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ORIGINAL ARTICLE

The clinical management of children with achondroplasia in Italy: results of clinician and parent/caregiver surveys

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Abstract

Purpose This study aimed to assess the real-world management of achondroplasia in Italy.

Methods Two online surveys addressed to (1) parents/caregivers of individuals with achondroplasia and (2) Italian clinicians managing individuals with achondroplasia were conducted to assess real-world perspectives on achondroplasia management. Both surveys collected data on either patient or clinician demographics, details on diagnoses and referrals, disease complications, and views/experiences with limb lengthening surgery.

Results In total, 42 parents/caregivers and 19 clinicians (from 18 hospitals) completed the surveys. According to parents/caregivers, achondroplasia diagnosis was most commonly made in the third trimester of gestation (55% of respondents), with a genetic test performed to confirm the diagnosis in all but one case. In contrast, the clinicians indicated that, while achondroplasia was typically suspected during the prenatal period (78%), diagnosis was more frequently confirmed postnatally (72%). Parents/caregivers reported that the greatest impact of achondroplasia-related complications occurred in their children between the ages of 2–5 years. The most significant complications were otitis, sleep apnoea, stenosis of the foramen magnum or pressure on the spinal cord, and hearing difficulties. Lengthening surgery had been presented as a treatment option to 92% of responding parents/caregivers, with 76% of clinicians viewing surgery favourably. Typically, clinicians' reasons for suggesting limb lengthening surgery were to improve patient quality of life, increase patient autonomy and self-acceptance, improve trunk-limb disproportion, short stature and walking, and ensure that all possible treatment options had been presented to the parents/caregivers.

Conclusion This survey provides insight into the real-world management of individuals with achondroplasia in Italy.

Keywords Achondroplasia · Clinician survey · Italy · Patient/caregiver survey · Real-world management

Introduction

Achondroplasia is a rare genetic disorder, caused by a recurrent pathogenic variant in the fibroblast growth factor receptor 3 gene (*FGFR3*) that results in short limb skeletal dysplasia [1]. Achondroplasia is the most common form of disproportionate short stature with an estimated worldwide birth prevalence of 3.7 to 4.6 cases per 100,000 births [1, 2]. The European Surveillance of Congenital Anomalies (EUROCAT) network reported a prevalence of achondroplasia from the Emilia-Romagna region in Italy for the years 1991 to 2015 of 5.70 per 100,000 births [1].

Individuals with achondroplasia show specific clinical features detectable at birth, including rhizomelia, macrocephaly, midface hypoplasia, frontal bossing, depressed nasal bridge, short broad hands with a trident hand configuration, hypoplastic foramen magnum, and a small skull base [1, 3, 4]. Complications of achondroplasia affect individuals throughout their lifetime [5]. In infancy, these complications include gross motor delay, hypotonia, otitis media, foramen magnum stenosis (which can lead to sudden death), and sleep apnoea, and in childhood, delayed motor and speech development, thoracolumbar kyphosis, genu varum, otitis media, sleep apnoea, obesity, symptomatic spinal stenosis, and pain. Many of these childhood complications persist into adolescence and adulthood [5].

Due to the wide range of complications associated with achondroplasia, a multidisciplinary team (MDT) is often involved in ongoing care, although the types of specialties involved differ between countries [6]. Differences between

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countries also exist in diagnostic methods, patient management, and the specialty of the lead clinician, and until 2021, there were no universally agreed European recommendations for the management of achondroplasia [6]. The European consensus on principles for the management of achondroplasia now provides a basis for the development of optimal care (Table 1) [1, 6]. An important step in the journey of many individuals with achondroplasia is limb lengthening surgery [7]. There are differences in many aspects of patient management for this procedure, including whether and when an individual is offered such surgery, as well as the surgical techniques employed. Here, we report the findings of surveys of parents and caregivers of individuals with achondroplasia and of clinicians managing individuals with achondroplasia, which were conducted to understand how this disorder is currently managed in Italy and to gain insight into the patient journey.

Methods

We conducted two surveys, one addressed to parents and caregivers of individuals with achondroplasia and another one to clinicians who manage individuals with achondroplasia, to assess the real-world management of achondroplasia in Italy from their perspectives.

Study design and study participants

MA Provider, an Italian healthcare consultancy company, drafted the clinician and parent/caregiver surveys with support and validation from clinicians. MA Provider (Italy) contacted hospitals throughout Italy and invited clinicians to complete the clinician survey. The survey was self-administered by clinicians online. The Italian parent/caregiver association 'Associazione per l'Informazione e lo Studio dell'Acondroplasia' (AISAC, the Italian Association for Achondroplasia Information and Study) made the parent/caregiver survey available on their website, and members were asked to complete the form (which was also self-administered). AISAC ensured the accuracy of the data collected from parents/caregivers and provided the data to MA Provider who then analysed the results, and produced the study report.

Data collected

The parent/caregiver survey collected the following information: demographic details; details regarding achondroplasia diagnosis and referrals made after diagnosis; complications of achondroplasia; patient care experience, including information regarding their treatment centre(s), which specialist made the diagnosis of achondroplasia, which specialist was in charge of follow-up, and the reasons for losing contact with the treatment centre; and their views/experiences with limb lengthening surgery, including which physician suggested this treatment option and when/how/where it was conducted.

The clinician survey collected the following information: clinician details (specialty, institution type) and institution details (type of institution, achondroplasia patient services, specialists managing individuals with achondroplasia); details of clinicians' patients (ages, complications); details of the specialities involved in diagnosis, referrals, and patient follow-up; details of patient follow-up (frequency of patient visits, reasons for loss to follow-up); and views on limb lengthening surgery and patient access to surgery.

Table 1 The 2020 European Achondroplasia Forum (EAF) guiding principles for the management of achondroplasia, modified from 'The first European consensus on principles of management for achondroplasia' by Cormier-Daire V et al. published in *Orphanet J Rare Dis* 2021;16(1):333 under a Creative Commons Attribution 4.0 International License [6]

Item	Guiding principles
1	Achondroplasia is a lifelong disorder requiring lifelong management by an experienced MDT, led by physicians/clinicians experienced in achondroplasia management. Close monitoring during the first 2 years of life is critical
2	When a diagnosis of achondroplasia is made or suspected, either in utero or after birth, the family should be referred as soon as possible to a clinician experienced in achondroplasia to discuss the prognosis and management of the disorder
3	Decisions around management should be made in the MDT setting jointly with the person with achondroplasia and/or their family
4	The primary goals of management are to enable anticipation, identification, and treatment of problems and provide education and support to encourage a healthy lifestyle, positive self-esteem and mental health, autonomy, and independence
5	Patients should have access to a variety of adaptive measures, support to ensure proper usage, and access to approved treatment options as they become available
6	Regular monitoring in adolescence and adulthood should continue under an MDT with expertise in achondroplasia management. Care should include genetic counselling, transition to adulthood, psychosexual well-being, and management of pregnancy

MDT Multidisciplinary team

Statistical methods

Due to the descriptive nature of this study, no sample size was determined. MA Provider (Italy) analysed the results of this survey. Descriptive statistics were used to describe the survey findings, with categorical variables expressed as counts and percentages.

Research ethics

All participants gave their informed consent for the collection and use of medical and health information in an aggregated and anonymised manner for the purposes of this research only. No parents and caregivers of individuals with achondroplasia or associated clinicians received any compensation for participation in the survey. The survey complied with Italian data protection laws and was conducted in accordance with the Declaration of Helsinki. As this was not an investigation of clinical outcomes with any particular intervention, neither ethics committee approval nor clinical trial registration was required. The research was conducted by MA Provider (Italy) and funded by BioMarin.

Results

Between 1 and 7 June 2022, 25 clinicians from a total of 18 hospitals across Italy were invited to participate in this study (Online Resource 1; Supplementary Table S1), of which 13 were 'University Hospitals' (i.e. teaching hospitals). Of the 25 invited clinicians, 19 (76%) completed the survey. At the time of the survey, a total of 493 individuals with achondroplasia were managed in these hospitals. The questions were not necessarily answered by all respondents; therefore, sample sizes varied between questions.

Parent/caregiver survey

A total of 42 surveys were received from the AISAC and reviewed by MA Provider.

Patient demographics

Most individuals with achondroplasia were aged between 2 and 12 years (Table 2). Parents/caregivers of children with achondroplasia from 14 different Italian regions participated in the survey, including Lombardy ($n=12$), Veneto ($n=7$), Piemonte ($n=6$), and Campania ($n=4$), with two cases each in Emilia-Romagna, Lazio and Calabria, and one case each in Liguria, Tuscany, Umbria, Molise, Puglia, Sicily, and Sardinia.

Diagnosis and referrals

The diagnosis of achondroplasia was most commonly made prenatally, usually in the third trimester of gestation (55%; Table 2). A genetic analysis was performed to confirm the clinical diagnosis of achondroplasia in all but one case (41/42). A diagnosis of achondroplasia was most likely to be made by a geneticist (19/42; 45%), followed by a gynaecologist (12/42; 19%), diagnostic medical sonographer (8/42; 14%), and neonatologist (6/42; 14%).

Most respondents were referred to a specialised centre for the care of individuals with achondroplasia (i.e. a reference centre) after diagnosis (20/42; 47%) or were already in a reference centre at the time of diagnosis (7/42; 17%). The referral to a reference centre was most frequently done by a geneticist (8/20; 40%), gynaecologist (5/20; 25%), diagnostic medical sonographer (4/20; 20%), or neonatologist (3/20; 15%).

Most respondents (27/42; 64%) answered that they were referred to a patient advocacy group (PAG) for support and contact with other families, while only 38% (16/42) were referred to a psychological support service (provided either by the local health authority, a PAG, or the reference centre for achondroplasia). A total of 27/38 answered yes to 'have you been informed of the social protections (e.g. civil disability, employment protection, etc.) that a person with achondroplasia is eligible for', most of whom received this information from either a PAG or other families (in seven cases each).

Complications

Thirty-nine per cent (15/44) of parents/caregivers reported the greatest impact of achondroplasia-related complications was during the ages of 2 to 5 years. The most significant complications were otitis, sleep apnoea, stenosis of the foramen magnum or pressure on the spinal cord, and hearing difficulties or hearing loss, with the distribution of these complications differing by age group (Fig. 1).

The reported aspects of achondroplasia that most affected the child's quality of life were reduced functional capacity (18/28; 67%), reduced self-acceptance (7/27; 26%), pain (5/27; 19%), low self-esteem (3/27; 11%), and hypotonia (1/27; 4%).

Patient care and follow-up

The routine care provided to individuals with achondroplasia was generally performed by the reference centre (26/40; 65%), with others receiving routine care by a specialist near

Table 2 Characteristics and demographics of children with achondroplasia reported by the parents/caregivers and clinicians

Item, *n*	Parent/caregiver survey	Clinician survey
Age at diagnosis	*n* = 42	
Prenatal period (2nd trimester)	3	NA
Prenatal period (3rd trimester)	23	NA
Neonatal period, before hospital discharge	8	NA
During first 2 months of life	2	NA
Between 2–6 months of life	5	NA
≥ 6 months of life	1	NA
Age at time of survey	*n* = 42	*n* = 493
0–1 years	1	15
2–5 years	11	93
6–8 years	7	103
9–12 years	15	128
13–16 years	5	73
> 16 years	3	81
Age at time of discussing/being offered lengthening surgery	*n* = 34	
At diagnosis	11	NA
0–1 years	11	NA
2–5 years	6	NA
6–8 years	4	NA
9–12 years	2	NA
Age at which limb lengthening surgery would be recommended by clinician		*n* = 17
≤ 6 years	NA	1
7–8 years	NA	3
8–9 years	NA	1
9–10 years	NA	2
11–13 years	NA	3
14–16 years	NA	3
Variable	NA	3
Can't answer	NA	1

NA Not applicable

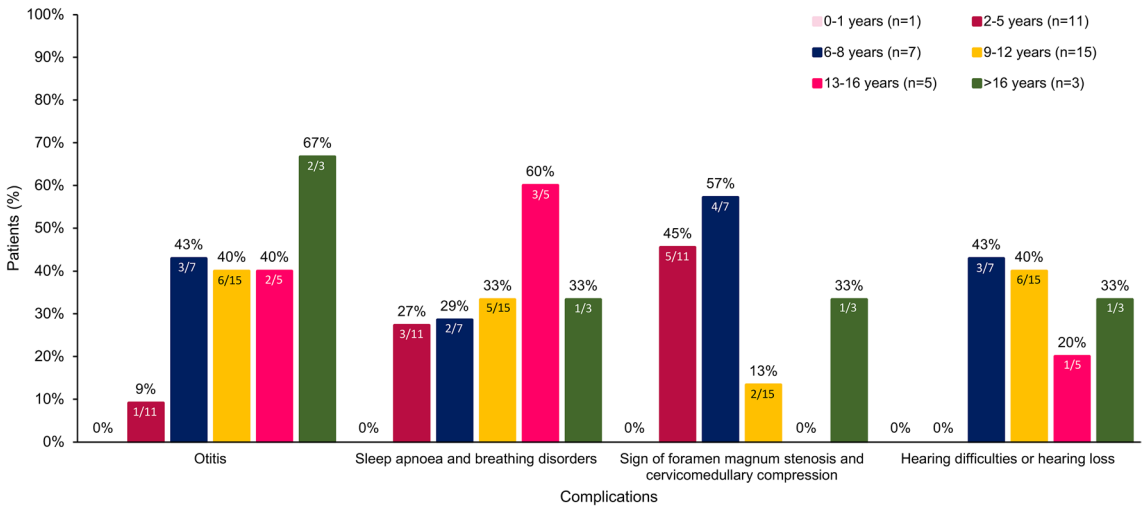

Fig. 1 Distribution of signs and symptoms by age group

their place of residence (13/40; 3%); the remaining respondents reported not needing assistance in daily life. Of those reporting that routine care was provided by a specialist, 6/11 (55%) saw their specialist once a year (Table 3). Specialists consulted in the last 2 years included orthopaedic surgeons, physiotherapists, ear, nose, and throat (ENT) specialists, neurosurgeons, clinical geneticists, and paediatric endocrinologists or endocrinologists (Fig. 2).

Most respondents reported that they consulted or contacted the reference centre to manage complications (32/39; 82%), with 7/39 (18%) reporting that they contacted their specialist; two respondents (5%) reported that no complications occurred.

Overall, 12/39 (31%) reported visiting the reference centre once per year, with 10/39 (26%) reporting visiting the reference centre once every 6 months and a further 10/39 (26%) visiting once every 3 months; 5/39 (13%) reported visiting the reference centre less than once per year (Table 3). The frequency of reference centre visits differed by patient age (Fig. 3).

In response to the question 'how far is it from your home to the reference centre that follows your child', 17/39 (44%) reported a distance of over 200 km.

While 19/40 (48%) respondents answered that their reference centre remained the same over time, 21/40 (52%) reported having changed their centre, with 9/20 (45%) reporting they changed their centre when their child was aged between 2 and 5 years. Of the 21 respondents who answered this question, the reasons for changing referral centres varied, with the most common reason being problems/dissatisfaction with the centre ($n=9$), transfer of the treating clinician ($n=3$), and that the former centre was not a reference centre for treatment of achondroplasia ($n=3$).

When asked what the main reasons for losing contact with the reference centre or the specialist were, 64% (16/25) of respondents reported 'no motivation', 12% (3/25) reported that it was because their reference centre was only for paediatric cases, and 8% (2/25) reported that distance to the reference centre or managing specialist was a factor. Dissatisfaction with the centre/specialist, difficulty in contacting the centre, 'COVID-19', and their child experiencing motor difficulties during the treatment period were each suggested by 4% (1/25) of respondents.

Table 3 Frequency of visits for specialists and reference centres

	Specialists[a] ($n=11$)	Reference centre[a] ($n=39$)
Frequency of visits, *n*		
More than once per month	1	1
Once per month	0	1
Once every 3 months	1	10
Once every 6 months	1	10
Once per year	6	12
Less than once per year	2	5

[a]11 parents/caregivers said routine care was provided by a specialist; 39 parents/caregivers specified the frequency of visits to a reference centre, but the responses are not mutually exclusive, nor was it established whether the specialists were at a reference centre or at a different type of clinical institution

Lengthening surgery

Lengthening surgery had been presented as a treatment option to 34/37 respondents (92%), at diagnosis in 11 cases

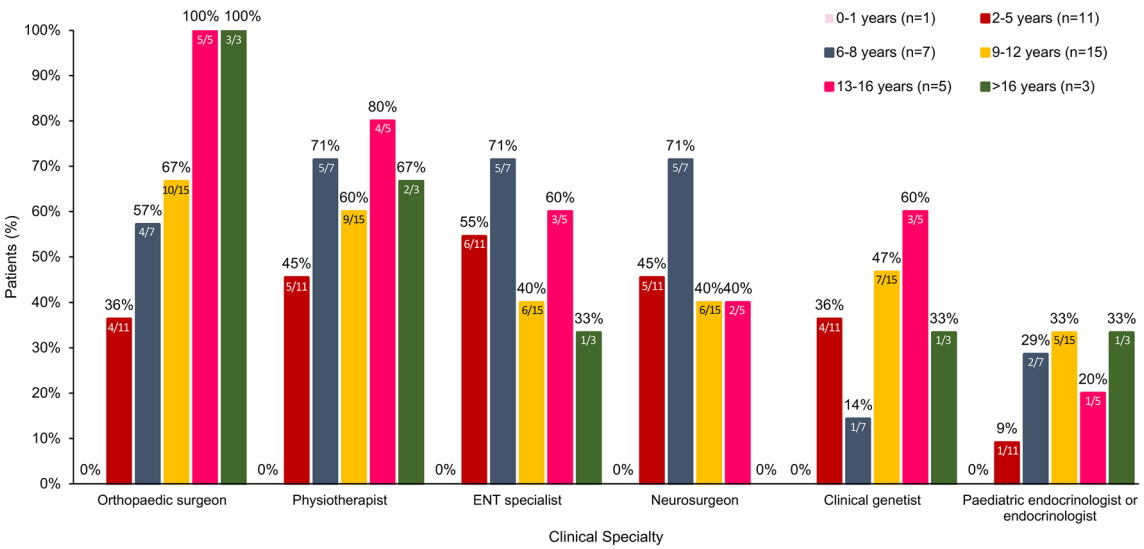

Fig. 2 Specialists consulted in the previous 2 years, by age group. *ENT* ear, nose, and throat

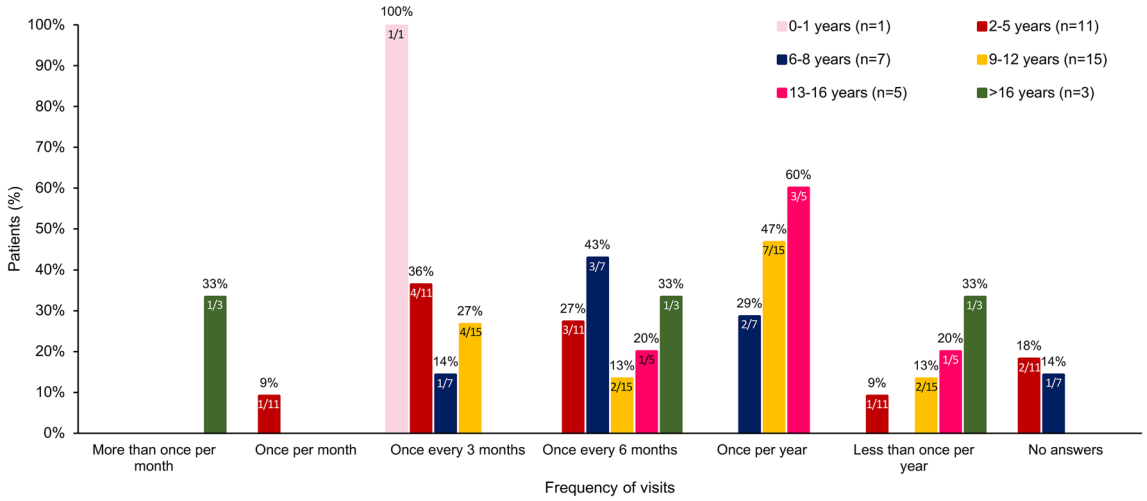

Fig. 3 Frequency of visits by age group

and between birth and 1 year of age in a further 11 cases (Table 2). This option was presented by an orthopaedic surgeon in 18/33 respondents (55%), with a further eight (24%) each presented lengthening surgery as an option by a paediatric endocrinologist/endocrinologist or a clinician expert in auxology.

In total, 11/37 respondents reported that their child had undergone lengthening surgery; four had the surgery at 8 years of age, two at 10 years of age, and one each at 6 and 14 years of age (three did not indicate age at surgery). Only eight respondents specified which limbs were operated on (lower limbs in all eight cases). The reasons for surgery were given by eight respondents and included to increase their child's autonomy ($n=3$), because it was requested by the child ($n=2$), a desire to increase their child's height ($n=2$), and to eliminate varus deformity ($n=2$). The reasons given for not undergoing surgery ($n=20$) included that the child was too young ($n=7$), the child was awaiting surgery ($n=6$), the parents were waiting to make a decision ($n=2$), and that the surgical procedure would have a great impact on the child's and their family's life ($n=2$). Lengthening surgery was performed at a reference centre in 41% (11/27) of cases and at other centres in the remaining 59% (16/27) of cases.

Improving the patient's journey

Respondents gave the following suggestions to improve the patient journey: (1) strengthening psychological support for families, (2) being managed by MDTs more assiduously, (3) reducing excessively long waiting times and hospitalisations, (4) increasing the efficiency of reference centres, (5) providing more information to families, especially at diagnosis; and (6) continuing patient follow-up after the age of 18 years.

Clinician survey

From the 27 hospital centres contacted, 25 clinicians completed 19 surveys (six were completed jointly by two clinicians). Paediatrics was the most common specialty participating in this survey (Online Resource 1; Supplementary Fig. S1). As some surveys were completed by more than one clinician, the sample sizes refer to the number of clinician surveys completed rather than the number of clinicians; however, for simplicity, the results are referred to as 'clinicians' instead of the more strictly correct 'clinician surveys'.

Diagnosis and referrals

The greatest proportion of individuals with achondroplasia currently managed by the clinicians in this survey were aged 6–8 years (103/493; 21%) or 9–12 years (128/493; 26%); only 3% (15/493) were infants (0–1 years; Table 2). Achondroplasia was suspected during the prenatal period (14/18; 78%) more often than during the postnatal period (4/18; 22%), but the diagnosis was confirmed more frequently in the postnatal than the prenatal period (13/18 [72%] vs. 5/18 [28%]). Clinicians usually confirmed the clinical diagnosis with molecular analysis (17/18; 94% of clinicians) of the *FGFR3* gene. Geneticists, neonatologists, and paediatricians most commonly made the diagnosis of achondroplasia (89%, 67%, 61% of 18 clinicians, respectively), and were the specialists who most frequently communicated the diagnosis to the parent/caregiver (83%, 44%, 67% of 18 clinicians, respectively) [Note: more than one choice of answer was allowed for these questions; therefore, the percentages did not add up to 100%]. Since most diagnoses were made at achondroplasia reference centres, the majority of clinicians

reported that diagnoses were not followed by referral to a reference centre (15/18; 83%).

At the clinicians' hospitals, there were 109 newly diagnosed individuals with achondroplasia treated within the last 2 years, of whom 23 were diagnosed after the age of 1 year and the remainder were diagnosed in the first year ($n=29$, aged 3–12 months; $n=30$, aged < 3 months; $n=14$, at birth); there were 13 prenatal diagnoses.

All clinicians reported that the parent/caregiver would be referred to a PAG, and that this referral was usually handled by the paediatrician (14/18; 78%).

Complications

The frequency of elective terminations of pregnancy because of an achondroplasia diagnosis in the 2 years prior to the survey was reported as 'never' by 9/17 (53%), 'sometimes' by 7/17 (41%), and 'often' by 1/17 (6%) clinicians.

The three most common clinician-reported complications seen in children with achondroplasia were hypotonia, foramen magnum stenosis, and lumbar kyphosis in infancy (Fig. 4a), varus/valgus knee, sleep apnoea, and lumbar kyphosis in children aged 2–4 years (Fig. 4b), varus/valgus knee, dental malocclusion, and obesity/overweight in children aged 5–10 years and 11–15 years (Fig. 4c and d), and varus/valgus knee, lumbar spinal stenosis, myelopathy/radiculopathy, and obesity/overweight in adolescents aged > 16 years (Fig. 4e).

Hospital and treatment team characteristics

Most of the hospitals included in this study were reference centres for achondroplasia (15/19; 79%); of the remaining hospitals, only one was not located in the same region as the closest reference centre.

The majority of clinicians (16/18; 89%) confirmed that their hospital used MDTs to manage individuals with achondroplasia. The co-ordinators of these MDTs were usually paediatricians (13/16; 81%) or geneticists (5/16; 31%). Other specialities occupying this role included endocrinologists,

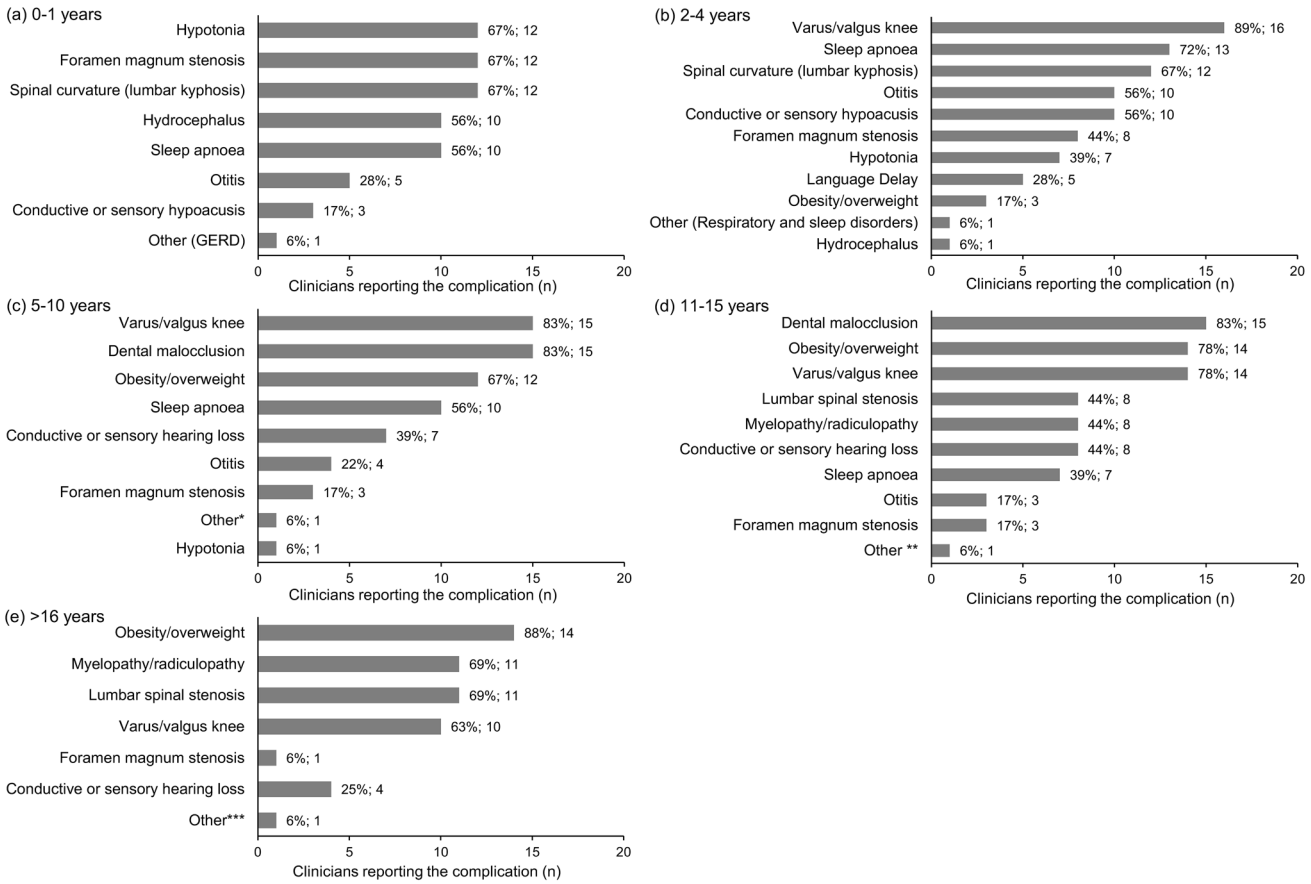

Fig. 4 Clinician-reported common complications in individuals with achondroplasia aged **a** 0–1 years, **b** 2–4 years, **c** 5–10 years, **d** 11–15 years, and **e** ≥16 years. Complications were not mutually exclusive; therefore, percentages do not add up to 100%. Eighteen clinician surveys were included in this analysis. *'Other' included lumbar lordosis, social problems, mobility problems, and respiratory disorders. **'Other' included pain, lumbar lordosis, social problems, quality of life problems, mobility problems, respiratory disorders, and lower limb pain and fatigue after prolonged effort. *GERD* gastroesophageal reflux disease

neonatologists, orthopaedic surgeons, and psychologists ($n = 1$ to 3). Medical specialists included within MDTs were mainly geneticists, endocrinologists, orthopaedic surgeons, and neurosurgeons (Online Resource 1; Supplementary Fig. S2).

Parent/caregiver counselling was most often the responsibility of geneticists (15/18; 83%) and paediatricians (9/18; 50%), although psychologists (5/18; 28%), neonatologists, and orthopaedic surgeons (1/18 each) could also be involved (categories of clinician were not mutually exclusive).

Services such as physiotherapy and psychological support for patients were provided in about two-thirds of hospitals according to the clinicians surveyed (11/19 [58%] and 12/19 [63%], respectively).

Patient management and follow-up

Individual visits to the hospital decreased in frequency with increasing age (Online Resource 1; Supplementary Table S2). Infants (aged 0–1 years) visited the hospital predominantly every 3 months (12/18 clinicians; 67%), preschoolers (aged 2–4 years) every 6 months (13/18; 72%), 5–10-year olds and 11–15-year olds once per year (9/17 [53%] and 7/16 [44%], respectively) or once every 6 months (8/17 [47%] and 7/16 [44%], respectively), and adolescents/adults aged > 16 years once a year (10/15; 67%). Only one hospital did not offer continuing patient support into late adolescence; nine hospitals followed individuals with achondroplasia up to the age of 16–18 years, and eight into adulthood (> 18 years).

The reasons most commonly cited by clinicians for individuals with achondroplasia being lost to follow-up were reaching the age of majority (10/18; 56% of clinicians) and undergoing limb lengthening surgery (6/18; 33%). Other reasons included difficulties for patients to get to the hospital (4/18; 22%), and 'other' (i.e. economic reasons, changing reference centre, and no need for the patient to visit the hospital) [Note: clinicians could cite more than one reason, i.e. reasons were not mutually exclusive].

Lengthening surgery

In response to an open-ended question, clinicians' reasons for asking parents/caregivers to consider limb lengthening surgery were to improve the child's quality of life, increase their autonomy and self-acceptance, improve trunk-limb disproportions and short stature, improve walking, and inform families of all available treatment options.

Nine of the 17 clinicians viewed surgery on both the upper and lower limbs favourably; four were in favour of surgery only on the lower limbs and none only on the upper limbs; four clinicians viewed surgery unfavourably. The clinicians' views on the age at which individuals should undergo limb lengthening surgery varied among the 17 respondents: three each suggested 7–8 years of age, 11–13 years, 15–16 years, and 'variable', and two suggested 9–10 years of age (Table 2). Two clinicians suggested ≤ 6 years and 8–9 years, respectively.

Accessibility to surgery was determined firstly by asking clinicians where surgery was conducted relative to their hospital. Six of 18 (33%) clinicians said their hospital was the location for the surgery, 7/18 (39%) reported that a centre in the same region of Italy did the surgeries, and 5/18 (28%) reported that surgery would have to be conducted at a hospital in another region of Italy. Access to surgery was also determined by asking whether clinicians perceived the parent/caregiver's level of education to be an influencing factor in the family's decision for/against limb lengthening surgery, to which four clinicians agreed, thirteen partially agreed, and only one said it was not an influencing factor. Clinicians were also asked if they thought family income level was an influencing factor in the decision to undergo surgery, to which 12/18 (67%) said 'partially', one said 'yes', and five said 'no'.

Discussion

Our survey of 42 parents/caregivers of children with achondroplasia and of 25 clinicians treating children with achondroplasia revealed that the real-world management of individuals with achondroplasia in Italy is generally consistent with the 2020 recommendations of the European Achondroplasia Forum [6]. Our findings were also generally consistent with the recommendations of the International Achondroplasia Consensus Statement Group [8].

While our clinician survey did not attempt to formally estimate the incidence and prevalence of paediatric achondroplasia, we asked clinicians to report the number of new diagnoses of achondroplasia at their hospital. A total of 109 new diagnoses were reported, which in our view seems high, given that the EUROCAT network reported an estimated achondroplasia prevalence of 5.70 per 100,000 births between 1991 and 2015 in Emilia-Romagna, Italy [1]. This high rate of new diagnoses could be attributable to parents taking their child to a different reference centre to get a second opinion on a diagnosis, and thus, the same individual may have been counted twice in our clinician survey.

Early diagnosis is important to allow access to effective counselling [6], as well as early treatment intervention [8]. According to the parents/caregivers, almost two-thirds of individuals received a prenatal diagnosis, and all but one had been diagnosed by 6 months of age. In contrast, only one-third of clinicians reported confirming a diagnosis in the prenatal period. The results of the parent/caregiver survey are consistent with the literature, which generally shows that

many cases of achondroplasia are diagnosed in early infancy [4]; however, it is lower than the overall prenatal diagnosis rate in Europe (65% of patients) [9]. The higher prenatal diagnosis rate in Europe may be influenced by data from France and countries other than Italy, as clinicians in these countries tend to perform diagnostic computed tomography (CT) scans during pregnancy if achondroplasia is suspected [10–12], whereas Italian clinicians do not carry out CT scans during pregnancy. One possible reason for this slight discrepancy between parents/caregivers and clinicians in the timing of achondroplasia diagnoses may be that parents think that the *first* time they were told about the possibility of their child having achondroplasia was a formal diagnosis; indeed the high proportion of parents/caregivers reporting that the diagnosis was made by a healthcare professional during a prenatal ultrasound examination seems to support this possibility. Nevertheless, it is reassuring that the clinicians surveyed confirmed a diagnosis by genetic analysis in all but one case, in concordance with recommendations [8].

According to the parents/caregivers, around 40% of them were required to travel a considerable distance (> 200 km) to access routine care for their child, which may represent a barrier to adequate care, particularly when close monitoring of children with achondroplasia is recommended [8]. While our survey was not able to directly ascertain whether the distance required to travel was a reason for the low frequency of visits for some individuals, it is plausible, given that previous research has highlighted distance to treatment centres as a barrier to accessing medical care [13]. All parents/caregivers reported that their children had reference centre visits once every 3 months in their first year of life, and most (12/18), but not all, clinicians reported the same frequency for this age group. In our view, this frequency is, on average, acceptable for close monitoring of children with achondroplasia.

We found that approximately half of the parents/caregivers changed their child's reference centre, of whom half again did so when their child was aged 2–5 years, with the principal reason being problems or dissatisfaction with the centre. While our survey did not capture any further information regarding specific problems or their source of dissatisfaction, the possible reasons for this include a lack of effective treatment for achondroplasia [7, 14], difficulties in communication, disagreement regarding clinical decisions, or attrition of healthcare professionals experienced in the disease. In our experience, other potential reasons why an individual with achondroplasia may change reference centre over the course of follow-up include reaching the age of majority, family and job commitments, fatigue, or because individuals with achondroplasia feel well and do not think they need a medical appointment at the centre. Some results from our parent/caregiver survey support these possibilities, as illustrated by their responses to being asked how their child's patient journey with achondroplasia could be improved: 'continuing follow-up after the age of 18 years', 'reducing excessively long waiting times and hospitalisation', 'higher efficiency of reference centres', and 'being followed by multidisciplinary teams more assiduously'.

An individual with achondroplasia should be managed by an experienced MDT throughout their life [6, 8]. Our survey results, although largely from children with achondroplasia, confirm that MDTs are usually used to manage achondroplasia in Italy. The composition of the MDT was variable given the diverse range of complications experienced by paediatric/adolescent individuals with achondroplasia.

The importance of supporting the individuals with achondroplasia and their family's mental health and providing education and counselling is recognised in the European and international guidelines [6, 8]. Our results show that psychologists were less frequently involved in parent/caregiver counselling than geneticists and paediatricians, even though two-thirds of the hospitals were reported by clinicians as being able to provide psychological support services. In our experience, psychological support is not usually provided at the reference centre, and psychologists are often not employed at smaller hospitals where individuals with achondroplasia are followed. Parents identified better psychological support for families and better provision of information to families as ways to improve the patient journey.

Our finding that the majority of clinicians reported individuals with achondroplasia aged over > 16 years having a visit frequency of once a year is surprisingly high; in our clinical experience, many of these individuals do not show up for follow-up appointments by this age, in part because they will have previously been hospitalised many times and no longer wish to interact with medical services. Over one-half of parents/caregivers in our survey reported that they may lose contact with the reference centre or their specialist due to 'no motivation', possibly reflecting a sense of fatigue with frequent hospital visits, medical assessments, and procedures. In general, follow-up of adults with achondroplasia can be less frequent (e.g. once every 2 years) than of children. And in our experience, the patient's general practitioner would usually provide routine follow-up care during adulthood. Our results indirectly support this: specialist services for adults were not as common as for children since only 8 of the 18 clinicians surveyed reported that their hospital continued care into adulthood (> 18 years of age). More than one-half of the clinicians reported that adolescents were likely to be lost to follow-up from the reference centre when they reach the age of majority. Reassuringly, from the parent/caregiver point of view, our results suggest that adolescents aged > 16 years experienced some continuity of care (frequency of visits was evenly split between less than once a year, once every 6 months, and once a month).

Overall, our survey results show that visit frequency is not standardised within or across age groups, or indeed across institutions, and that this represents an important unmet need in the management of individuals with achondroplasia across Italy. Similarly, we also found that each reference centre conducts lengthening surgery at different ages. This is not surprising, given the lack of evidence-based consensus on this issue [15].

Limitations

Our study has some limitations. We did not include any formal rating scales or quality of life questionnaires in our surveys and all data were parent/caregiver- or clinician-reported and are subject to recall bias. Furthermore, sample bias may exist as not all reference centres in Italy were approached to be included in the survey. While our surveys showed that the age of 2–5 years was the age at which there was the greatest impact on the child and their family due to the complications/comorbidities of achondroplasia (excluding lengthening surgery), parents could only comment on their experiences up to the age of their own child at the time they completed the survey. Further, a substantial proportion of patients had not yet reached adolescence; thus, the age period of greatest impact could be different if parents were surveyed again in 10 years' time, for example. As a result, our data are limited to the impressions of parents and caregivers, and we did not collect data from the children themselves, which may have been possible at least for those in older age groups. Lastly, the small sample size limits the generalisability of the results, but does provide a useful starting point in terms of the current state of the patient journey for individuals with achondroplasia in Italy.

Conclusions

Our survey of those involved in the care of children with achondroplasia provides important insight into the real-world management of this disorder in Italy and has the potential to help improve the management and outcomes of this rare genetic disorder.

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Author contributions MFB, MS, RR, and MM contributed to conceptualization, methodology, and writing—original draft; MFB, SM, FA, SB, RR, GS, AS, MA, FV, GZ, and MM were involved in writing—review and editing. All the authors discussed their clinical experiences and have read and approved the final version for submission.

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Data availability The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest MFB is/has been a consultant for BioMarin and Sanofi. SM is/has been a consultant for BioMarin, Kyowa Kirin, Alexion, and Ascendis. FA has received research support from Merck Serono and Sandoz and is/has been a consultant for Kyowa Kirin, BioMarin, Novo Nordisk, and Abiogen Pharma. SB is/has been consultant for BioMarin, Sanofi, and Citieffe. GS is/has been a consultant for BioMarin and Lilly. AS is/has been a consultant for BioMarin (scientific boards, observational trial) and Pfizer (ongoing observational trial). MS is/has been consultant for BioMarin. GZ is receiving/has received research support from BioMarin, Pfizer, MSD, ArQule, Theracon, LabCorp, and Incyte. MM has received research support from Pfizer and Merck Serono and is/has been a consultant for Pfizer, Novo Nordisk, Merck Serono, Ferring, BioMarin, and Ascendis. RR and FV declare that they have no competing interests.

Ethical approval The survey complied with Italian data protection laws. As this was not an investigation of clinical outcomes with any particular intervention, neither ethics committee approval nor clinical trial registration was required. No parents and caregivers of patients with achondroplasia or associated clinicians received any compensation for participation in the survey.

Consent to participate All participants gave their informed consent for the collection and use of medical and health information in an aggregated and anonymised manner for the purposes of this research only.

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