

RESEARCH

Open Access



Adults with achondroplasia exhibit a high probability of specific micronutrient inadequacy and low physical activity levels: a cross-sectional study

Inês Alves^{1,2*}, Maria António Castro^{3,4}, Sofia Tavares⁵, Orlando Fernandes¹ and Cidália D. Pereira^{3,6,7,8}

Abstract

Purpose Achondroplasia is a rare skeletal dysplasia, characterized by disproportionate short stature and predisposition to obesity. There is limited evidence on nutritional adequacy in adults with achondroplasia. This study aimed to assess nutrient intake and adequacy in adults with achondroplasia, exploring associations with anthropometric characteristics and physical activity patterns.

Methods An exploratory cross-sectional study evaluated 16 Portuguese adults with achondroplasia (10 women), aged 38.4 ± 13.8 years). Nutrient intake was assessed using a validated food frequency questionnaire and evaluated against reference values from the European Food Safety Authority. Anthropometric body composition parameters were assessed using standardized methods and physical activity levels using the International Physical Activity Questionnaire.

Results Most participants (62.5%) exhibited high body mass index (≥ 30 kg/m²), with 43.8% presenting waist-to-hip ratio above WHO cut-offs and elevated fat mass percentage (27.0 ± 10.5). Macronutrient distribution largely aligned with recommendations, yet 43.8% exceeded saturated fat intake while 100% presented lower intakes of omega-3 fatty acids and 57.3% lower fiber intake. High probability of inadequacy was found for vitamin D, vitamin K, biotin, manganese, and molybdenum. Pantothenic acid, vitamin E, and iodine intakes were also concerning. Sodium intake exceeded recommendation in 75% of participants. Physical activity levels were low, with 56.3% of participants categorized as inactive.

Conclusions This study provides novel insights into nutritional inadequacies and sedentary lifestyle in adults with achondroplasia, highlighting the need for tailored dietary interventions and adapted physical activity programs. Promotion of the Mediterranean dietary patterns may also offer benefits for nutritional adequacy in this population.

Keywords Skeletal dysplasia, Macronutrients; Micronutrients, Food intake, Rare condition

*Correspondence:

Inês Alves

ines.alves@uevora.pt

Full list of author information is available at the end of the article



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

Introduction

Achondroplasia (ACH) is a rare skeletal dysplasia, occurring in 1 in 25,000 live births [61]. It is caused by a gain-of-function mutation in the fibroblast growth factor receptor 3 (FGFR3) gene, leading to impaired endochondral ossification and characteristic skeletal features [44]. This results in a disproportionate short stature with shorter arms and legs, with an average trunk size [54, 55]. While extensive research exists on genetic and physical aspects of ACH, a critical knowledge gap remains concerning nutritional requirements and dietary patterns in this population. ACH is related to a high prevalence of several comorbidities, such as obesity, obstructive sleep apnea (OSA), spinal stenosis [74], and pain, which may be interconnected [32]. The exact mechanisms for obesity prevalent in ACH are not well understood, both genetic and environmental aspects may be involved [68, 89]. Environmental factors, in particular dietary intake and physical activity, may play a crucial role in body mass management and obesity prevention [18, 54]. It is well known that obesity is a systemic issue affecting multiple organ systems and has several associated comorbidities, such as diabetes, depression, cardiovascular disease, and venous thromboembolism [47].

Nutritional adequacy is the concept related to the sufficient intake of an essential nutrient in relation to the nutrient requirement for adequate health and is determined by comparing nutrient requirements and intakes of an individual or population. Assessment of the adequacy of nutrient intake of an individual or population is based on the probability of adequacy [15]. Adequacy also implies that nutrients must satisfy the dietary needs considering age, gender, body size, and physical activity level [15]. There is a scarcity of information on dietary intake and nutritional adequacy in adults with achondroplasia (ACH). However, a study by Madsen et al. [54] demonstrated that individuals with ACH tend to follow a dietary pattern similar to the typical Western diet, characterized by high consumption of processed meats and high-fat dairy products, and low intake of fish, fruits, and vegetables [54]. Such dietary patterns are associated with increased risks of obesity and cardiovascular disease [16, 43, 54]. Individuals with achondroplasia exhibit characteristic body features and an increased risk of obesity, which may further limit their ability to engage in regular physical activity [6]. These factors can contribute to metabolic abnormalities, consistent with observations in the general population [34]. Improving diet quality and promoting physical activity are central components of the World Health Organization's global strategy to prevent non-communicable diseases [82]. Also, gender-specific considerations are particularly important in achondroplasia research, as emerging evidence suggests

differential patterns in metabolic profiles [69], musculoskeletal complications, physical activity tolerance [18] and psychosocial challenges [4] between men and women with this condition, though comprehensive data remain limited.

Therefore, this exploratory study aimed to investigate nutritional intake adequacy and physical activity patterns in Portuguese adults with achondroplasia, providing preliminary insights into potential areas of nutritional inadequacy and activity limitations in this rare population.

Methods and materials

Study design and participants

This cross-sectional study involved 16 Portuguese adults with ACH recruited by the National Association for Skeletal Dysplasia between November 2022 and June 2023. Inclusion criteria included age over 18 years and a clinically confirmed diagnosis of ACH. While no formal exclusion criteria were applied to maximize sample representativeness in this rare condition, participant medical histories were documented to assess potential confounding factors including food allergies and mobility-limiting comorbidities. The STROBE guidelines [25] and the SAGER guidelines [31] for sex and Gender Equity in research were used for reporting. This study was approved by the Ethics Committee of University of Évora, registry number 22056. A written informed consent was provided to all participants for their review before their inclusion in the study, and all participants gave consent in adherence to the 1964 Declaration of Helsinki and its later amendments.

Data collection

This study and data presented are openly available in Open Science Framework repository at <https://osf.io/qjtvz/>.

Anthropometry and body composition assessment

Anthropometric measurements including body mass, height, waist and hip circumferences, and upper arm girth were measured using standardized techniques [33, 58]. Body composition was assessed using a multi-frequency segmental analyzer (Tanita MC780-PMA) providing estimates of fat mass, lean mass, and bone mineral mass, with values presented as percentages. BMI was calculated as body mass in kilograms divided by height in meters squared. Obesity in the general population is typically defined as $BMI \geq 30 \text{ kg/m}^2$. However, in individuals with achondroplasia, BMI is a less reliable indicator of adiposity due to disproportionate short stature and altered body proportions, which may lead to overestimation of body fat [29, 33, 65]. Therefore, waist-to-hip ratio (WHR), a height-independent calculation to measure

obesity, was included to better assess central adiposity, using WHO cut-offs of ≥ 0.85 for women and ≥ 0.90 for men [83].

Comorbidities assessment

Participants responded to a tailored questionnaire on medical history based on specific guidance [27], which included respiratory complications (obstructive sleep apnea, current ventilation therapy use), orthopedic conditions (spinal stenosis, chronic pain requiring medication), neurological conditions (history of foramen magnum stenosis, decompression surgery), and lifestyle factors (smoking status). All participants provided self-reported medical history information, with responses categorized as confirmed diagnosis, absence of condition, or unknown status.

Dietary assessment

The dietary intake of participants was assessed using a semi-quantitative food frequency questionnaire (FFQ) (Lopes C, 2000), validated for the Portuguese population (Lopes C, 2000; [50]) and administered by a trained dietitian (CDP) to collect information about participants' food consumption over the last year. A standardized photographic manual, the Food Quantification Photographic Manual from the National food and Physical activity Survey 2015–2016 [76] was used for more accurate quantification of the participants' food intake. Nutrient intake values were calculated using validated algorithms by the Nutritional Epidemiology research team at the Institute of Public Health, University of Porto (ISPUP) [77], which processed the FFQ data through standardized nutrient composition databases.

Briefly, to obtain food consumption, the frequency of each item was multiplied by the respective average standard portion in grams (g) and by a seasonal variation factor for foods consumed in specific seasons (0.25, considering the average seasonality of 3 months). Foods were converted into nutrients using the Food Processor Plus computer programme (ESHA Research, Salem, OR, USA), with nutritional information taken from the US Department of Agriculture food composition tables, adapted to typical Portuguese foods [48–50].

The prevalence of nutritional adequacy was obtained by the comparison of the participants' estimated intake of energy, macro- and micronutrients with the dietary reference values (DRV) established by the European Food Safety Authority, EFSA [22] or with Dietary Reference Intakes by the Institute of Medicine, IOM, whenever a DRV was not established by EFSA. As proposed by EFSA, energy intake was adjusted by age, sex, and physical activity. The Reference Intake ranges (RI) for macronutrients, expressed as % of the energy intake, were used as cut-offs

for macronutrients [22]. The range defined by EFSA was used for carbohydrates and total fat, and the IOM range for proteins [35]. For saturated and trans fatty acids, WHO guidelines were considered [86]. For monosaturated and polyunsaturated fatty acids and omega 3 and omega 6 fatty acids, Nordic guidelines were accounted [11]. The European Society of Cardiology guidelines for the management of dyslipidaemias were followed for cholesterol [52]. Therefore, the prevalence of nutritional adequacy was described as the percentage of participants whose intake was within the reference range for macronutrients and above AR or AI for micronutrients and not exceeding the tolerable upper intake level whenever defined. For sodium and chloride, nutritional adequacy was considered whenever intake was equal to or below safe and adequate intake [20, 35].

Physical activity

Physical activity levels were evaluated using the short version of the International Physical Activity Questionnaire (IPAQ) [73], which is widely validated and used in diverse populations. The IPAQ enables comparability of physical activity data across studies and provides a flexible framework for capturing the duration and intensity of walking, moderate, and vigorous activities without the need for specialized equipment. This makes the instruments especially suitable for populations with physical limitations, as those with ACH. Physical activity is quantified in metabolic equivalents of task (MET-minutes/week) and categorized as inactive (PAL1), minimally active (PAL2), or highly active (PAL3).

Data analysis

Statistical analysis was performed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA) with a significance level set at $p < 0.05$. Descriptive statistics were calculated for continuous variables, with frequencies and percentages used to summarize categorical variables like gender and physical activity levels. Shapiro–Wilk test was used to assess the normality of continuous variables. Variables not normally distributed were analysed using non-parametric tests. Independent *t*-test was used to compare normally distributed continuous variables between men and women, including anthropometric and body composition variables with effect size measured by Cohen *d*, and the Mann–Whitney *U* test was applied for non-normally distributed variables to compare differences in nutrient intake and physical activity levels between genders, with effect size measured by rank biserial correlation (rbc). The critical value for 2-tailed Mann–Whitney *U* test, $p < 0.01$ was 7. Spearman's rank correlation coefficient (rho) was used to evaluate relationships between physical activity measures and nutrient intake. This approach was

prioritized over multiple regression modelling, considering the exploratory nature of this study and small sample. No missing data were present for primary outcomes. For dietary recalls, any incomplete entries (<5%) were handled using multiple imputations. Given the rarity of ACH (1:25,000) and an estimated Portuguese population of 10 million, our sample of 16 participants represents approximately 3.2% of the estimated ACH population in Portugal (≈ 500 individuals). Effect sizes for Cohen *d* were considered as small (*d*=0.2), medium (*d*=0.5), and large (*d*≥0.8), while for Spearman’s rank correlation (ρ , ρ) these were also interpreted according to Cohen’s conventions: small (ρ =0.10–0.29), medium (ρ =0.30–0.49), and large (ρ ≥0.50) [24]. All statistical comparisons are reported regardless of significance threshold, with effect sizes provided to support interpretation given the exploratory sample size.

While this sample size limits statistical power, it provides valuable exploratory data for this rare condition. Post-hoc power analysis indicated adequate power (0.8) to detect large effect sizes (*d*=0.8) at α =0.05 for primary outcomes.

Results

Anthropometric and body composition characteristics

This study included 16 adults with ACH (10 women, 6 men) with a mean age of 38.2±13.8 years (21 to 57 years old). Among our participants, 62.5% (10/16) presented

a body mass index (BMI) > 30 kg/m² (95%CI 24.7–58.7). Yet, on the other side, 43.75% (7/16) presented a waist-to-hip ratio over WHO cut-off points, with just 1 woman presenting a ratio of 0.85 and all men (6/6) a ratio above ≥0.90 [83], with significant gender differences observed. The mean fat mass percentage (FM%) was high among participants (95%CI 7–47.6). Values from our study sample are shown in Table 1, as well as reference values for body composition from (a) a study in the general Portuguese population (PT) [7]; (b) another study in adults with achondroplasia (ACH) [54] and (c) a study with 10 adult men with achondroplasia [72].

Comorbidity Profile

Comorbidity analysis revealed sleep apnea in 25% (4/16) of participants, spinal stenosis symptoms in 18.75% (3/16), with 6.25% (1/16) having a history of foramen magnum decompression surgery. Additionally, 18.75% (3/16) used medication for chronic pain. Among all participants, 18.75% were smokers (3/16). These comorbidities may influence both dietary patterns and physical activity engagement.

Nutritional adequacy

The consumption of additional foods beyond those listed in the FFQ was also asked of participants, and the following additional foods have been mentioned: 3 participants (vegetarians) reported eating veggie burgers, seitan, tofu,

Table 1 Anthropometric measurements and body composition parameters of adults with achondroplasia, with significant differences between genders identified. Means and standard deviation presented comparison between women and men were performed using independent sample t-tests and effect size (Cohen *d*). Reference data from studies a., b. and c. is also presented. All p-values are reported

	<i>a. Reference values</i> PT (n = 392)	<i>b. Reference values</i> ACH (M = 15 W = 18)	Total sample (n = 16)	Women (n = 10)	Men (n = 6)	p-value	Effect size (Cohen <i>d</i>)
Age (years)	49.5±10.6	40±15	38.4±13.8	36.6±15.2	41.0±11.8	0.555	0.312
Height (cm)	164±9.2	130±6.9 (W) 135±9.2 (M)	126.0±12.7	123.1±11.4	130.0±14.5	0.307	0.548
Body mass (kg)	71.7±14.4	55.6±9.5 (W) 66.3±16.4 (M)	53.5±14.7	48.9±10.4	61.1±18.5	0.112	0.875
Body mass index-BMI (kg/m ²)	26.3±4.5	34.1±7	35.8±11.4	32.5±6.8	36.8±13.1	0.400	0.4548
Waist circumference (cm)		82.2 (W) 94.1 (M)	83.9±14.6	79.3±10.5	91.7±18.0	0.103	0.901
Hip circumference (cm)			102.2±11.4	103.0±8.23	100.0±16.2	0.625	0.258
Waist-to-hip ratio			0.82±0.09	0.77±0.07	0.91±0.05	<0.001	2.258
Mid upper arm girth (cm)			30.1±3.9	30.1±4.4	30.3±3.3	0.926	0.049
Fat mass (%)	20.7±8.8	c. 29.3±2.9	27.0±10.5	27.4±7.5	26.5±15.2	0.872	0.085
Lean mass (%)			68.6±11.3	67.3±9.3	70.8±14.8	0.567	0.302
Bone mineral mass (%)			3.8±0.6	3.7±0.4	3.8±0.8	0.815	0.123
Body water (%)			55.0±9.5	52.7±6.4	58.8±12.9	0.226	0.654

soy drinks, and vegetable yogurts weekly; 1 participant reported eating blueberries, blackberries, and raspberries 5 to 6 times a week, and another participant reported eating mango once weekly.

Energy and macronutrient intake

The median (percentile 25–75) for daily total energy intake (TEI) was 1742.42 kcal (1381–2497), with a macronutrient distribution of 16.85 ± 4.0% for proteins, 50.62 ± 8.80% for total carbohydrates, and 33.13 ± 5.37% for total fat.

EFSA DRVs finder online tool was applied to verify TEI for each participant according to the specific age and considering their specific physical activity level (PAL=1.4, 1.6, 1.8, and 2.0). Significant gender differences with large size effects were observed for TEI, with women consuming a median of 1416.82 kcal while men presented a median intake of 2643.40 kcal (*d*=2.69, *p*<0.001). Differences were also observed for total carbohydrates (*d*=2.19, *p*<0.001), proteins (*d*=2.09, *p*=0.001) and total fat (*d*=1.76, *p*=0.004). To highlight that 25% (4/16) of our participants presented a TEI above average requirement (3/6 men, 1/10 women). Daily energy and macronutrient intake of participants are presented in Table 2.

All participants had intakes within the protein recommendations [21]. However, when the total protein intake (in g) was adjusted for each participant’s body mass, we

found that 50% (8/16) had an intake between 0.66 and 1.5 g/kg body mass, 18.75% (3/16) had an intake above 1.5 and below 2 g/kg body mass, and 25% (4/16) had an intake above 2 g/kg body mass. Only one participant had a protein intake below 0.66 g/kg body mass. For carbohydrates, 12.5% (2/16) had intakes above the reference range and 12.5% (2/16) did not reach 45% of the TEI. For total fat intake, 25% (2/16) had an intake greater than 35% of the TEI, with 43.75% (7/16) exceeding reference values for saturated fat and the same proportion for cholesterol. However, the recommended intakes of polyunsaturated fatty acids (PUFAs), especially omega-3, were not met by any of the participants. In addition, 56.25% (9/16) of participants did not meet fiber intake recommendations. Positive correlations were observed between waist to hip ratio with caloric intake (*r*=0.67, *p*=0.005) and with carbohydrates (*r*=0.65, *p*=0.006).

Micronutrients intake

In our study, the micronutrients vitamin D, vitamin K, biotin, manganese, and molybdenum were those with the highest probability of inadequacy, as none of the participants reached the AI. Iodine and vitamin E were also at risk of inadequacy, with only 18.75% of participants reaching the AI. Sodium intake exceeded the safe and adequate intake in 75% of participants. Importantly, the intake of micronutrients did not exceed the tolerable upper intake level, whenever defined, in any of the

Table 2 Daily energy and macronutrients intake of adults with achondroplasia. Values presented as medians, percentiles and percentages. All p-values are reported and significant gender differences in energy and macronutrients intake when *p*<0.05

Macronutrients	Dietary reference values	% Within adequacy	All (n = 16) median (P25–P75)	Women (n = 10) median	Men (n = 6) median	p-value	Effect size (Cohen d)
Energy intake (kcal)	a)	75.00	1742.47 (1381–2497)	1416.82	2643.40	<0.001	2.690
Protein (g)	–	–	85.39 (55.2–113.0)	56.59	125.47	0.001	2.090
Total carbohydrates (g)	–	–	225.46 (168.0–311.0)	171.55	311.52	<0.001	2.190
Total fat (g)	–	–	61.59 (52.4–95.8)	54.63	101.66	0.004	1.760
Protein (%TEI)	10–35%	100	16.85 (14.6–19.7)	16.72	17.94	0.507	0.352
Total carbohydrates (%TEI)	45–60%	75	50.62 (47.3–53.4)	49.39	51.60	0.444	0.407
Total fat (% of TEI)	20–35%	68.75	34.13 (32.1–34.9)	34.13	34.09	0.614	0.266
Saturated fatty acids (%TEI)	< 10%	56.25	9.74 (8.88–10.7)	10.53	8.94	0.464	0.389
Trans fat acids (%TEI)	< 1%	100	0.42(0.34–0.51)	0.50	0.34	0.166	0.755
MUFA (%TEI)	10–20%	87.5	15.03 (14.1–16.0)	14.57	15.76	0.975	0.016
PUFA (%TEI)	5–10%	75	5.60 (4.94–6.14)	5.86	5.16	0.399	0.449
Omega 3 (%TEI)	At least 1%	0	0.53 (0.44–0.60)	0.53	0.53	0.733	0.180
Omega 6 (%TEI)	At least 3%	87.5	4.01 (3.55–4.49)	4.20	3.75	0.055	1.081
Omega 6/omega 3 ratio	–	–	7.38 (6.90–8.41)	7.61	7.0	0.449	0.403
Cholesterol (mg)	< 300 mg	56.25	294.37 (217–410)	250.58	386.39	0.173	0.742
Dietary fiber (g)	≥ 25 g	43.75	23.37 (8.17–26.80)	20.56	25.02	0.117	0.864

Abbreviations: TEI, total energy intake. a) EFSA DRVs finder online tool was applied to verify TEI for each participant accordingly the specific age and considering their specific physical activity level

respondents. Significant differences with large effect sizes ($d=1.37$ to 2.74) were found between gender for many micronutrients, with men presenting higher intake, except for vitamin K, as presented in Table 3. It is important to note that in the study population, it was observed that only three participants were on a vegetarian diet, one of whom was on a vegan diet. In addition, only three participants reported taking multivitamin supplements, including the vegan participant. These supplements were not considered for nutrient adequacy.

Physical activity patterns

Physical activity level (PAL) obtained using the IPAQ revealed two groups: PAL1, with low physical activity or “inactive” representing 56.25% (9/16) and PAL2 with moderate activity or “minimally active” representing 43.75% (7/16), with our participants presenting a markedly lower percentage of moderate activity than those reported in the general Portuguese population. The

IAN-AF 2015–2016 study, which found that 57.7% of Portuguese adults achieved moderate to high physical activity levels [51] while in our study only 43.75% (7/16) met WHO minimum recommendation of 600 MET-minutes/week[85]. The mean total physical activity score was 878.2 ± 816.7 MET-minutes/week, positively influenced by two more active participants, both men. Significant gender differences were observed for moderate physical activity, as presented in Table 4.

Associations between physical activity and nutritional variables

Significant differences ($p < 0.05$) with small effect sizes were found between physical activity levels (PAL1 and PAL2) for dietary fiber ($rb = 1.11$), vitamin A ($rb = 1.23$), calcium ($rb = 1.38$), biotin ($rb = 1.38$), chloride ($rb = 1.51$, $p = 0.01$) and iodine ($rb = 1.23$). Strong correlations ($p < 0.001$) were found between physical activity score and fat mass % ($\rho = 0.802$), lean mass % ($d = 0.786$) and

Table 3 Daily energy and micronutrients intake of adults with achondroplasia. Values presented as medians, percentiles and percentages. All p-values are reported and significant gender differences in micronutrients intake when $p < 0.05$

Micronutrients	Daily reference values	% Within adequacy	All (n = 16) Median (P25–P75)	Women (n = 10) Median	Men (n = 6) Median	p-value	Effect size (Cohen d)
Total vitamin A (µg)	570 µg	93.75	1455.38 (892–1974)	1480.40	1455.38	0.928	0.047
Thiamine (mg/MJ)	0.072 mg/MJ	100	0.18 (0.17–0.19)	0.18	0.17	<0.001	2.382
Riboflavin (mg)	1.3 mg	68.75	1.74 (1.2–2.4)	1.25	2.53	<0.001	2.695
Niacin (mg/MJ)	1.3 mg/MJ	100	2.45 (2.1–2.8)	2.46	2.25	0.007	1.643
Vitamin B6 (mg)	1.5 mg M; 1.3 mg F	75.00	1.85 (1.3–2.5)	1.415	2.52	0.020	1.352
Vitamin B12 (µg)	4 µg	75.00	5.54 (4.3–11.0)	4.7	12.74	0.003	1.828
Folate (µg)	250 µg	68.75	315.06 (231–375)	294.83	329.62	0.392	0.456
Pantothenic acid (mg)	5 mg	25.00	4.05 (2.8–4.9)	2.88	5.38	<0.001	2.744
Vitamin C (mg)	90 mg M; 80 mg F	81.25	138.01(114–161)	127.13	148.71	0.563	0.306
Vitamin D (mg)	15 mg	0	2.86 (1.5–4.7)	1.89	4.21	0.397	0.451
Vitamin E (mg)	13 mg M; 11 mg F	18.75	9.12 (6.3–12.3)	7.09	12.46	0.011	1.502
Vitamin K (µg)	70 µg	0	17.82 (11.0–25.9)	18.54	16.72	0.818	0.121
Calcium (mg)	A:860 mg; B:750 mg	56.25	827.18 (521–1146)	609.67	1412.34	<0.001	2.410
Copper (mg)	1.6 mg M; 1.3 mg F	56.25	1.52 (1.1–1.9)	1.09	2.18	0.002	2.007
Iron (mg)	6 mg (pre-M 7 mg)	100	15.27 (9.9–17.3)	10.67	18.18	0.003	1.872
Magnesium (mg)	350 mg M; 300 mg F	50.00	331.51 (223–393)	225.5	402.24	<0.001	2.193
Manganese (µg)	3 mg	0	3.41 (2.5–3.5)	2.58	3.50	0.011	1.561
Phosphorous (mg)	550 mg	93.75	1416.88 (817–1623)	858.6	1832.6	<0.001	2.563
Potassium (mg)	3500 mg	43.75	3263.87 (2231–4238)	2314.5	4764.6	<0.001	2.407
Selenium (µg)	70 µg	56.25	81.52 (58.2–107)	63.95	112.8	0.019	1.367
Sodium (mg)	2 g	25.00	3321.5 (2293–3815)	2476.1	3956.1	0.002	1.956
Zinc (mg)	7.5 mg M; 6.2 mg F	93.75	10.96 (6.9–14.0)	7.2	14.8	<0.001	2.535
Biotin (µg)	40 µg	0	11.81 (6.0–14.3)	7.9	18.1	0.013	1.470
Chloride (mg)	3.1 g	100	653.67 (430–978)	513.1	983.7	0.009	1.552
Iodine (µg)	150 µg	18.75	52.50 (30.8–107.0)	35.4	174.6	0.001	2.044
Molybdenum (µg)	65 µg	0	7.19 (3.8–9.4)	6.8	7.6	0.414	0.435

Abbreviations: pre-M pre-menopausal, M male, F female, A:18 to 24 years, B: ≥25 years

Table 4 Physical activity measures of adults with achondroplasia represented as MET-min total/week and levels. All p-values are reported. Reference value for physical activity level from Lopes et al. [51]

Measure	Reference values %	All (n = 16)	Women (n = 10) mean	Men (n = 6) mean	p-value	Effect size (rbc)
MET-min total/week		878.2 ± 816.7	696 ± 614	1181 ± 1071	0.551	0.200
W_MET (MET-min)		486.0 ± 486.0	516 ± 497	434.0 ± 507.0	0.549	0.200
M_MET (MET-min)		113.0 ± 173.0	20.0 ± 43.2	267.0 ± 202.0	0.006	0.783
V_MET (MET-min)		280.0 ± 521.0	160.0 ± 320.0	480.0 ± 744.0	0.381	0.250
PAL 1 (%)		56.3	70.0	33.3		
PAL 2 (%)	57.7	43.8	30.0	66.7		

Abbreviations: W_MET walking, M_MET moderate-intensity activities, V_MET vigorous-intensity activities, PAL physical activity level

bone mass % ($d=0.782$). Other correlations were found between moderate intensity activities (M_MET) with carbohydrates intake ($\rho=0.734$, $p=0.001$), and also with riboflavin ($\rho=0.768$, $p<0.001$), calcium ($\rho=0.643$, $p=0.007$), magnesium ($\rho=0.693$, $p=0.003$), manganese ($\rho=0.693$, $p=0.002$), potassium ($\rho=0.718$, $p=0.002$), and iodine ($\rho=0.633$, $p=0.008$). Also, moderately strong associations were found between M_MET and calcium ($R^2=0.50$, $p=0.002$) and with iodine ($R^2=0.609$, $p<0.001$).

Discussion

This exploratory study provides novel insights into nutritional adequacy and physical activity patterns in Portuguese adults with ACH. Our findings reveal an interplay of factors related to this rare condition: high obesity, specific micronutrient inadequacies affecting bone and metabolic health, and low physical activity levels in most participants. The distinct anthropometric features of achondroplasia, disproportionate short stature with reduced limb-to-torso ratio, appear to be associated with these outcomes, particularly in regard to obesity tendency and physical activity engagement [1]. Obesity in achondroplasia appears to involve mechanisms beyond traditional energy balance, including potential FGFR3-related metabolic alterations and atypical fat distribution patterns that distinguish it from typical obesity. This finding suggests that standard obesity prevention and management strategies may require population-specific adjustments for individuals with achondroplasia [69]. Given the exploratory nature of this study and the multifactorial relationships identified, our study results provide groundwork for larger and longitudinal investigations to establish evidence-based interventions for this population.

Anthropometry, body composition, and obesity

The elevated fat mass percentage and high prevalence of BMI > 30 kg/m² observed in 62.5% of our participants

aligns with previous research demonstrating elevated obesity risk in individuals with ACH. When comparing the results from our participants to those found in a larger Portuguese study with 393 adults [7], our participants' BMI was superior (35.8 ± 11.4 kg/m² vs 26.3 ± 4.5 kg/m², respectively) as well as the FM% ($27.0 \pm 10.5\%$ vs 20.7 ± 8.8 , respectively), yet when comparing to values from a study by Sims et al. [72] with 10 adult men with achondroplasia, our participants presented lower FM% (29.3 ± 2.9 vs 27.0 ± 10.5 , respectively). While we observed discrepancies between BMI and fat mass percentage (FM%) among our participants, these findings likely reflect the inherent limitations of BMI as a measure of adiposity in individuals with achondroplasia [33]. Skeletal dysplasias such as achondroplasia are characterized by disproportionate short stature and altered body proportions, which can lead to BMI underestimating or misclassifying adiposity compared to direct body composition analyses. Additionally, standard bioelectrical impedance (BIA) and dual-energy X-ray absorptiometry (DXA) methods may also be less accurate in this population due to unique limb geometry and fat distribution patterns [17, 29]. These challenges highlight the importance of using multiple assessment tools and interpreting body composition data with caution in skeletal dysplasia populations.

The waist-to-hip ratio results provide additional context for obesity assessment. While nearly all women met WHO standards (<0.85), men exceeded the recommended threshold (≥ 0.90), indicating central adiposity concerns despite the complex BMI interpretation. These findings emphasize the necessity of employing multiple anthropometric tools when assessing adiposity in achondroplasia populations. Alternative indices, such as trunk fat mass divided by sitting height squared (TF/sH²), may provide a more accurate obesity assessment in this population [5].

Macronutrient nutritional adequacy

The macronutrient distribution in our study population largely aligned with EFSA/IOM recommendations for reference intake range (RI), expressed as the proportion (%) of energy derived from that macronutrient, with most participants falling within the recommended ranges for proteins, total fat, and carbohydrates. Most participants showed energy intakes within DRV, with 9 out of 10 women presenting an adequate energy intake that may underline a conscious effort to manage weight, given the propensity for obesity in ACH. Importantly, although protein intakes are within the IOM range of 10–35% of TEI for all participants when protein intakes (g) are adjusted for participants' body mass, 25% have intakes greater than 2 g/kg body mass. Although this higher intake occurs almost exclusively in participants with a high PAL, and given the musculoskeletal challenges associated with ACH, it is important to consider this aspect individually in the dietary management of adults with ACH, as chronic protein intake above 2 g/kg of body mass may be associated with metabolic disturbances [41, 56, 88]. Although our participants presented lower median saturated fat intake compared to general Portuguese adult populations (IAN-AF 2015–2016) [51] 9.74% vs 10.2% TEI respectively, still 43.75% of participants had an intake of saturated fat above 10% of TEI. The same percentage showed an intake of cholesterol above 300 mg/day, which combined with the high probability of omega 3 fatty acid inadequacy (none of the participants met the Nordic recommendations), may increase the risk of metabolic and cardiovascular diseases [14, 38, 39, 79]. This situation may reinforce the increased omega-6/omega-3 ratio observed in our study. According to research, the human body can maintain optimal health with an intake ratio of omega-6/omega-3 of 5:1. As the intake of n-6 PUFA-rich diets increases, so does the incidence of metabolic syndromes, which may be caused by the activation of inflammatory pathways [10]. It is also important to note that more than half of the participants did not meet the recommended 25 g of dietary fiber per day [22], yet still, our participants presented a higher dietary fiber intake compared to the general Portuguese adult populations (IAN-AF), with a median intake of 23.4 g vs 17.2, respectively.

Fiber has important physiological roles, not only in increasing satiety but also in modulating the gut microbiome and lipoprotein metabolism, which together are important for obesity and its associated metabolic abnormalities prevention [36, 45, 46, 78] and should be promoted in this particular population.

Micronutrient nutritional adequacy

In terms of micronutrient intakes, vitamin D, vitamin K, biotin, manganese, and molybdenum stand out as having the highest probability of inadequacy, as none of the participants reached the AI, and there is also a high risk of inadequacy for iodine, vitamin E, and pantothenic acid. In addition, sodium intake exceeded the safe and adequate intake in 75% of participants.

The high probability of inadequacy for vitamin D observed in our study aligns with the findings from Madssen et al. [54], who also reported low vitamin D intake in Norwegian adults with ACH. And while an adequate vitamin D intake is critical for bone health and may have additional benefits in reducing inflammation and improving muscle function [12], an insufficient intake among individuals with ACH, who are already predisposed to skeletal complications, may negatively influence the occurrence of spinal stenosis [42] and osteoarthritis [2, 32]. Furthermore, emerging research suggests that vitamin D deficiency may contribute to increased inflammation, which could potentially worsen the chronic pain often experienced by individuals with ACH [42]. Although 56.25% of participants in our study presented an intake within DRV for calcium, this combined with low vitamin D could potentially be an added challenge to bone health in adults with ACH [57].

In the IAN-AF study [51], there was also a high prevalence of inadequacy for sodium, with 76.4% of Portuguese (63.2% of women and 88.9% of men) exceeding the maximum tolerated value (UL). This prevalence was higher in adults (79.7%) and adolescents (74.7%) which is aligned with our study, with only 25% of participants presenting an intake within recommendations. In addition, many studies demonstrate that populations worldwide consume much more sodium than is physiologically necessary, exceeding 2 g sodium/day (equivalent to 5 g salt/day) [84]. This higher sodium intake observed among our participants, associated with a probable potassium inadequacy in more than half of the participants, can add extra concern as it may contribute to increased blood pressure and cardiovascular risk [80, 84]. Another important and related finding, as magnesium depletion may contribute to hypertension and cardiovascular events [3] is that only 50% of the participants reached the reference values for magnesium. Together, these findings highlight the importance of monitoring sodium intake and additionally promoting potassium and magnesium intake to prevent hypertension and cardiovascular risk in this population.

Inadequate iodine intake has been observed for decades in populations considered to be iodine sufficient [13]. Machado et al., using a 24-h dietary recall, found a median iodine intake of 58 µg/day (51 and 68 µg/day in women and men, respectively) [53] which is in line with

the median found in our study, 52.50 µg/day. However, in our study, women have a significantly lower median than men (35.4 µg/day versus 174.6 µg/day). In a recent report, the World Health Organization (WHO)/Europe and the Iodine Global Network noted that the increasing popularity and availability of plant-based alternatives to major iodine sources, such as milk, dairy products, and fish, is contributing to persistent and increasing iodine insufficiency in the WHO European Region. This situation can put women at increased risk, particularly during pregnancy when iodine requirements are higher [87]. Salt iodization is the main strategy to prevent iodine deficiency at the population level [9, 13] and may be an important nutritional strategy for this population.

Gender differences in vitamin E intake ($d=1.52$, $p=0.011$) persisted after adjustment for energy intake. A high probability of vitamin E inadequacy was also found in different studies [71] [60, 71, 75]. In our study, women had a significantly lower median intake of vitamin E compared to men (7.09 mg versus 12.46 mg). Interestingly, a study in the north region of Portugal reported high vitamin E inadequacy (83%) in women prior to pregnancy [63]. Vitamin E deficiency seems more likely in situations of fat restriction or fat malabsorption, as it is a fat-soluble vitamin, which can be found in several diseases such as inflammatory bowel disease [75].

Regarding vitamin K, there is less evidence on the adequacy; however, given that the concentration of vitamin K in most foods is very low (< 10 µg/100 g) and that most of the vitamin is obtained from a few green leafy vegetables and four vegetable oils (soya, cottonseed, rapeseed and olive), which contain high levels, inadequacy may occur. Contrary to our results, a cross-sectional study of 238 adults from the Algarve region of Portugal found that only 10% of participants had a vitamin K intake below the adequate intake [63].

Biotin, manganese, molybdenum, and pantothenic acid deficiencies due to inadequate dietary intake are rare [40, 62] and research on dietary adequacy is lacking. It was therefore quite unexpected to observe that none of the participants reached the AI for the above micronutrients (except for pantothenic acid, but only 25% achieved the AI), as they are widely available in a variety of foods.

Comorbidity impact on nutritional and physical activity outcomes

The substantial comorbidity burden observed among our participants provides important context for interpreting our nutritional and physical activity findings. The 25% prevalence of sleep apnea is very low compared to previous studies that found nearly 50% of sleep apnea in adults with achondroplasia [28]. This may be due to the self-reported data and underestimate of the diagnosis by

the participants. Sleep-disordered breathing affects appetite regulation through documented alterations in key hormonal pathways [70] that promote increased appetite and preference for high-calorie, energy-dense foods [66].

The 18.75% prevalence of chronic pain requiring medication is consistent with literature reporting chronic pain in 64–70% of adults with achondroplasia [27]. Pain-related medications can also affect appetite and nutrient absorption, while chronic pain-associated mood changes may influence food choices through comfort eating behaviors or appetite suppression [59, 67]. The strong correlation observed between physical activity scores and body composition ($r=0.78$ – 0.80) may be partially mediated by pain-related activity limitations.

Physical activity and nutrition interactions

The physical activity levels observed in our study population are below recommended levels, with 56.25% categorized as inactive or with low physical activity, which may have significant implications for nutritional needs and overall health. Participants showed having lower weekly activity compared to the general adult population [30] and below the threshold of WHO recommendation of at least 600 MET-minutes/week of physical activity [85]. The reduced physical activity levels in adults with ACH may be attributed to various factors, including physical limitations, pain, or fear of injury [19]. This inactivity contributes to decreased energy expenditure, while concurrent obesity exacerbates mobility restrictions through increased joint loading, chronic inflammation, and metabolic dysfunction [23, 37]. Likely, the observed physical activity limitations in ACH adults likely represent a self-perpetuating cycle.

Moreover, sedentary behavior has been associated with increased inflammation and insulin resistance, which could exacerbate the glucose metabolic changes identified in this population [8, 69]. The strong correlation between physical activity score and fat mass percentage indicates robustly that, in this population, a complex relationship between energy intake, expenditure, and body composition may exist.

Higher physical activity levels often correlate with better dietary habits, as demonstrated by comprehensive reviews of European adult populations, which show that more active individuals tend to have healthier dietary patterns and overall better diet quality [26].

Positive correlations and associations were found between M_MET and some micronutrients, whose intake has been associated with physical activity. One of these micronutrients is riboflavin, which is crucial for energy production and the metabolism of fats, drugs, and steroids; riboflavin plays a role in maintaining a healthy metabolism. This sheds light on its association with

physical activity levels [64]. Another correlation was with potassium, which is vital for muscle function and cardiovascular health, important for electrolyte balance, and essential during physical activity [81]. Concerning iodine, this micronutrient is essential for thyroid function, which regulates metabolism. Adequate iodine intake can influence energy levels and metabolic rate [90] what may potentially affect physical activity capacity.

Implications and recommendations

The results of this study highlight the importance of nutritional assessment in adults with ACH. Personalized intervention with energy prescriptions adapted to requirements, considering individual physical activity levels, and monitoring of macro- and micronutrient intakes are important. Although the overall macronutrient intake is adequate, it is important to promote the consumption of omega-3 fatty acids and fiber in this population. Regarding micronutrients, given universal vitamin D inadequacy and skeletal comorbidities, routine supplementation (≥ 600 IU/day) should be prioritized alongside dietary counseling. Nutritional strategies to promote vitamin E and iodine adequate intake and to reduce sodium intake are also extremely important. In addition, considering the lack of research on vitamin K, biotin, manganese, pantothenic acid, and molybdenum adequacy, future studies with larger groups of individuals with ACH are important to confirm these findings.

Beyond nutritional adequacy, the strong M-MET-iodine association ($R^2=0.609$) suggests activity levels may indirectly influence thyroid metabolism, which should be further evaluated for weight management. Tailored physical activity program interventions to increase overall activity levels in this population should be developed. These programs should focus on low-impact exercises that improve cardiovascular health without putting excessive strain on the joints. Overall, regular monitoring of nutritional status and body composition using methods appropriate for individuals with ACH should be applied. Incorporating elements of the Mediterranean diet, such as increased consumption of fruits, vegetables, whole grains, legumes, fish, and olive oil, could potentially address some of the nutritional gaps observed in our study population.

Limitations

The small sample size reflects the condition rarity. The non-random sampling due to recruitment by one advocacy organization may differ from the overall community of people with achondroplasia, and being a study conducted solely in Portugal limits the generalizability of our findings. These factors may affect the representativeness of the results to broader populations

with achondroplasia. The multi-frequency bioelectrical impedance analyser used may have reduced accuracy in individuals with achondroplasia due to altered limb proportions and other potential factors still to unveil. Moreover, standard BMI calculations have not been validated for individuals with disproportionate short stature, potentially leading to misclassification of obesity status, and when existent, specific indices validated for this population should be used.

The tools used in this study, the FFQ and the IPAQ, rely on self-reported data, which can be subject to recall bias and misreporting. While FFQ is validated for general populations, ACH-specific portion size adaptations may improve accuracy given unique anthropometrics. Although the use of a FFQ with a 1-year recall period may be subject to recall bias, it is nonetheless considered a reference method for dietary assessment. By covering a longer reference period, the FFQ enables the estimation of usual intake, including foods that are consumed infrequently or seasonally, which may not be adequately captured by short-term dietary assessment methods. Although our analysis identified a high probability of micronutrient inadequacy, it is important to note that this does not equate to clinical micronutrient deficiency. The assessment reflects potential inadequacy in dietary intake, which, if sustained over time, may increase the risk of developing nutritional deficiencies. Further validation through biochemical assessment would be necessary to confirm actual deficiency status. The IPAQ is a general assessment tool and can under- or overestimate physical activity levels due to recall or social desirability bias, which could be assessed by cognitive debriefing to identify adapted physical activity metrics. The overall limitations can be overcome by future research that includes larger, more diverse, and multi-national participants to validate and extend these findings.

Conclusions

This exploratory study provides novel insights into nutritional adequacy and physical activity patterns in Portuguese adults with achondroplasia. Key findings reveal micronutrient inadequacies, particularly for vitamin D, biotin, and iodine, alongside low physical activity levels and high obesity prevalence. While macronutrient distributions aligned with recommendations, excessive saturated fat intake and insufficient omega-3 and fiber consumption present opportunities for dietary improvements. The disproportionate stature characteristic of ACH presents a challenge in obesity assessment using standard BMI thresholds. Our data reinforce the need for achondroplasia-specific adiposity metrics, as BMI may induce misclassifications. Future studies should validate these findings through biochemical assessments and

explore longitudinal relationships between diet, activity, and comorbidities in ACH.

Clinical trial number

Not applicable.

Acknowledgements

The authors gratefully acknowledge Sofia Almeida Costa and Catarina Campos Silva, members of the Nutritional Epidemiology research team, Institute of Public Health, University of Porto (ISPU) for the technical support in providing the semi-quantitative food frequency questionnaire applied in this study and for converting food consumption data into nutrient intake values.

Author contribution

I. A.: conceptualization, methodology, investigation, data curation, writing—original draft, writing—review and editing, visualization. MAC, ST, and OF: writing—review and editing. CDP: conceptualization, methodology, writing—review and editing, supervision.

Funding

This research is part of the doctoral project “Physical, biomechanical and psychological characterization associated with physical activity of individuals with ACH” supported by the Fundação para a Ciência e Tecnologia (FCT) fund, with reference UI/BD/154535/2022 and DOI <https://doi.org/10.54499/UI/BD/154535/2022>.

Data Availability

This study and data presented are openly available in Open Science Framework repository at <https://osf.io/qjtvz/>

Ethics approval and consent to participate

This study was approved by the Ethics Committee of University of Évora, under the number 22056, on the 6th of June 2022. A written informed consent was provided to all participants for their review before their inclusion in the study, and all participants gave consent, in adherence to the 1964 Declaration of Helsinki and its later amendments.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹School of Health and Human Development, CHRC, University of Évora, 7005 Évora, Portugal. ²ANDO Portugal, National Association for Skeletal Dysplasia, 7005 Évora, Portugal. ³School of Health Sciences, ciTechCare, CDRSP, Polytechnic University of Leiria, 2411 Leiria, Portugal. ⁴RoboCorp Lab, i2a-IPC Polytechnic Institute of Coimbra and CEMPRE (Centre for Mechanical Engineering, Materials and Processes), ARISE, University of Coimbra, 3030 Coimbra, Portugal. ⁵Department of Psychology and Education and Psychology Research Center, University of Évora, 7005 Évora, Portugal. ⁶ciTechCare-Center for Innovative Care and Health Technology, Leiria, Portugal. ⁷Laboratory of Separation and Reaction Engineering-Laboratory of Catalysis and Materials (LSRE-LCM), ESTG-IPLeia, Leiria 2411, Portugal. ⁸ALICE-Associate Laboratory in Chemical Engineering, University of Porto, Porto 4200, Portugal.

Received: 20 April 2025 Accepted: 18 July 2025

Published online: 23 July 2025

References

- Alade Y, Schulze K, McGready J, Koerner C, Henry B, Dlugash R, J H-F. Cross-sectional study of physical activity in adults with achondroplasia. *Adv Rare Dis*. 2014;1(2). <https://doi.org/10.12715/ard.2014.1.2>
- 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(3):237–43. <https://doi.org/10.1111/cge.12045>.
- AlShanableh Z, Ray E. Magnesium in hypertension: mechanisms and clinical implications. *Front. Physiol -Sec. Renal Physiology and Pathophysiology*. 2024;15. <https://doi.org/10.3389/fphys.2024.1363975>
- Alves I, Fernandes O, Castro M, & S.T. Physical Activity and Psychosocial Outcomes in Adults with Achondroplasia: An Exploratory Study. *Int J Environ Res Public Health*. 2024a;31(9):1160. <https://doi.org/10.3390/ijerph21091160>
- Alves I, Fernandes O, Castro MA, Tavares S, Pereira CD. Obesity and abdominal fat in adults with achondroplasia - PO54 XXII Congresso de Nutrição e Alimentação, Porto. 2023. https://actaportuguesadenutricao.pt/edicoes/https-actaportuguesadenutricao-pt-wp-content/uploads-2022-09-resumos_cna-2022_po-pdf-3/
- Alves I, Koromani F, Lemos C, Tavares S, Fernandes O, Pereira CD, Castro MA, Rivadeneira F. Facilitators and constraints of physical activity in adults with achondroplasia: a scoping review. *J Rare Dis*. 2024b;3(22). <https://doi.org/10.1007/s44162-024-00048-9>
- Araujo J, Farias F, Severo M, Ramos E, Lopes C, Nogueira L. Assessment of fat mass and fat-free mass in Portuguese youth and adults: calibration of bioelectrical impedance with dual-energy x-ray absorptiometry. *Research Square*. 2023. <https://doi.org/10.21203/rs.3.rs-3822008/v1>
- Ashok T, Puttam H, Tarnate V, Jhaveri S, Avanthika C, Treviño A, Ahmed N. Role of Vitamin B12 and Folate in Metabolic Syndrome. *Cureus*. 2021;13(10): e18521. <https://doi.org/10.7759/cureus.18521>.
- Bath S, Verkaik-Kloosterman JS, Borg M, Eilander S, Hora K, Aksoy B, Hristozova N, van Lieshout L, Besler H, Lazarus J. A systematic review of iodine intake in children, adults, and pregnant women in Europe—comparison against dietary recommendations and evaluation of dietary iodine sources. *Nutr Rev*. 2022;80(11):2154–77. <https://doi.org/10.1093/nutrit/nuac032>.
- Bishehkolaei M, Pathak Y. Influence of omega n-6/n-3 ratio on cardiovascular disease and nutritional interventions. *Human Nutrition & Metabolism*. 2024;37: 200275. <https://doi.org/10.1016/j.jhnm.2024.200275>.
- Blomhoff R, Andersen R, Arnesen E, Christensen J, Eneroth H, Erkkola M. Nordic Nutrition Recommendations 2023: Integrating Environmental Aspects. 2023. <https://doi.org/10.6027/nord2023-003>
- Bouillon R, Marcocci C, Carmeliet G, Bikle D, White J. Skeletal and Extraskelatal Actions of Vitamin D: Current Evidence and Outstanding Questions. *Endocr Rev*. 2019;40(4):1109–51. <https://doi.org/10.1210/er.2018-00126>.
- Brantsæter A, Knutsen H, Johansen N, Nyheim K, Erlund I, Meltzer H, Hensjum S. Inadequate iodine intake in population groups defined by age, life stage and vegetarian dietary practice in a Norwegian convenience sample. *Nutrients*. 2018;10(2):230. <https://doi.org/10.3390/nu10020230>.
- Briggs M, Petersen K, Kris-Etherton P. Saturated fatty acids and cardiovascular disease: replacements for saturated fat to reduce cardiovascular risk. *Healthcare*. 2017;21(2):29. <https://doi.org/10.3390/healthcare502029>.
- Castro-Quezada I, Román-Viñas B, Serra-Majem L. The Mediterranean diet and nutritional adequacy: a review. 2014;6(1):231–48. <https://doi.org/10.3390/nu6010231>.
- Clemente-Suárez V, Beltrán-Velasco A, Redondo-Flórez L, Martín-Rodríguez A, Tornero-Aguilera J. Global impacts of western diet and its effects on metabolism and health: a narrative review. *Nutrients*. 2023;15(12):2749. <https://doi.org/10.3390/nu15122749>.
- Coppini L, Waitzberg D, Campos A. Limitations and validation of bioelectrical impedance analysis in morbidly obese patients. *Curr Opin Clin Nutr Metab Care*. 2005;8(3):329–32. <https://doi.org/10.1097/01.mco.0000165013.54696.64>
- de Vries OM, Johansen H, Fredwall SO. Physical fitness and activity level in Norwegian adults with achondroplasia. *Am J Med Genet A*. 2021;185(4):1023–32. <https://doi.org/10.1002/ajmg.a.62055>.
- Dhiman N, Albaghdadi A, Zogg CK, Sharma M, Hoover-Fong JE, Ain MC, Haider AH. Factors associated with health-related quality of life (HRQOL) in adults with short stature skeletal dysplasias. *Qual Life Res*. 2017;26(5):1337–48. <https://doi.org/10.1007/s11136-016-1455-7>.
- EFSA. (2009). Scientific Opinion of the Panel on Dietetic products, Nutrition and Allergies on a request from European Commission related to labelling reference intake values for n-3 and n-6 polyunsaturated fatty acids. *The EFSA Journal*. 1176(11). <https://doi.org/10.2903/j.efsa.2009.1176>

21. EFSA. Scientific Opinion on Dietary Reference Values for protein. *EFSA J*. 2012;10(1):2557. <https://doi.org/10.2903/j.efsa.2012.2557>.
22. EFSA. Dietary reference values for nutrients summary report. European Food Safety Authority Supporting publication. 2017;14(12):e15121. <https://doi.org/10.2903/sp.efsa.2017.e15121>
23. Elagizi A, Kachur S, Carbone S, Lavie C, Blair S. A Review of Obesity, Physical Activity, and Cardiovascular Disease. *Curr Obes Rep*. 2020;9(4):571–81. <https://doi.org/10.1007/s13679-020-00403-z>.
24. Ellis P. *The Essential Guide to Effect Sizes: Statistical Power, Meta-Analysis, and the Interpretation of Research Results*. Cambridge University Press. 2010. <https://doi.org/10.1017/CBO9780511761676>.
25. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61(4):344–9.
26. European Commission, D.-G. f. H. a. F. S. (2018). Reviews of scientific evidence and policies on nutrition and physical activity. Objective B1: A comprehensive review of the scientific evidence about the source of calories consumed and types and frequency of physical activity among Europeans. EW-06–18–318-EN-N).
27. Fredwall S, AlSayed M, Ben-Omran T, Boero S, Cormier-Daire V, Fauroux B, Guillén-Navarro E, Innig F, Kunkel P, Lampe C, Maghnie M, Mohnike K, Mortier G, Pejin Z, Sessa M, Sousa SB, M I. European achondroplasia forum practical considerations for following adults with achondroplasia. *Adv Ther*. 2024;41(7):2545–2558. <https://doi.org/10.1007/s12325-024-02880-3>
28. Fredwall S, Øverland B, Berdal H, Berg S, Weedon-Fekjær H, Lidal I, Savarirayan R, Månung G. Obstructive sleep apnea in Norwegian adults with achondroplasia: a population-based study. *Orphanet J Rare Dis*. 2021;16(1):156. <https://doi.org/10.1186/s13023-021-01792-7>.
29. Fredwall SO, Linge J, Leinhard OD, Kjonigsen L, Eggesbo HB, Weedon-Fekjær H, Lidal IB, Manum G, Savarirayan R, Tonstad S. Cardiovascular risk factors and body composition in adults with achondroplasia. *Genet Med*. 2021;23(4):732–9. <https://doi.org/10.1038/s41436-020-01024-6>.
30. Haseler T, Haseler C. Lack of physical activity is a global problem. *BMJ*. 2022;376(8576): o348. <https://doi.org/10.1136/bmj.o348>.
31. Heidari S, Babor T, De Castro P, Tort S, Curno M. Sex and gender equity in research: rationale for the SAGER guidelines and recommended use. *Res Integr Peer Rev*. 2016;1(2):2. <https://doi.org/10.1186/s41073-016-0007-6>.
32. Hoover-Fong J, Cheung MS, Fano V, Hagenas L, Hecht JT, Ireland P, et al. Lifetime impact of achondroplasia: Current evidence and perspectives on the natural history. *Bone*. 2021;147:115902. <https://doi.org/10.1016/j.bone.2021.115872>.
33. Hoover-Fong J, Semler O, Barron B, Collett-Solberg P, Fung E, Irving M, Kitaoka T, Koerner C, Okada K, Palm K, Sousa S, Mohnike K. Considerations for anthropometry specific to people with disproportionate short stature. *Adv Ther*. 2025. <https://doi.org/10.1007/s12325-024-03061-y>.
34. Hruby A, Hu F. The epidemiology of obesity: a big picture. *Pharmacoeconomics*. 2015;33(7):673–89. <https://doi.org/10.1007/s40273-014-0243-x>.
35. IOM. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Institute of Medicine. 2005. <https://doi.org/10.17226/10490>
36. Ioniță-Mîndrican CZ, K, Mititelu M, Oprea E, Neacșu S, Moroșan E, et al. Therapeutic benefits and dietary restrictions of fiber intake: a state of the art review. *Nutrients*. 2022;26(13):2641. <https://doi.org/10.3390/nu14132641>
37. Jacinto M, Matos R, Alves I, Lemos C, Monteiro D, Morouço P, Antunes R. Physical activity, exercise, and sports in individuals with skeletal dysplasia: what is known about their benefits? [Review]. *Sustainability*. 2022;14(8).
38. Kaur G, Mason R, Steg G, Bhatt D. Omega-3 fatty acids for cardiovascular event lowering. *Eur J Prev Cardiol*. 2024;31(8):1005–14. <https://doi.org/10.1093/eurjpc/zwae003>.
39. Khan S, Lone A, Khan M, Virani S, R, B, et al. Effect of omega-3 fatty acids on cardiovascular outcomes: A systematic review and meta-analysis. *EClinicalMedicine*. 2021;8(38):100997. <https://doi.org/10.1016/j.eclinm.2021.100997>
40. Kippler M, Oskarsson A. Manganese – a scoping review for Nordic Nutrition Recommendations 2023. *Food & Nutrition Research*. 2024. <https://doi.org/10.29219/fnr.v68.10367>
41. Kitada M, Oguraa Y, Monnoa I, Koya D. The impact of dietary protein intake on longevity and metabolic health. *eBioMedicine*. 2019;43:632–40. <https://doi.org/10.1016/j.ebiom.2019.04.005>
42. Ko S, Kim H, Kwon J. The effectiveness of vitamin D3 supplementation in improving functional outcome of non-surgically treated symptomatic lumbar spinal stenosis: Randomized controlled clinical trial - Pilot study. *Medicine (Baltimore)*. 2023;102(40): e32672. <https://doi.org/10.1097/MD.00000000000032672>.
43. Kopp W. How Western diet and lifestyle drive the pandemic of obesity and civilization diseases. *Diabetes Metab Syndr Obes*. 2019;24(12):2221–36. <https://doi.org/10.2147/DMSO.S216791>.
44. Laederich M, Horton W. Achondroplasia: pathogenesis and implications for future treatment. *Curr Opin Pediatr*. 2010;22(4):516–23. <https://doi.org/10.1097/MOP.0b013e32833b7a69>.
45. Li H, Zhang L, Li J, Wu Q, et al. Resistant starch intake facilitates weight loss in humans by reshaping the gut microbiota. *Nat Metab*. 2024;6:578–97. <https://doi.org/10.1038/s42255-024-00988-y>
46. Li Y, Xia D, Chen J, Zhang X, Wang H, Huang L, et al. Dietary fibers with different viscosity regulate lipid metabolism via ampk pathway: roles of gut microbiota and short-chain fatty acid. *Poult Sci*. 2022;101(4):101742. <https://doi.org/10.1016/j.psj.2022.101742>.
47. Lim Y, Boster J. Obesity and Comorbid Conditions. In *StatPearls* (Ed.). 2024. <https://www.ncbi.nlm.nih.gov/books/NBK574535/>
48. Lopes C. Reprodutibilidade e Validação de um questionário semi-quantitativo de frequência alimentar. In: *Alimentação e Enfarte Agudo do Miocárdio: um estudo caso-controlado de base populacional*. Universidade do Porto]. Porto, Portugal. 2000.
49. Lopes C. Reprodutibilidade e Validação de um questionário semi-quantitativo de frequência alimentar In: *Alimentação e enfarte agudo do miocárdio: um estudo caso-controlado de base populacional*. 2000.
50. Lopes C, Azevedo A, Ramos E, Barros H. Intake and adipose tissue composition of fatty acids and risk of myocardial infarction in a male Portuguese community sample. *J Am Diet Assoc*. 2007;107(2):276–86. <https://doi.org/10.1016/j.jada.2006.11.008>.
51. Lopes C, Torres D, Oliveira A, Severo M, Alarcão V, Guiomar S, et al. Inquérito Alimentar Nacional e de Atividade Física, IAN-AF 2015–2016: Relatório de resultados. 2017. www.ian-af.up
52. Mach, F, Baigent, C., Catapano, A., Koskinas, K., M., C., L., B., M., C., G., D. B., V., D., B., F., I., G., A., H., T., L., & al, e. (2020). ESC Scientific Document Group. ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2019;1(1):111–88. <https://doi.org/10.1093/eurheartj/ehz455>.
53. Machado A, Gonçalves C, Moreira P, et al. Iodine intake assessment in the staff of a Porto region university (Portugal): the iMC Salt trial. *Eur J Nutr*. 2023;62:2245–56. <https://doi.org/10.1007/s00394-023-03149-1>.
54. Madsen A, Fredwall SO, Maanum G, Henriksen C, Slettaahjell HB. Anthropometrics, diet, and resting energy expenditure in Norwegian adults with achondroplasia. *Am J Med Genet A*. 2019;179(9):1745–55. <https://doi.org/10.1002/ajmg.a.61272>.
55. Maghnie M, Semler O, Guillen-Navarro E, Wiesel A, Maria Allegri AE, Seli-corni A, Lopez AGM, Heath K, Zampino G, Haeusler G, Hagenäs L, Leiva-Gea A, González VL, Raimann A, Simarro FS, Tajé S, Ertl DA, Gregersen PA, Landfeldt E, Mohnike K. Health-related quality of life (HRQoL) in achondroplasia: findings from a multinational, observational study [Conference Abstract]. *Mol Genet Metab*. 2021;132:127–8. [https://doi.org/10.1016/s1096-7192\(21\)00280-8](https://doi.org/10.1016/s1096-7192(21)00280-8).
56. Malhotra R, Cavanaugh K, Blot W, Ikizler T, Lipworth L, Kabagambe E. Higher protein intake is associated with increased risk for incident end-stage renal disease among blacks with diabetes in the Southern Community Cohort Study. *Nutr Metab Cardiovasc Dis*. 2016;26(12):1079–87. <https://doi.org/10.1016/j.numecd.2016.07.009>.
57. Matsushita M, Kitoh H, Mishima K, Kadono I, Sugiura H, Hasegawa S, Nishida Y, Ishiguro N. Low bone mineral density in achondroplasia and hypochondroplasia. *Pediatr Int*. 2016;58(8):705–8. <https://doi.org/10.1111/ped.12890>.
58. Merker A, Neumeyer L, Hertel N, Grigelioniene GM, K K, Hagenäs L. Development of body proportions in achondroplasia: Sitting height, leg length, arm span, and foot length. *Am J Med Genet A*. 2018;176(9):1819–29. <https://doi.org/10.1002/ajmg.a.40356>
59. Mohn E, Kern H, Saltzman E, Mitmesser S, McKay D. Evidence of drug-nutrient interactions with chronic use of commonly prescribed medications: an update. *Pharmaceutics*. 2018;20(1):36. <https://doi.org/10.3390/pharmaceutics10010036>.

60. Moshfegh A, Goldman J, Cleveland L. What we eat in America, NHANES 2001-2002 usual nutrients intakes from food compared to dietary reference intakes. 2005.
61. Pauli RM. Achondroplasia: a comprehensive clinical review. *Orphanet J Rare Dis*. 2019;14(1):1. <https://doi.org/10.1186/s13023-018-0972-6>.
62. Perry C, Butterick T. Biotin *Advances in Nutrition*. 2024;15(7): 100251. <https://doi.org/10.1016/j.advnut.2024.100251>.
63. Pinto E, Barros H, Santos Silva I. Dietary intake and nutritional adequacy prior to conception and during pregnancy: a follow-up study in the north of Portugal. *Public Health Nutr*. 2009;12(7):922–31. <https://doi.org/10.1017/S1368980008003595>.
64. Powers H. Riboflavin (vitamin B-2) and health. *Am J Clin Nutr*. 2003;77(6):1352–60. <https://doi.org/10.1093/ajcn/77.6.1352>.
65. Purnell J. Definitions, classification, and epidemiology of obesity (Vol. MDText.com, Inc.; 2000 [Updated 2023]). 2023. <https://www.ncbi.nlm.nih.gov/books/NBK279167/>
66. Reid M, Maras J, Shea S, Wood A, Castro-Diehl C, Johnson D, et al. Association between diet quality and sleep apnea in the Multi-Ethnic Study of Atherosclerosis. *Sleep*. 2019;42(12):zsy194. <https://doi.org/10.1093/sleep/zsy194>
67. Roche C, Burton A, Newton-John T. Eating to Feel Better: The Role of Comfort Eating in Chronic Pain. *J Clin Psychol Med Settings*. 2025. <https://doi.org/10.1007/s10880-025-10064-6>.
68. Saint-Laurent C, García S, Sarrazay V, Dumas K, Authier F, Sorel S, et al. Early postnatal soluble FGFR3 therapy prevents the atypical development of obesity in achondroplasia. *PLoS One*. 2018;13(4):e0196232.
69. Saint-Laurent C, Garde-Etayo L, Gouze E. Obesity in achondroplasia patients: from evidence to medical monitoring. *Orphanet J Rare Dis*. 2019;14(1):253. <https://doi.org/10.1186/s13023-019-1247-6>.
70. Sharma S, Kavuru M. Sleep and metabolism: an overview. *Int J Endocrinol*. 2010;2010: 270832. <https://doi.org/10.1155/2010/270832>.
71. Shim J, Kim K, Lee J, Yoon M, Lee H. Dietary intake and major source foods of vitamin E among Koreans: findings of the Korea National Health and Nutrition Examination Survey 2016–2019. *Nutr Res Pract*. 2022;16(5):616–27. <https://doi.org/10.4162/nrp.2022.16.5.616>.
72. Sims D, Onambele-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(3): e0213806. <https://doi.org/10.1371/journal.pone.0213806>.
73. Sjostrom M, Ainsworth B, Bauman A, Bull F, Hamilton-Craig C, Sallis J. Guidelines for data processing analysis of the International Physical Activity Questionnaire (IPAQ) - Short and long forms. 2005. <http://www.scienceopen.com/document?vid=b223350f-d159-4043-9b48-e2031f210a3c>
74. Stender M, Pimenta JM, Cheung M, Irving M, Mukherjee S. Comprehensive literature review on the prevalence of comorbid conditions in patients with achondroplasia. *Bone*. 2022;162: 116472. <https://doi.org/10.1016/j.bone.2022.116472>.
75. Szewczyk K, Górnicka M. Dietary vitamin E isoforms intake: development of a new tool to assess tocopherols and tocotrienols intake in adults. *Nutrients*. 2023;28(17):3759. <https://doi.org/10.3390/nu15173759>.
76. Torres D, Sousa N, Teixeira S, Soares R, Amorim H, Guiomar S, et al. Inquérito Alimentar Nacional e de Atividade Física, IAN-AF 2015–2016: Manual Fotográfico de Quantificação de Alimentos. (U. d. Porto, Ed.) 2017. www.ian-af.up.pt
77. Torres R, Real H. Literacia nutricional e literacia alimentar: uma revisão narrativa sobre definição, domínios e ferramentas de avaliação. *Acta Port Nutr*. 2021;24:56–63. <https://doi.org/10.21011/apn.2021.2411>
78. Waddell I, Orfila C. Dietary fiber in the prevention of obesity and obesity-related chronic diseases: From epidemiological evidence to potential molecular mechanisms. *Crit Rev Food Sci Nutr*. 2022;63(27):8752–67. <https://doi.org/10.1080/10408398.2022.2061909>.
79. Wang T, Zhang X, Zhou N, Shen Y, Li B, Chen B, Li X. Association between omega-3 fatty acid intake and dyslipidemia: a continuous dose–response meta-analysis of randomized controlled trials. *JAHA*. 2023;12(11): e029512. <https://doi.org/10.1161/JAHA.123.029512>.
80. Wang Y, Yeh T, Shih M, Tu Y, Chien K. Dietary sodium intake and risk of cardiovascular disease: a systematic review and dose-response meta-analysis. *Nutrients*. 2020;25(10):2934. <https://doi.org/10.3390/nu12102934>.
81. Weaver C. Potassium and health *Adv Nutr*. 2013;1(3):368S-377S. <https://doi.org/10.3945/an.112.003533>.
82. WHO. (2004). Global strategy on diet, physical activity and health.
83. WHO. (2008). Waist Circumference and Waist–Hip Ratio: Report of a WHO Expert Consultation W. Press.
84. WHO. (2012). WHO Guideline: Sodium intake for adults and children. (ISBN 978 92 4 150483 6).
85. WHO. (2020). WHO guidelines on physical activity and sedentary behaviour (ISBN 978–92–4–001512–8).
86. WHO. (2023). Saturated fatty acid and trans-fatty acid intake for adults and children: WHO guideline summary (World Health Organization, Issue. <https://iris.who.int/handle/10665/375034>
87. WHO. (2024). Prevention and control of iodine deficiency in the WHO European Region adapting to changes in diet and lifestyle [Licence: CC BY-NC-SA 3.0 IGO](ISBN 978–92–890–6119–3).
88. Wu G. Dietary protein intake and human health. *Food Funct*. 2016;7(3):1251–65. <https://doi.org/10.1039/c5fo01530h>.
89. Wynn J, King TM, Gambello MJ, Waller DK, Hecht JT. Mortality in achondroplasia study: a 42-year follow-up [Article]. *Am J Med Genet Part A*. 2007;143(21):2502–11. <https://doi.org/10.1002/ajmg.a.31919>.
90. Zimmermann M. Iodine deficiency. *Endocr Rev*. 2009;30(4):376–408. <https://doi.org/10.1210/er.2009-0011>.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.