Physical Activity, Exercise, and Sports in Individuals with Skeletal Dysplasia: What Is Known about Their Benefits?

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Abstract: There is a lack of knowledge about the practice of physical activity, exercise, and sports in people with skeletal dysplasia (SD). This study aimed to characterize the physical fitness of people with SD; investigate the benefits of physical activity, exercise, or sports programs for people with SD; identify the adapted physical activities that can be prescribed to individuals with SD; and identify the most common and effective structural characteristics and guidelines for the evaluation of individuals with SD and corresponding activity prescriptions. Electronic searches were carried out in the PubMed, Scopus, SPORTDiscus, Psycinfo, and Web of Science databases in October 2021 and March 2022 and included papers published until 3 March 2022. The search strategy terms used were “dwarfism”, “dwarf”, “skeletal dysplasia”, “achondroplasia”, “pseudoachondroplasia”, “hypochondroplasia”, “campomelic dysplasia”, “hair cartilage hypoplasia”, “x-linked hypophosphatemia”, “metaphyseal chondrodysplasia schmid type”, “multiple epiphyseal dysplasia”, “three M syndrome”, “3-M syndrome”, “hypophosphatasia”, “fibrodysplasia ossificans progressive”, “type II collagen disorders”, “type II collagenopathies”, “type II collagenopathy”, “physical activity”, “exercise”, “sport”, “training”, and “physical fitness”, with the Boolean operators “AND” or “OR”. After reading the full texts of the studies, and according to previously defined eligibility criteria, fifteen studies met the inclusion criteria; however, there was not a single intervention study with physical exercise. Several cross-sectional, review, or qualitative studies presented a set of essential aspects that future intervention studies can consider when evaluating, prescribing, and implementing physical exercise programs, as they allowed the physical characterization of the SD population. This study demonstrated an apparent scarcity in the literature of experimental studies with physical exercise implementation in the SD population.

Keywords: adapted physical activity; physical fitness; physical exercise program; skeletal dysplasia; achondroplasia
1. Introduction

Bone ossification, or osteogenesis, is the process of bone formation, which develops from a template, which is mostly cartilage. Osteogenesis can be intramembranous or endochondral, and in this last type, several transcription factors are involved [1]. Skeletal dysplasia (SD) occurs due to genetic mutations. It is characterized by a general structural abnormality in the growth and shape of bone, cartilage, and dentin, namely, in the genes that encode proteins [2]. Some researchers claim that SD occurs due to mutations in the FGFR1, FGFR2, and FGFR3 genes [3–6]. There are currently 461 SDs, nonlethal and lethal, divided into 42 groups according to 4 criteria: phenotypic (physical), radiological, biochemical, and genetic. Although considered rare, they have a prevalence of 1 case in every 5000 births. The most common skeletal dysplasia is achondroplasia [6–8], with 3.7 cases for every 100,000 births [9], and the most common characteristics present in individuals with achondroplasia are short stature combined with a trunk length almost identical to an individual without this condition and shortening of the limbs [10,11].

In addition to several and often chronic medical complications, the prevalence of pain is high [12–15] and increases with age [12] across all SDs. Most of the pain felt, associated with physiological issues, can compromise participation in physical activity, which negatively influences physical fitness [16,17] and, in the case of achondroplasia, increases the occurrence of obesity [18] being associated with increased mortality rates from heart disease [19–22]. Across the majority of SDs, the factors presented above result in health problems, limitations in physical functioning and activities of daily living, and a lower quality of life for these individuals compared with the general population [13,23–26], which, in turn, affects mental health [23].

In the general population, physical activity and physical exercise are affordable and inexpensive options to promote physical fitness, reduce the risk of metabolic and cardiovascular diseases, and promote mental health and quality of life [27–29]. However, there is a lack of knowledge about adapted physical activity, exercise, or sports in people with SD, which reinforces the need to verify whether regular practice leads to the beneficial effects observed in the general population beyond the occurrence of medical complications [30]. Likewise, there is the need to verify how these activities are adapted, modified, and created (taking into account the concept of adapted physical activity) to meet the special needs of people with functional diversity, as is the case for individuals with SD. It is essential to carry out future studies with adequate prescriptions and interventions toward a positive and rewarding experience [30]. Therefore, the objectives of this study were to characterize the physical fitness of individuals with SD; assess the benefits of adapted physical activity, exercise, or sports in individuals with SD; identify the physical activities that can be prescribed to individuals with SD; and identify the most common and effective guidelines for prescribing adapted physical activity, exercise, or sports to individuals with SD.

2. Materials and Methods

This review was carried out in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) protocol [31] and the methods suggested by Bento [32]. The protocol was registered in PROSPERO, under the number CRD42021286409. The PICOS strategy [33,34] was used to obtain a final sample of studies that included: (i) “P” (patients) corresponding to participants with any type of skeletal dysplasia, of any age, gender, ethnicity, or race; (ii) “I” (intervention) corresponding to the practice of adapted physical activity, physical exercise program, or sports, implemented in the population mentioned above, regardless of the duration of the intervention; (iii) “C” (comparison) corresponding to comparisons before and after the intervention or between the control group and the intervention group; (iv) “O” (outcome) corresponding to the effects of the practice of adapted physical activity, physical exercise, or sports; (v) “S” (study design) corresponding to any type of study (intervention studies, randomized controlled trials (RCTs) or not RCTs, pilot studies, cross-sectional studies, or reviews). A preliminary
analysis of several studies related to the main purpose of this study was conducted to identify the most appropriate databases and keywords prior to starting.

2.1. Information Sources and Search Strategy

This study was carried out during October 2021 and March 2022, in English, by searching the databases PubMed, Web of Science, Scopus, Psycinfo, and SPORTDiscus, considering the maximum period of retrieval allowed by the databases. The descriptors used were “dwarfism”, “dwarf”, “skeletal dysplasia”, “achondroplasia”, “pseudoachondroplasia”, “hypochondroplasia”, “campomelic dysplasia”, “hair cartilage hypoplasia”, “x-linked hypophosphatemia”, “metaphyseal chondrodysplasia Schmid type”, “multiple epiphyseal dysplasia”, “three M syndrome”, “3-M syndrome”, “hypophosphatasia”, “fibrodysplasia ossificans progressive”, “type II collagen disorders”, “type II collagenopathies”, “type II collagenopathy”, “physical activity”, “exercise”, “sport”, “training”, and “physical fitness”, with the Boolean operators “AND” or “OR”, as shown in Table 1. The search was updated until 2 March.

**Table 1. Search Strategy.**

| Search Strategy | Use of descriptors |
|-----------------|--------------------|
| (“dwarfism” OR “dwarf” OR “skeletal dysplasia” OR “rare bone disease” OR “short stature” OR “achondroplasia” OR “pseudoachondroplasia” OR “hypochondroplasia” OR “campomelic dysplasia” OR “hair cartilage hypoplasia” OR “x-linked hypophosphatemia” OR “metaphyseal chondrodysplasia Schmid type” OR “multiple epiphyseal dysplasia” OR “three M syndrome” OR “3-M syndrome” OR “hypophosphatasia” OR “fibrodysplasia ossificans progressive” OR “type II collagen disorders” OR “type II collagenopathies” OR “type II collagenopathy”) AND (“physical activity” OR “exercise” OR “sport” OR “training” OR “physical fitness”) |

2.2. Eligibility Criteria

To be included in this review, studies had to meet the following criteria: (i) intervention studies (RCTs or not RCTs) or pilot studies; (ii) population with SD; (iii) no restrictions on age, race, ethnicity, sex, or gender; (iv) studies with any number of participants. The primary exclusion criteria used in the study were the following: (i) comments or abstracts published in congress or conference proceedings; (ii) articles that are not published in English; (iii) studies that do not describe the intervention protocol.

2.3. Selection and Data Collection Process

Two researchers carried out the research independently and downloaded information to the ENDNOTE X7 software (Clarivate, London, UK). Duplicate articles were eliminated, and all the articles that did not meet the inclusion criteria were removed. The studies selected in the previous phase were thoroughly reviewed by two independent reviewers (M. J. and R. A.) according to the specific eligibility criteria.

3. Results

By searching the various databases, 1785 studies were identified. In the first phase, after eliminating duplicate articles and on the basis of the titles and abstracts, a sample of 24 studies with relevant potential for the study were identified. After reading the full texts of the studies, and according to the eligibility criteria previously defined, the study sample was constituted by fifteen studies, as shown in Figure 1.

Brooks et al. [35] and Carneiro [36] did not analyze physical exercise. The studies of Bal et al. [37], Saffarian et al. [38], Moura et al. [39], and Dummer et al. [40] did not correspond to an intervention study with physical exercise and/or did not assess physical fitness. Several studies were excluded for other reasons, such as: for being grey literature, communications at conferences, book chapters, articles not online/available, and so on [41–45].
Although we considered the choice of databases and terms to be comprehensive, no study was extracted for analysis, most likely because these are rare conditions and the limited research available has a medical care focus. Although we were not able to answer a part of our aim, several studies reported important information regarding physical fitness, allowing us to answer a part of our research question (Table 2).

Figure 1. PRISMA flowchart of this review.
Table 2. Included studies for a qualitative discussion.

| Author            | Aims                                                                                                                                                                                                 | Participants                                                     | Type of Study                  | Data Collection Methodology                                                                 | Main Results                                                                                                                                                                                                 |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|--------------------------------|-------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Brooks et al. [35] | (1) Evaluate the prevalence of anterior cruciate ligament and posterior cruciate ligament injuries, (2) compare with the general population, (3) determine how many patients with anterior cruciate ligament or posterior cruciate ligament injuries underwent operation, (4) determine the levels of patient activity. | \( n = 430; 35 \pm 18 \text{ years}; \) and patients with achondroplasia. | Cross-sectional.              | Phone call—questions.                                                                     | Total of 29% reported low physical activity, 51% moderate physical activity, and 17% high physical activity.                                                                                               |
| Carneiro et al. [36] | Use the 6 min walk test to follow and assess mobility and quality of life in a young woman with achondroplasia and morbid obesity.                                                                     | \( n = 1; 28 \text{ years}; \) and achondroplasic dwarfism (achondroplasia). | Case report.                  | A 6 min walk test.                                                                        | The 6 min walk test may be a good method for assessing cardiorespiratory capacity, mobility, and quality of life.                                                                                               |
| Cumming et al. [46] | Follow two brothers with accentuated dwarfism (11 and 19 years old).                                                                                                                                   | \( n = 2; 11 \text{ and 19 years}; \) and dwarfism.              | Case reports.                 | Electromyography.                                                                         | No changes in neuromuscular capacity.                                                                                                                                                                         |
| De Vries et al. [47] | Cross-sectional study comparing cardiorespiratory fitness (peak VO2), six-minute walk test, muscle strength, balance, and self-reported physical activity level in Norwegian adults with achondroplasia with the reference values for individuals of average height. | \( n = 43; 37.5 \pm 16.8; \) and achondroplasia.               | Cross-sectional.              | Spirometry; VO2 peak; 6 min walk test; 30 s sit-to-stand; Balance Error Scoring System, International Physical Activity Questionnaire (IPAQ). | Men performed better at VO2 peak; sufficient physical activity; 6 min walk test and 30 s sit-to-stand were feasible; and correlation between the 6 min walk test and 30 s sit-to-stand (men: \( r = 0.63, p = 0.007; \) women: \( r = 0.71, p < 0.001 \)).  |
| Hanson et al. [48] | Investigate whether massage increases the distance she can walk before the onset of muscle fatigue.                                                                                                    | \( n = 1; 63 \text{ years}; \) and hypochondroplasia.            | Case report.                  | Walk.                                                                                     | Muscle fatigue at an early stage.                                                                                                                                                                          |
| Hoover-Fong et al. [49] | Through health screening research, blood pressure was measured in short-stature adults.                                                                                                               | \( n = 403; 38.6 \pm 14.1 \text{ years}; \) and skeletal dysplasia. | Cross-sectional.              | Blood pressure (systolic and diastolic)—blood pressure equipment (e.g., Dinamap, Tampa, FL, USA).      | Prevalence of hypertension.                                                                                                                                                                               |
| Hoover-Fong et al. [50] | Lifetime impact of achondroplasia.                                                                                                                                                                     | -                                                               | Review.                        | -                                                                                         | Lower quality of life in all domains, including physical; restriction on basic activities of daily living (bathing/dressing themselves, toileting independently, etc.); higher metabolic cost when walking as stride length is shorter; delays in gross motor skill development (adolescents and children); and high prevalence of sedentary behaviour, obesity, and pain. |

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Table 2. Cont.

| Author            | Aims                                                                 | Participants                                    | Type of Study         | Data Collection Methodology                                                                 | Main Results                                                                 |
|-------------------|----------------------------------------------------------------------|------------------------------------------------|-----------------------|---------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Hyvönen et al. [14] | Information about functioning and equality in individuals with skeletal dysplasia compared with matched controls without skeletal dysplasia. | $n = 80$; 43 ± 14.7 years; and skeletal dysplasia. | Cross-sectional. | Questionnaire—formed by operationalizing International Classification of Functioning, Disability, and Health. | Restriction of function, which affected activities of daily living. |
| Low et al. [51]    | This paper detailed the structural, intellectual, motor, orthopedic, and medical characteristics of several types of dysplasia. | -                                              | Review.               | -                                                                                           | Implications and modifications for participation of individuals with SD in physical activity. |
| Madsen et al. [52] | Describe the anthropometrics, diet, and resting energy expenditure in adults with achondroplasia. | $n = 40$; 40 ± 15 years; and skeletal dysplasia. | Cross-sectional. | -                                                                                           | High frequency of central obesity and unhealthy dietary habits. |
| Orlando et al. [53] | Describe muscle strength and power, functional capacity, mobility and physical activity level in adults with X-linked hypophosphatemia. | $n = 26$; 44 ± 16.1 years; and X-linked hypophosphatemia. | Prospective cohort study. | -                                                                                           | Deficit in lower limb muscle power, reduced functional capacity, and high incidence of impaired mobility and inactivity. |
| Pfeiffer et al. [54] | Analysis of the impact of achondroplasia on children’s quality of life. | $n = 36$ parents.                             | Qualitative research study (interviews). | Qualitative analysis of concept elicitation interviews informed the development of a preliminary theoretical model of the symptoms and/or complications. | Pain and low stamina/tiring easily. |
| Pfeiffer et al. [55] | Explore how having achondroplasia affects older children and adolescents’ day-to-day functioning and well-being. | $n = 32$; 9 to 18 years; and achondroplasia. | Individual/focus group interviews. | Adapted grounded theory approach informed the qualitative analysis of interview data. | Low stamina/tiring easily; back pain; and difficulty walking long distances. |
| Steele et al. [56]  | Impact of musculoskeletal manifestations on physical function in adults with X-linked hypophosphatemia. | $n = 9$; 53.6 ± 5.3 years; and X-linked hypophosphatemia. | Cross-sectional. | Occupational therapy assessment (passive range of motion, Berg Balance Score, manual muscle testing, Lower Extremity Functional Scale, and kinematic measurements) and a semi-structured interview by social worker. | Limitations throughout the gait cycle. |
| Author              | Aims                                                                 | Participants                      | Type of Study | Data Collection Methodology                                                                                                                                                                                                 | Main Results                                                                                       |
|---------------------|----------------------------------------------------------------------|-----------------------------------|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Takken et al. [17]  | Study in children with achondroplasia the response to exercise, muscle strength, exercise capacity, anthropometric factors, and physical activity. | \( n = 17; \) 11.8 ± 3.3 years; and achondroplasia. | Cross-sectional | Standing height, sitting height, arm span, and head circumference were measured; weight—electronic scale; BMI—kg \times m^{-2}; body composition—7 skin folds; leg volume—anthropometric method (Janes and Pearson, 1969); fat-free mass—bioelectric measurement system (Xitron Technologies Inc., San Diego, CA, USA); maximal exercise capacity—treadmill exercise testing; breath-by-breath minute ventilation, oxygen consumption, carbon dioxide production, and respiratory exchange ratio—metabolic stress test software; strength muscles in lower and upper extremities—hand-help dynameter; energy expenditure—3 day activity record; and perceived functional ability—Activity Scale for Kids. | Cardiopulmonary exercise capacity and muscle strength were reduced. |

\( n \)—participants.
Although our research resulted in 1785 studies, none had an experimental methodology. Seven were cross-sectional studies [14,17,35,47,49,52,56], three were case reports [36,46,48], two were review studies [50,51], and two were qualitative studies [54,55].

4. Discussion

Adapted sports are a source of multiple benefits, mainly for emotional and social aspects, as they are inclusive and contribute to the overall development of a person with a disability [57].

This review was dual-aimed: (1) analyze and characterize the physical fitness of individuals with SD, through studies that performed physical assessments; (2) analyze the effects of adapted physical activity, exercise, or sports in individuals with SD on the basis of the characterization of implemented programs and establish effective guidelines for prescribing adapted physical activity, namely, duration, weekly frequency, appropriate assessment methods, and types of exercise.

Although no experimental studies with physical exercise were extracted for analysis, which compromised a part of our aim, several studies presented a set of essential aspects, in physical terms, for future intervention studies to consider when evaluating, prescribing, and implementing their interventions, as presented in Table 2. The information that we present and discuss throughout the remainder of this document should be considered important tools for future intervention studies.

In the specific case of achondroplasia, two theoretical models were described that contained potentials and limitations for individuals carrying out different experiences in their daily lives, which should be known to professionals working with this population, namely, physical exercise professionals [54,55].

Hyvänen et al. [14], through a questionnaire based on the International Classification of Functioning Disability and Health (ICF) [58], concluded that the sample questioned had disturbances in body functions and in the success in carrying out activities (difficulties at the level of body function are related exercise tolerance, mobility, and joint stability). These conclusions are in line with the studies of Alade et al. [12], Krüger et al. [26], Hoover-Fong et al. [50], Orlando et al. [53], and Pfeiffer et al. [54], who affirmed the existence of functional problems in this population. Extending to the SD population, in addition to these difficulties, they face barriers in their environmental and social participation (acquisition of materials; use of services, such as ATMs, disabled-persons bathrooms, etc.; and stigmatized attitudes from society) [14,59].

In the scarce literature found, most referred to achondroplasia. In addition to creating guidelines for the assessment and prescription of adapted physical activity and exercise, there is also a need to characterize and understand the specific needs and physical impairments in other types of skeletal dysplasia.

4.1. Physical Activity

There is limited research on participation in physical activities, and on the benefits or risks and harms of its practice by individuals with SD. Regarding achondroplasia, in the study of Brooks et al. [35], in which 148 people were questioned by phone calls, 43 (29%) reported low levels of physical activity, 75 (51%) reported moderate physical activity, and 26 (17%) reported a high prevalence of physical activity. On the other hand, Takken et al. [17], Hoover-Fong et al. [50], and Orlando et al. [53] noted that in addition to poor physical fitness, people with achondroplasia also showed low participation in physical activities and reduced energy expenditure compared with normal individuals. At the same time, when engaging in physical activities, the cost of carrying out such actions is higher, as the stride length is shorter [50]. In the study by Vries et al. [47], people with achondroplasia had low levels of physical fitness compared with reference values from normal individuals. Yet, beyond the anatomic differences, there are disabling barriers that limit the ability to engage in physical activity, and a deep assessment of environmental limitations should also be conducted toward improving the access and practice of adapted physical activity.
4.2. Anthropometry

Regarding anthropometry, individuals with SD may have a higher body mass index [12,60] and percentage of body fat [52] and lower values of bone mineral content, bone mineral density, and fat-free mass compared with reference values from similar-aged individuals [61–64]. Individuals with SD, namely, achondroplasia and hypochondroplasia, demonstrate reduced bone mineral density values associated with osteoporosis and osteopenia [62]. These values are positively correlated with body mass index [62]. This fact reveals the special care that must be taken when evaluating, prescribing, and conducting physical activities. Measuring the degree of obesity using the body mass index equation may not be the most appropriate anthropometric measure, given its relationship with height [18,65,66]. However, several efforts have been made to define reference values for our focus population [67,68]. In addition, there is evidence of its relationship with waist circumference [52]. Waist circumference measurement may be a good method to estimate obesity and the risk of the onset of metabolic or cardiovascular diseases [69,70]. However, there are no common reference values [71]. These levels of obesity may be associated with sleep apnea in children with achondroplasia [72,73].

4.3. Hemodynamic Profile

The literature is scarce in studies that assessed hemodynamic variables. As Hoover-Fong et al. stated [49], for blood pressure assessment, it is essential to consider the choice of blood pressure equipment with an adjustable sleeve up to the length of the upper limbs, without covering the shoulder and elbow. In some cases, this measurement is performed on the forearm due to the constraints described before. Hypertension was previously observed in people with SD, compared with age-adjusted data, which made them susceptible to the onset of diseases. These values correlate with sex, age, and body mass index [49].

4.4. Cardiorespiratory Capacity

Pulmonary capacity and exercise capacity are reduced in people with SD compared with healthy people [17,74,75], as is maximum oxygen volume (VO$_2$max) [47] compared with reference values [76], so they fatigue at an earlier stage [48,54,55]. People with achondroplasia must ventilate more frequently to absorb 1 L of oxygen, compared with reference values from individuals of similar ages and sex [17], which may be explained by a reduction in vital capacity [74,75]. Heart rate is high for the amount of oxygen absorbed [74,75], implying a reduced stroke volume because of a smaller chest volume. VO$_2$max is also lower as body weight increases [47]. Regarding gender, men with dysplasia have a higher VO$_2$max than women [47].

Carneiro et al. [36] and Vries et al. [47] noted that for achondroplasia, the 6 min walk test may be an effective, adaptable, and viable method to assess not only cardiorespiratory capacity but also mobility and quality of life in individuals with SD, while using the Borg scale to measure intensity [77]. In this population, the 6 min walk test values increased with good muscle strength [47].

4.5. Neuromuscular Capacity

Cumming et al. [46] found that people with achondroplasia do not show muscle changes and maintain intact neuromuscular function. In turn, Takken et al. [17] noted that the muscle tone of this population is not ideal due to the short length of their bones, causing hypotonia [78]. Piróg and Briggs [79] noted that the muscle complications observed in SD are usually mild, but they can occur due to a muscle anomaly or changes in the musculoskeletal system. However, in the case of achondroplasia, neuromuscular capacity is reduced compared with ordinary healthy people [17,53,80,81], which may be explained by the low percentage/amount of muscle mass achieved. This leads to muscle fatigue at an early stage [48]. While the mean muscle strength for men with achondroplasia was reduced compared with reference values, women with achondroplasia had results similar to the reference values, both for absolute values and ranges [47,82]. This population also presents
a reduction in muscle volume and a high prevalence of fat infiltration [80]. Similar to the 6 min walk test, the 30s sit-to-stand test is an easy-to-perform option for measuring muscle strength [47], and the chair used to perform the 30s sit-to-stand test must be proportional to the height of the participants.

4.6. Balance Capacity

A test that is apparently difficult to perform, not recommended, and not feasible for assessing balance in people with achondroplasia is the Balance Error Scoring System [83]. Although the literature is not abundant in studies that assessed balance in a population with dysplasia, Vries et al. [47] and Sims et al. [80] stated that there might be a decrease in balance with achondroplasia.

4.7. Neurological Symptoms—Neuropathies and Spinal Stenosis

Symptomatic spinal stenosis has a very high prevalence in adults with achondroplasia (kyphosis, lordosis, scoliosis, and spine deformity) [81,84,85] and increases with age [60,81]. These symptoms are associated with reduced walking capacity, activity limitations, and pain [81,86]. Early intervention and careful follow-up should be undertaken after the onset of neuropathy or spinal stenosis symptoms [85].

4.8. Pain

Many studies have described the prevalence of pain in people with SD [12–15,54,55,87], often associated with neuropathies or spinal stenosis. Particular attention should be given to this aspect, acting as a facilitator in the rehabilitation process and not harming the current situation. On the other hand, this prevalence of pain impacts daily functioning and the ability to work [88]. In this sense, physical exercise can be an excellent co-adjutant to attenuate/decrease pain and diminish its intensity, especially in the joints [89,90].

4.9. Hearing, Voice, and Vision

A clinical study by Tunkel et al. [91] found that 16 of 29 participants (55%) failed a hearing screening in one or both ears, but few reported the use of hearing aids. Although less frequent, individuals with SD may present voice and vision impairment [85]. Ear infections and fluid in the ear are frequent [54]. This highlights the importance of the physical exercise professional when evaluating, prescribing, and implementing physical exercise to use strategies with demonstrations or personalized feedback and taking special care with instructions [29].

4.10. Evaluation and Prescription of Physical Exercise

A gap in the literature is the lack of validated physical fitness assessments and instruments for SD [47] and reference values for different types of SD. For instance, for evaluating and prescribing cardiorespiratory exercise, consideration should be given to the short stature and length of the lower limbs. As anthropometric features lead to shorter steps, the process used for assessment must be a function of time and not distance [51]. Changing the dimensions of the area where physical activities occur (i.e., game fields) is also essential. Tasks that require manipulation also need to be adapted as the focus population has small hands, short fingers, and other anomalies (e.g., use of smaller balls or use of smaller handles) [51,92].

Before starting any sport, a neurological assessment is suggested to evaluate the possible deformation of the spine. It should be carried out according to the degrees of kyphosis, lordosis, and scoliosis, which have been presented in individuals with SD several times [81,84]. Exercise that recruits the posterior plane can benefit posture [93]. At the same time, because hypotonia and lordosis are aggravated by a lack of tonus in the abdominal cavity, exercises that reinforce the abdominal wall are critical. It is also essential to pay special attention to spinal instability and be careful when prescribing exercises that involve loads and impact. When possible, we should avoid prescribing activities such
as jumping, diving, heading a ball, or contact sports [51]. In achondroplasia, due to the prevalence of ligament laxity, it is vital to consider the range and speed of movement to avoid injuries [16,94].

A functional analysis shows any movement restrictions that individuals may have [95], and the 6 min walk test and 30s sit-to-stand test are also good options for functional assessment variables [36,47]. For example, people with achondroplasia cannot fully extend the elbow joint due to a deformity of the distal part of the humerus and subluxation of the radial head [16,96].

4.11. Recommendations

First of all, it is essential to capture and assess the needs and expectations of people with SD regarding physical exercise and sports.

It is essential to be aware that the population with SD experiences activities and tasks differently than the average population. The proposed activity must be as adapted as possible, considering that user-specific needs depending on age and physical limitations can vary between individuals with the same type of skeletal dysplasia. Adapted physical activity leads to a multitude of physiological, social, and psychological benefits [27].

It is also important, in terms of recommendations, that the implementation of physical exercise programs is adapted (also in terms of neuromuscular and metabolic profiles) and led by a physical exercise professional. A better understanding of intervention strategies for people with SD is fundamental to structuring effective methodologies that, in addition to improving physical abilities, promote positive adaptations in quality of life, including social and psycho-emotional aspects.

We also highlight that this is a population with a prevalence of mental health disorders, namely, anxiety and depression [25,97], which affects their quality of life [13]. Anecdotal evidence showed a higher rate of suicide prevalence in adults with SD compared with the general population [98]. Although we did not find any intervention studies in the population with SD with physical activity, exercise, or sports, they have been shown to promote the mental health of individuals with other types of comorbidities, namely, disabilities [99] and cancer [100]. At the same time, the practice of physical activity, exercise, or sports is associated with anti-inflammatory processes, protecting central functions, and delaying cognitive decline and premature aging, which may be promising for individuals with SD [101].

Likewise, it is necessary to further research this topic to allow the development of specific training protocols/programs, from the level of initial training to continuous training and with the integration of a syllabus covering the dimensions of exercise for people with SD. Training should be focused on the characterization of inherent physical, physiological, psychological, social, and emotional aspects and aim to update technical skills and the professional development of physical exercise with a holistic view; therefore, an adjusted schedule and the execution of various sessions of physical exercise programs may be attained that consider concerns health and quality of life.

The results of this study only allowed us to characterize the individuals’ physiques, but we now have a greater overview of the current knowledge; therefore, this document is a starting point in the process of evaluating and prescribing adapted physical activity for people with SD. What is currently known about the levels of physical activity in individuals with SD relate to anthropometric characteristics; hemodynamic profiles; cardiorespiratory, neuromuscular, and balance capacities; neurological symptoms related to pain, hearing, voice, and vision problems; and some recommendations for the evaluation and prescription of exercise. Above all, it is necessary to include qualitative methodologies to understand which types of adapted physical activities are more motivating for individuals and promote adherence and maintenance in sports practice.
4.12. Limitations

Through the methodology used, we found that there is limited research and available studies (i.e., experimental studies) on adapted physical activities and exercise for people with SD. However, before starting this systematic review, an exploratory search was carried out in the databases to better understand the potential of this research and the search terms and methodologies to focus on in order to be as comprehensive as possible. Also, most studies focused on one SD, i.e., achondroplasia, so information was limited and needed to be carefully interpreted to avoid generalizations.

5. Conclusions

The assessment of physical fitness and prescription and implementation of adapted physical exercise must consider the individual needs of people with SD. Each type of SD is distinct and varies depending on age and individuals’ medical history; therefore, such individuals require a personalized assessment so that physical complications are avoided and the activities/exercise are catered to the type of SD.

Assessing limitations is essential; however, above all, to promote individual physical capacities and the recommendations of the World Health Organization, adapted, inclusive physical activities or sports for people with SD should be personalized.

This work is a call to action for the design and development of studies in the context of biomechanics, sport physiology, and vocational education.

When reading studies, we saw that there is no consensus on the practice of physical activity by individuals with SD, but that barriers at various levels can negatively influence this practice. These individuals have unfavorable anthropometric values and hemodynamic structures, particularly in SDs with restrictive chest and lung capacities as well as neuromuscular and balance capacities. They also have a high prevalence of neurological symptoms; pain; and, at times, hearing, voice, and vision deficits.

Our search presented a clear scarcity in the literature of experimental studies with adapted physical exercise implemented in the SD population, which represents a clear knowledge gap. We believe that this work is an important tool as a first step toward better interventions as it characterized the physical fitness of the population in focus. It is necessary to carry out urgent research on this topic, namely, the impact of physical exercise on the physical fitness, health, and quality of life of individuals with SD and the psychological benefits of structure-adapted sports for SD populations.

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References
1. Breeland, G.; Sinkler, M.A.; Menezes, R.G. Embryology, Bone Ossification. In StatPearls; StatPearls Publishing: Treasure Island, FL, USA, 2021.
2. Horton, W.A. Skeletal development: Insights from targeting the mouse genome. Lancet 2003, 362, 560–569. [CrossRef]
3. Geister, K.A.; Camper, S.A. Advances in Skeletal Dysplasia Genetics. *Annu. Rev. Genom. Hum. Genet.* 2015, 16, 199–227. [CrossRef] [PubMed]

4. Rousseau, F.; Bonaventure, J.; Legeai-Mallet, L.; Pelet, A.; Rozet, J.-M.; Maroteaux, P.; Le Merrer, M.; Munich, A. Mutations in the gene encoding fibroblast growth factor receptor-3 in achondroplasia. *Nature* 1994, 371, 252–254. [CrossRef] [PubMed]

5. Warnan, M.L.; Cormier-Daire, V.; Hall, C.; Krakow, D.; Lachman, R.; LeMerrer, M.; Mortier, G.; Mundlos, S.; Nishimura, G.; Rimoin, D.L.; et al. Nosology and classification of genetic skeletal disorders: 2010 revision. *Am. J. Med. Genet. Part A* 2011, 155, 943–968. [CrossRef]

6. Mortier, G.R.; Cohn, D.H.; Cormier-Daire, V.; Hall, C.; Krakow, D.; Mundlos, S.; Nishimura, G.; Robertson, S.; Sangiorgi, L.; Savarirayan, R.; et al. Nosology and classification of genetic skeletal disorders: 2019 revision. *Am. J. Med. Genet. Part A* 2019, 179, 2393–2419. [CrossRef]

7. Shirley, E.D.; Ain, M.C. Achondroplasia: Manifestations and Treatment. *J. Am. Acad. Orthop. Surg.* 2009, 17, 231–241. [CrossRef]

8. Vajo, Z.; Francomano, C.A.; Wilkin, D.J. The Molecular and Genetic Basis of Fibroblast Growth Factor Receptor 3 Disorders: The Achondroplasia Family of Skeletal Dysplasias, Muenke Craniosynostosis, and Crouzon Syndrome with Acanthosis Nigricans. *Endocr. Rev.* 2000, 21, 23–39. [CrossRef]

9. Simmons, K.; Hashmi, S.S.; Scheuerle, A.; Canfield, M.; Hecht, J.T. Mortality in babies with achondroplasia: Revisited. *Birth Defects Res. Part A Clin. Mol. Teratol.* 2014, 100, 247–249. [CrossRef]

10. Horton, W.A.; Hall, J.G.; Hecht, J.T. Achondroplasia. *Lancet* 2007, 370, 162–172. [CrossRef]

11. Pauli, R.M. Achondroplasia: A comprehensive clinical review. *Orphanet J. Rare Dis.* 2019, 14, 1. [CrossRef]

12. Alade, Y.; Tunkel, D.; Schulze, K.; McGready, J.; Jallo, G.; Ain, M.; Yost, T.; Hoover-Fong, J. Cross-sectional assessment of pain and physical function in skeletal dysplasia patients. *Clin. Genet.* 2013, 84, 227–243. [CrossRef] [PubMed]

13. Dhiman, N.; Albaghdadi, A.; Zogg, C.K.; Sharma, M.; Hoover-Fong, J.E.; Ain, M.C.; Haider, A.H. Factors associated with health-related quality of life (HRQOL) in adults with short stature skeletal dysplasias. *Qual. Life Res.* 2017, 26, 1337–1348. [CrossRef] [PubMed]

14. Hyvönen, H.; Anttila, H.; Tallqvist, S.; Muñoz, M.; Leppäjoki-Tiistola, S.; Teittinen, A.; Mäkitie, O.; Hiekkala, S. Functioning and equality according to International Classification of Functioning, Disability and Health (ICF) in people with skeletal dysplasia compared to matched control subjects—A cross-sectional survey study. *BMC Musculoskelet. Disord.* 2020, 21, 808. [CrossRef] [PubMed]

15. Wright, M.J.; Irving, M.D. Clinical management of achondroplasia. *Arch. Dis. Child.* 2012, 97, 129–134. [CrossRef] [PubMed]

16. Haga, N. Management of disabilities associated with achondroplasia. *J. Orthop. Sci.* 2004, 9, 103–107. [CrossRef]

17. Takken, T.; van Bergen, M.W.M.; Sakkers, R.J.B.; Helders, P.J.M.; Engelbert, R.H.H. Cardiopulmonary Exercise Capacity, Muscle Strength, and Physical Activity in Children and Adolescents with Achondroplasia. *J. Pediatr.* 2007, 150, 26–30. [CrossRef]

18. Hecht, J.T.; Hood, O.J.; Schwartz, R.J.; Hennessey, J.C.; Bernhardt, B.A.; Horton, W.A.; Opitz, J.M.; Reynolds, J.F. Obesity in achondroplasia. *Am. J. Med Genet.* 1988, 31, 597–602. [CrossRef]

19. Hecht, J.T.; Francomano, C.A.; Horton, W.A.; Annegers, J.F. Mortality in achondroplasia. *Am. J. Hum. Genet.* 1987, 41, 454–464. [CrossRef]

20. Kodama, S.; Saito, K.; Tanaka, S.; Maki, M.; Yachi, Y.; Asumi, M.; Sugawara, A.; Totsuka, K.; Shimano, H.; Ohashi, Y.; et al. Cardiorespiratory Fitness as a Quantitative Predictor of All-Cause Mortality and Cardiovascular Events in Healthy Men and Women: A meta-analysis. *JAMA* 2009, 301, 2024–2035. [CrossRef]

21. Ladenvall, P.; Persson, C.U.; Mandelakisz, Z.; Wilhelmens, L.; Grimby, G.; Svärdsudd, K.; Hansson, P.-O. Low aerobic capacity in middle-aged men associated with increased mortality rates during 45 years of follow-up. *Eur. J. Prev. Cardiol.* 2016, 23, 1557–1564. [CrossRef]

22. Wynn, J.; King, T.M.; Gambello, M.J.; Waller, D.K.; Hecht, J.T. Mortality in achondroplasia study: A 42-year follow-up. *Am. J. Med. Genet. Part A* 2007, 143A, 2502–2511. [CrossRef] [PubMed]

23. Constantinides, C.; Landis, S.H.; Jarrett, J.; Quinn, J.; Ireland, P.J. Quality of life, physical functioning, and psychosocial function among patients with achondroplasia: A targeted literature review. *Disabil. Rehabil.* 2021, 1–13. [CrossRef] [PubMed]

24. Gollust, S.E.; Thompson, R.E.; Gooding, H.C.; Biesecker, B.B. Living with achondroplasia in an average-sized world: An assessment of quality of life. *Am. J. Med. Genet. Part A* 2003, 120, 447–458. [CrossRef] [PubMed]

25. Johansen, H.; Andresen, I.-L.; E Naess, E.; Hagen, K.B. Health status of adults with Short Stature: A comparison with the normal population and one well-known chronic disease (Rheumatoid Arthritis). *Orphanet J. Rare Dis.* 2007, 2, 10. [CrossRef]

26. KräGer, L.; Pohjolainen, T.; Kaitila, I.; Kautianen, H.; Arkela-Kautianen, M.; Hurri, H. Health-related quality of life and socioeconomic situation among diastrophic dysplasia patients in Finland. *J. Rehabil. Med.* 2013, 45, 308–313. [CrossRef]

27. ACSM. *American College of Sports Medicine-Guidelines for Exercise Testing and Prescription*, 10th ed.; Wolters Kluwer: Philadelphia, PA, USA, 2017.

28. Blair, S.N.; Morris, J.N. Healthy Hearts—And the Universal Benefits of Being Physically Active: Physical Activity and Health. *Ann. Epidemiol.* 2009, 19, 253–256. [CrossRef]

29. World Health Organization. *Guidelines on Physical Activity and Sedentary Behaviour*; World Health Organization: Geneva, Switzerland, 2020; p. 24.

30. Joseph, W.; David, P. *Adapted Physical Education and Sport*, 6th ed.; Human Kinetics: Champaign, IL, USA, 2016.
31. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021, 372, 105906. [CrossRef]

32. Bento, T. Revisões sistemáticas em desporto e saúde: Orientações para o planeamento, elaboração, redação e avaliação. Motricidade 2014, 10, 107–123. [CrossRef]

33. Methley, A.M.; Campbell, S.; Chew-Graham, C.; McNally, R.; Cheraghi-Sohi, S. PICO, PICOS and SPIDER: A comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. BMC Health Serv. Res. 2014, 14, 579. [CrossRef]

34. Nang, C.; Piano, B.; Lewis, A.; Lycett, K.; Woodhouse, M. Using the PICO Model to Design and Conduct a Systematic Search: A Speech Pathology Case Study. Edith Cowan University Western Australia: Joondalup, WA, Australia, 2015; p. 51.

35. Brooks, J.T.; Ramji, A.F.; Lyapustina, T.A.; Yost, M.T.; Ain, M.C. Low Prevalence of Anterior and Posterior Cruciate Ligament Injuries in Patients With Achondroplasia. J. Pediatr. Orthop. 2017, 37, e43–e47. [CrossRef]

36. Carneiro, J.; Da Silveira, V.; Vasconcelos, A.; De Souza, L.; Xerez, D.; Da Cruz, G.; Quaresma, J.; Macedo, R.; De Oliveira, J. Bariatric Surgery in a Morbidly Obese Achondroplastic Patient—Use of the 6-Minute Walk Test to Assess Mobility and Quality of Life. Obes. Surg. 2007, 17, 255–257. [CrossRef] [PubMed]

37. Bal, S.; Kocygjit, H.; Turan, Y.; Gurgan, A.; Bayram, K.B.; Güvenc, A.; Kocaaga, Z.; Dirim, B. Spondyloepiphyseal dysplasia tarda: Four cases from two families. Rheumatol. Int. 2009, 29, 699–702. [CrossRef] [PubMed]

38. Saffarian, M.R.; Swampillai, J.J.; Andary, M.T.; Sylvain, J.V.; Halliday, S.E.; Bratta, B. Incidence of injury and illness during the 2013 world dwarf games. Inj. Epidemiol. 2019, 6, 13. [CrossRef] [PubMed]

39. Moura, D.L. Correcting stigma through the spectacle: The case of soccer team of dwarfs. Revista Brasileira Ciências Esportes 2015, 37, 341–347. [CrossRef]

40. Dummer, G. Sports Preferences of Dwarf Athletes. Res. Q. Exerc. Sport 1992, 63, A90.

41. Arndt, D. The Relationship between Skeletal Dysplasia and Incidence and Recurrence of Knee and Ankle Sprains among College Sports Participants. Ph.D. Thesis, Springfield College, Springfield, MA, USA, 1966.

42. Parent-Nichols, J.; Chamberlain, D. Use of a Knee Orthosis to Advance Motor Control in a 3-Year-Old with Achondroplasia: A Case Report. J. Prosthet. Orthot. 2021, 34, e61–e68. [CrossRef]

43. Takken, T.; Bergen, M.V.; Sakkers, R. Respiratory Gas Exchange and Metabolic Responses during Exercise in Children and Adolescents with Achondroplasia. In Children and Exercise XXIV; Routledge: London, UK, 2008.

44. Wagner, T.; Sandt, D. Physical Education Programming for Students with Achondroplasia. J. Aust. Strength Cond. 2012, 26, 35–39.

45. Lane, C. Strengthening Considerations for a Dwarf Track and Field Thrower. J. Aust. Strength Cond. 2017, 25, 42–52.

46. Cumming, G.R.; Kerr, D.; Ferguson, C.C. Constrictive pericarditis with dwarfism in two siblings (Mulibrey nanism). J. Pediatr. 1976, 88, 569–572. [CrossRef]

47. De Vries, O.M.; Johansen, H.; Fredwall, S.O. Physical fitness and activity level in Norwegian adults with achondroplasia. Am. J. Med. Genet. Part A 2021, 185, 1023–1032. [CrossRef] [PubMed]

48. Hansson, A.A. Improving mobility in a client with hypochondroplasia (dwarfism): A case report. J. Bodyw. Mov. Ther. 2010, 14, 172–178. [CrossRef] [PubMed]

49. Hoover-Fong, J.; Alade, A.Y.; Ain, M.; Berkowitz, I.; Bober, M.; Carter, E.; Hecht, J.; Hoershemeyer, D.; Krakow, D.; MacCarrick, G.; et al. Blood pressure in adults with short stature skeletal dysplasias. Am. J. Med. Genet. Part A 2020, 182, 150–161. [CrossRef] [PubMed]

50. Hoover-Fong, J.; Cheung, M.S.; Fano, V.; Hagenas, L.; Hecht, J.T.; Ireland, P.; Irving, M.; Mohnike, K.; Offiah, A.C.; Okenfuss, E.; et al. Lifetime impact of achondroplasia: Current evidence and perspectives on the natural history. Bone 2021, 146, 115872. [CrossRef] [PubMed]

51. Low, L.J.; Knudsen, M.J.; Sherrill, C. Dwarfism: New Interest Area for Adapted Physical Activity. Adapt. Phys. Act. Q. 1996, 13, 1–15. [CrossRef]

52. Madsen, A.; Fredwall, S.O.; Maanum, G.; Henriksen, C.; Slettabjell, H.B. Anthropometrics, diet, and resting energy expenditure in Norwegian adults with achondroplasia. Am. J. Med. Genet. Part A 2019, 179, 1745–1755. [CrossRef]

53. Orlando, G.; Bubbear, J.; Clarke, S.; Keen, R.; Tetlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021, 372, 105906. [CrossRef]

54. Orlando, G.; Bubbear, J.; Clarke, S.; Keen, R.; Tetlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021, 372, 105906. [CrossRef]

55. Pfeiffer, K.M.; Brod, M.; Smith, A.; Gianettoni, J.; Viuff, D.; Ota, S.; Charlton, R.W. Assessing physical symptoms, daily functioning, and well-being in children with achondroplasia. Inj. Epidemiol. 2019, 6, 13. [CrossRef] [PubMed]

56. Pfeiffer, K.M.; Brod, M.; Smith, A.; Gianettoni, J.; Viuff, D.; Ota, S.; Charlton, R.W. Assessing physical symptoms, daily functioning, and well-being in children with achondroplasia. Inj. Epidemiol. 2019, 6, 13. [CrossRef] [PubMed]

57. Steele, A.; Gonzalez, R.; Garbalosa, J.C.; Steigbigel, K.; Grgurich, T.; Parisi, E.; Feinn, R.S.; Tommasini, S.M.; Macica, C.M. Osteoarthritis, Osteophytes, and Enthesophytes Affect Biomechanical Function in Adults With X-linked Hypophosphatemia. J. Clin. Endocrinol. Metab. 2020, 105, e1798–e1814. [CrossRef]

58. Rueda, Z.R.R.; Florez, K.T.C.; Ibarra, A.G.F.; Cardona, M.R.M.; Gomez, F.L. Intervención fisioterapéutica en deportista con acondroplasia practicante de levantamiento de potencia adaptado y natación paralímpica. Reporte de caso. Case Rep. 2021, 7, 81–90. [CrossRef]

59. Cieza, A.; Fayad, N.; Bickenbach, J.; Prodinge, B. Refinements of the ICF Linking Rules to strengthen their potential for establishing comparability of health information. Disabil. Rehabil. 2019, 41, 574–583. [CrossRef] [PubMed]
59. Da Rocha, L.; Wagner, D. Pessoas com nanismo acondroplasia: Um estudo acerca dos aspectos psicossociais e as contribuições da atividade física na sua inclusão social. Ciência Movimento 2018, 20, 17–29. [CrossRef]

60. Ain, M.C.; Abdullah, M.A.; Ting, B.L.; Skolasky, R.L.; Carlisle, E.S.; Schkrohowsky, J.G.; Rigamonti, D. Progression of low back and lower extremity pain in a cohort of patients with achondroplasia. J. Neurosurg. Spine 2010, 13, 335–340. [CrossRef]

61. Sims, D.; Onambélé-Pearson, G.; Burden, A.; Payton, C.; Morse, C. Whole-body and segmental analysis of body composition in adult males with achondroplasia using dual X-ray absorptiometry. PLoS ONE 2019, 14, e0213806. [CrossRef] [PubMed]

62. Matsushita, M.; Kito, H.; Mishima, K.; Kadono, I.; Sugiyama, H.; Hasegawa, S.; Nishida, Y.; Ishiguro, N. Low bone mineral density in achondroplasia and hypochondroplasia. Pediatr. Int. 2016, 58, 705–708. [CrossRef] [PubMed]

63. Arita, E.S.; Pippa, M.G.B.; Marcucci, M.; Cardoso, R.; Cortes, A.R.G.; Watanabe, P.C.A.; Oliveira, J.X. Assessment of osteoporotic alterations in achondroplastic patients: A case series. Clin. Rheumatol. 2013, 32, 399–402. [CrossRef] [PubMed]

64. Taşoğlu, Ö.; Onat, S.; Yenigün, D.; Aslan, M.D.; Nakipoğlu, G.F.; Özgirgin, N. Low bone density in achondroplasia. Clin. Rheumatol. 2014, 33, 733–735. [CrossRef]

65. Owen, O.E.; Smalley, K.J.; D’Alessio, D.A.; Mozzoli, M.A.; Knerr, A.N.; Tappy, L.; Boden, G. Resting Metabolic Rate and Body Composition of Achenodrolastic Dwarfs. Medicine 1990, 69, 56–67. [CrossRef]

66. Schulze, K.J.; Alade, Y.A.; McGready, J.; Hoover-Fong, J.E. Body mass index (BMI): The case for condition-specific cut-offs for overweight and obesity in skeletal dysplasias. Am. J. Med. Genet. Part A 2013, 161, 2110–2112. [CrossRef]

67. Del Pino, M.; Mejía, R.R.; Fano, V. Leg length, sitting height, and body proportions references for achondroplasia: New tools for monitoring growth. Am. J. Med. Genet. Part A 2018, 176, 896–906. [CrossRef]

68. Hoover-Fong, J.; McGready, J.; Schulze, K.; Alade, A.Y.; Scott, C. A height-for-age growth reference for children with achondroplasia: Expanded applications and comparison with original reference data. Am. J. Med. Genet. Part A 2017, 173, 1226–1230. [CrossRef] [PubMed]

69. Katzmarzyk, P.T.; Janssen, I.; Ross, R.; Church, T.S.; Blair, S.N. The Importance of Waist Circumference in the Definition of Metabolic Syndrome: Prospective Analyses of Mortality in Men. Diabetes Care 2006, 29, 404–409. [CrossRef] [PubMed]

70. Siren, R.; Eriksson, J.G.; Vanhanen, H. Waist circumference a good indicator of future risk for type 2 diabetes and cardiovascular disease. BMC Public Health 2012, 12, 631. [CrossRef] [PubMed]

71. Saint-Laurent, C.; Garde-Etayo, L.; Gouze, E. Obesity in achondroplasia patients: From evidence to medical monitoring. Orphanet J. Rare Dis. 2019, 14, 253. [CrossRef] [PubMed]

72. Tenconi, R.; Khirani, S.; Amaddeo, A.; Michot, C.; Baujat, G.; Couloigner, V.; De Sanctis, L.; James, S.; Zerah, M.; Cormier-Daire, V.; et al. Sleep-disordered breathing and its management in children with achondroplasia. Am. J. Med. Genet. Part A 2017, 173, 868–878. [CrossRef]

73. Kohler, M. Risk factors and treatment for obstructive sleep apnea amongst obese children and adults. Curr. Opin. Allergy Clin. Immunol. 2009, 9, 4–9. [CrossRef]

74. Stokes, D.C.; Pyeritz, R.E.; Wise, R.A.; Fairclough, D.; Murphy, E.A. Spirometry and Chest Wall Dimensions in Achondroplasia. Chest 1988, 93, 364–369. [CrossRef]

75. Stokes, D.C.; Wohlf, M.E.B.; Wise, R.A.; Pyeritz, R.E.; Fairclough, D.L. The Lungs and Airways in Achondroplasia: Do Little People Have Little Lungs? Chest 1990, 98, 145–152. [CrossRef]

76. Edvardsen, E.; Hansen, B.H.; Holme, I.M.; Dyrstad, S.M.; Anderssen, S.A. Reference Values for Cardiorespiratory Response and Fitness on the Treadmill in a 20– to 85-Year-Old Population. Chest 2013, 144, 241–248. [CrossRef]

77. Borg, G. Borg’s Perceived Exertion and Pain Scales; Human Kinetics: Champaign, IL, USA, 1998.

78. Savarirayan, R.; Rimoin, D.L. The skeletal dysplasias. Best Pr. Res. Clin. Endocrinol. Metab. 2002, 16, 547–560. [CrossRef]

79. Pirlò, K.A.; Briggs, M.D. Skeletal Dysplasias Associated with Mild Myopathy—A Clinical and Molecular Review. J. Biomed. Biotechnol. 2010, 2010, 686457. [CrossRef] [PubMed]

80. Sims, D.T.; Onambélé-Pearson, G.L.; Burden, A.; Payton, C.; Morse, C.I. Specific force of the vastus lateralis in adults with achondroplasia. J. Appl. Physiol. 2018, 124, 696–703. [CrossRef] [PubMed]

81. Fredwall, S.O.; Steen, U.; De Vries, O.; Rustad, C.F.; Eggshba, H.B.; Weeden-Fekjær, H.; Lidal, I.B.; Savarirayan, R.; Mánun, G. High prevalence of symptomatic spinal stenosis in Norwegian adults with achondroplasia: A population-based study. Orphanet J. Rare Dis. 2020, 15, 123. [CrossRef]

82. Tveter, A.T.; Dagfinrud, H.; Moseng, T.; Holm, I. Health-Related Physical Fitness Measures: Reference Values and Reference Equations for Use in Clinical Practice. Arch. Phys. Med. Rehabil. 2014, 95, 1366–1373. [CrossRef] [PubMed]

83. Brown, H.J.; Siegmund, G.P.; Guskiewicz, K.M.; van den Doel, K.; Cretu, E.; Blouin, J.-S. Development and Validation of an Objective Balance Error Scoring System. Med. Sci. Sports Exerc. 2014, 46, 1610–1616. [CrossRef] [PubMed]

84. Vanlandewijck, Y.; Thompson, W. Handbook of Sports Medicine and Science—The Paralympic Athlete; Wiley-Blackwell: Hoboken, NJ, USA, 2011.

85. Fredwall, S.O.; Maanum, G.; Johansen, H.; Snekkevik, H.; Savarirayan, R.; Lidal, I. Current knowledge of medical complications in adults with achondroplasia: A scoping review. Clin. Genet. 2020, 97, 179–197. [CrossRef]

86. Unger, S.; Bonafé, L.; Gouze, E. Current Care and Investigational Therapies in Achondroplasia. Curr. Osteoporos. Rep. 2017, 15, 53–60. [CrossRef]

87. Gamble, C.; Nguyen, J.; Hashmi, S.S.; Hecht, J.T. Pseudoachondroplasia and painful sequelae. Am. J. Med. Genet. Part A 2015, 167, 2618–2622. [CrossRef]
88. Breivik, H.; Borchgrevink, P.C.; Allen, S.M.; Rosseland, L.A.; Romundstad, L.; Hals, E.K.B.; Kvarstein, G.; Stubhaug, A. Assessment of pain. Br. J. Anaesth. 2008, 101, 17–24. [CrossRef]
89. Ambrose, K.R.; Golightly, Y.M. Physical exercise as non-pharmacological treatment of chronic pain: Why and when. Best Pract. Res. Clin. Rheumatol. 2015, 29, 120–130. [CrossRef]
90. Geneen, L.J.; Moore, R.A.; Clarke, C.; Martin, D.; Colvin, L.A.; Smith, B.H. Physical activity and exercise for chronic pain in adults: An overview of Cochrane Reviews. Cochrane Database Syst. Rev. 2017, 2017, CD011279.
91. Tunkel, D.; Alade, Y.; Kerbavaz, R.; Smith, B.; Rose-Hardison, D.; Hoover-Fong, J. Hearing loss in skeletal dysplasia patients. Am. J. Med. Genet. Part A 2012, 158, 1551–1555. [CrossRef] [PubMed]
92. Watt, A.J.; Chung, K.C. Generalized Skeletal Abnormalities. Hand Clin. 2009, 25, 265–276. [CrossRef] [PubMed]
93. Katz, J.N.; Harris, M.B. Clinical Practice. Lumbar Spinal Stenosis. N. Engl. J. Med. 2008, 358, 818–825. [CrossRef]
94. Ireland, P.J.; McGill, J.J.; Zankl, A.; Ware, R.; Pacey, V.; Ault, J.E.; Savarirayan, R.; Sillence, D.O.; Thompson, E.M.; Townshend, S.; et al. Functional performance in young Australian children with achondroplasia. Dev. Med. Child Neurol. 2011, 53, 944–950. [CrossRef]
95. Cook, G.; Burton, L.; Hoogenboom, B. Pre-Participation Screening: The Use of Fundamental Movements as an Assessment of Function—Part 2. N. Am. J. Sports Phys. Ther. 2006, 1, 132–139.
96. Kitoh, H.; Kitakoji, T.; Kurita, K.; Katoh, M.; Takamine, Y. Deformities of the elbow in achondroplasia. J. Bone Jt. Surgery. Br. Vol. 2002, 84, 680–683. [CrossRef]
97. Jennings, S.E.; Ditro, C.P.; Bober, M.B.; Mackenzie, W.G.; Rogers, K.J.; Conway, L.; Duker, A.L. Prevalence of mental health conditions and pain in adults with skeletal dysplasia. Qual. Life Res. 2019, 28, 1457–1464. [CrossRef]
98. Ritchie, H.; Roser, M.; Ortiz-Ospina, E. Suicide, Our World in Data. 2015. Available online: https://ourworldindata.org/ (accessed on 20 March 2022).
99. Jacinto, M.; Frontini, R.; Matos, R.; Antunes, R. Effects of Exercise Programs on Anxiety in Individuals with Disabilities: A Systematic Review with a Meta-Analysis. Healthcare 2021, 9, 1047. [CrossRef]
100. Zyzniewska-Banaszak, E.; Kucharska-Mazur, J.; Mazur, A. Physiotherapy and Physical Activity as Factors Improving the Psychological State of Patients with Cancer. Front. Psychiatry 2021, 12, 772694. [CrossRef]
101. Scheffer, D.D.L.; Latini, A. Exercise-induced immune system response: Anti-inflammatory status on peripheral and central organs. Biochim. Biophys. Acta (BBA) Mol. Basis Dis. 2020, 1866, 165823. [CrossRef] [PubMed]