosarcoma (11), *n* = 1	Content of the SICG-Peds	NA
Zadeh, 2015, USA [56]	A: To provide guidelines in the use of Voicing My Choices for health-care providers D: Ethical guide for health-care providers for Voicing My Choices	AYAs living with cancer or pediatric HIV (NS), *n* = NA	Guidelines in the use of Voicing My Choices	NA

ACP: advance care planning; AYAs: adolescents and young adults; CF: cystic fibrosis; EOL: end of life; HCP: health care provider; HIV: human immunodeficiency virus; NS: not specified; NA: not applicable; RCT: randomized controlled trial; * Country where study was conducted.

3.2. Intervention Characteristics

Table 7 presents an overview of the characteristics of the 18 pACP tools. Most interventions focused on conversations with children and their parents or surrogates as a key element of ACP [11,31,33–37,39,42–47,50,52–55,57,58,60]. Seven articles were only concerned with patients [40,48,49,51,56,59]. Two interventions targeted parents of children [38,41,47]. Some tools were used to study specific disease groups, such as oncology (*n* = 6) [35–39,41–43,46,52,58,59] and HIV/AIDS (*n* = 1) [31–34,53], whilst most tools focused on children with life-limiting conditions in general (*n* = 12) [11,40,44,45,47–51,54–57,60]. Twenty-five articles specified their research population's age, ranging from zero to 28 years. Figure 2 displays the children's ages of the target population per article. The authors of one article studied children from the age of 13 years [43]. A few studies did not specify the age of the child [44,54–56,58,59]. Nine studies researched children of all ages, including young adults [11,37,38,40,41,45,47,50,60]. Most articles were focused on adolescents and young adults [11,16,31–43,45,48–50,52,53,60], and only a few included young children [11,37,38,40,41,45–47,50,57,60]. Three studies described a specific age in their research population but did not explain their choice of this age [46,51,57]. Among those intervening in the care were a broad diversity of clinicians including pediatricians, nurses, clinicians, and unspecified certified facilitators. Conversation topics included: disclosing hopes, wishes, goals (of care), preferences for care and treatment, family and patient needs, and the planning of future or end-of-life care. The ACP was approached as a longitudinal face-to-face process with multiple conversations. Most articles did not specify the race or ethnicity of their target population [11,40,43–45,50–52,54–60]. The most common population backgrounds were Caucasian [35,36,38,41,42,46,47,49] and African American [31–34,39,48,53]. The importance of a culturally appropriate pACP intervention was mentioned in most articles (*n* = 20) [11,31–36,42,44,45,47,48,50,52–56,58,60].

Table 7. Intervention characteristics.

Intervention (Country)	Intervention Characteristics				Publications Included
	Materials (Ma), Mode (Mo) and Setting (Se)	**Aim**	**Interventionist**	**Target Population**	
1. Comfort Care Communication Tool (USA)	Ma: Four-quadrant design document Mo: Face-to-face longitudinal conversations Se: NS	To enhance adolescents' disclosure and person-centered care based on families' goals	Pediatric Advanced Comfort Care Team Nurse	Adolescents with life-threatening or life-limiting health care conditions	Christenson, 2010 [51]
2. Family-Centered pediatric Advance Care Planning (USA)	Ma: Family-centered ACP survey (session 1), Respecting Choices interview (session 2), and Five Wishes document (session 3) Mo: Three-session face-to-face conversation Se: Outpatient clinic	To facilitate EOL discussions for adolescents and their families	Certified facilitator	Adolescents with cancer, HIV or AIDS and their surrogates	Curtin, 2017 [52] Dallas, 2012 [53] Dallas, 2016 [31] Friebert, 2020 [42] Jacobs, 2015 [39] Lyon, 2009 [32] Lyon, 2009 [33] Lyon, 2010 [34] Lyon, 2013 [35] Lyon, 2014 [36]
3. Family-Centered pediatric Advance Care Planning Rare (USA)	Ma: Conversation card, documentation tool Mo: Four-session interviews, face-to-face or via telemedicine conversation Se: NS	To identify and meet caregiver-centered palliative care needs	Certified clinician	Family caregivers of children and adolescents with rare diseases	Lyon, 2019 [47]
4. Implementing Advance Care Planning Toolkit (NL)	Ma: Information leaflets, preparation cards (child and parent), and conversation guides Mo: Face-to-face conversations, on-off conversation, or multiple conversations Se: Home, inpatient, or outpatient clinic	To prepare children, clinicians and parents for future care, to guide documentation, and to elicit the voice of the child and stimulate a patient-centered approach	Clinician involved in the patient's care	Children with life-limiting conditions and their families	Fahner, 2020 [11]
5. DAY 100 Talk (UK)	Ma: Family preparatory and summary worksheet and a conversation guide Mo: Fill in up-front and face-to-face longitudinal conversations Se: Outpatient clinic	To enhance families' disclosure and interdisciplinary guidance	Trained pediatric oncologist and psychosocial clinician	Children, adolescents, and young adults with cancer and their families	Feraco, 2018 [43]
6. 3 × 3 Lifetime Framework (UK)	Ma: 3 × 3 Framework Document Mo: Face-to-face longitudinal conversations Se: NS	To enhance family engagement in EOL planning	Clinicians	Children with non-malignant, life-limiting illnesses and their families	Finlay, 2008 [45]
7. The Wishes Document (UK)	Ma: Hand-held document Mo: Face-to-face longitudinal conversations Se: NS	To enhance family engagement in EOL planning	Clinician involved in the patient's care	Children, young people with life-limiting conditions and their families	Fraser, 2010 [54]
8. The ADVANCE toolkit (UK)	Ma: Ethical guide Mo: Face-to-face longitudinal conversations Se: Private place	To enhance provider guidance, families' disclosure, and families' engagement in EOL planning	Clinician involved in the patient's care	Young persons with learning disabilities (who are approaching the end of life) and their families	Gallagher, 2018 [55]
9. Holistic Needs Assessment (UK)	Ma: Comprehensive assessment of needs Mo: Face-to-face conversation Se: NS	To enhance person-centered care based on family needs	Senior member of staff	Children in palliative care settings and their family	Hartley, 2016 [44]

Table 7. *Cont.*

Intervention (Country)	Intervention Characteristics				Publications Included
	Materials (Ma), Mode (Mo) and Setting (Se)	Aim	Interventionist	Target Population	
10. Decision-making Communication Tool (USA)	Ma: Four domains of decision making Mo: Face-to-face longitudinal conversations Se: Outpatient clinic	To enhance patient–provider communication, decision making, and quality of life, as well as to identify goals of care	Supportive care team clinicians	Pediatric palliative care: infants, children, and adolescents with potentially life-limiting illnesses (oncology) and their families	Kline, 2012 [46] Hays, 2006 [37]
11.Communication Plan: Early through End of Life (USA)	Ma: Conversation guide and visual aids Mo: Three face-to-face conversation sessions, longitudinal revision Se: During clinic appointments	To reduce parental distress	Trained oncology providers	Parents of children with cancer	Hendricks, 2017 [38] Moody, 2020 [41]
12. Voicing my choices (USA)	Ma: Guide adapted from the Five Wishes, completion of the document guide Mo: Longitudinal revision Se: NS	To enhance communication between the patient and caregiver in EOL preferences and care	Clinicians	Adolescents and young people living with a serious illness	Wiener, 2012 [48] Kazmerski, 2016 [40] Zadeh, 2015 [56]
13. My Choices/Choices for My Child Booklets (UK)	Ma: Booklets for children and parents, possibility Mo: To fill in/initiate thinking or face-to-face conversations Se: Home or outpatient clinic	To enhance family engagement in future planning and the disclosure of family preferences	NA	Children with life-limiting conditions from diagnosis onwards and their parents	Noyes, 2013 [50]
14. The Serious Illness Conversation Guide-Peds (SICG-Peds) (Canada)	Ma: Conversation guide Mo: Longitudinal face-to-face or by phone conversations Se: Home or clinic	To enhance understanding of illness and care preferences	Trained pediatrician	Children with serious illness and their parents	Van Breemen, 2020 [57]
15. Five Wishes® (USA)	Ma: Legal document consisting of five wishes Mo: Fill in document Se: NS	To enhance communication in EOL care	Clinicians	Adolescents and young adults living with serious illnesses	Wiener, 2008 [49]
16.Individualized care planning and coordination (USA)	Ma: Advance care planning documentation tool Mo: Longitudinal revision on timely basis Se: NS	To facilitate integration of palliative care into ongoing care	Clinicians	Children with cancer and their parents	Baker, 2008 [58]
17. MyPref (USA)	Ma: Preference report up-front cancer therapy Mo: Fill in document, longitudinal revision Se: NS	To clarify AYAs' preferences and to enhance engagement in medical decision making	Oncology providers or other clinicians	AYA patients with relapsed/progressive cancer	Snaman, 2019 [59]
18. FOOTPRINTS (USA)	Ma: Conversation guide, using a discharge order sheet Mo: Longitudinal face-to-face conversations Se: During the interdisciplinary "care conference"	To provide quality of care for the patient, their families, and providers through anticipating their needs on a continual basis	Hospital-based "continuity" pediatrician	Children with life-limiting illnesses and their families	Toce, 2003 [60]

AYA: adolescents and young adults; ACP: advance care planning; AIDS: acquired immunodeficiency syndrome; EOL: end of life; HIV: human immunodeficiency virus; NA: not applicable; NS: not specified.

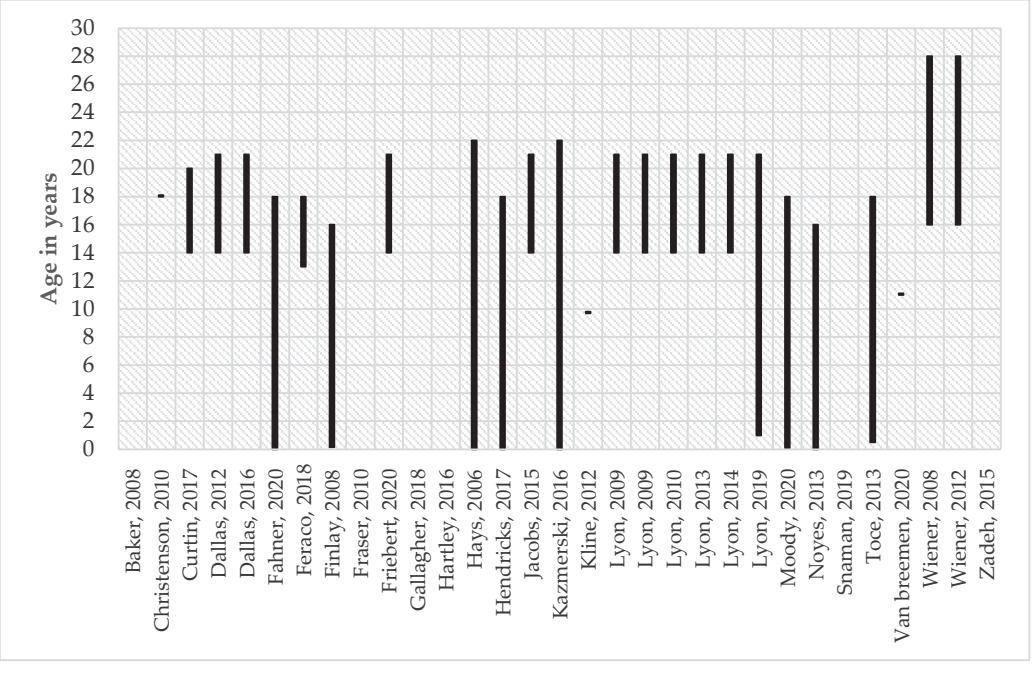

Figure 2. Age range in study population per article [11,31–60].

3.3. Attention to Age Appropriateness

Age-appropriate characteristics are summarized in Table 8. The concept of an age-appropriate approach was mentioned in two thirds of the articles [11,32,33,35–37,42,44,48–60] in an implicit or explicit way. However, no clear definition of an age-appropriate approach to pACP was described. Seventeen articles mentioned the age-appropriate concept in an implicit way without linking the importance of adapting the tools to the development of the child [35–37,40,42,44,48–55,57,58,60]. An example of an implicit description of the age-appropriate concept is cited in Box 1.

Box 1. Example of implicit description of the concept of age appropriateness.

"Most adolescents aged 14 years and older do not differ from adults in their capacity to make informed treatment decisions, and their understanding of death is no less mature than that of adults" [42] (p. 2).

Few articles referred to the concept in an explicit way by describing any implications of using the concept [11,32,33,56,59]. An explicit description of the age-appropriate concept is presented in Box 2.

Box 2. Example of explicit description of the concept of age appropriateness.

"Developmentally, the AYA period is characterized by emerging abstract thinking and an evolving sense of vulnerability. Given this complex developmental stage, AYA patients may benefit from the use of specialized tools to facilitate abstract consideration of factors involved in decision making" [59] (p. 2).

Although most articles referred to age appropriateness as a concept in some way, this was generally not translated into specific elements of the described tools nor specified for different levels of development. Twelve articles provided general recommendations to implement age appropriateness in pACP tools [11,32,37,48–51,54–56,58,59]. Fourteen

studies claimed their tools to be age-appropriate [11,32,33,36,48–53,56,57,59,60], yet only seven articles implemented elements adjusted to the age of their population. Most of these articles adapted the language to the child's age [11,48,50,51,56,57], used age-appropriate images [49,50], or added a glossary [48,56]. One article referred to their pACP guide as containing family-centered language [57]. These elements mainly focused on adolescents and young adults [48,49,51] or did not specify a particular age of their target population [56,57]. None of the articles explained why these adaptations meet the development needs or capacities of studied children nor explored the development needs of children in general.

Another way to contribute to the age-appropriate concept was by evaluating a tool for its age appropriateness. Most articles did not report any empirical study data regarding the age appropriateness of the tool used by participants. Twenty-eight studies described or evaluated the effectiveness and the child and family preferences of their tools, but none of them specifically evaluated their age appropriateness [11,31–39,41–47,50–60]. Only three studies examined the age appropriateness of their tool by asking adolescents and young adults if the tool was considered appropriate for themselves and other participants of their age [40,48,49]. The development stage or capacities to participate in the pACP of the children were not described or researched. None of the articles examined age appropriateness in young children. Age-appropriate outcomes were reported by providers in one article [40] and by AYAs in three articles [40,48,49]. These studies showed that AYAs considered pACP tools to be age-appropriate [40,49] and could be introduced before the age of 18 [40]. AYAs experienced the tools as helpful [49]. Only one article examined the perspective of the providers, revealing that pACP tools were considered less appropriate for AYAs and therefore contradicting AYAs' opinion on age appropriateness. About half of the providers reported thinking that pACP conversations should occur after the age of 18 [40].

Table 8. Age-appropriate characteristics.

Article	Description Concept	Implementation in the Tool Described		Evaluation on Age Appropriateness Stated by Patient/Provider/Family			Recommendations
		Statement of Concept Applied	Elements of Tool	Patient	Provider	Family	
Baker, 2008 [58]	Implicit	No	NS	NS	NS	NS	Yes
Christenson, 2010 [51]	Implicit	Yes	Questions adjusted for age and maturity	NS	NS	NS	Yes
Curtin, 2017 [52]	Implicit	Yes	NS	NS	NS	NS	No
Dallas, 2012 [53]	Implicit	Yes	NS	NS	NS	NS	No
Dallas, 2016 [31]	No Description	No	NS	NS	NS	NS	No
Fahner, 2020 [11]	Explicit	Yes	Booklets and conversation guides, with language adapted to the children	NS	NS	NS	Yes
Feraco, 2018 [43]	No Description	No	NS	NS	NS	NS	No
Finlay, 2008 [45]	No Description	No	NS	NS	NS	NS	No
Fraser, 2010 [54]	Implicit	No	NS	NS	NS	NS	Yes
Friebert, 2020 [42]	Implicit	No	NS	NS	NS	NS	No
Gallagher, 2018 [55]	Implicit	No	NS	NS	NS	NS	Yes
Hartley, 2016 [44]	Implicit	No	NS	NS	NS	NS	No
Hays, 2006 [37]	Implicit	No	NS	NS	NS	NS	Yes
Hendricks,2017 [38]	No Description	No	NS	NS	NS	NS	No
Jacobs, 2015 [39]	No description	No	NS	NS	NS	NS	No

Table 8. *Cont.*

Article	Description Concept	Implementation in the Tool Described		Evaluation on Age Appropriateness Stated by Patient/Provider/Family			Recommendations
		Statement of Concept Applied	Elements of Tool	Patient	Provider	Family	
Kazmerski, 2016 [40]	Implicit	No	NS	90% considered VMC (Voicing My Choices) to be age-appropriate; 66% considered ACP to be appropriate to introduce before the age of 18 or at any age	58% considered VMC to be appropriate for patient population/age group; 50% found the ideal patient age for ACP discussion was >18 years	NS	No
Kline, 2012 [46]	No Description	No	NS	NS	NS	NS	No
Lyon, 2009 [32]	Explicit	Yes	NS	NS	NS	NS	Yes
Lyon, 2009 [33]	Explicit	Yes	NS	NS	NS	NS	No
Lyon, 2010 [34]	No Description	No	NS	NS	NS	NS	No
Lyon, 2013 [35]	Implicit	No	NS	NS	NS	NS	No
Lyon, 2014 [36]	Implicit	Yes	NS	NS	NS	NS	No
Lyon, 2019 [47]	No Description	No	NS	NS	NS	NS	No
Moody, 2020 [41]	No Description	No	NS	NS	NS	NS	No
Noyes, 2013 [50]	Implicit	Yes	Booklets content and images adapted for age	NS	NS	NS	Yes
Snaman, 2019 [59]	Explicit	Yes	NS	NS	NS	NS	Yes
Van Breemen, 2020 [57]	Implicit	Yes	Family-centered language	NS	NS	NS	No
Wiener, 2008 [49]	Implicit	Yes	Age-appropriate images	90% declared that all statements on EOL care were appropriate and helpful for someone their age	NS	NS	Yes
Wiener, 2012 [48]	Implicit	Yes	Wording and questions adjusted for development and a glossary added	No significant tool differences in the degree of help or stress in age groups or differences in document content; AYAs disagreed on whether medical care wishes in the Five Wishes versus MTMWMV (My Thoughts, My Wishes, My Voice) was more appropriate for someone of their age	NS	NS	Yes
Zadeh, 2015 [56]	Explicit	Yes	Wording and questions adjusted for development and a glossary added	NS	NS	NS	Yes
Toce, 2003 [60]	Implicit	Yes	NS	NS	NS	NS	No

ACP: advance care planning; AYA: adolescents and young adults; EOL: end of life; NS: not specified.

3.4. Factors Influencing Age Appropriateness

We identified four factors related to age appropriateness that might influence the pACP approach: willingness to participate, ability to participate, social identity, and legal responsibilities. How these factors function at certain development stages was not clearly described. Table 9 shows an overview of these factors per article. Articles were marked with an 'x' when contributing to this factor.

Table 9. Factors related to age appropriateness.

		Ability to Participate				
	Willingness to Participate	**Decision-Making Capacity**	**A Child's Understanding of Their Own Medical Process**	**Cognitive Impairment**	**Developing Social Identity**	**Legal Responsibilities**
Baker, 2008 [58]		x	x			
Christenson, 2010 [51]	x	x	x		x	
Curtin, 2017 [52]				x		
Dallas, 2012 [53]	x	x	x	x		x
Dallas, 2016 [31]	x			x		x
Fahner, 2020 [11]	x	x				
Feraco, 2018 [43]	x			x		
Finlay, 2008 [45]						
Fraser, 2010 [54]		x				
Friebert, 2020 [42]	x	x	x	x		
Gallagher, 2018 [55]		x	x		x	
Hartley, 2016 [44]		x				
Hay, 2006 [37]						
Hendricks, 2017 [38]						x
Jacobs, 2015 [39]	x			x		x
Kazmerski, 2016 [40]	x					
Kline, 2012 [46]						
Lyon, 2009 [32]	x	x		x	x	
Lyon, 2009 [33]	x	x	x	x		x
Lyon, 2010 [34]	x			x		x
Lyon, 2013 [35]	x	x	x	x		
Lyon, 2014 [36]	x	x	x	x		
Lyon, 2019 [47]						
Moody, 2020 [41]						
Noyes, 2013 [50]						
Snaman, 2019 [59]	x		x			
Toce, 2003 [60]		x				
van Breemen, 2020 [57]			x			
Wiener, 2008 [49]		x	x			x
Wiener, 2012 [48]	x	x	x		x	x
Zadeh, 2015 [56]	x	x	x		x	x

Sixteen articles stated that children, especially AYAs, show a willingness to participate in pACP conversations [11,31–36,39,40,42,43,48,51,53,56,59]. Articles explored the child's willingness to participate by asking this to the children themselves and their parents. Willingness reflects the motivation of the child to be involved in a pACP conversation and clarifies to what extent this may be so. Many articles cited previous research on this subject, which showed that adolescents and young adults have a desire to participate in pACP. Few declared the same desire among young children and teenagers [11,34,43,56].

Another factor we identified was the ability to participate in pACP. This was referred to by three different sub-themes. Firstly, multiple articles reported that children and adolescents are cognitively able and sufficiently mature to make decisions, medical or otherwise, and that they therefore should be involved in pACP [11,32,33,35,36,42,44,48,49,51,53–56,58,60]. Most articles did not specify which cognitive capacities are needed but described cognitive capacities in general. The second sub-theme was the understanding of how a child's own disease process contributes to their participation in pACP. This may indicate whether or not they are able to understand the content of a pACP conversation [33,35,36,42,48,49,51,53,55–59]. The subjects we identified were an understanding of the consequences of decision making [33,35,53,56,58], medical concepts (health, illness, death) [36,42,48,51,55,57,59], and an understanding of treatment decisions in general [36,55,56,58]. The final sub-theme was cognitive impairment. Many articles excluded patients with cognitive impairment because they experienced this as limiting or complicating age-appropriate pACP [31–36,39,42,43,52,53]. However, separate from decision-making capacity and understanding, cognitive impairment was identified as a factor on its own that influences the ability of a child to participate in conversations.

Five articles described a developing social identity in adolescence as a factor related to age appropriateness [32,48,51,55,56]. During adolescence, children develop an awareness of themselves and others, which influences children's preferences and goals in pACP.

Some articles described the law requesting an advance directive, or living will, starting from a certain age [31,33,34,38,39,48,49,53,56]. These legal documents or conversations were sometimes described as part of the pACP conversations. Laws determine what is considered a legal age in participating in own health-care decisions. In some articles, younger age groups (18 years old or younger) were excluded from such topics or conversations [31,33,34,38,39,48,53,56].

4. Discussion

To our knowledge, this is the first systematic review examining age-appropriate characteristics and outcomes in pACP interventions for children with life-limiting conditions. Thirty-one articles reporting on 18 unique pACP tools were identified. Although pACP is aimed to emphasize the preferences and goals of children and their parents, the voices of children are explored by the interventions to a very limited extent. Two thirds of the studied articles referred to the age-appropriate concept; however, none of the studies comprehensively examined the development stage of their target population. Few interventions contained elements adjusted to the development of the child, or evaluated the intervention on age appropriateness [40,48,49]. The factors contributing to age appropriateness identified from the studies we investigated were: willingness to participate, ability to participate, developing a social identity, and legal responsibilities.

4.1. Defining Age Appropriateness in pACP

In this review, we have defined age appropriateness as the level of cognitive development of a child corresponding to a certain age. Cognitive development can differ between individuals of the same age and can fluctuate in children with life-limiting conditions [61–63]. Age-appropriate pACP tools would therefore benefit from adjustments to the development stage of a child with a life-limiting illness.

In this review, we identified different factors (willingness to participate, ability to participate, legal responsibilities and social identity) that might characterize or influence

the development stage. Piaget described different stages in cognitive development in children [17]. The literature is not, however, clear about whether these stages could be used for children with life-limiting illnesses. However, it does provide general information on the development capacities and the comprehension of topics related to ACP. As ACP is intended to be used to discuss future care preferences, children might benefit from an understanding of the medical concepts involved and also from a greater role in medical decision making. A review of medical decision making in children and adolescents showed that four cognitive capacities are needed: communicating a choice, understanding, reasoning, and appreciation [64]. In this way, the development stage of the child, with corresponding cognitive capacities, determines their ability in medical decision making. Expressing a choice, the first criterion, can either be accomplished via language or non-verbal communication [65,66]. Starting from the age of five years, children have a proper understanding of language, and this is a first step towards medical decision making. Non-verbal communication helps in assessing a child's preferences but is excluded as legal consent [67]. The second criterion, understanding information on one's own medical treatment, requires different neurological capacities in decision making [65,66]. Previous studies have shown that children from the ages of seven to ten years can orient and maintain attention [68–70], those from six to 12 years old can memorize [71,72], and those from the age of ten years old can recall received information [73–75]. Aside from understanding information on treatment, the comprehension of understanding of concepts such as illness, life, and death depends on the cognitive understanding of death as a biological act [76–80]. This can be fully understood starting from the ages of five to seven years old [78–81]. The understanding of sub-concepts such as irreversibility, universality, personal mortality, inevitability, causality, and unpredictability might even begin at the age of three [77–81]. The articles we researched provided some basis to this theory, implying that children, starting from a young age, should not be excluded from these topics in pACP. Children from the ages of six to eight years can logically reason [82,83] about decision-making consequences, including risks and benefits, which is the third criterion [65,66,84]. This capacity further develops in adolescence, therefore meaning that they can understand more complex issues [82]. Few of the articles we researched mentioned that children can understand the consequences of decisions, indicating that children are able to reason regarding logically their own pACP decisions and should therefore be included in weighing different treatment options. The last criterion, appreciation, indicates that children from the ages of three to four years start recognizing their own norms and values, as well as the effect of these on their own life [67,85,86]. This implies that preferences and hopes in pACP could be explored in a more simple manner and early in childhood. Most studied articles focused on pACP interventions for older children and may have underestimated the value for younger children. Adolescence is considered an interesting development phase in decision making in which children develop a social identity and awareness of themselves and their peers [87]. They highly value the acceptance of peers, which influences decision making [88]. Adolescents make more decisions offering swift rewards in the presence of the other peers [89]. Altogether, Grootens-Wiegers et al. stated that children from the age of 12 are expected to be competent in decision making [64]. Legally, children from the age of 12 years are allowed to make joint decisions on medical issues with their parents. From the age of 16, they can make decisions on their own [90]. In the USA starting from the age of 18 they are allowed to give informed consent for participating in clinical trials [91]. pACP can play a valuable role in preparing children for decision making. However, ACP was not developed for contemporaneous medical decision making; rather, it was developed for preparing certain decisions in the future. In this way, children can participate and have a feeling of control in their own disease process. This can only be achieved when the child's level of development is assessed as part of pACP or prior to the initiation of pACP.

We identified cognitive impairment as a factor influencing the concept of development. Approximately half of the children with life-limiting illnesses also suffer a degree of cognitive impairment [92]. Multiple articles excluded children with cognitive impairment,

indicating that it could complicate participation in pACP. Cognitive impairment is defined as a deficiency in cognitive function consisting of multiple capacities: memory, general intelligence, learning new things, language, orientation, perception, attention, and concentration and/or judgment [93]. Cognitive impairment is a broadly used term in which one or more cognitive functions are affected in general. Engaging these children in pACP would therefore benefit from adaptations to the development of their cognitive functions.

Most pACP articles on children with life-limiting conditions reported that pACP interventions need to be culturally appropriate. Preferences in discussing pACP topics differ between cultures [94]. However, the literature is not clear what is considered age-appropriate pACP participation in different cultures. Cognitive development, and therefore level of the child's participation in conversations and decision making, is influenced by cultural differences that affect parenting roles, government guidelines and education [95]. To involve children in pACP in an adequate and age-appropriate manner, their ethnical background should be considered.

Even though defining different stages in the development of children with life-limiting illnesses would be helpful, evidence indicates that the development, cognitive or otherwise, of a child is an individual, fluctuating, culturally-dependent and differentiating process with regard to different topics [61–63]. The development of a child can progress or regress individually during the life or disease process. When a child deteriorates, cognitive development can regress and changes in level of development and rate of assent could appear [90]. On the other hand, clinical experience has shown that children, especially adolescents, with life-limiting illnesses often seem to have a better understanding of death and dying compared to healthy children of their age [61]. This can be due to their greater experience with death than other children of their age [62]. However, the literature is inconsistent. Experiencing death through media [62] and what parents teach their children about biology and natural processes [63] stimulates children with regard to the concept of death and dying [62,63]. Diverse ACP topics might have different levels of development in one individual. A comprehension of life and death is only one aspect of the topics discussed in pACP. Other topics, such as preferences and hopes in general, could be easier for children to talk about and could be comprehended on another level of development. The comprehension of diverse topics in pACP differs in the development in children and should therefore determine their level of participation in that topic. The comprehension of one's own body, for example, develops between the ages of four to six years [96], while the understanding of death develops later, between the ages of five and seven years [62,78–81].

4.2. Recommendations for Future Research

Development is an individual, fluctuating, culturally dependent, and differentiating process between topics and cognitive functions. The stage of development, rather than age, therefore gives direction in how to appropriately engage children with regard to their development. Research is needed to identify the specific characteristics of each development stage for children with life-limiting conditions. Elements that depend upon developments can then be determined and incorporated to create age-appropriate pACP interventions. Most pACP tools lack a comprehensive inclusion or description of age-appropriate pACP elements. Current literature on pACP does not provide sufficient insight in characteristics of age-appropriate elements. This complicates the appraisal of the usefulness of current tools. Two interventions were evaluated on age appropriateness by their target population of AYAs and their providers [40,48,49]. They were considered acceptable and useful for this age group. Age-appropriate elements, such as language and images, were incorporated, but an explanation of why these elements met the child's developmental needs and capacities was lacking. Examining the intervention by the target population provides a first indication of the level of age appropriateness of a tool. However, more insight is needed regarding which development characteristics apply to certain age groups that are relevant in pACP. In this way, a framework of age-appropriate pACP elements can be designed and incorporated into existing and newly developed

interventions. pACP tools can be ranked for their level of age appropriateness, which might be an indicator of high-quality family-centered tools. We were not able to apply any qualification to the level of age appropriateness of the pACP tools studied in this review without such a framework.

Creating and examining different stages in development for children with life-limiting illnesses would benefit from other fields of expertise. Experts in developmental psychology, even children themselves and their families, could determine what information or elements are considered age-appropriate [40,48,49]. The development stage should be frequently assessed because it fluctuates, which may require a separate tool. Creating an intervention that determines the level of development of a child regarding pACP topics could provide an indication of how clinicians can involve children in pACP conversations, e.g., which topics providers have to raise or questions to ask. The same fluctuating cognitive phenomena have been observed in dementia patients [97,98] in which cognitive capacities for ACP participation were assessed [97,99]. The literature shows that even patients with severe dementia can still share their preferences or wishes on a certain level [99]. Therefore, we should always explore children's cognitive development and involve children in their own disease processes on a level that corresponds with their cognitive capacities.

Future research should investigate what is considered age-appropriate participation in different cultures, which has not yet been described in the literature. In creating an age-appropriate intervention, cultural norms and values should be incorporated to involve children in a way that is appropriate for their developmental stage.

4.3. Strengths and Limitations

This systematic review contributes to the body of knowledge of the young and evolving field of pACP. The research team assessed the content and characteristics of different pACP tools regarding age appropriateness. A team offering broad expertise evaluated the different aspects of age appropriateness. This review comprises the first steps towards the incorporation of age appropriateness in pACP. The results show that age appropriateness is considered important; however, the comprehensive elaboration of this concept is still in its infancy. These findings limit the opportunities for clinical implications for current practice while emphasizing the need for ongoing research to be able to develop a comprehensive age-appropriate approach in pACP. In addition, the variety of different study designs complicates any comparison of the role of the separate intervention elements. pACP may be an upcoming field of expertise, but it is still relatively new in advance care planning and there might be more influencing factors than we have discovered. Other fields of expertise might contribute to these factors. Most reviewed articles were published and conducted in the USA. This might limit the applicability of the findings to other countries. The USA articles were mainly dominated by one research group, which might have biased the results.

5. Conclusions

In this review, we have summarized the age appropriateness of existing pACP tools in children with life-limiting conditions. The relevance of an age-appropriate approach was mentioned in most articles, though mainly in an implicit way. None of the articles comprehensively examined the development stage of their target population. Four factors influencing age appropriateness were identified: willingness to participate, ability to participate, developing social identity, and legal responsibilities. Three articles evaluated their tools regarding age appropriateness. The tools integrated age-appropriate elements to a very limited extent, mainly focusing on adolescents and young adults. The involvement of children of all ages in pACP needs a more comprehensive approach.

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Appendix A

Tables A1–A3 show a score overview per article, conducting the risk of bias and quality of reporting assessment.

Table A1. Risk of bias assessment trials according to Cochrane risk of bias tool.

		Dallas, 2016 [31]	Lyon, 2009 [32]	Lyon, 2009 [33]	Lyon, 2010 [34]	Lyon, 2013 [35]	Lyon, 2014 [36]
1.	Random sequence generation	+	+	+	+	?	+
2.	Allocation concealment	+	+	+	+	+	+
3.	Blinding of participants	-	-	-	-	-	-
4.	Blinding of outcome assessment	+	-	?	?	-	?
5.	Incomplete outcome data	+	+	?	+	+	+
6.	Selective reporting	+	-	+	+	+	+
7.	Total score (6)	5	3	3	4	3	4

+ = criterion with low risk of bias, a score of one point was assigned; - = criterion with high risk of bias, a score of zero points was assigned; ? = criterion with unclear risk of bias, no score was assigned.

Table A2. Risk of bias assessment observational studies according to an adapted risk of bias assessment tool.

	Hays, 2006 [37]	Hendricks, 2017 [38]	Jacobs, 2015 [39]	Kazmerski, 2016 [40]	Kline, 2012 (MM) [46]	Lyon, 2019 (MM) [47]	Moody, 2020 [41]	Wiener, 2008 (MM) [49]	Wiener, 2012 (MM) [48]	Friebert, 2020 [42]	Noyes, 2013 (MM) [50]
1. Selection process of study population	+	+	+	+	+	+	+	+	+	+	-

Table A2. *Cont.*

	Hays, 2006 [37]	Hendricks, 2017 [38]	Jacobs, 2015 [39]	Kazmerski, 2016 [40]	Kline, 2012 (MM) [46]	Lyon, 2019 (MM) [47]	Moody, 2020 [41]	Wiener, 2008 (MM) [49]	Wiener, 2012 (MM) [48]	Friebert, 2020 [42]	Noyes, 2013 (MM) [50]
2. Comparability of compared groups	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
3. Standardized protocol for the use of the ACP tool	-	+	+	+	-	+	+	+	+	+	+
4. Standardized protocol for measuring the outcome	+	+	+	-	+	+	+	+	+	+	+
5. Missing data with regard to inclusion of follow-up or incomplete data	+	+	+	-	-	+	-	-	-	+	-
6. Adjustment for confounders	-	-	NA	NA	+	-	-	NA	NA	+	NA
7. Selective outcome reporting	+	+	+	-	+	+	+	+	+	+	-
Total score (out of 7)	4	5	5	2	4	5	4	4	4	6	2

+ = criterion with low risk of bias, a score of one point was assigned; - = criterion with high risk of bias, a score of zero points was assigned; ? = criterion with unclear risk of bias, no score was assigned; MM = mixed methods; NA: Not Applicable.

Table A3. Quality of reporting in qualitative studies according to the Comprehensive consolidated criteria for Reporting Qualitative research.

		Fahner, 2020 [11]	Feraco, 2018 [43]	Finlay, 2008[45]	Hartley, 2016[44]	Noyes, 2013 (MM) [50]	Kline, 2012 (MM) [46]	Lyon, 2019 (MM) [47]	Wiener, 2012 (MM) [48]	Wiener, 2008 (MM) [49]
1.	Interviewer/facilitatorc	+/-	+	-	+/-	-	+/-	-	-	+
2.	Credentials	-	+	-	-	-	-	-	+	+
3.	Occupation	-	-	-	-	-	-	-	-	-
4.	Gender	-	+	-	-	-	-	-	-	-
5.	Experiences or training	-	-	-	-	-	-	+/-	-	+
6.	Relationships established	-	-	-	-	-	-	-	-	-
7.	Participant knowledge of the interviewer	-	-	-	-	-	-	-	-	-
8.	Interviewer characteristics	-	-	-	-	-	-	-	-	-
9.	Methodological orientation	+	+	+	+	+	+	+	-	+

Table A3. *Cont.*

		Fahner, 2020 [11]	Feraco, 2018 [43]	Finlay, 2008[45]	Hartley, 2016[44]	Noyes, 2013 (MM) [50]	Kline, 2012 (MM) [46]	Lyon, 2019 (MM) [47]	Wiener, 2012 (MM) [48]	Wiener, 2008 (MM) [49]
10.	Sampling	-	+	-	+	+	-	-	-	-
11.	Method of approach	-	+	-	-	+	-	-	-	-
12.	Sample size	+	+	+	+	+	+	+	+	+
13.	Non-participation	-	+/-	-	-	+	+/-	+/-	-	+
14.	Setting of data collection	-	+/-	-	-	+/-	-	-	-	-
15.	Presence of non-participants	-	-	-	-	-	-	+	-	-
16.	Description of sample	+	+	+/-	-	+/-	+	+	+	+
17.	Interview guide	-	+	-	+	+/-	-	+	-	+
18.	Repeat interview	-	-	-	-	-	-	-	-	+
19.	Audio-visual recording	+	+	-	+	+	+	+	-	-
20.	Field notes	-	-	-	-	+	-	-	-	-
21.	Duration	-	+	-	-	-	-	+	-	+
22.	Data saturation	-	-	-	+	-	-	-	-	-
23.	Transcripts returned	-	-	-	-	-	-	-	-	-
24.	Number of data coders	-	+	-	-	-	-	-	-	-
25.	Description of coding three	-	-	-	-	-	-	-	-	-
26.	Derivation of themes	-	+	-	+	-	-	-	-	-
27.	Software	-	+	-	-	+	-	-	-	-
28.	Participant checking	-	-	+	-	-	-	-	-	-
29.	Quotations presented	+	+	-	+	+/-	+/-	+/-	+/-	-
30.	Data and findings consistent	+	+	+/-	+	+	+	-	+	+
31.	Clarity of major themes	+	+	-	+	+	-	-	-	-
32.	Clarify of minor themes	+	-	-	-	-	-	-	-	-
Total +		8.5	18	4	10.5	12	6	8.5	4.5	11

+ = criterion was properly described, one point was assigned; +/- = criterion was incompletely described, 0.5 points were assigned; - = criterion was not described, zero points were assigned.

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children

MDPI

Review

Psychosocial Considerations for the Child with Rare Disease: A Review with Recommendations and Calls to Action

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Abstract: Rare diseases (RD) affect children, adolescents, and their families infrequently, but with a significant impact. The diagnostic odyssey undertaken as part of having a child with RD is immense and carries with it practical, emotional, relational, and contextual issues that are not well understood. Children with RD often have chronic and complex medical conditions requiring a complicated milieu of care by numerous clinical caregivers. They may feel isolated and may feel stigmas in settings of education, employment, and the workplace, or a lack a social support or understanding. Some parents report facing similar loneliness amidst a veritable medicalization of their homes and family lives. We searched the literature on psychosocial considerations for children with rare diseases in PubMed and Google Scholar in English until 15 April 2022, excluding publications unavailable in full text. The results examine RD and their psychosocial ramifications for children, families, and the healthcare system. The domains of the home, school, community, and medical care are addressed, as are the implications of RD management as children transition to adulthood. Matters of relevant healthcare, public policies, and more sophisticated translational research that addresses the intersectionality of identities among RD are proposed. Recommendations for interventions and supportive care in the aforementioned domains are provided while emphasizing calls to action for families, clinicians, investigators, and advocacy agents as we work toward establishing evidence-based care for children with RD.

Keywords: rare disease; children; families; medical complexity; care coordination; psychosocial; policy; advocacy

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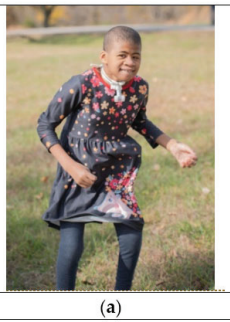
1. Introduction

Rare diseases (RD) affect children, adolescents, and their families infrequently, but have a significant impact. While the US National Institutes of Health defines such conditions as occurring with a frequency of 1 in 200,000 or less, definitions vary around the world [1]. The US definition is linked to what is known as the 1983 Orphan Drug Act—a measure taken to provide incentives to the pharmaceutical industry to research and develop new treatments for infrequently occurring conditions [2]. Another name for these conditions in the US is "orphan diseases" as the law was called the Orphan Drug Act (www.eurordis.org/about-rare-diseases accessed on 15 June 2022).

In the European Union (EU), RDs have been defined as those occurring in less than 1 per 2000 people [3]. Like the US orphan drug laws, attention to orphan diseases and pharmaceuticals exists in the EU and Japan [4]. However, the absence of governmental attention to RDs and their impact continues to be heralded worldwide [5]. This is certainly understandable as 40 per 100,000 individuals have RD [1]. In such a calculus, it is likely that around the world there are hundreds of millions of people affected by RD with estimates of 25 million people or more in North America and up to 36 million in Europe [1]. Genetic disorders account for a large majority of RD [6]. While identifying a genetic basis for RD may allow refined definitions and approaches in research and development for therapeutics, it also makes the recognition and attention to certain disease features difficult due to the specificity of gene-mediated processes. Features may entail a phenotypic expression that is recognizable to the clinician, such as seizures, yet be minimally responsive to typical therapeutic agents and require symptom-driven genomic investigation or specific tests. In the case of RD presenting as epilepsy, this may involve special testing of the cerebrospinal fluid. Other conditions may involve metabolic processes impacting vital organ function, or significant developmental behavioral differences [7]. The diagnostic odyssey that must be undertaken as part of having a child with RD is immense and carries with it practical, emotional, relational, and contextual issues that are not well understood by those caring for or impacted by the child's RD.

Children with RD often have chronic, complex medical conditions requiring a complicated milieu of care by numerous clinical caregivers. They may feel isolated, have anxiety or depression, and may feel stigmas in settings of education, employment and the workplace, lacking self-sufficiency, and feel a lack a social support or understanding by others [8]. Families of children with RD face a multitude of challenges, too. Parents of children with neurodevelopmental differences have expressed feelings of social isolation and being overwhelmed [9]. Other parents report not being understood by their peers with more typically developing children and facing a veritable medicalization of their homes and family lives [10–13].

This review examines RDs and their psychosocial ramifications for children, families, and the healthcare team. The domains of the home, school, community, and healthcare are addressed, as are the implications of RD management as children transition to adulthood while families must access and advocate for their healthcare needs. To this end, matters of relevant healthcare and public policy and more sophisticated translational research that address the intersectionality of identities among RD are proposed. Finally, recommendations for evidence-based interventions and supportive care in the aforementioned domains are presented. Calls to action for families, clinicians, investigators, and advocacy agents are stated to prompt continued work toward establishing evidence-based care for these children. See Figure 1.



Meet Miya, a 10-year-old girl who is nicknamed 'Lovey' because she is so affectionate and caring. She loves to be alongside of her loved ones and finds a way to be in the middle of anything happening in her home. Miya is defying the odds every day and thriving because of the comprehensive care she receives. She lives with 4p Trisomy, a clinical syndrome first described in 1970 by M.G. Wilson. Still, today only about 85 people with this rare disease have their story recorded in the medical literature.

(**a**) (**b**)

Figure 1. (**a**) Photo Captions: #RareDisease #RareIsntRare; (**b**) Miya's Story [14].

2. Materials and Methods

The initial search of the literature was conducted in PubMed and Google Scholar databases for peer-reviewed articles published until 15 April 2022, in English. The secondary search included articles from reference lists that were identified in the primary search. Records were screened initially by title and abstract and then full-text articles were retrieved for full review and eligibility evaluation. The searches combined a range of key terms including "Pediatric" OR "Children" AND "Rare Disease" AND "Psychosocial" OR "Social." Duplicate manuscripts and those unable to be obtained by interlibrary loan or through library access online were removed after exporting references to Endnote Online (https://www.myendnoteweb.com/EndNoteWeb.html, accessed on 1 February 2022). The reader is referred to this Special Issue (https://www.mdpi.com/journal/children/special_issues/psychosocial_considerations accessed on 10 June 2022) for research on the following relevant topics that were published outside of the time range for inclusion in the current review article, e.g., psychosocial difficulties among preschoolers, advance care planning, social support for siblings of children with cancer, transition to adulthood among youth with RD, and experiences in youth with rare cancers.

3. Results

3.1. The Child with RD

Individuals with RD are surviving and living lives not previously thought possible, yet are not well understood [15]. Existing knowledge about children with RD describes the psychosocial experiences of their families and caregivers [16,17] yet the child with RD must remain the focal point. Children with RD are more likely to encounter significant challenges in their functioning at home, at school, and in their community [18]. However, there is scant research characterizing the child's own experiences. What is known about RD is drawn from the intersection of groups of children with chronic disease. For example, children (and youth) with special healthcare needs (CSHCN or CYSHCN, used interchangeably in this review) have, or are at increased risk of having, a chronic physical, developmental, or emotional condition requiring more healthcare services than is needed by most typically developed children [19]. Children with medical complexity (CMC) are a sub-population of CSHCN and children with RD, often with functional impairment and dependence on medical technology and equipment (such as gastrostomy tubes).

The medical and psychosocial needs of CMC and their families are not well met by many existing healthcare models, and CMC are more than twice as likely as typically developing children to have unmet healthcare needs [20]. They represent a small portion of children but account for more than one third of pediatric healthcare resources consumed annually [21]. Children with RD require multidisciplinary care coordination among multiple sectors of care [22–24], experience a higher frequency of inpatient stays than others, and experience significant obstacles to having their voices heard. Studies have shown variable efforts for care teams to involve the child with an RD in their own care, relying on parent caregiver reports predominantly [25]. While not all CSHCN and CMC have RD, many do, and the intensity and acuity of their medical and psychosocial needs make this a valuable group to consider when assessing the psychosocial needs of children with RD.

3.1.1. Intersecting Identities and Experiences

The intersecting facets of the child's identity and experiences are ignored in studies about RD. Understandably, studies about RD may be impacted by the small number of individuals with a rare diagnosis. Yet, without attention to intersectionality and understanding our care models and for whom and under what conditions they are effective, the insights gained can be limited in their utility and application [26]. Social determinants of health (SDH) are known to contribute to inequity in outcomes, although the impact on children with RD has not been fully characterized. Diagnostic genetic testing can be a powerful tool, although it may not be available to all in need [27]. In the USA, CSHCN are disproportionately of Black, non-Hispanic/Latinx heritage and are believed to experience inequities

in health and healthcare access due to historical marginalization [28]. When inequities are examined based upon race and ethnicity, primary language spoken in the household, insurance type, and poverty status, children with medical complexity are found to be twice as likely to have at least one unmet need, compared to children without medical complexity. However, in one study, children with medical complexity had disproportionately higher unmet needs than children without medical complexity across all categories of race and ethnicity [20]. Because racial, geographic, and socioeconomic inequities impact healthcare globally, these SDH are estimated to have substantial impact on children with RD.

3.1.2. Behavioral Health

Health-related quality of life (HRQOL) in children with chronic disease is known to be related to both self-management and self-efficacy [29]. Children living with RD experience barriers that impact their quality of life (QOL) and psychosocial functioning [30] as demonstrated by higher levels of mental health needs [31]. In a recent cross-sectional study conducted in Western Australia, 43.9 percent of parents of children with RD reported that their child experienced mental health difficulties [32]. Lum and colleagues found that parents of children with chronic illnesses were 2.2 times more likely to report that their child experienced emotional distress and lower levels of self-confidence [33].

3.1.3. Communication

Understandably, children with RD that have emotional distress or comorbid developmental behavioral conditions are at risk for having communication challenges. These children may experience communication barriers, some negatively impacting their care, or they may have a comorbid speech or language disorder. The psychosocial impacts of having a speech or language disorder have been documented and include bullying, delays in adaptive functioning, and difficulties with emotion regulation [34,35]. Others noted that children with language disorders are more likely to experience anxiety, depression, ADHD, and externalizing behaviors compared to those without language disorders [36]. In examining psychosocial outcomes, Lewis and colleagues found that adolescents with early childhood speech sound disorder experienced poorer psychosocial outcomes when combined with language impairment [37]. Thus, children with RD coupled with communication disorders may require a different type of support in promoting positive psychosocial outcomes.

3.2. RD in the Family

RDs impact the entire family. Recently, Hoover and colleagues poignantly acknowledged that the ongoing COVID-19 pandemic has brought new visibility to difficult experiences that are commonplace among families of CSHCN [38]. Examples of such a family impact include being forced into homeschooling, being homebound, stretching oneself to meet the social and educational needs of the child while meeting their health needs, inequities in quality of healthcare, and the injustices of their outcomes linked to race, ethnicity, or socioeconomic status. The authors make clear that this previously invisible role of family caregiving—including the work of nurturing, tasks, resources and services to meet day-to-day needs—is not yet adequately recognized [38]. In fact, despite challenges they face, families must consistently respond to both routine day-into-night cares as well as the crises that arise [13] regardless of whether prior knowledge or support services are available to help. This is especially important to acknowledge given families' resilience in the face of adversity.

3.3. Social Determinants of Health

SDHs have a significant impact on children with RD and their families. Families of children with complex chronic conditions, including those with RD, are more likely to experience medical financial hardship [39,40]. Medical financial hardship is correlated with negative child health outcomes regardless of a family's socioeconomic status or other financial resources [41]. There is a strong association between foregone family employ-

ment [42] and family-provided medical care [43–45]. CSHCN have elevated risk for food insecurity and malnutrition, which has a dramatic impact upon daily and long-term functioning [46,47]. Reduced access to household materials is associated with increased acute healthcare utilization and unmet healthcare needs among CSHCN [48,49]. Beyond housing stability, this also relates to accessible housing adaptations for children with disabilities. Families face difficult trade-offs when it comes to identifying viable housing options [50]. High acuity medical episodes, such as prolonged intensive care hospitalization or development of new medical technology dependence may bring heightened vulnerability [51]. For example, the proportion of families with unmet basic needs increases during chemotherapy treatment for newly diagnosed pediatric cancers [52]; the same may be true for acute changes in health status with other conditions such as RD.

3.4. Home Care

Some children with RD have complex medical needs that require chronic home health services. Private duty nursing (PDN), also called "home nursing care," is an integral part of care for some children [53]. Examples of PDN services include tracheostomy/ventilator and other airway and pulmonary care, providing tube feedings, administration of medications, performance of ordered home therapy exercises, and other essential health services. Without PDN, some children may not live safely at home. Limited access to home healthcare services and staffing in North America, Europe, and globally has been identified as a crisis for families. PDN is known to be inextricably linked with child survival and family stability due to family life being intertwined with home healthcare schedules, staffing, and services [54]. In fact, gaps in PDN staffing threaten family physical, mental, and financial wellbeing. Families must continually fight payors and government agencies for their allotted services, with out-of-pocket costs being customary although unjust. This long-standing widespread shortage of home nurses and geographic heterogeneity of both quality and quantity of nursing services mean that many children do not receive the number of hours for which they qualify [43,55]. This results in family caregivers improvising nursing care, which has the potential to place the child's health at risk, can result in parent(s) foregoing employment and income [44], and negatively impact marital and family dynamics [56].

3.5. The Search for Answers

Families experience myriad psychosocial challenges in providing loving care to their child with RD. Initially, the diagnostic odyssey of identifying the genetic underpinnings of a rare disease can raise many poignant issues for families [57,58]. Mendelian genetic disorders are primarily caused by alterations in one gene or abnormalities in the genome and may be seen since birth or visible in the family history. Although Mendelian genetic disorders are individually rare, they are collectively more common and contribute disproportionately to pediatric morbidity and mortality [27]. Genetic testing allows for the benefit of individualized treatment plans in addition to ending the diagnostic odyssey, which not only halts further unnecessary testing but may also result in immense psychological benefit, leading to improved quality of life. However, genetic testing may reveal that other family members carry the same gene or disorder, which can be difficult for families to navigate [59]. Furthermore, ensuring equitable application of these advances in genomic technology has been challenging. Technology has limits, too. Even when expanded genome sequencing is available, it may not yield an interpretable answer, or after many years answers obtained may only facilitate a small step toward better understanding or treating RD.

3.6. Barriers to Wellbeing

While genetic diagnosis may provide timely medical intervention, informed choices, access to clinical trials and engagement in disease-specific support [59] for some with RD, significant barriers to wellbeing also emerge. This includes isolation and loneliness. At times, in being one of the only or few to receive a specific diagnosis, often with little known about its course, prognosis, or known interventions, loneliness prevails [60]. While

in most circumstances outside of RD, a diagnosis brings understanding, treatment and reasonable prognostication, a diagnosis of an RD is accompanied by uncertainty. This can increase anxiety about the future, create instability, and lead to a variety of sequelae for family members. Finding a new normal following this journey may be daunting for many [7]. For example, parents of CMC report lower health-related quality of life (HRQOL) when compared to parents of non-CMC, and ratings of mental health QOL are lower than physical ones [61]. However, families may experience lack of access to suitable mental health services or experience a "lack of fit" in peer support groups [62]. Behavioral health challenges for family caregivers are largely known to include caregiver stress [63,64]. Family caregivers often perceive that they do not have time to address their own behavioral health needs [60,61]. When they do try to attend to their own needs, they may not be able to access appropriate services due to caregiving-specific barriers to care [65–67].

Cardinali and colleagues noted that challenges reported in caring for a child with RD often varied for mothers and fathers [68]. Both valued information about the diagnosis, perceived the lack of an organized medical system, and shared many feelings and behaviors as a couple. Fathers noted challenges with finances, education, feelings, and behaviors. Mothers noted problems with career, adaptation to the child's needs, their role in education, their own feelings, and how the family functioned as a system. While finding others who truly relate to the unique aspects of the individual RD is valuable to the family, they may find that others with RD share themes of common experiences [68]. Positive family functioning has been demonstrated to positively influence the QOL for children with RD [69,70]. Family cohesiveness, positive intrafamily relationships, and acceptance are related to positive family and child functioning; in fact, some families have created positive meaning from their experiences [70,71].

Parents describe feeling misunderstood by family and friends regarding the realities of their daily caregiving experience, and many describe difficulty connecting with a supportive community [9]. Social support and respite care are known to sustain caregiver wellbeing [13] and reduce stress and burden [11,72]. However, the logistics of accessing these helpful resources are rife with barriers [73]. Access to informational and interactive peer support for parent caregivers of children with RD is a substantial service to families [13,74]. These may take the form of in-person events, group offerings, virtual live meeting rooms, or asynchronous communication forums such as social media or chat rooms [57]. Despite the accessibility of virtual social support options, parent caregivers may experience significant behavioral health challenges that can be exacerbated by caregiving demands and all that comes with caring for RD [75].

3.7. Coordination of Care

Access to coordination of needed services represents a significant challenge. RDs typically require multiple specialists and thus multiple appointments that must be coordinated and attended by the family, many of which may have little experience in complex care settings [60,61,64]. While a patient- and family-centered care (PFCC) approach to children's chronic conditions is often emphasized [76], care programming has a long way to go to address the needs that arise for families of a child with RD [11]. Often, children with RD are seen in clinics without established care pathways and this can be experienced by the family as an ongoing struggle to advocate for their child's needs [77]. Additionally, healthcare teams may not be familiar with the RD.

3.8. Access to Information

In addition to challenges accessing coordinated care, it can be challenging to access accurate and helpful information pertinent to the RD. Lack of or limited access to accurate evidence-based information about their child's condition can contribute to additional caregiver stress. Managing the unknown and when contending with situations where there is no answer or information is a challenge that is salient to families of a child with RD. Families search the internet often for answers to questions, with information quickly at their

fingertips that may or may not be accurate. The dangers of misinformation are substantial with this approach. Even in cases where information is available about the disease, it may not be available in a caregiver's primary language, compounding access inequities and stress [78,79]. Families report asking healthcare providers for answers and being told they do not know, or that information is not yet known. While care teams seek the most up to date information in the care of their patients, families may be asked to tolerate ambiguity.

Caring for children with RD requires adequate personal health literacy including the skills to find, understand and use information to inform health-related decisions. These skills include reading, listening, speaking and numeracy skills as well as the ability to seek and find information from reputable sources [80]. An individual's personal health literacy can be dynamic and may be lower in times of stress [81]. A child with RD may also have multiple caregivers who are expected to follow complicated instructions relating to medical care such as medications, nutrition, and equipment.

3.9. The Family Is Part of the Care Team

Despite the challenges that families report, the experience they gain over time can be significant. They become 'expert medical caregivers' by experience, sometimes about RD, but most certainly about their own child and their care [38]. Parents become to the intermediary between care teams and their child or may even find themselves in a teaching role in explaining their child's RD to the care team.

3.9.1. Advisory Councils and Boards

One pathway for care coordination and patient- and family-centered care builds upon the expertise of the family caregiver. Patient and family engagement refers to the process through which these individuals are included in the diagnostic, treatment, and administrative processes. These groups bring patients and families together to provide guidance on how to improve the patient and family experience. Involvement in these councils is one way to ensure patients and family members are engaged with their healthcare experience. In fact, many hospitals and healthcare organizations have formed patient and family engagement programs, such as patient family advisory councils (PFAC) or family advisory boards (FAB) that recruit parents of a child with an RD to serve on a patient family advisory council or board.

These parent or patient volunteers serve to provide valuable input to care teams about issues that directly impact patient care and family wellbeing. Through this partnership, parents assist in the expert care of other children served by the healthcare system. Parents may feel heard and healthcare teams may stay connected to the true purpose and concerns of families. Parents or patients engaged in this role may enhance intervention outcomes as told by families in real-time so that iterative improvements may be made to impact their child(ren) and others served in the organization. The challenge, however, is that families serving in these roles may not be representative of the entire population they represent. Additionally, parents of children with rare diseases or medical complexity may not have time to volunteer in this role. See Figure 2.

Meet·Ryan,·Miya's·mother·who·adopted·Miya·into·their·forever·family·from·medical·foster·care.·Ryan·works·as·a·master's-level·nurse·and·is·an·"expert·medical·parent"·providing·24/7·care·to·a·child·with·RD·and·her·siblings.·
She·serves·as·the·chief·elect·on·a·patient·family·advisory·council·within·a·large·pediatric·health· system· where· she· demonstrates· the· value· of· a· true· partnership· between· the·healthcare·team,·specialists,·and·parent·caregivers.·
Ryan's·top·advice·to·parents·and·care·teams·is·to·"Know·that·there·is·much·to·learn·from·a·parent·who·has·earned·what·equates·to·a·professional·degree·in·their·child."

Figure 2. The Expert Medical Parent [14].

3.9.2. The Siblings

Sometimes, the family member that is unseen or in the background, siblings of children with RD, present unique experiences and serve roles in the family that differ from families without RD. Deavin and colleagues conducted a meta-synthesis of multiple qualitative studies to draw conclusions from the direct reports of siblings themselves to better describe the psychosocial commonalities experienced by siblings in order to improve care for families [82]. They identified two overarching themes experienced by siblings: (a) relationship changes and (b) managing change. Within these themes existed the family's relational changes in cohesion and relationship between parents and the sibling, as well as the sibling's relationship to self and contending with the emotional experience of foregoing their own needs and serving new roles and responsibilities.

The Committee on Psychosocial Aspects of Child and Family Health of the American Academy of Pediatrics summarized challenges for siblings as follows [83]. A common role that siblings report is that of the assistant caregiver. Siblings may feel overshadowed or neglected due to the constraints of the child patient's needs and the impact on limiting parental time and resources toward the sibling. They can feel embarrassed if others stare at or make comments about the family member with RD because they look different. They may become angry if they are asked to assume more household chores or guilty when they resent their added responsibilities in the family. Additionally, siblings report feeling guilty about being healthy and not having RD. Siblings who may be genetic carriers of an RD that is not phenotypically apparent may feel guilt and anxiety about what this means for their own decisions to have families of their own. Additionally, siblings may feel anxious about becoming ill themselves and experience a higher rate of medical trauma related to witnessing intense medical experiences of their sibling at home or within the medical setting. While academically siblings may experience more missed school, some studies report academic challenges that extend beyond missed days due to hospitalizations or medical visits for their sibling [84].

3.10. Access Barriers in the Community

Children with RD and their families may experience barriers to engagement in community activities due to exclusion or limited access for individuals with physical or intellectual differences. This affects the families' ability to thrive in the communities where they and their families live, learn, work, and play.

3.10.1. Community Activities and Transportation

Lack of wheelchair accessible transportation, as well as other adaptations to meet the mobility needs of some children with RD, create significant barriers to attendance at medical appointments, engagement in educational and therapeutic activities, and play [85–88]. Some legal statutes exist to help ensure accessibility, such as the Americans with Disabilities Act (ADA) in the USA, although in reality these provisions often fall short and can at times require costly and time-intensive enforcement measures if not being followed. Without reliable community options for accessible transportation, families face the choice to either pay to adapt a personal vehicle or limit participation in activities outside the home. The sheer cost and lack of funding mechanisms for these adaptations create an insurmountable barrier for many families, exacerbating social isolation and limiting access to medical and educational services in the community. Families in both rural and urban areas face significant, although at times different, barriers to accessible transportation.

Social exclusion and isolation are commonly described among parents of children with RD [89]. Parents of children with rare neurodevelopmental disorders have described experiencing social taboo and stigma when interacting with families of neurotypical children [9]. Exclusion can be related to limitations of the built environment or structure of an activity (e.g., playground without accessible equipment) or to assumptions about the nature of a child's disability (e.g., child excluded from a reading activity due to the assumption they would not comprehend it). Some children experience barriers to support services and

special programs due to the rare nature of their qualifying condition [15]. For example, a child with a progressive neurodegenerative disorder caused by a novel genetic mutation may not be technically eligible for a waiver program because their diagnosis is not one of the listed eligible conditions. Eligibility criteria for support programs are heterogenous, the application processes can be onerous, and once accepted the waitlist for services can be years long.

3.10.2. Appropriate and Fair Education

Children with RD have the right to an appropriate education in the least restrictive environment possible, but school districts and service providers are not always equipped with the resources and skills to meet that need. Legal statutes such as the Individuals with Disabilities Education Act (IDEA) in the USA set expectations for school-based services for children with disabilities, but the unfortunate reality is that individual school districts do not always have the necessary resources to fulfill these expectations. Parents of children who have neurocognitive differences, including children with RD, often find themselves having to advocate for their children's educational and therapy needs. The lack of appropriate support services to allow for appropriate access to places of learning may prevent children with RD from attending school or being educated according to their rights and abilities.

Children with RD may also experience social difficulties by way of stigma and bullying and face greater misunderstandings of their experiences by peers and teachers [30,32,90] and are more likely to be bullied compared to their peers [91]. Delays in diagnosis may impact school planning and access to resources for children with RD [92,93]. Given that schooling may be disrupted by the child's medical needs, official recognition of abilities, coordination of care, curricular adaptation, emphasis on autonomy, and peer support may all influence an equitable education [92,93]. Furthermore, children with RD experience disruptions in their school experience and are more likely to have higher academic, medical, and social–emotional needs but do not experience school-based support at the same level [33]. Common themes in a qualitative study where children with RD experienced reduced school attendance included increased discrimination, reduction in participation, and facing students and teachers who lack knowledge and understanding of their experiences [92].

3.11. The Healthcare Team

Caring for a child with RD is a 'team sport' and 'takes a village.' Due to frequent healthcare utilization and fragmentation of the healthcare system, individuals with RD and their families often must update new providers about their child's complex history and care needs, feeling more like an expert than the professional, telling the story over and over. Turnover of health professionals has also been identified as a concern for those with RD. Families have identified the need to continually update existing or new "continuity" providers as a stressor and dissatisfier. Healthcare organizations and healthcare teams can optimize care coordination in multiple ways. Practices should work to minimize wait times for acute and chronic care and maximizing access to services. Children with RD and their families may rely on a multidisciplinary coordinated care team in that children with chronic conditions often are higher utilizers of social work services than their healthy counterparts [73].

Healthcare teams not only consist of many professionals, but also trainees. Trainees need to be made aware of unique needs of individuals with RD. It is important that clinicians model principles of patient- and family-centered care to their trainees. Teams should have shared goals, clear roles, mutual trust at effective communication as well as measurable outcomes [94]. Healthcare teams should model and instill these principles in medical trainees and other interprofessional education. Healthcare teams can learn from one another as well as from patients and families. Project ECHO is one model that has proven effective across disciplines and uses a "spoke and hub" model for bidirectional education and case-based learning via tele-mentoring [95]. This type of model moves knowledge

instead of people. For healthcare teams, educators or individuals with RD, the ECHO model may serve as a potential way to rapidly share best practices and information [95].

Medical Homes are one example of a system that meets patient needs, improves the patient experience, and also improves provider efficiency and support [96]. A Medical Home is a beneficial component of care for all children, especially those with RD, disabilities, or other medical complexity [9]. In the USA, they have demonstrated healthcare cost reductions to families and insurance payors as well as reductions in emergency services utilization [97]. As children with RD have so many healthcare providers, it is sometimes difficult to identify the primary person or team responsible to see the whole picture and coordinate care [13]. The Medical Home provider may be a specialist (such as geneticist or neurologist office that has a care team familiar with the RD) or a primary care provider that is the central 'home' for general healthcare and coordination for the child with RD [98]. The healthcare team that serves as the Medical Home may differ at times by health condition and geographic resources; it may also change over time as patient and family needs or resources shift. Centering care within the Medical Home model ensures continuity and minimizes the need for families or individuals with RD to retell their story. The model also enables a big picture view of the health and wellbeing of the whole child with RD, not only one aspect of care, and how different medical recommendations from multiple specialists interact [99]. While some conditions have entire clinics dedicated to individuals with a certain diagnosis (e.g., a Down syndrome clinic, or Neurofibromatosis clinic), individuals with RD will not typically find such clinics for their condition based on its low prevalence. Rather, multidisciplinary complex care clinic programs with interprofessional healthcare teams (dietician, pharmacist, primary provider, social worker, psychologist, nursing, etc.) are an example of care coordination programs for individuals with RD or multiple health conditions [97,98].

3.12. Transition to Adult Care

Transitioning pediatric and adolescent care to Adult Care is challenging for any child, including many children with RD [100]. The change in family support that comes with increased independence from caregivers to self-management of one's own care brings many challenges and needs. In the past, individuals with childhood onset RD may have had a poor prognosis and may or may not have lived into adulthood. With advances in medicine, these children are living longer and adult healthcare teams to whom they turn may be even less familiar with the childhood onset RD than those with pediatric training. Additionally, expectations may be different in adult settings. For some children, chronological adulthood does not mean caregiving needs are gone. When some individuals with RD become legal adults, they may need various levels of ongoing assistance. Some children with RD have intellectual disabilities or differences and find it difficult to negotiate the expectation of being independent and capable of their own decision-making without someone else present. Additionally, for children who have neurodevelopmental delays, supportive services such as those of Child Life Specialists are not typically available in adult hospital or clinic settings. Child Life Specialists are trained in promoting developmentally appropriate coping skills to minimize adverse effects of stressors related to healthcare encounters and procedures [101]. In some countries, legal structures require that youth with RD be evaluated or determined to require a guardian to manage certain aspects of their livelihood. This may be required to access funds allotted for their housing or care in adulthood. Considerations may include medical decision making, financial holdings, housing, legal rights, navigation of healthcare systems, and optimizing independent functioning and safety as possible given their needs [102]. There are many complexities and hurdles to determining if assistance needed and legal and insurance changes to navigate. Additionally, for individuals with RD and physical differences or disabilities, accessible transportation, services, and healthcare offices may be difficult to negotiate independently.

4. Recommendations

The material presented here represents an overview of the many facets of caring for children with RD that impact their psychosocial wellbeing. While some evidence exists for improving systems of care and care delivery, much remains to be done to advance the state of supports across settings for children with RD and their families. In what follows, specific pathways are proposed to achieve high priority recommendations that may further herald this call to action for leaders in healthcare, education, research, and policy.

4.1. Support Pathways

4.1.1. The Child and Family

In Germany, CAREFAMNET examined the many gaps between medical and psychosocial health for children with RD and their families [103]. They found that psychosocial care is not standard part of routine care for these children and families. They highlight a need for improvement to facilitate access to psychosocial care and support, expand services to all family members, strength, and expert patient organizations, simplify application procedures and more cooperation between funding agencies, strengthen low threshold services, integrate psychosocial care, and promote interdisciplinary collaboration and networking. Many families of children with RD face substantial burdens related to the time and intensity of daily cares, frequent tradeoffs to balance caregiving with employment and other family needs, the social isolation of their unique caregiving experience, and navigating a complex and often fragmented healthcare system. Improving caregiver supports can help decrease caregiver burden and help families connect with peers [40]. Many communities have peer support networks both for parent caregivers and for children with RD themselves. Such networks may allow families with a child having an RD to connect with another family of a child with the same condition. If that is not possible, connecting with a family with similar lived experiences of RD, such as the challenges of a diagnostic odyssey or daily life with medical technology dependence, can offer valuable support. Diagnosis-specific national organizations and support groups are also a resource for caregivers to connect with other families affected by an increasing number of rare diseases. In the USA, the National Organization for Rare Disorders (NORD) has established a database of these organizations on their website [104]. There are also organizations that provide support and resources based on a child's developmental or medical needs rather than a specific diagnosis. Clinicians should help families connect with community organizations that support educational and community advocacy efforts on behalf of children with complex medical needs.

An additional support for families may come through connecting them with community organizations that support educational and community advocacy efforts on behalf of children with an RD or complex medical needs. Such support groups may take the form of being informational, resource-oriented, providing a peer mentor, or family-to-family support. Parents are recommended to seek support with others who have shared similar lived experiences although some RD specific connections may be available. One such parent support program with global accessibility and impact includes Parent to Parent online support groups that are arranged by country [105]. In New Zealand, for example, Parent to Parent has support groups in twelve different locations [106]. These resources aim to connect parent caregivers across the globe with other parents who understand their unique circumstance. Parents may choose to match with another parent, for example, by disease, location, or special healthcare need [107]. In-person community and social connection may be built by attending informational, disease specific group events, or supportive gatherings. One example in the USA is Hope Kids which provides ongoing events, activities and a powerful, unique support community for families who have a child with a life-threatening medical condition [108]. The mission is to surround these remarkable children and their families with the message that hope is a powerful medicine.

4.1.2. The Siblings

The presence of a family member with RD provides opportunities for increased empathy, responsibility, adaptability, problem solving and creativity. Siblings themselves highlight that obtaining support from friends, peers, and support groups were essential as a positive force in managing changes in their lives, while negative reactions from others was a detriment. What mediated this was coping, acceptance and adjustment [82]. They note that families and healthcare teams may underestimate the emotional responses and needs of siblings due to their presentation of self-sufficiency and adaptation to additional responsibilities despite experiencing elevated levels of stress. Such evidence about the importance of addressing sibling's psychosocial needs has led sibling interventions to be incorporated as a standard of care in pediatric oncology, for example. Thus, this is a great opportunity for parents and healthcare providers to meet siblings' needs in numerous ways.

1. Parents, be aware that while attending to the needs of the child with RD, you may be neglecting—or creating unfair expectations for—your other children.
2. Siblings can learn to participate in the family and feel pride and love in helping their brother or sister with their health.
3. Try to establish some balance between the needs of your child with a chronic health problem or disability and those of your other children.
4. Keep in mind that siblings need to have honest information about the condition and to have their questions listened to and answered.
5. Spending small amounts of quality time with each child individually as much as possible may help.
6. Support groups involving other siblings in a comparable situation can play a pivotal role in siblings' coping and thriving amidst this challenging situation.

One example of a resource for sibling support that has a global impact includes the Sibling Support Project and Sibshops including SibTeen, Sib20, and SibNet [109]. These are online communities for siblings across various age groups, which allow thousands of siblings of youth with complex medical conditions from around the world to connect with their peers to both receive and provide much needed support [109] and can be accessed here: (https://siblingsupport.org accessed on 4 December 2021).

4.2. Support and Collabortion Pathways

4.2.1. Behavioral Health

Supportive care coordination and shared care plans have been associated with improved parental mental health for families of CSHCN [63,64]. To address behavioral health needs in the settings where children with RD and their families are found, certain adaptations to an integrated care model such as the Medical Home, or specialty care center, may prove useful. Integrated care embeds behavioral health providers such as psychologists and social workers and counselors into the healthcare setting. Visits to the Medical Home provider may yield a consult with an embedded mental health provider as a first point of contact for an emotional, behavioral, or psychosocial need, providing immediate access to care [110]. To optimize family wellbeing, it is important that psychosocial care be needs-oriented for children and their families rather than diagnosis-oriented [103]. Families may prefer not to add another care provider to their family's team nor to add more appointments on the family calendar. However, there are situations such as depression with suicidal ideation or reduced effectiveness in completing demands due to depression, anxiety impacting sleep and daily effectiveness, sleep disorders reducing one's restoration that could sustain caregiving and wellbeing. These are examples when evidence based behavioral healthcare is recommended and can be positively impactful for the parent caregiver and the child patient [111]. Services for adult caregivers of a child with RD may be identified through your healthcare system that cares for your child. Families are encouraged to ask the provider for the child with RD for vetted referrals who understand the unique circumstances of caregivers of a child with RD. Telehealth counseling or psychotherapy

may be available that would be otherwise not accessible due to location or transportation and other time- and- effort- based barriers.

4.2.2. Partnership

The overarching model that best accommodates psychosocial needs of children with RD and their families is the PFCC approach because it is known to improve patient and family satisfaction, patient self-management, and physical and mental health outcomes. The foundational principles of patient- and family-centered care include valuing patients and families as members of the healthcare team, ensuring inclusive communication, and harnessing technology to promote access to health information [112].

4.3. Patient Family Advisory Councils or Boards

Family advisory boards, councils, and volunteer service opportunities that provide shared experiences and social support, sense of community. Importantly, for patient family engagement to be effective in partnering in the healthcare of RD, those serving on the boards must reflect the views, needs, and culture of those they represent. In one large pediatric health system in the USA, barriers to participation in PFACs were found to vary by race/ethnicity and socioeconomic status, with those from Black or less affluent families underrepresented in these boards [113]. If a sizable portion of those served by the health system are of a particular racial or ethnic group, or spoken language, their SDH should be addressed by the institutional policies advocated for by the representatives of the current board. Richard and colleagues outlined recommendations for developing, implementing, and sustaining PFACs [114]. These included four themes and are summarized as follows:

- Use evolving recruitment methods
- Prepare for effective participation
- Ensure diversity within PFACs
- Outline terms for orientation and participation.

PFACs should recruit in an ongoing manner to maintain adequate participant numbers in light of the ongoing changes in circumstances and needs of families. Important to acknowledge is that members may agree to serve a particular term (e.g., one year) with the option to renew their commitment annually, but that they should feel free to withdraw their participation at any time should their needs change. PFACs should produce "living" reference documents that establish regulations around membership and recruitment that provide guidelines to PFAC members, including how to recruit and retain members and outline how they would be involved in the council. Training was completed using an orientation manual that includes expectations, ways to stay engaged and connected, legislative requirements such as accessibility and privacy as well as in-person orientation on how they can tell their story, teaching them about the organization and what they can expect. Members should be the ones who choose when the meeting dates are going to be, how they want to set up the council. In a pediatric setting diverse representation would include the pediatric voice as well as various ethnic, religious, geographic, and socioeconomic backgrounds [114]. It was stated that the PFAC should look like your waiting room. Some strategies utilized to promote diversity within the PFAC include targeted recruitment for members of underrepresented groups; recruitment of individuals who work with members of minority and underrepresented groups [113].

Next, for the PFAC to thrive, the authors recommended the PFAC leaders to address logistics to promote attendance, for example, virtually or in person. On an ongoing basis, address open communication and all barriers to participation among members. This may be accomplished by setting a standard for continuous communication that is established from the outset of the PFAC. Provision of certified interpreter services that allow individuals with language barriers to participate effectively and efficiently; virtual participation options for those who may not always be able to physically attend meetings; and finally, meeting with individual groups outside the institution to gather information from minority groups that can be brought back to the PFAC. One recommendation is to consider compensation

of parents who donate their time and expertise to PFACs rather than considering them vetted volunteers for the health system. This may improve the ability for parents who have not participated due to financial barriers or related circumstances to participate through financial support for their time. This could enhance diversity and inclusion and representation of all families within these advisory boards which is so important to guide health systems in serving diverse populations.

5. Calls to Action

Healthcare Teams.

5.1. Include the Child Directly

Families and healthcare teams can positively influence the child's acute care experience by intentionally including the child in decision making processes while admitted to the hospital and this is expected to increase coping through improved engagement and control with their own outcomes [25]. Although there is limited research on communication between healthcare staff and children with communication barriers or who are nonverbal, parents have recommended that we speak directly to their child rather than rely on the parent to serve as a go-between. In fact, parents report feeling more anxious if they are the only communicator for their child and want health team to make more of an effort to involve the child in their care. It is known that children feel and need competence in medical visits and being a part of medical decision -making about their lives is empowering. Specifically, parents ask the care staff to show the child what to expect and help them feel in control using communication at their level. Parents ask that staff learn about the child's unique way of communicating and learn how to use it. For example, if a child uses an adaptive communication device, sign language, or a communication board be prepared so that the child can interact in the visit. Communicating with the child can increase their sense of safety and security. Finally, parents ask that if one member of the healthcare team learns about ways to communicate effectively with the child, share this with the rest of the team so that the family does not have to "start over" in retelling their story with each visit [115]. See Figure 3.

- In the USA, better care coordination between health providers who care for my child is essential. Specialists and care teams must have time and space to communicate with each other to optimize care for the whole child.
- Pharmacy and hospital discharge paperwork must communicate and align in their instructions to parents to avoid confusion and errors in dosing. Discharge medication instructions for Miya were dosed in milligrams but Miya takes medication in milliliters requiring Ryan to covert dosages to give Miya her medicine. Ryan expressed, "This creates a lot of confusion and worry for parent caregivers that could be avoided."
- "Care teams, please ask what my child wants in her life. See my child as more than her rare disease. See her as a person who will thrive within her ability … not just live out the disease."

Figure 3. A Parent Voice: Calls to action that Ryan values most for Miya [14].

5.2. Leverage Collaborative Communication

Taking time to hear the child and family's concerns and to partner with them in their care is the aim of care conferences. These are meetings with the parent and medical specialists to discuss the patient's care, express concerns, and share information. Care Conferences are often non-billable and thus can be rife with limitations in the medical system driven by revenue productivity. However, care conferences add value to the collaboration between patient, family and healthcare team that cannot be built elsewhere through other methods of consultation among providers or in office visits. The electronic health record (EHR) provides a means for messaging to facilitate information sharing and communication with families. This allows for documentation to be saved and referenced

later by the family and the care team. Families are recommended to keep a journal or binder of information with questions, answers, and concerns to bring up in visits. This allows the parent and the care team to ensure that all questions are addressed, and that solutions and interventions are tracked over time. Parents are encouraged to ask for Infographics and visual aids for difficult to understand routines, cares, or medication regimens, mobile apps and pill minders for timed dosing and improved adherence to prescription medication plans. Parents are recommended to offer their assistance to the care team as an observer or data collector in the home to inform medical or behavioral health decision making. Behavioral health providers may provide charts or checklists to help parents or school staff track and share with the care team any clinically relevant home behaviors and symptoms.

Care coordination for CMC with RD may improve parental mental health [63,116], in addition to the other expected benefits for the child. While not all healthcare providers will have the same resources, healthcare teams must proactively communicate to ensure coordinated care. There are tools to help with care coordination. Proactive guidance when available such as use of emergency information forms, action plans, comprehensive care plans can be useful in helping families to communicate essential information. Families and individuals with RD are part of the care team and should participate in creation and updates of care plans. Additionally, inclusion of the parent voice in clinical practices and improvement work is key to optimizing care for children with RD. Healthcare teams are encouraged to approach the provider-patient/family relationship with curiosity and an open mind, and frame caregiver expertise as an asset to that partnership.

Care mapping is a family-driven, person-centered process to highlight a family's strengths and communicate both the big picture and small details of all the resources needed to support a child and family in a snapshot. The process of care mapping has served as a useful tool for care coordination and patient and family engagement [117]. See Figure 4 for links to instructions and additional resources to engage with families in care mapping.

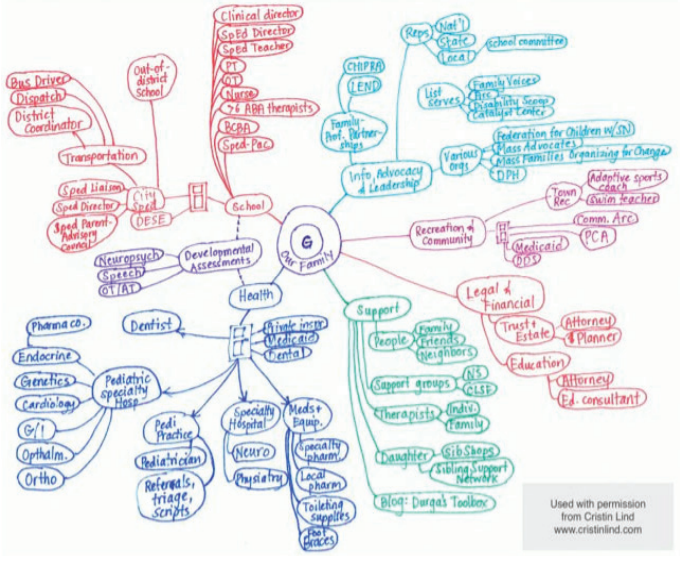


Figure 4. Care map created by the mother of a child with medical complexity to pictorially represent aspects of the care her son requires to be coordinated. Used with permission from Cristin Lind, http://www.childrenshospital.org/integrated-care-program/care-mapping accessed on 4 December 2021.

A care map depicts that the web families navigate is not limited to medical providers alone. The healthcare team may include professionals from many fields such as a phar-

macist, social worker, psychologist, dietician, nurse, care coordinator, patient navigator, therapist, genetic counselor, or a medical librarian. The child and family are also an essential and integral and central member of the care team. Regular communication between care teams, outpatient and inpatient and use of care co-management guidelines or customized care plans can enhance care coordination and ensure healthcare teams are on the same page. Medical care is only one aspect of the experience of a child with RD and coordination with community and educational services is also essential. An integrated care model is recommended, when possible, as it may increase behavioral healthcare access (embedding behavioral health and psychosocial supports within the medical setting and team). Care teams can collaborate with a patient and their parents and the child's school and home- and community-based care providers to develop a shared plan of care that reflects the many settings that contribute to a child's care. Partner with schools and other agencies working with the family to glean data points to guide decision making about interventions such as medication dosing, behavioral interventions. Examples of care coordination tools can be found here: https://www.ahrq.gov/ncepcr/care/coordination.html (accessed on 11 March 2022) [118].

1. *Facilitate Transition to Adult Care*

To improve transition to adult care for individuals with RD, healthcare teams should discuss transition early starting in adolescence. Teams can discuss ways to prepare individuals with RD and their families for adult healthcare and system navigation. These may include initiating testing if it is unclear if an individual with RD will need any level of legal guardianship or other supports and discussing the process. Healthcare teams can aid by creating a transition summary and communicating with potential or new adult healthcare teams during the transition period [119]. Healthcare systems must recognize this challenge as well to better support individuals with RD and provide resources but also adequate training for adult physicians [120]. Providing a transition coordinator is one intervention that may be useful for facilitating a smooth transition. The 'why' behind transition cannot be understated; when young adults with RD reach the age of transition to adult care, this opens space for new young children with RD and their families to access high quality care [102].

2. *Access and Share Essential Information*

Individuals with RD and their families often have a long quest for a diagnosis or understanding the RD. Healthcare teams are encouraged to partner with families and to encourage the search for answers. One mechanism of action is participation in clinical trials and in helping families to connect to case reports in the medical literature that will provide added information about their child's RD. Teams can encourage and facilitate connection with other families or networks to share and learn. Families and healthcare teams are also encouraged to discuss where to find reliable sources of information. This may range from online sources, but also expert medical consultations or second opinions, clinical trial opportunities, and expertise from other families with lived experience. Families should be encouraged to bring questions to their visits, including any information found online to discuss. Utilizing and providing access to a medical librarian may also be critical in helping to find accurate information for both providers and individuals with RD and their family. Families are encouraged to ask their care providers what reputable sources or societies are disseminating innovative, up to date, evidence-based or vetted information about their child's condition. From this starting point, families may find they are able to determine sources they can trust and references they can rely upon. Families are encouraged to ask questions on what is known and what is being explored in clinical trials, for example, but not know how much weight and hope to place on what may or may not be possible.

To address challenges related to accessing available information and care instructions, healthcare teams should use health-literacy-informed strategies. Healthy people 2030 recognizes that it is not just the individual that determines health literacy, but it is also affected by the degree to which organizations equitably enable individuals to find,

understand and use information and services [79]. Many standard patient education child health handouts may not always be applicable or sensitive to the needs of individuals with RD and must be further personalized. For instance, individuals with RD may have complicated medication regimens or care routines or dietary needs. Additionally, an individual's health literacy can worsen during times of stress [81]. It is known that individuals with RD may have complicated care instructions and their parents may experience elevated levels of stress. To promote understanding of instructions, the use of plain language with primary-grade-level readability (sixth grade or lower in the USA system), and visual graphics when possible, are recommended [121]. The "teach back' method can be used to check for understanding by asking children and parents to teach back what they heard in their own words. Although this technique can cause some discomfort at first, with practice, it is effective to increase patient-centered communication and effective engagement [122]. Healthcare teams can mitigate disparities associated with low health literacy by using health-literacy-informed strategies including limiting information, action-oriented instructions, plan language, demonstration, teach back, supplementing verbal with written information and pictographic and multimedia materials [121]. Additionally, for those individuals or families that do not share a common language with the healthcare team, having interpreter services and translation for written materials is essential for communication.

Health literacy is one social determinant of which there is no need to screen for, as all individuals benefit from clear communication. However, healthcare teams should screen for the impact of SDH. While this is a recommended practice for all pediatric patients, there is a particularly high likelihood of SDH factors impacting health outcomes for children with rare diseases, given their likelihood of having complex chronic medical needs. The complex financial burdens these families experience should be considered, and families should be helped to connect with financial supports and assistance programs for which they qualify [123]. Integration of social work into the healthcare team can be extremely beneficial to families of children with RD, particularly when it is structured as longitudinal case management to address these families' dynamic needs over time.

3. Sustain Strategically

Provider wellbeing is a vital consideration in sustaining the medical provider role alongside a child with RD and their families' difficult journey. While provider wellbeing initiatives are emerging within healthcare globally, recommendations for medical providers to bolster their longevity and wellbeing and reduce 'burnout' are a key consideration when caring for the child with RD. Turnover of health professionals has also been identified as a concern for those with RD. Families have identified as a stressor or dissatisfier the need to continually update new providers. Health systems are recommended to utilize collaborative care teams to sustain each other more than sole providers. Care teams may hire professional roles for time-sensitive and time-intensive tasks. For example, a clinical pharmacist can supplement the care team for children with RD to manage polypharmacy, medication reconciliations and this has been shown to improve provider burnout [119]. They may also partner with schools and other agencies working with the family to glean data points to guide decision making about interventions such as medication dosing and behavioral interventions.

Improving electronic health record functionality with documentation, correspondence, consultation, and communication among team members, and reduce time-wasters and duplication of efforts with processes can improve provider wellbeing [124,125]. In fact, simply using messaging within the EHR for consultation reduces provider burnout [124,125]. Utilize the team's expertise rather than trying to do it all yourself. Plan joint or cascading visits so that the family may come to clinic for a visit but see multiple professionals either in person or virtually in the context of that visit. Engage with families as partners through efficient communication, for example, using modalities that double as documentation such as patient portal that populates into the electronic health record [126]. Honor the expert medical parent with partnership to serve as your eyes and hands in the home setting toto increase efficiency in your outpatient diagnostic workup and treatment planning [38].

5.3. Educators

Schools are called to provide inclusive education through intentional collaboration with families and healthcare teams. When teachers and students understand the child's experience and acknowledge their disease, a student may experience a reduction in "feeling different," an increase in their emotional wellbeing, and a reduction in caregiver worry [92]. Schools have the opportunity to provide a safe, accepting, and inclusive environment for children and may improve quality of life [93]. To reduce disadvantages in their education process and to promote a supportive environment, it is recommended that schools increase their awareness of the experiences of children with RD and take actionable steps to make the school environment most accessible [92,93]. Healthcare teams have an opportunity to promote communication and shared understanding between the settings where the child spends their time. Additionally, healthcare teams are recommended to ask families for their permission (release of information) to communicate with the school and enhance the connections between the school and healthcare setting to coordinate needs for the child.

5.4. Investigators

At this time, three areas of advancement in research have been identified. First, research to date focuses on the experiences of caregivers, but the voices and experiences of the child with RD are not quantified or described. This is concerning as many of the psychosocial and medical treatments are focused on improving the child or adolescents' wellbeing, but there are scant data guiding clinicians on best practices that are congruent and affirming based on these youths' experiences. Thus, a first step is to direct the investigator's attention to exploring and describing the experiences of youth with RD and to include them in the research process. A model that might be beneficial to apply is community-based participatory research, where youth are guiding the research developmental process. Researchers may serve as a vehicle to elevate caregiver voices in these spaces in appropriate and effective collaboration. Second, there is a need for translational research, where studies highlight whom interventions will benefit and under what specific conditions. While correlational studies are necessary, at this time there is a lack of clarity and direction in how these research findings may best be applied in clinical settings. Third, there is a lack of intersectionality in understanding youth with RD, where there is limited knowledge on race, ethnicity, gender, SES, geographic location, and access to specific resources. Within the context of the USA, the social construct of race has been the main driver in inequities in service access. Studies that lack this intersectional lens are doing a disservice to a large section of the population and are further perpetuating inequities. Thus, investigators are encouraged to use an intersectional framework in their research design, while using a wholistic rather than additive approach.

5.5. Policy Advocates and Change-Makers

Investigators may collaborate with caregivers to not only examine their experiences but to also elevate their voices in policy spaces. Policy change relies on advocacy by families of RD, who are already stretched thin by constant caregiving responsibilities. Expecting these families to speak up to promote change represents a major barrier to progress addressing the policy needs of this population. Policy change requires the perspectives of caregiver and patient advocates to highlight and address their needs. However, caregivers of youth with RD are often prevented from participation due to practical barriers, such as providing round-the-clock care. This is a major barrier that prevents progress in policy that is reflective of this population's needs. Policy-makers are urged to act on the significant gaps in equity and provision for this population with specific recommendations highlighted here.

5.5.1. Improve SDH at Multiple Levels

SDH are defined by the World Health Organization as the conditions in which people are born, grow, live, work and age [127]. When considering the modifiable contributors to an individual's health outcomes, medical care is estimated to account for ten to twenty

percent [128], with social determinants of health dwarfing the impact of direct clinical services. Interventions to address SDH should be focused on the community and population levels in addition to individual screening, in order to systematically address these common needs, which have a disproportionate effect on families of children with chronic medical needs [129]. Connecting families with care coordination services either within the medical home or in partnership with a community organization may be a successful means of addressing SDH which may also improve the family's experience of other aspects of their child's care [130]. The provision of care coordination services is often limited by poor reimbursement within established payment models for pediatric medical services, making it financially unsustainable for centers to offer. Recognize the impact of caregiver-provided medical care for children with RD, and advocate for enrollment in home nursing care and patient care aide services when medically appropriate [38,45,131]. Augmenting existing funding streams and creating new financial incentives for care coordination has the potential to improve access to this important service for families of children with RD [130].

5.5.2. Improve Home and Community Based Services

Improve funding for home-based services including private duty nursing, skilled nursing visits, and patient care aide services. The authors are writing from the perspective of the USA where there is a long-standing shortage of pediatric home nursing services. Improved funding and support for these services would allow children to receive care in the least restrictive environment possible, decrease preventable hospitalizations [131] and contribute to family wellbeing by decreasing parents' need to improvise this skilled caregiving on their own. While other countries' statuses may differ regarding this service, this USA perspective highlights the importance of bolstering the fragile network of home- and community-based services on which these families rely. It is recommended that policy-makers invest in robust paid family leave policies, childcare programs equipped to serve CSHCN with RD, and paid family caregiving, which can mitigate the impact of children's chronic health needs on families [44]. Additionally, advocating for the establishment and expansion of these services and local, regional, and national levels is necessary.

5.5.3. Improve Accessibility in Communities

It is recommended to improve access to wheelchair-accessible transportation and accessibility of community spaces and activities to allow children with RD to participate fully in family and community activities regardless of disability status [85,86]. As many existing legal statutes are not sufficient for ensuring this accessibility, policy-makers should consider bolstering this legislation to improve its effectiveness and provide resources for communities and organizations to adapt their spaces and programs more successfully to be inclusive.

6. Limitations

There are limitations to account for when considering the results of this review. First, our sampling of the literature may have missed articles not included in English or within the databases used. Second, our recommendations may not represent consensus among all healthcare professionals caring for this population and may reflect the sampling of the available literature. Third, the authors all practice in the USA which may bias or slant our approach to the topic influencing how recommendations are framed. Finally, very little research specifically addresses the psychosocial needs of children with rare diseases. Therefore, much of the current knowledge is gleaned from a sampling of studies that address one or more facets of either a subset of the population or more global the psychosocial concerns. There is much to be learned from the growing body of literature regarding relevant intersectionality of multiple identities represented by children with RD, including children with medical complexity or disabled children, and these populations' needs may not capture those of children with RD.

7. Conclusions

This review has endeavored to provide a thorough examination of psychosocial considerations for the child with RD. In doing so, several gaps in the medical literature to bolster evidence-based care, psychosocial support, and access to resources in society at large for children with RD have been identified. Therefore, existing information on the psychosocial considerations of populations of children with chronic conditions, including CSHCN, CMC, and what little is known about RD specifically, is examined. In summarizing literature through a purposeful sampling of the scientific literature, recommendations to integrate what is known of current best practices, accessing optimal resources, and proposals framed as 'calls to action' are given to elevate the quality of life and promote evidence-based care for children with RD, their families, and healthcare teams. Understanding the psychosocial considerations for children with RD will hopefully energize future endeavors to better understand and address the needs of these remarkable children and their families.

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