Anthropometrics, diet, and resting energy expenditure in Norwegian adults with achondroplasia

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Abstract
Individuals with achondroplasia have a high prevalence of obesity and increased risk of cardiovascular disease. Fat distribution, diet, and caloric intake are known risk factors, but the literature concerning diet and energy balance in achondroplasia is limited. The main aim of this study was to describe the anthropometrics, diet, and resting energy expenditure (REE) in a Norwegian adult achondroplasia population. Here, we present a descriptive cross-sectional study with the following variables: anthropometrics, the SmartDiet questionnaire, and dietary records. In addition, REE was measured and estimated using indirect calorimetry and prediction equations. A total of 33 adults with achondroplasia participated with a mean age of 40 years. Mean body mass index was 34.1 kg/m², and mean waist circumference was 94.1 cm for men and 82.2 cm for women. Their diets were classified as unhealthy (38%) or in need of improvement (62%). The mean REE values for the total group were 21 kcal/kg for the male ($n = 15$) and 20 kcal/kg for the female ($n = 18$). This study revealed a high frequency of central obesity and unhealthy dietary habits in Norwegian adults with achondroplasia. Mean energy intake was low and only 10% higher than the mean REE, and does not explain the high prevalence of abdominal obesity in our population.

KEYWORDS
achondroplasia, body composition, body mass index, diet, resting energy expenditure, waist circumference

1 | INTRODUCTION

Achondroplasia (AHC [MIM: 100800]) is the most common skeletal dysplasia and results in a disproportionally short stature (Horton, Hall, & Hecht, 2007; Waller et al., 2008). The arms and legs are short, while the trunk has an almost normal size (Merker et al., 2018a). Previous studies have reported that individuals with achondroplasia have an increased risk of obesity starting from childhood, cardiovascular disease (CVD), and mortality (Hecht et al., 1988; Hecht, Francomano, Horton, & Annegers, 1987; Paajanen, Oksala, Kuukasjarvi, & Karhunen, 2010; Saint-Laurent et al., 2018; Wynn, King, Gambello, Waller, & Hecht, 2007). The reasons for this are currently unknown (Hecht et al., 1988; Paajanen et al., 2010; Wynn et al., 2007), but both genetic and lifestyle factors are likely involved (Hecht et al., 1988; Saint-Laurent et al., 2018; Trenkwalder, Kessler, Schunkert, & Erdmann, 2015).

Achondroplasia is caused by a mutation in the gene coding for fibroblast growth factor receptor 3 (FGFR3) (Ornitz & Legeai-Mallet, 2017) that results in increased FGFR3 signaling. This causes increased inhibition of chondrocyte differentiation and proliferation, resulting in decreased bone elongation (Ornitz & Legeai-Mallet, 2017).
Obesity and an unhealthy diet are two of the many identified risk factors for CVD in the general population (Hajar, 2017; Micha, Penalvo et al., 2017; Mongraw-Chaffin, Peters, Hudley, & Woodward, 2015). Obesity is defined as having a body mass index (BMI) over 30 kg/m² and is positively associated with CVD (Huxley, Mendis, Zheleznyakov, Reddy, & Chan, 2010; Mongraw-Chaffin et al., 2015). BMI, calculated from the body weight in kilograms divided by the square of the body height in meters, is the most common anthropometric tool used to assess weight and to classify obesity (Bastien, Poirier, Lemieux, & Despres, 2014). However, it is highly debated whether this is the most appropriate anthropometric measure to define excess body weight across ethnic groups (Huxley et al., 2010). Given its dependence on height, using BMI to measure body fat content may be problematic in achondroplasia (Hecht et al., 1988; Owen et al., 1990; Schulze, Alade, McGready, & Hoover-Fong, 2013). An increased waist circumference reflects central obesity among adults with average height, and waist circumference values of over 94 cm for men and over 80 cm for women increase the risk of metabolic complications (Nishida, Ko, & Kumanyika, 2010; Yusuf et al., 2005).

It is well established that diet affects the risk of CVD, directly and indirectly through factors such as blood pressure and cholesterol (Bechthold et al., 2017; Mente, de Koning, Shannon, & Anand, 2009; Micha, Shulkin et al., 2017). There is strong evidence for a causal link between dietary patterns and CVD risk (Mente et al., 2009). Micronutrient status is also important, for example, vitamin D and folate have been found to play protective roles in the cardiovascular system (Lamberg-Allardt, Brustad, Meyer, & Steingrimsdottir, 2013; Li et al., 2016; Staniewicz & Kenney, 2017; Van Guelpen et al., 2009; Zittermann, 2017). The Mediterranean diet is significantly associated with a reduced risk of CVD, while the Western diet is significantly associated with increased CVD risk (Mente et al., 2009; Micha, Penalvo et al., 2017).

Total energy expenditure (TEE) is the total amount of energy a person uses per day and includes resting energy expenditure (REE), thermogenesis, and physical activity (Mahan, Escott-Stump, & Raymond, 2012). TEE accounts for approximately 65–70% of an individual’s daily energy expenditure and is the amount of energy expended to sustain standard body functions, such as the maintenance of body temperature and circulation (Mahan et al., 2012; Owen et al., 1986; Owen et al., 1987). REE is an important factor in establishing daily energy requirements and evaluating adequate energy intake.

Obesity is an increasing problem in the general population but may confer even greater adverse consequences for individuals with achondroplasia. Excess weight can exacerbate common complications in achondroplasia such as sleep apnea, spinal stenosis, and leg deformities and probably also the risk of CVD (Hecht et al., 1988; Hoover-Fong, Schulze, McGready, Barnes, & Scott, 2008). To the best of our knowledge, there are no studies exploring the diets of adults with achondroplasia, and the knowledge of energy intake and expenditure is limited. The main aim of this study was to describe the anthropometrics, diets, and REEs of a Norwegian adult achondroplasia population.

### 2 | SUBJECTS AND METHODS

#### 2.1 | Subjects

Individuals were recruited from “The Norwegian Adult Achondroplasia Study”; a population-based cross-sectional study conducted at the Sunnaas Rehabilitation Hospital in collaboration with the TRS National Resource Centre for Rare Disorders. The subjects were successively recruited for nutritional screening on day 1 of admission. Participants were provided written and verbal information on the nutritional assessment methods by a doctor upon admission and consent was collected from all of the included subjects. The clinical diagnosis of achondroplasia was molecularly confirmed in all participants.

#### 2.2 | Methods

##### 2.2.1 | Anthropometrics

All investigations and measurements were performed during a 2.5-day stay at the Sunnaas Rehabilitation Hospital. Height and weight were measured in the morning with patients wearing light clothes and no shoes. Height was measured while patients were in a standing position, in centimeters, using a wall-mounted measuring tape (KaWe E-44444, Kirchner & Wilhelm GmbH + Co. KG, Asperg, Germany). Weight was measured using a digital weight (ADE Model M320600, ADE GmbH & Co. KG, Hamburg, Germany). Waist circumference was measured according to the recommendations provided by the World Health Organization in a standing position, using a nonstretchable measuring tape, from the midpoint between the lower margin of the lateral lower rib and the iliac crest (Nishida et al., 2010).

##### 2.2.2 | Diet and nutrient intake

A 4-day weighed dietary record and a food frequency questionnaire (SmartDiet) were used to collect dietary data. The SmartDiet questionnaire is a retrospective self-administered food and lifestyle questionnaire developed in Norway (Svilaas et al., 2002). It includes 21 questions about food choices and lifestyle habits, and the total score indicates how healthy and heart friendly the diet is. A score at or above 36 points indicates a heart-friendly diet according to Norwegian dietary recommendations; low intakes of saturated fat, salt, and sugars; good sources of dietary fiber and mono- and polyunsaturated fat (Helsedirektoratet, 2014). The SmartDiet questionnaire was used to record information about the participants’ general diet in addition to their self-reported dietary intake log. The participants were instructed on how to fill out the SmartDiet questionnaire when they were admitted to the Sunnas Rehabilitation Hospital and had access to a dietitian before and after filling out the questionnaire to address any questions or uncertainties. The participants required approximately 15 minutes each to complete the questionnaire.

Dietary record-keeping is a prospective method that provides detailed information about food and beverage consumption over a specified period of time (Ortega, Perez-Rodrigo, & Lopez-Sobaler, 2015). Participants were asked to fill out the dietary record on 4 consecutive
days including the weekend. To assist the participants in defining portion sizes, a picture book developed by the Department of Nutrition at the University of Oslo was used that contains photographs of food items at different stated amounts and weights (Totland et al., 2012). The participants were instructed not to change their eating habits during the 4 days of investigation. Data on intake of macro- and micronutrients were obtained from the 4-day dietary records calculated through an online diet tool from the Norwegian Directorate of Health and the Norwegian Food Safety Authority (Matportalen, 2017). Diet composition and intake of macro- and micronutrients were evaluated against the Nordic Nutrition Recommendations of 2012 (Tetens et al., 2014).

2.2.3 | Resting energy expenditure

The participants’ REE was measured at 8:00 a.m. in the morning in a room below the patient ward. Participants were instructed to take the elevator down to the test room and not to eat or drink for 12 hours prior to the test. A computerized standard open-circuit technique involving a breath-by-breath spirometer was used ($V_{max}$ Encore 229D, CareFusion Corporation, San Diego, CA). The equipment was calibrated before each test. To calibrate the gas analyzers, room air and medically certified calibration gases (16% O$_2$ and 4% CO$_2$/26% O$_2$ and 0% CO$_2$) were used. A 3-L calibration syringe was used for the volume calibration. The total test time was 15 minutes and the mean of the last 5 minutes was used in the statistical analyses. REE was also calculated using two different predictive equations: the Harris–Benedict equation (Roza & Shizgal, 1984) and the Mifflin–St. Jeor equation (Mifflin et al., 1990). Prediction of the daily heat production is made by the use of multiple regression equations. The Harris–Benedict equation for men is

$$h = 66.47 + 13.75w + 5.00s - 6.76a$$

and for women is

$$h = 655.10 + 9.56w + 1.85s - 4.68a$$

where $h$ = total heat production per 24 hours, $w$ = weight in kilograms, $s$ = stature in centimeters, and $a$ = age in years (Frankenfield, Muth, & Rowe, 1998). The Mifflin–St. Jour equation is

$$9.99w + 6.25h - 4.92a + 166 + s (males, 1; females, 0) - 161$$

(Mifflin et al., 1990).

2.2.4 | Statistical analysis

Descriptive statistics were used for the analyses on demographic data and test data from the nutritional screening. For parametric and normally distributed data, independent or paired sample t tests were used and the Mann–Whitney U-test was used for nonparametric analyses. Results are presented as means and SDs or as medians with their 25th and 75th percentiles. The Spearman correlation ($r$) coefficient was calculated to investigate the relationship between BMI and waist circumference. The statistical significance level was set at a $p$ value of <.05. All analyses were performed using the SPSS Statistics v25 software package (IBM United States Software).

2.2.5 | Ethical considerations

This study was approved by the Norwegian Regional Committee for Medical and Health Research Ethics South East (Approval No. 2016/2271). The project was carried out in accordance with The Declaration of Helsinki—ethical principles for medical research involving human subjects. All participants provided their written consent prior to inclusion in the study.

3 | RESULTS

3.1 | Study population

As shown in Figure 1, 33 adult individuals with achondroplasia participated in the study, 18 of which were women. A total of 32 participants completed the SmartDiet questionnaire and 20 participants completed the 4-day investigation. The characteristics of the study population are presented in Table 1. The mean age of the study population was 40 years ($\pm$15). A total of 12 of the participants worked or studied full time, 4 worked part time, 10 received full disability benefits, 4 received part-time disability benefits, two were unemployed, and one was retired.

3.2 | Height, weight, BMI, and waist circumference

The mean height for men and women was 135.1 cm and 130.7 cm, and the mean weight for men and women was 66.1 kg and 55.2 kg, respectively. The mean BMI of the study population ($N = 33$) was 34.1 kg/m$^2$, and its distribution is shown in Figure 2. None of the participants were classified as underweight, 3 individuals were of healthy weight, 5 were overweight, and 25 were classified as obese according to BMI. The BMI increased significantly with age ($r = .459, p < .01$).

The mean waist circumference was 94.1 cm and 82.2 cm for men and women, respectively. An increased waist circumference (>94 cm for men and 80 cm for women) was associated with increased BMI ($r = .345, p < .05$).
men and >80 cm for women) was found in 17 individuals, of which 9 were women. A substantial increase in waist circumference (≥102 cm for men and ≥88 cm for women) was found in 10 individuals, of which 5 were women. There was a strong correlation between BMI and waist circumference ($r = .817, P < .001$; see Figure 3). Participants with increased waist circumferences had BMIs between 30 and 35 kg/m², and participants with substantially increased waist circumferences had BMIs between 35 and 40 kg/m² (see Figure 3). Waist circumference also significantly correlated with age ($r = .508, P < .01$).

### 3.3 Dietary intake

Data from the SmartDiet questionnaire and the self-reported dietary information are presented in Table 2. An unhealthy diet (score ≤27) was found in 12 of the participants and 20 scored between 28 and 35, indicating that their diet could be improved. None of the participants scored above 36, which is the cutoff indicative of a healthy and heart-friendly diet. Cheese, fat, processed snacks, and red and processed meats were the biggest sources of saturated fat in the participants’ diets. Their reported intake of whole grains and fruits, berries, and vegetables was low. Only two participants reported consuming over four servings of fruits, berries, and/or vegetables per day (≥600 g).

The 4-day dietary record was completed by 20 out of 33 participants, of which 12 were women. The median intake of nutrients, together with the number of participants, is presented in Table 3. The median intake was in accordance with recommendations for all nutrients except dietary fiber, saturated fatty acids, iron, iodine, vitamin D, and folate. The median intake of dietary fiber was 16.5 g/day, and only one individual had a fiber intake in accordance with the recommendations (25–35 g/day). The median intake of saturated fatty acids was 12 E% and three participants had an intake in accordance with the recommendations (<10 E%). The median intake of vitamin D was 0.8 μg/MJ and five participants had intake in accordance with the recommendations (1.4 μg/MJ). The median folate intake was 34 μg/MJ and five participants were in accordance with the recommendations (45 μg/MJ).

### 3.4 REE and energy intake

REE was measured and calculated for all participants ($n = 33$; see Table 4). The mean REE/kg measured by indirect calorimetry was

**TABLE 1** Characteristics of the study population

|                      | Mean* (SD) |
|----------------------|------------|
| **Age (years)**      |            |
| All ($n = 33$)       | 40 (15)    |
| Men ($n = 15$)       | 41 (17)    |
| Women ($n = 18$)     | 40 (14)    |
| **Height (cm)**      |            |
| Men ($n = 15$)       | 135.6 (9.2)|
| Women ($n = 18$)     | 130.7 (6.9)|
| **Weight (kg)**      |            |
| Men ($n = 15$)       | 66.3 (16.4)|
| Women ($n = 18$)     | 55.6 (9.5) |
| **BMI (kg/m²)**      |            |
| All ($n = 33$)       | 34 (7)     |
| Men ($n = 15$)       | 36 (7)     |
| Women ($n = 18$)     | 33 (6)     |
| **Work**             | N (%)      |
| Full-time job/student| 12 (37%)   |
| Part-time job        | 4 (12%)    |
| Unemployed           | 2 (6%)     |
| Retired              | 1 (3%)     |
| Disability benefit (50–95%) | 4 (12%) |
| Disability benefit (100%) | 10 (30%) |

*Higher education (education at the university or college level).

Notes: cm = centimeter, kg = kilogram, and m = meter.

*SD (standard deviation).

**FIGURE 2** Distribution of BMI in the population. BMI, body mass index [Color figure can be viewed at wileyonlinelibrary.com]

**FIGURE 3** Correlation (Spearman’s) between BMI and waist circumference ($r = .817, P < .001$). BMI, body mass index

and waist circumference ($r = .817, P < .001$; see Figure 3). Participants with increased waist circumferences had BMIs between 30 and 35 kg/m², and participants with substantially increased waist circumferences had BMIs between 35 and 40 kg/m² (see Figure 3). Waist circumference also significantly correlated with age ($r = .508, P < .01$).
### TABLE 2  Intake of food groups from SmartDiet

| Food groups | % (n) | Food groups | % (n) |
|-------------|-------|-------------|-------|
| Milk        |       | Bread, crisp bread and cereals |       |
| Do not use/use rarely | 25 (8) | Do not use bread/crisp bread/cereals | 6 (2) |
| Skimmed milk | 22 (7) | Products low in fiber | 34 (11) |
| Low-fat milk | 47 (15) | Products rich in fiber | 60 (19) |
| Whole milk | 6 (2) | Fruits, berries and vegetables |       |
| Yogurt      |       |              |       |
| Do not use yogurt weekly | 50 (16) | ≤2 servings/day | 56 (18) |
| 1–2 units of 1 dL/week | 31 (10) | 2–4 servings/day | 38 (12) |
| 3–4 units of 1 dL/week | 6 (2) | >4 servings/day | 6 (2) |
| ≥5 units of 1 dL/week | 13 (4) | Beverages and spreads high in sugar | 68 (22) |
| Cream/sour cream |       |              |       |
| Do not use/use rarely | 22 (7) | ≥3 times/day | 16 (5) |
| With low fat content | 19 (6) | Snacks |       |
| With medium fat content | 40 (13) | 0–1 times/day | 31 (10) |
| With high fat content | 19 (6) | 2 times/week | 56 (18) |
| Cheese      |       | Weekly intake of legumes |       |
| Do not use/use rarely | 6 (2) | ≥3 times/week | 13 (4) |
| With low fat content | 0 | No | 72 (23) |
| With medium fat content | 16 (5) | Yes | 28 (9) |
| With high fat content | 78 (25) | Potato/rice/pasta |       |
| Meatproducts on bread |       | Do not use | 9 (3) |
| Do not use/use rarely | 16 (5) | 0–1 portion/day | 66 (21) |
| With low fat content | 56 (18) | 2 portions/day | 6 (2) |
| With high fat content | 28 (9) | ≥3 portions/day | 19 (6) |
| Meat and meatproducts for dinner | Weekly intake of nuts |       |
| Do not use/use rarely | 9 (3) | No | 66 (21) |
| With low fat content | 47 (15) | Yes | 34 (11) |
| With medium fat content | 28 (9) | Weekly intake of avocado/olives |       |
| With high fat content | 16 (5) | No | 72 (23) |
| Fishproducts on bread |       | Yes | 28 (9) |
| On 1 slice of bread/week or never | 50 (16) | Coffee |       |
| On 2–4 slices of bread/week | 34 (11) | No | 16 (5) |
| On ≥5 slices of bread/week | 16 (5) | Yes | 84 (27) |
| Fish for dinner | Alcohol consumption |       |
| 1 time/week or never | 34 (11) | No | 25 (8) |
| ≥2 times/week | 53 (17) | <1 unit/week | 47 (15) |
| ≥3 times/week | 13 (4) | 1–7 units/week | 28 (9) |
| Fatty fish 1–2 times/week | 8–14 units/week | 0 |       |
| No | 38 (12) | ≥15 units/week | 0 |       |
| Yes | 62 (20) | Eggs per week |       |
| Mayonnaise, remoulade, and caviar | Meals per day |       |
| On ≤1 slice of bread/week | 47 (15) | 1–2 | 25 (8) |
| On 2–7 slices of bread/week | 44 (14) | 3–4 | 34 (11) |
| On ≥8 slices of bread/week | 9 (3) | ≥5 | 22 (7) |
| Butter or margarine on bread |       |       |       |
| Meals per day | (Continues) |       |       |
21 kcal/kg for the male (n = 15) and 20 kcal/kg for the female (n = 18). The mean REEs (measured by indirect calorimetry) were 1,416 and 1,110 kcal/day for men and women, respectively, and 1,249 kcal/day for the total group (see Table 4). The male participants had significantly higher REEs compared to the females, with a mean difference of 306 kcal/day (p < .001). The mean REE estimations from the Harris–Benedict equation for the whole population were 1311 kcal/day (men: 1383 kcal/day; women: 1249 kcal/day). The estimations from the Mifflin–St. Jeor equation for the total and male populations did not differ significantly from the measured REEs. However, the equation-based estimations for the female participants were significantly higher by a mean of 140 kcal/day (p = .001). The mean REEs from the Mifflin–St. Jeor equation for the total, male, and female populations were 1552, 1719, and 1413 kcal/day, respectively. The Mifflin–St. Jeor equation significantly overestimated REE on the group level (p < .001) with 303 kcal/day for the male (p < .001) and female (p < .001) participants, which led to an overestimation of 24% on the group level. The calculated REE is considered acceptable if the difference is no more than ±10% compared to the values measured by indirect calorimetry (Frankenfield, Roth-Yousey, & Compher, 2005). Hence, 10 participants (30.3%) had their REE correctly estimated with the Mifflin–St. Jeor equation, whereas 15 participants (45.5%) had a correct REE estimation with the Harris–Benedict equation.

According to the 4-day dietary record collected from 20 (60%) of the participants, the men (n = 8) and women (n = 12) had mean energy intakes of 1,569 kcal/day and 1,287 kcal/day, respectively. The mean energy intake for the whole group was estimated to be 1400 kcal/day (Table 4). Mean REE measured by indirect calorimetry (n = 20) was not significantly different from the mean REE measured for the whole study group (n = 33).

4 | DISCUSSION

The results from this cross-sectional study indicate a high prevalence of obesity in the Norwegian adult achondroplasia population, assessed by BMI and waist circumference. The findings also revealed that none of the participants had healthy and heart-friendly diets. The mean energy intake was low and approximately 10% above the measured REE.

4.1 | Anthropometrics

Half of the study population had increased waist circumferences, and 10 out of 33 had a substantially increased waist circumference, indicating a high prevalence of abdominal obesity. Three out of four adults were categorized as obese according to BMI. This is much higher than in the general Norwegian population, in which approximately one out of five adults is obese according to the Norwegian HUNT study (Midthjell et al., 2013). Our findings correspond with reported BMI measures in other achondroplasia populations (Ain et al., 2010; Alade et al., 2013; Hecht et al., 1988; Merker et al., 2018b; Saint-Laurent et al., 2018). BMI being dependent on height may lead to an overestimation of the prevalence of obesity in the achondroplasia population due to the short stature characteristic of the disease (Schulze et al., 2013). However, the strong correlation between BMI and waist circumference found in the present study supports a high frequency of abdominal obesity. BMI has been found to correlate with waist circumference in the average height population, although to varying degrees (Nishida et al., 2010). In the present study, we found that men and women with achondroplasia and an increased waist circumference had BMIs between 30 and 35 kg/m² and those with a substantially increased waist circumference had BMIs between 35 and 40 kg/m². These findings indicate that a BMI between 25 and 29.9 kg/m² could be regarded as typical for adults with achondroplasia, as also suggested by Schulze et al. (2013). We also found that both BMI and waist circumference increased with age, indicating that a sedentary lifestyle may contribute to the high frequency of obesity in this population. However, further research is needed to investigate body composition, fat distribution, and clinical implications, as well as the level of physical activity in adults with achondroplasia.
4.2 | Dietary intake

The results of the SmartDiet questionnaire revealed a dietary pattern with a high intake of unhealthy foods, such as processed meats and high-fat dairy products, and a low intake of healthy foods such as fish, fruits, vegetables, and legumes, reflective of the typical Western diet. This is consistent with the high intake of saturated fatty acids and the low intake of fiber, folate, and vitamin D reported in the dietary record. A high intake of saturated fatty acids increases the risk of CVD by increasing low-density lipoprotein cholesterol (Briggs, Petersen, & Kris-Etherton, 2017), and 17 of 20 participants in the present study had an intake of saturated fatty acids above the recommended levels. Daily consumption of fiber has also been shown to reduce the risk of CVD (Estruch et al., 2009; Ho et al., 2016; Ho et al., 2016; Hollaender, Ross, & Kristensen, 2015; Wu et al., 2015), but only one participant consumed the recommended dietary fiber intake of 25–30 g/day. Intake of vitamin D and folate was generally low among the participants, and none of the women met the recommended intake of folate. Although vitamin D fortified milk was frequently used in this population, the intake was not high enough to provide the adequate intake of vitamin D.

### TABLE 3  Intake of nutrients from dietary record

| Nutrients                      | All (n = 20) | *Recommended intake | Intake in accordance with recommendations (%) |
|-------------------------------|-------------|---------------------|-----------------------------------------------|
|                               | Median      | (25th, 75th)        |                                               |
| Carbohydrates (E%)            | 47          | (45, 51)            | 45–60                                         | 75                                           |
| Carbohydrates (g/day)         | 177         | (152, 199)          |                                               |                                              |
| Dietary fiber (g/day)         | 16.5        | (11.1, 18.3)        | 25–35                                         | 5                                            |
| Sugar (E%)                    | 6           | (3, 9)              | <10                                           | 80                                           |
| Protein (E%)                  | 18          | (17, 19)            | 10–20                                         | 80                                           |
| Protein (g/day)               | 60          | (50, 75)            |                                               |                                              |
| Fat (E%)                      | 36          | (31, 39)            | 25–40                                         | 80                                           |
| Fat (g)                       | 53          | (41, 64)            |                                               |                                              |
| Saturated fatty acids (E%)    | 12          | (10, 15)            | <10                                           | 15                                           |
| Monounsaturated fatty acids (E%) | 14          | (10, 17)            | 10–20                                         | 85                                           |
| Polyunsaturated fatty acids (E%) | 6           | (4, 7)              | 5–10                                          | 75                                           |
| Omega-3 (E%)                  | 2           | (1, 2)              | ≥ 1                                           | 100                                          |
| Cholesterol (mg)              | 168         | (117, 240)          | <300                                          | 90                                           |
| Vitamin A (bRAE/MJ)           | 91          | (58, 189)           | 80                                            | 55                                           |
| Vitamin D (μg/MJ)             | 0.8         | (0.4, 1.3)          | 1.4                                           | 25                                           |
| Vitamin E (a-alpha-TE/MJ)     | 1.6         | (1.4, 2.8)          | 0.9                                           | 90                                           |
| Thiamin (mg/MJ)               | 0.23        | (0.17, 0.27)        | 0.12                                          | 100                                          |
| Riboflavin (mg/MJ)            | 0.24        | (0.19, 0.30)        | 0.14                                          | 100                                          |
| Niacin (mg/MJ)                | 2.3         | (2.1, 2.8)          | 1.6                                           | 100                                          |
| Vitamin B<sub>6</sub> (mg/MJ) | 0.21        | (0.18, 0.26)        | 0.13                                          | 100                                          |
| Folate (μg/MJ)                | 34          | (26, 43)            | 45                                            | 25                                           |
| Vitamin B<sub>12</sub> (μg/MJ)| 0.8         | (0.7, 1.0)          | 0.2                                           | 100                                          |
| Vitamin C (mg/MJ)             | 13          | (6, 17)             | 8                                             | 70                                           |
| Calcium (mg/MJ)               | 115         | (89, 147)           | 100                                           | 65                                           |
| Iron (mg/MJ)                  | 1.2         | (1.0, 1.6)          | 1.6                                           | 25                                           |
| Potassium (g/MJ)              | 0.43        | (0.37, 0.52)        | 0.35                                          | 90                                           |
| Magnesium (mg/MJ)             | 39          | (35, 51)            | 32                                            | 95                                           |
| Zinc (mg/MJ)                  | 1.3         | (1.2, 1.8)          | 1.2                                           | 85                                           |
| Iodine (μg/MJ)                | 15          | (9, 23)             | 17                                            | 40                                           |
| Selenium (μg/MJ)              | 6.8         | (5.5, 7.5)          | 5.7                                           | 70                                           |
| Copper (mg/MJ)                | 0.1         | (0.1, 0.2)          | 0.1                                           | 100                                          |
| Phosphorus (mg/MJ)            | 196         | (182, 222)          | 80                                            | 100                                          |

Notes: E% (% intake of total energy intake), g (gram), mg (milligram), μg (microgram), and MJ (megajoule).

* Nordic Nutrition Recommendations 2012, 5th Ed, Denmark; 2014.

bRAE (retinol activity equivalents).
aAlpha-TE (alpha-tocopherol equivalents).
TABLE 4 Mean REE and total energy intake in the study population

|                      | Mean (SD)       |       |       |
|----------------------|-----------------|-------|-------|
|                      | All (n = 33)    | Men (n = 15) | Women (n = 18) |
| REE measured by IC   | 1.249 (208)     | 1.416 (161) | 1.110 (121)    |
| REE predicted by HBEs| 1.311 (158)     | 1.383 (182) | 1.250 (106)    |
| REE predicted by MSJE| 1.552 (258)     | 1.719 (267) | 1.413 (147)    |
| Total energy intake  |                 |       |       |
| (kilocalories)       | 1.400 (356)     | 1.569 (239) | 1.287 (385)    |
| Total energy intake  |                 |       |       |
| (megajoules)         | 5.6 (1.6)       | 6.6 (1.0)  | 5.1 (1.3)      |

Note: REE (resting energy expenditure [kilocalories/day]).
Abbreviations: HBEs, Harris–Benedict equations; IC, indirect calorimetry; MSJE, Mifflin–St. Jeor equations; SD, standard deviation.

4.3 | REE and energy intake

The reasons underlying the predisposition for obesity in achondroplasia are unknown and could be related to excessive caloric intake or decreased energy expenditure (Hecht et al., 1988). The present study showed that Norwegian men and women with achondroplasia had lower daily REEs compared to those of average height (Muller et al., 2018; Owen et al., 1986; Owen et al., 1987; Redman et al., 2014). The mean REE was 1416 kcal/day for men and 1110 kcal/day for women. This is consistent with findings from the American and Canadian achondroplastic population published by Owen et al. (1990). Metabolically active tissues, such as skeletal muscle, brain, and liver, are the major contributors to REE (Mahan et al., 2012). However, when looking at REE per unit body weight, men and women with achondroplasia in the present study had REE/kg values similar to men and women of average height (Muller et al., 2018; Redman et al., 2014). This is inconsistent with the findings by Owen et al. that achondroplastic individuals had higher REE/kg values compared to men and women of typical height (Owen et al., 1990). A possible explanation for this discrepancy is the differences in age and BMI between the populations, as the subjects from Owen et al. were younger and had lower BMIs. There were also differences in the REE assessment method. The participants in Owen et al.’s study had complete bed rest for at least 1 hour in the morning before REE measurement. The limitation of not being able to perform bedside REE measurement in our study would likely produce somewhat elevated REE values compared to the protocol used by Owen et al. This strengthens our findings of significantly lower REE measured from indirect calorimetry.

The REE estimated using the Harris–Benedict equation was not significantly different from the REE measured on the group level or for the male participants but overestimated the REE of the female participants by 13%. Estimation of REE using the Mifflin–St. Jeor equation was significantly different from the measured REE and overestimated REE by 24% on the group level (21% for male and 27% for female participants). These findings indicate that the Harris–Benedict equation could be more accurate in estimating REE in achondroplastic individuals than the Mifflin–St. Jeor equation relative to indirect calorimetry. This is inconsistent with the majority of previous reports on prediction equations in the average-height population in which the Mifflin–St. Jeor equation is most accurate for estimating REE, especially for overweight and obese individuals (Frankenfield, 2013; Frankenfield, Rowe, Smith, & Cooney, 2003; Mifflin et al., 1990; Rao, Wu, Liang, Wang, & Hu, 2012). However, both predictive equations are developed from studies on populations with average stature and have height as a dependent factor. Moreover, fat-free mass is shown to be a single predictor of REE measured by indirect calorimetry (Mifflin et al., 1990). Therefore, we recommend measuring individual REE by indirect calorimetry in achondroplasia. However, if equations are used to predict the REEs of those with achondroplasia, it should be noted that the results might be overestimated by 100–300 kcal.

The achondroplastic population in the present study had lower REE values compared to men and women of average height, indicating lower energy requirements in achondroplasia. Moreover, the reported energy intake was only 10% above the REE. TEE is unknown in this study population; however, TEE is probably greater than 10% above REE and the energy intake is commonly underestimated among study subjects (Lichtman et al., 1992; Schoeller, 1995). An excessive total energy intake may contribute to the high frequency of obesity in achondroplasia, but probably does not explain the propensity for obesity in achondroplasia alone. Several studies have reported a high prevalence of childhood obesity in achondroplasia (Hecht et al., 1988; Hoover-Fong et al., 2008). Saint-Laurent et al. (2018) found an abnormal fat distribution in children and adolescents with achondroplasia, with predominantly abdominal obesity, but without developing the classical complications such as diabetes or dyslipidemia (Saint-Laurent et al., 2018). In an achondroplasia mouse model, the authors demonstrated that treatment with soluble FGFR3 restored the abnormal fat distribution and metabolism, suggesting that the obesity and uncommon metabolism could be directly linked to the FGFR3 mutation. Clinical trials on children with achondroplasia with a C-type natriuretic peptide (CNP) analog are ongoing (Ornitz & Legeai-Mallet, 2017). Human studies with soluble FGFR3 are also underway. Outcome measurements should include body composition and fat distribution. BMI and other anthropometric measurements are all indirect measures and are poor predictors of fat distribution (Thomas, Fitzpatrick, Malik, Taylor-Robinson, & Bell, 2013). Magnetic resonance imaging is currently accepted as the gold standard for evaluating body fat content and distribution (Thomas et al., 2013), and should be considered as outcome measures in future research on body composition and metabolism in achondroplasia.

4.4 | Strengths and limitations

To the best of our knowledge, the present study is the first to investigate the diet of individuals with achondroplasia. Although the number of participants is limited, the study group is considered to be the representative of the adult achondroplasia population in Norway. This study provides important insight into the diet of a population that has been
shown to have an increased risk of obesity and CVD, for which diet is a modifiable risk factor. To generate dietary data that are as accurate as possible, two different collection methods were used.

The limitations of this study should also be addressed. Due to the lower completion of the 4-day dietary record, a nonresponse bias may exist in the dietary data. As anthropometrics and diet were recorded on only one occasion, the results can only provide associations, not causal relationships. Studies have shown that there is a tendency to overreport the consumption of healthy foods such as fish, fruits, and vegetables and to underreport foods rich in sugar and fat (Heitmann & Lissner, 1996; Sviaas et al., 2002). Hence, the participants’ intake of fruits, berries, vegetables, folate, and vitamin D might have been even lower than reported and their intake of saturated fatty acids even higher. Our findings show that the Norwegian achondroplastic population has a lower daily REE compared to people of average height. A corresponding lower total daily energy intake is thus required to prevent becoming overweight. As indicated by our results, this may be challenging especially in terms of covering their nutritional requirements through diet; therefore, we recommend regular individual nutrition assessments and dietary guidance for this population.

As data collection on physical activity is still ongoing, associations between activity and total daily energy requirements for this study population are not yet estimated.

5 | CONCLUSION

The adult achondroplastic population in the present study had lower daily REEs compared to men and women of average height. A strong correlation was found between BMI and waist circumference. Half of the study population had an increased waist circumference and about 30% had a substantially increased waist circumference, suggesting a high prevalence of abdominal obesity in the achondroplastic population. The mean energy intake was low and only 10% higher than the mean REE, and does not explain the high prevalence of abdominal obesity in our population. Metabolism, body fat content, and distribution need to be further explored in achondroplasia, and outcome measures assessing body composition should be included in future clinical trials.

The study population had unhealthy diet patterns similar to the Western diet and the general Norwegian population. As the combination of achondroplasia, unhealthy and low-intake diets, and central obesity may lead to both malnutrition and increased cardiometabolic risk, the Norwegian adult achondroplasia population should be offered dietary counseling.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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