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Research Report

The Relation Between Nutritional Intake and Body Weight in 4–18 Year Old Patients with DMD: What could possibly be done to prevent weight gain?

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Abstract.
Background: Overweight is a common problem in Duchenne muscular dystrophy (DMD) and is associated with reduced mobility and quality of life. The influence of nutritional intake on (over)weight is unclear.
Objective: To investigate weight and energy and macronutrients intake compared to age-specific requirements in DMD patients (4–18 years).
Methods: We assessed weight and body mass index (BMI) and the amount of energy (kcal/day) and macronutrients based on self-reported nutrition diaries. Nutritional intake was compared to requirements for 3 age-groups according to the Dutch Healthy Diet Guideline (4–8/9–13/14–18 years) using a student's *t*-test, and relations with age and BMI were investigated by means of Pearson's correlations.
Results: Forty-eight patients participated, 22 ambulatory, median age 10.8 years. The majority used corticosteroids (N = 41). Overweight (BMI z-score > 2.07) was present in 19 patients; 6% (4–8 years), 73% (9–13 years) and 47% (14–18 years). Overweight was more common in non-ambulatory (61.6%) than ambulatory patients (13.6%). Patients aged 4–8 received 290 kcal/day more than required ($p < 0.001$). Patients aged 9–13 received 349 kcal/day ($p = 0.005$) less than required. Overall, intake of fibre, nuts, meat/fish/eggs/legumes and dairy was lower than recommended ($p < 0.05$). The difference between energy intake versus requirement correlated moderately to age ($r = –0.549$, $p < 0.001$) and BMI ($r = –0.562$, $p < 0.001$).
Conclusions: Overweight was found especially in patients aged 9–18 even though they received less energy than required. Younger patients (4–8) had good weight but consumed more energy than required. All patients did not consume enough fibre, nuts, meat/fish/eggs/legumes and dairy. Limiting energy and increasing fibre/protein intake at an early age may prevent overweight at a later age.

Keywords: Duchenne muscular dystrophy, dietary intake, nutritional intake, body mass index, body weight

INTRODUCTION

Duchenne muscular dystrophy (DMD) is characterized by progressive muscle damage leading to muscle weakness, motor delays, loss of mobility and altered body composition [1–3]. Most DMD patients

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have symptoms of muscle weakness before the age of six and become non-ambulant around the age of ten without treatment [4]. Use of corticosteroids has led to beneficial effects on mobility, muscle strength and muscle function but at the expense of significant side effects including low bone density, constipation, increased appetite, increased caloric intake and weight gain [1, 5–7]. In the late ambulatory and early non-ambulatory stage of the disease, obesity is a common feature due to a disturbed metabolism, a decrease in physical activity and the use of corticosteroids [8]. Many patients become overweight before the age of thirteen and overweight is related to respiratory problems (i.e. respiratory muscle fatigue, pneumonia and respiratory failure), low self-esteem, reduced mobility and a deteriorated quality of life [9–11].

It is unclear how a healthy weight can be achieved in DMD patients because true prospective intervention studies have not been conducted. Observational research that has been conducted recommended that DMD patients require a distinct treatment combination of weight management and education on micronutrients and healthy eating [12]. However, the relation between nutritional intake and weight in the different stages of DMD has not yet been investigated [13].

Nutritional recommendations for the Dutch healthy population are proposed in the Dutch Healthy Diet Guideline based on scientific research and the National Food Consumption Survey [14]. The guideline differentiates dietary recommendations based on the age-groups (1–3, 4–8, 9–13 and 14–18 years old) for general recommended daily nutritional intake used by the Netherlands Nutrition Centre [15]. In 2015 the Dutch Dietary Treatment Guideline for DMD patients was proposed on the basis of the Dutch Healthy Diet Guideline stating that DMD patients should receive the same proportion of carbohydrates (40–45% of total calories), fat (20–40%), fluid, fibre and micronutrients as the healthy population [16]. It recommends slightly higher amounts of proteins (at least 10–15%) and stresses the importance of adequate calcium and vitamin D intake [17–19]. The caloric needs of DMD patients are estimated with the Schofield equation with adjustment for activity level [16]. However, it is unknown whether the use of this equation is completely suitable to use in DMD because the resting energy expenditure in DMD boys is lower than in the healthy population [20–22]. The DMD guideline suggests a balanced calory restriction in case of excessive weight.

Although the DMD dietary guideline is applied in practice, implementation has not been studied. It is not known how dietary intake in the DMD population compares to the disease specific nutritional requirement of DMD patients as presented in the guideline. In addition, no data is available regarding the difference in dietary intake between patients within different age groups and according to ambulatory status. Insights in nutritional intake may help to identify nutrients that could potentially contribute to maintaining a healthy weight in DMD patients and improve quality of life. Therefore, the aim of this study was to compare nutritional intake to dietary reference intake and to compare energy and macronutrients intake to requirements at different ages. The second aim was to evaluate the association between nutritional intake and age and BMI in ambulatory and non-ambulatory patients with DMD.

MATERIALS AND METHODS

A cross-sectional prospective study was conducted in the Leiden University Medical Centre (LUMC) with data from April 2018 till March 2020. This research was approved by the Medical Ethical Science Committee (N19.046) of the LUMC.

Study population

Patients with DMD between the age of 1 and 18 years who were treated in the LUMC by the multidisciplinary neuromuscular team who monitored their nutritional intake for at least one day in a nutrition diary were eligible for the study.

Study characteristics

Age, diagnosis, ambulatory status, activity level, body mass index, weight, height, corticosteroid use and type of corticosteroids were retrospectively collected from the electronic medical records.

Energy and macronutrients intake

Prior to the outpatient visit, patients were asked to monitor their nutritional intake for three days in a nutrition diary which was cross-checked by registered dieticians (DB and KC). The mean intake of energy and macronutrients (proteins, carbohydrates, fat and fibre) was calculated. Values of the Dutch Food Composition Database (NEVO-online 2019, version 6.0) were used to determine the intake of energy in kilo-

calories and the intake of macronutrients in grams [23]. The average daily intake of the patients was determined by calculating the average intake from the number of useable nutrition diaries, i.e. data for at least one day with a note for breakfast, lunch, dinner and snacks. In case no quantity or type of product was mentioned the minimum quantities and products according to the Dutch Healthy Diet Guideline were selected and used for analysis.

Energy and macronutrients requirements

The Schofield equation was used to calculate energy requirement, with height, weight and age as variables and was corrected for physical activity (factor 1 (sedentary) for non-ambulant boys and 1.1 (low active) for ambulant boys) [24, 25]. Individual requirements of macronutrients were established on the basis of the Dutch Dietary Treatment Guideline for DMD patients [16]. The amount of proteins, carbohydrates and fat intake and requirement was converted into energy percentage to determine the ratio between macronutrients. The energy percentage was calculated by dividing the total energy intake or requirement in kcal by the number of kcal per gram per macronutrient. Subsequently, the outcome was divided by the amount of proteins, carbohydrates or fat in grams.

Nutritional intake and dietary references

Nutritional intake was compared to the recommended daily amount according to the Dutch Healthy Diet Guideline [14]. To evaluate these recommendations the nutrients were classified into categories, namely: vegetables, fruits, bread, (whole) grains, nuts, meat, fish, eggs and legumes, dairy products, cheese, fatty products (e.g., soft margarine, liquid baking and cooking fat and vegetable oils) and drinks. To compare the nutritional intake with the requirement and dietary references intake, patients were categorized into age-related groups, namely 4–8 years, 9–13 years and 14–18 years. This categorization was based on the age-groups for general recommended daily amounts used by the Netherlands Nutrition Centre [15].

Anthropometric measurements

Height (m) and weight (kg) were measured during consultation. To calculate height of non-ambulatory patients the length of the ulna was measured and subsequently entered into the formula proposed by Gauld [26]. BMI was calculated as weight (kg) divided by the squared height (m). Z-scores of weight and BMI (kg/m^2) were calculated by subtracting the mean weight and BMI from the observation and dividing this result by the standard deviation. The BMI scores were used for analysis and categorized in underweight, adequate weight, overweight and obese according to age-specific international values of the World Obesity Organization [27].

Statistical analysis

Statistical analysis was performed using SPSS Statistics for Windows, version 25.0 (IBM Corp. Released 2017, Armonk, NY). Kolmogorov-Smirnov test was used to verify if data were normally distributed. All continuous variables were expressed as means with standard deviations (SD). Energy, proteins, carbohydrates and fibre intake was compared to the requirement for each age group using student's *t*-test. Fat requirement is presented as interval value instead of a mean value. In order to compare fat intake with requirement, an average *p*-value was calculated using the interval-null hypothesis [28]. The mean nutritional intake was also compared to the recommended daily amount and to intake of the Dutch healthy population of the same age group for all ten nutrient categories using one sample *t*-test. Associations between the difference in energy and fibre intake versus the requirements and age and weight were analysed using Pearson's correlations. Correlation strength was defined as weak (0.3–0.5), moderate to good (0.5–0.75) and good-excellent (>0.75) [29]. Difference in BMI, energy and fibre intake between ambulant and non-ambulant patients was tested using student's *t*-test. All statistical tests performed were two-tailed tests and executed for each age subgroup. A p-value < 0.05 was considered statistically significant. The Bonferroni-Holm method was used to counteract the multiple comparisons problem.

RESULTS

Forty-eight boys with DMD with an age between 4 and 18 years (mean 10 years and 8 months) were included in the study. Twenty-six were non-ambulatory, 41 used intermittent corticosteroids (seven never used corticosteroids) and 41 fulfilled the nutritional diary for three days. Seven patients kept the nutritional diary for only one or two days.

Table 1
Characteristics and anthropometric measurements of the participating DMD patients

	4–8 years	9–13 years	14–18 years
Patients, n	18	15	15
Mean age (years)	6.8 ± 1.3	11.2 ± 1.7	15.1 ± 1.1
Body weight (kg)	22.7 ± 4.3	53.2 ± 20.2	69.2 ± 17.2
z-score	–0.6 ± 1.0	1.4 ± 1.7	1.1 ± 1.4
Height (cm)	121.3 ± 9.4	148.5 ± 14.6	167.7 ± 10.2
z-score	–0.9 ± 0.6	–0.7 ± 0.9	–1.1 ± 1.2
BMI (kg/m^2)	15.2 ± 1.7	23.4 ± 5.4	24.8 ± 5.2
z-score	–0.2 ± 1.5	2.2 ± 1.4	1.8 ± 1.5
Corticosteroid use, n (%)	12 (66.7)	14 (93.3)	15 (100.0)
prednisone, n (%)	11 (61.1)	5 (33.3)	5 (33.3)
deflazacort, n (%)	1 (5.6)	9 (60.0)	10 (66.7)
Non-ambulatory boys, n (%)	1 (5.6)	10 (66.7)	15 (100.0)
Three nutrition diaries available, n (%)	16 (88.9)	12 (80.0)	13 (86.7)

BMI, body mass index. Data expressed as mean ± standard deviation. Corticosteroid use and wheelchair-bound are expressed as amount of patients and percentage.

The characteristics and anthropometry of the patients stratified according to age are shown in Table 1.

Weight status

The majority of patients aged 4–8 years had an adequate weight (66.7%), however underweight (27.8%) and overweight (5.6%) also occurred in this patient group. In patients 9–13 years overweight (53.3%) and obesity (20.0%) were most common and almost half of the patients aged 14–18 years were overweight (13.3%) or obese (33.3%) (Fig. 1a). Overweight was less common in ambulatory boys (13.6% overweight, 0% obese) compared to non-ambulatory boys (30.8% overweight and 30.8% obese) ($p < 0.001$) (Fig. 1b).

Energy and macronutrients

The mean energy intake (in kilocalories per day) was significantly different from the mean energy requirement for the age groups 4–8 and 9–13 (Table 2). The youngest age group (4–8 years) received 290 kcal/day more than required ($p < 0.001$), while patients aged 9–13 received 349 kcal/day less than required ($p = 0.005$). The amount of energy supplied by the intake of proteins was significantly higher than required for all age groups ($p < 0.05$). Protein intake in grams per kilogram body weight per day was also significantly higher than the requirement for 4–8 and 9–13 years ($p < 0.05$), as was carbohydrate intake based on energy percentage ($p < 0.05$). Fat intake was not significantly different from the requirement among all age groups, while fibre intake was significantly lower than required for all patients ($p < 0.001$). A moderate negative correlation was found between the difference in energy intake versus requirements

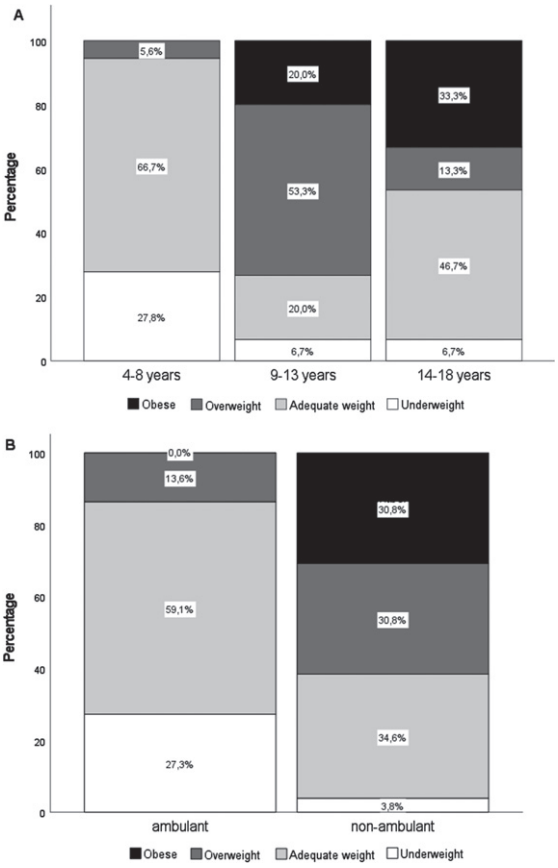

Fig. 1. Percentage of DMD patients with underweight, adequate weight, overweight or obesity based on body mass index according to age group (a) and ambulatory status (b).

and age ($r = –0.549$, $p < 0.001$) and body mass index ($r = –0.562$, $p < 0.001$) (Fig. 2). A weak negative correlation was found between fibre intake and age ($r = –0.418$, $p = 0.003$) and no correlation was found

Table 2
Difference between nutritional intake and requirement of boys with Duchenne muscular dystrophy according to age group

	Age group	Intake	Requirement	Difference intake and requirement	*p*-value
Energy					
(kcal/day)	4–8 years	1582 ± 320	1158 ± 99	424 ± 294	**<0.001**
	9–13 years	1346 ± 401	1695 ± 336	–349 ± 410	**0.005**
	14–18 years	1551 ± 406	1944 ± 297	–393 ± 539	0.014
Protein					
(g/kg/day)	4–8 years	2.7 ± 0.6	1.4 ± 0.2	1.3 ± 0.5	**<0.001**
(% of E/day)		15.5 ± 2.6	10.0 ± 0.0	5.5 ± 2.6	**<0.001**
(g/kg/day)	9–13 years	1.3 ± 0.7	0.9 ± 0.2	0.4 ± 0.6	**0.011**
(% of E/day)		18.7 ± 5.1	10.0 ± 0.0	8.7 ± 5.1	**<0.001**
(g/kg/day)	14–18 years	1.0 ± 0.4	1.1 ± 0.1	0.0 ± 0.3	0.712
(% of E/day)		18.0 ± 3.3	15.0 ± 0.0	3.0 ± 3.3	**0.003**
Carbohydrates					
(% of E/day)	4–8 years	66.1 ± 17.9	45.0 ± 0.0	21.1 ± 17.9	**<0.001**
	9–13 years	37.5 ± 10.4	45.0 ± 0.0	–7.5 ± 10.4	**0.014**
	14–18 years	38.5 ± 13.6	42.0 ± 2.5	–3.5 ± 13.2	0.319
Fat					
(% of E/day)	4–8 years	35.6 ± 9.7	20.0–40.0	0.0	0.144
	9–13 years	24.7 ± 9.7	20.0–40.0	0.0	0.161
	14–18 years	26.6 ± 10.6	20.0–40.0	0.0	0.184
Fibre					
(g/1.000 kcal)	4–8 years	13.2 ± 2.6	19.6 ± 2.1	–6.4 ± 2.5	**<0.001**
	9–13 years	9.3 ± 3.6	17.4 ± 3.2	–8.6 ± 4.7	**<0.001**
	14–18 years	9.0 ± 2.8	21.0 ± 3.1	–12.0 ± 2.6	**<0.001**

Data expressed as mean ± standard deviation. Macronutrient intake and requirement are represented as the amount of energy supplied by the macronutrient per day in percentages (% of E/day). Protein intake and requirement is also expressed as grams per kilogram body weight per day (g/kg/day). Requirements are based on the Dutch Dietary Treatment Guideline for DMD patients.[16] *P*-value for fat intake and requirement is expressed as a lower limit of the average *p*-value of interval-null hypothesis.[28] A p-value < 0.05 is considered as statistically significant. All outcomes are adjusted for multiple testing with the Bonferroni–Holm method.

between fibre intake and body mass index ($r = 0.040$, $p = 0.789$) (Fig. 3). In addition, ambulatory patients received a significantly higher amount of energy and fibre than non-ambulatory patients ($p < 0.05$).

Nutritional intake and dietary references

Patients between 4–8 years received an adequate amount of vegetables and bread compared to the recommended daily amount according to the Dutch Healthy Diet Guideline (Fig. 4 and Table 3). The amount of fruits was significantly higher than required for this age group ($p < 0.05$). Nutritional intake for other categories was significantly lower than the recommended daily amount ($p < 0.05$). For patients aged 9–13 years only vegetables and cheese intake was equal to the recommended amount. Intake of the remaining categories was significantly lower ($p < 0.05$). Nutritional intake of patients aged 14–18 years was significantly lower than recommended for all categories ($p < 0.01$). The categories (whole) grains and nuts deviated the most from the recommended amount for all age groups ($p < 0.01$). For all age groups fluid intake, such as water, coffee and tea, was less than half of the requirement ($p < 0.01$). The intake of DMD patients aged 4–8 years compared to the Dutch healthy population of the same age was significantly different for fruit, dairy and cheese ($p < 0.01$). The intake of vegetables, bread, whole grains and fatty products was significantly different between patients aged 9–13 years compared to the healthy population ($p < 0.01$). Overall, the intake of patients and healthy children aged 14–18 years was not significantly different except for bread and nuts ($p < 0.01$).

DISCUSSION

In this study, we observed that more than half of the patients aged 9–18 years was overweight, although they received less calories than recommended. This was in contrast to the youngest group (4–8 years) of whom the majority had a healthy weight but consumed too many calories. Overweight was less common in ambulatory boys compared to non-ambulatory boys, although ambulatory patients consumed more energy and fibre. In DMD patients of

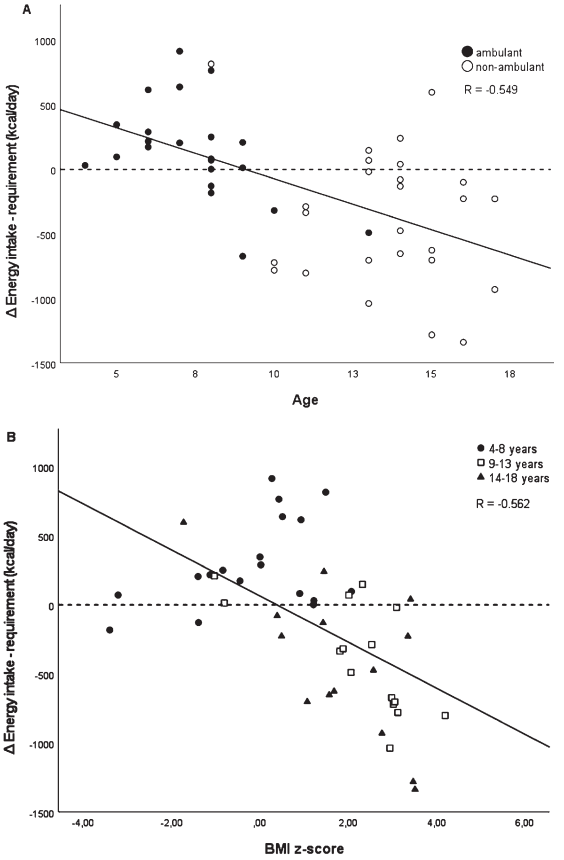

Fig. 2. Δ Delta energy intake and requirement according to age in ambulatory and non-ambulatory patients (a). Δ Delta energy intake and requirement according to BMI z-score in different age groups (b). Δ energy intake and requirement is expressed as kilocalories per day. Dotted line is no difference between intake and requirement.

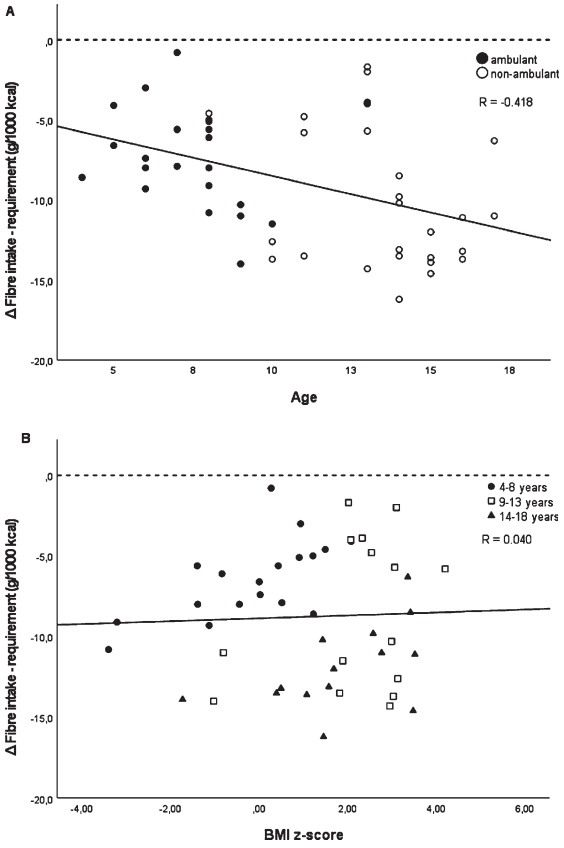

Fig. 3. Δ fibre intake and requirement according to age in ambulatory and non-ambulatory patients (a). Δ fibre intake and requirement according to BMI z-score in different age groups (b). Δ fibre intake and requirement is expressed as grams per 1000 kilocalories. Dotted line is no difference between intake and requirement.

all age groups energy and fibre intake did not equal the requirement. Moreover, consumption of fibre,meat, fish, eggs, legumes and dairy in DMD patients is limited from an early age.

To the best of our knowledge, our study is the first study investigating macronutrient intake and specific food intake in DMD patients. Limited studies are performed into the relationship between energy intake and body weight. Previous research showed that DMD children of 2–12 years received more energy than the requirement and that the majority of patients aged 9–18 years were overweight, which is consistent with our results [9–11, 13]. Caloric requirements for boys with DMD are supposed to be 20–30% lower compared to average healthy controls and this could be due to a decreased resting energy expenditure caused by loss of muscle mass [20–22]. Dieticians often recommend an energy restriction when BMI is too high, which may explain the lower energy intake in older DMD patients [22].

Energy intake decreases with age and ambulatory patients expend more energy compared to non-ambulatory patients. This could be explained by the energy requirement that stagnates when mobility decreases. In the end, energy requirement is between 1000 and 1500 kilocalories according to the Duchenne Dietary Treatment Guideline [16]. Despite this, body weight is higher in patients who have a lower energy intake. This indicates that weight change is multifactorial and does not depend solely on dietary intake. For example, factors such as growth, metabolic changes, decrease in physical activity and the use of corticosteroids play an important role in weight status as well [1].

An explanation for the decrease in protein intake (g/kg/day) in the older age groups could be that nutri-

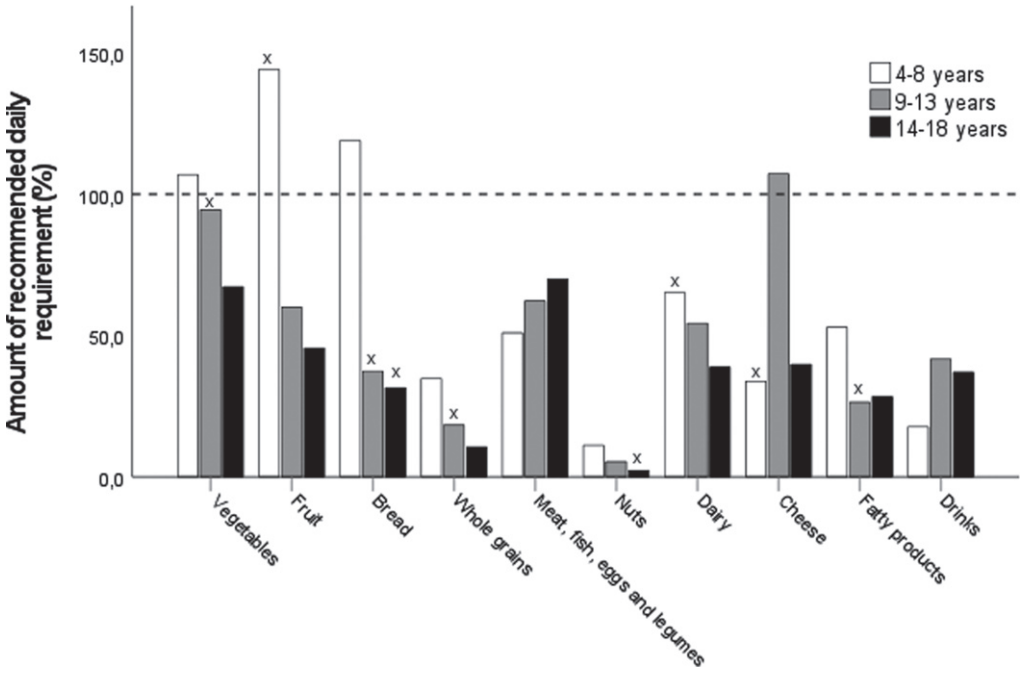

Fig. 4. Percentage of nutritional intake of DMD patients with the age of 4–8, 9–13 and 14–18 years compared to the recommended daily amount according to the Dutch Healthy Diet Guideline. Dotted line is the recommended daily amount. [x] indicates a significant lower intake of DMD patients compared to the Dutch healthy population of the same age group. A p-value < 0.05 is considered as statistically significant. All outcomes are adjusted for multiple testing with the Bonferroni–Holm method.

tional intake remains the same as the patient's body weight increases. As a result, patients receive a limited amount of grams per kilogram body weight. Nevertheless, there is no evidence suggesting that patients require additional protein intake compared with the requirement [30]. This applies to the intake of carbohydrates as well. Advice based on the dietary guideline is at least 40 energy percent carbohydrates per day to prevent unwanted muscle loss, but the influence of carbohydrate consumption on muscle breakdown in DMD patients has not yet been sufficiently investigated [16].

Our results showed no relationship between fibre intake and weight in DMD patients. Nevertheless, it is difficult to draw a conclusion based on these results because patients of all age groups have a fibre intake far below the minimum. Literature shows that high-fibre intake helps to reduce body weight in healthy adults, independently of calorie intake and other confounders [31, 32]. This is probably because fibre intake ensures satiety resulting into loss of appetite. Fibre intake decreased when comparing age groups and ambulation status, but the intake of fibre in the youngest patients is already below the recommended amount. This is not surprising, because the healthy Dutch population also consumes less fibre than recommended [33]. However, it is an important result as nearly half of the DMD patients suffer from constipation caused by reduced mobility and an insufficient fibre and fluid intake which contributes to a reduced quality of life and possible complications, such as dehydration and malnutrition [7, 34, 35]. Still, constipation in DMD patients is often underestimated and maltreated [36, 37]. Although an adequate amount of fibre is not the only way to maintain weight and to prevent constipation, high-fibre intake may have a positive effect on body weight and bowel movement of DMD patients.

We found that patients received a limited amount of whole grains and products like nuts, meat, fish, eggs, legumes and dairy compared to the recommended daily amount. These product groups contain various vitamins and minerals, such as vitamin A, D, E, B vitamins, calcium, magnesium, iron and zinc, which are involved in, among other things, body growth, bone and muscle preservation, oxygen supply and cell metabolism [38]. Currently, little is known about vitamin and mineral supplementation in DMD patients [39]. The Dietary Treatment Guideline for DMD patients only recommends vitamin D

Table 3
Difference between nutritional intake of DMD patients and the Dutch healthy population of the same age group compared to the recommended daily amount according to the Dutch Healthy Diet Guideline

	Age group	Requirement	Intake healthy population	Intake DMD patients	Difference intake patients and healthy population	*p*-value
Vegetables						
(gram/day)	4–8 years	100.0	72.5	106.9 ± 55.6	34.4	0.02
	9–13 years	150.0	79.8	141.7 ± 61.2	61.9	**0.002**
	14–18 years	250.0	102.9	168.1 ± 90.1	65.2	0.014
Fruit						
(gram/day)	4–8 years	150.0	118.4	216.2 ± 122.4	97.8	**0.003**
	9–13 years	200.0	80.5	120.0 ± 78.2	39.5	0.072
	14–18 years	200.0	67.6	91.0 ± 68.6	23.4	0.208
Bread						
(gram/day)	4–8 years	70.0	114.8	83.4 ± 55.6	–31.4	0.027
	9–13 years	175.0	138.5	65.1 ± 40.9	–73.4	**<0.001**
	14–18 years	210.0	163.0	66.0 ± 48.3	–97.0	**<0.001**
Whole grains						
(gram/day)	4–8 years	150.0	78.9	52.5 ± 48.6	–26.4	0.017
	9–13 years	300.0	112.7	54.5 ± 52.8	–58.2	**<0.001**
	14–18 years	450.0	146.9	47.5 ± 60.8	–99.4	0.239
Meat, fish, legumes, eggs						
(gram/day)	4–8 years	67.5	22.5	33.8 ± 28.1	11.3	0.125
	9–13 years	67.5	35.1	41.9 ± 34.4	6.8	0.488
	14–18 years	67.5	41.9	46.8 ± 35.5	4.9	0.564
Nuts						
(gram/day)	4–8 years	15.0	0.9	1.7 ± 4.4	0.8	0.465
	9–13 years	25.0	1.9	1.4 ± 5.2	–0.5	0.677
	14–18 years	25.0	2.5	0.6 ± 2.1	–1.9	**0.004**
Dairy						
(gram/day)	4–8 years	300.0	325.8	195.7 ± 173.9	–130.1	**0.006**
	9–13 years	450.0	312.0	244.4 ± 197.2	–67.6	0.207
	14–18 years	600.0	278.7	233.0 ± 168.7	–45.7	0.308
Cheese						
(gram/day)	4–8 years	20.0	17.9	6.7 ± 10.8	–11.2	**<0.001**
	9–13 years	20.0	20.5	21.5 ± 22.4	1.0	0.873
	14–18 years	40.0	26.1	15.9 ± 16.3	–10.2	0.029
Fatty products						
(gram/day)	4–8 years	30.0	15.2	15.8 ± 10.9	0.6	0.803
	9–13 years	45.0	20.5	11.8 ± 6.6	–8.7	**<0.001**
	14–18 years	55.0	22.4	15.5 ± 10.4	–6.9	0.023
Drinks						
(gram/day)	4–8 years	1000.0	219.6	176.9 ± 192.3	–42.7	0.355
	9–13 years	1000.0	379.8	416.7 ± 268.0	36.9	0.605
	14–18 years	1500.0	589.4	554.2 ± 331.5	–35.2	0.686

Data healthy population expressed as mean. Data DMD patients expressed as mean ± standard deviation. *P*-values indicate significant difference between the intake of DMD patients and the Dutch healthy population of the same age group. A p-value < 0.05 is considered as statistically significant. All outcomes are adjusted for multiple testing with the Bonferroni–Holm method.

and calcium supplementation under the guidance of a healthcare professional in case of corticosteroid treatment [16]. These micronutrients play an important role in the prevention of osteoporosis that can arise from prolonged corticosteroid use [19]. As most of the DMD patients use corticosteroids, focussing on dietary products containing vitamin D and calcium, such as dairy, cheese and nuts, would be beneficial.

Data on nutritional intake were collected through diaries in this study. Research shows that filling in nutritional diaries by parents is a simple and cost-effective method for assessing energy intake in boys with DMD [40, 41]. Our study is one of the first studies to extensively collect data on the dietary intake of DMD patients and the results of this study may contribute to more specific nutritional guidelines in this patient group.

A limitation of the research is that the nutritional intake may slightly deviate from the actual intake because of under- or overreporting and because not

all diaries were completely filled out. Missing data were imputed with data on the minimum quantities according to the Dutch Healthy Diet Guidelines which may have affected outcomes. However, the imputation of data was limited in our study due to the cross-checking of the nutrition diaries by registered dieticians during regular care. Besides, these missing data were random, therefore we do not expect that this will influence the results of our study. Moreover, this study is not a long-term follow-up and nutritional data were only measured at one time possibly leading to confounding (e.g. when a patient had two birthdays in a row this could lead to a less adequate dietary intake). Other external factors (e.g. no time to cook, mood) may have influenced the diet of DMD children as well, possibly affecting the results. Another limitation is the calculation of the energy requirements. This was calculated by means of the Schofield equation with weight and height. The question remains whether this equation is reliable in DMD patients. On the other hand, the Schofield weight equation shows the smallest deviation of various formulas to calculate energy requirement in DMD patients [24].

Furthermore, the comparison of the daily intake with the intake of the general population for the age group 4–18 years can be questioned. These data were obtained from the Dutch National Food Consumption Survey 2012–2016. Since this year does not correspond to the research years, the data may not be entirely comparable. Moreover, in the Dutch National Food Consumption Survey no distinction had been made between normal and whole grain products and fatty products included all types of fats. Although the data is not 100% comparable, trends that have been developed can be used for comparison. For example, in recent years the Dutch population has started eating more fruit and vegetables and drinking less sugary drinks [42]. This trend may have continued into 2018–2020. If the intake has changed in the general population, it will probably also have in DMD patients.

Follow-up research is needed to investigate what is appropriate nutritional care in this patient population to prevent or reduce overweight and obesity. A good research method would be to conduct an intervention study with nutrition and exercise. Indirect calorimetry has been confirmed to be the best method of calculating energy expenditure in clinical settings [43]. This measurement can possibly be applied in follow-up research to investigate the nutritional intake and requirement even more accurately. Besides, due to the change of body composition and the fact that body weight is disproportionately distributed in patients with DMD, the question remains whether body weight and the regular growth charts are accurate parameters for identifying the risk of becoming under- or overweight in patients with DMD. Disease specific growth charts might be more reliable for patients and dieticians to judge an individual nutritional status.

In conclusion, DMD patients 9–18 years old receive less calories than recommended but are still overweight, in contrast to the youngest group (4–8 years). Applying an energy restriction when weight gain has occurred may have no effect in older DMD patients, but might be beneficial to prevent excessive weight gain when implemented during early age. Nutritional interventions must be started at a young age and dieticians should mainly focus on the intake of fibre, proteins and fluid to achieve satiety. Therefore, DMD patients should consume enough whole grains, nuts, meat, fish, eggs, legumes and dairy. Although weight change is multifactorial, nutrition can play an important role. By taking pre-cautionary nutritional measures at an early age, preferably in the age of 4–8 years, overweight can possibly be prevented.

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CONFLICT OF INTEREST

The authors have no conflict of interest to report. We confirm that this report is consistent with the journal's guidelines on ethical publication, which all authors have read.

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REFERENCES

[1] Birnkrant D, Bushby K, Bann C, Apkon S, Blackwell A, Brumbaugh D, Case L, Clemens P, Hadjiyannakis S, Pandya S, Street N, Tomezsko J, Wagner K, Ward L, Weber D. Diagnosis and management of Duchenne muscular dystrophy, part 1: Diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. The Lancet Neurology. 2018;17(3):251-67. doi:10.1016/s1474-4422(18)30024-3.

[2] Skalsky A, Han J, Abresch R, Shin C, McDonald C. Assessment of regional body composition with dual-energy X-ray absorptiometry in Duchenne muscular dystrophy: Correlation of regional lean mass and quantitative strength. Muscle & Nerve. 2009;39(5):647-51. doi:10.1002/mus.21212.

[3] Leroy-Willig A, Willig T, Henry-Feugeas M, Frouin V, Marinier E, Boulier A et al. Body composition determined with MR in patients with Duchenne muscular dystrophy, spinal muscular atrophy, and normal subjects. Magnetic Resonance Imaging. 1997;15(7):737-44. doi:10.1016/s0730-725x(97)00046-5.

[4] Kim S, Campbell K, Fox D, Matthews D, Valdez R. Corticosteroid Treatments in Males With Duchenne Muscular Dystrophy. Journal of Child Neurology. 2014;30(10):1275-80. doi:10.1177/0883073814558120.

[5] Moxley R, Pandya S, Ciafaloni E, Fox D, Campbell K. Change in Natural History of Duchenne Muscular Dystrophy With Long-term Corticosteroid Treatment: Implications for Management. Journal of Child Neurology. 2010;25(9):1116-29. doi:10.1177/0883073810371004.

[6] Griggs R, Miller J, Greenberg C, Fehlings D, Pestronk A, Mendell J et al. Efficacy and safety of deflazacort vs prednisone and placebo for Duchenne muscular dystrophy. Neurology. 2016;87(20):2123-31. doi:10.1212/wnl.0000000000003217.

[7] Kraus D, Wong B, Horn P, Kaul A. Constipation in Duchenne Muscular Dystrophy: Prevalence, Diagnosis, and Treatment. The Journal of Pediatrics. 2016;171:183-8. doi:10.1016/j.jpeds.2015.12.046.

[8] Saure C, Caminiti C, Weglinski J, de Castro Perez F, Monges S. Energy expenditure, body composition, and prevalence of metabolic disorders in patients with Duchenne muscular dystrophy. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2018;12(2):81-5. doi:10.1016/j.dsx.2017.08.006.

[9] Willig T, Carlier L, Legrand M, Rivière H, Navarro J. Nutritional assessment in Duchenne muscular dystrophy. Developmental Medicine & Child Neurology. 2008;35(12):1074-82. doi:10.1111/j.1469-8749.1993.tb07925.x.

[10] Martigne L, Salleron J, Mayer M, Cuisset J, Carpentier A, Neve V et al. Natural evolution of weight status in Duchenne muscular dystrophy: A retrospective audit. British Journal of Nutrition. 2011;105(10):1486-91. doi:10.1017/s0007114510005180.

[11] Birnkrant D, Bushby K, Bann C, Alman B, Apkon S, Blackwell A et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: Respiratory, cardiac, bone health, and orthopaedic management. The Lancet Neurology. 2018;17(4):347-61. doi:10.1016/s1474-4422(18)30025-5.

[12] Chou E, Lindeback R, D'Silva A, Sampaio H, Neville K, Farrar M. Growth and nutrition in pediatric neuromuscular disorders. Clinical Nutrition. 2021. doi:10.1016/j.clnu.2021.01.013.

[13] Bernabe-García M, Rodríguez-Cruz M, Atilano S, Cruz-Guzmán O, Almeida-Becerril T, Calder P et al. Body composition and body mass index in Duchenne muscular dystrophy: Role of dietary intake. Muscle & Nerve. 2018;59(3):295-302. doi:10.1002/mus.26340.

[14] Health Council of the Netherlands. Guidelines for Good Nutrition. 2015:11-93. Available from: https://www.gezondheidsraad.nl/documenten/adviezen/2015/11/04/richtlijnen-goede-voeding-2015

[15] Guidelines Wheel of Five [Internet]. The Netherlands Nutrition Centre. [cited 5 April 2020]. Available from: https://www.voedingscentrum.nl/professionals/schijf-van-vijf/richtlijnen-schijf-van-vijf.aspx

[16] Wijnen, C. Dietary treatment guideline for Duchenne muscular dystrophy. 2010 Uitgevers. 2015:1-44. Available from: https://www.dieetbehandelingsrichtlijnen.nl/

[17] Health Council of the Netherlands. Dietary standards: Energy, proteins, fats and digestible carbohydrates. 2001:1-174. Available from: https://www.gezondheidsraad.nl/documenten/adviezen/2001/07/18/voedingsnormen-energie-eiwitten-vetten-en-verteerbare-koolhydraten

[18] Health Council of the Netherlands. Fibre Consumption Guideline. 2006:1-90. Available from: https://www.gezondheidsraad.nl/documenten/adviezen/2006/03/21/richtlijn-voor-de-vezelconsumptie

[19] Sertpoyraz FM. The relationship of bone mineral density and vitamin D levels with steroid use and ambulation in patients with Duchenne muscular dystrophy. Turkish Journal of Physical Medicine and Rehabilitation. 2019;65(3):216-21. doi:10.5606/tftrd.2019.3565.

[20] Bianchi M, Biggar D, Bushby K, Rogol A, Rutter M, Tseng B. Endocrine Aspects of Duchenne Muscular Dystrophy. Neuromuscular Disorders. 2011;21(4):298-303. doi:10.1016/j.nmd.2011.02.006.

[21] Hankard R, Gottrand F, Turck D, Carpentier A, Romon M, Farriaux JP. Resting Energy Expenditure and Energy Substrate Utilization in Children with Duchenne Muscular Dystrophy. Pediatric Research. 1996;40(1):29-33. doi:10.1203/00006450-199607000-00006.

[22] Shimizu-Fujiwara M, Komaki H, Nakagawa E, Mori-Yoshimura M, Oya Y, Fujisaki T, et al. Decreased resting energy expenditure in patients with Duchenne muscular dystrophy. Brain and Development. 2012;34(3):206-12. doi:10.1016/j.braindev.2011.05.005.

[23] Dutch Nutrient Database (Nevo) [Internet]. National Institute for Public Health and the Environment (RIVM). [cited 21 April 2020]. Available from: https://nevo-online.rivm.nl/

[24] Elliott SA, Davidson ZE, Davies PSW, Truby H. Predicting resting energy expenditure in boys with Duchenne muscular dystrophy. European Journal of Paediatric Neurology. 2012;16(6):631-5. doi:10.1016/j.ejpn.2012.02.011.

[25] Kruizenga H, Wierdsma N. Zakboek Diëtetiek. Amsterdam: VU University Press, 2014.

[26] Gauld LM, Kappers J, Carlin JB, Robertson CF. Height prediction from ulna length. Developmental Medicine & Child Neurology. 2007;46(7):475-80. doi:10.1111/j.1469-8749.2004.tb00508.x.

[27] Obesity Classification [Internet]. World Obesity Federation. [cited 5 June 2020]. Available from: https://www.worldobesity.org/about/about-obesity/obesity-classification

[28] Cohen MP. Why Not an Interval Null Hypothesis? Journal of Data Science. 2021;17(2):383-90. doi:10.6339/jds.201904_17(2).0008.

[29] Portney LG, Watkins MP. Foundations of clinical research: Applications to practice. London: Pearson Prentice Hall; 2010.

[30] Salera S, Menni F, Moggio M, Guez S, Sciacco M, Esposito S. Nutritional Challenges in Duchenne Muscular Dystrophy. Nutrients. 2017;9(6):594. doi:10.3390/nu9060594.

[31] Menni C, Jackson MA, Pallister T, Steves CJ, Spector TD, Valdes AM. Gut microbiome diversity and high-fibre intake are related to lower long-term weight gain. International Journal of Obesity. 2017;41(7):1099-105. doi:10.1038/ijo.2017.66.

[32] Kranz S, Brauchla M, Slavin JL, Miller KB. What Do We Know about Dietary Fiber Intake in Children and Health? The Effects of Fiber Intake on Constipation, Obesity, and Diabetes in Children. Advances in Nutrition. 2012;3(1):47-53. doi:10.3945/an.111.001362.

[33] Food consumption survey, fibre intake [Internet]. National Institute for Public Health and the Environment [cited 21 March 2020]. Available from: https://www.wateetnederland.nl/resultaten/energie-en-macronutrienten/inname/vezel

[34] Pane M, Vasta I, Messina S, Sorleti D, Aloysius A, Sciarra F, et al. Feeding problems and weight gain in Duchenne muscular dystrophy. European Journal of Paediatric Neurology. 2006;10(5-6):231-6. doi:10.1016/j.ejpn.2006.08.008.

[35] Brumbaugh D, Watne L, Gottrand F, Gulyas A, Kaul A, Larson J, et al. Nutritional and Gastrointestinal Management of the Patient With Duchenne Muscular Dystrophy. Pediatrics. 2018;142(Supplement 2). doi:10.1542/peds.2018-0333g.

[36] Lionarons J, de Groot I, Fock J, Klinkenberg S, Vrijens D, Vreugdenhil A et al. Prevalence of Bladder and Bowel Dysfunction in Duchenne Muscular Dystrophy Using the Childhood Bladder and Bowel Dysfunction Questionnaire. Life. 2021;11(8):772. doi: 10.3390/life11080772.

[37] Houwen-van Opstal S, Heutinck L, Jansen M, Krom Y, Cup E, Hendriksen J, et al. Occurrence of symptoms in different stages of Duchenne muscular dystrophy and their impact on social participation. Muscle & Nerve. 2021;1-9. doi: 10.1002/mus.27406.

[38] Zhang Y, Zhou W-e, Yan J-qing, Liu M, Zhou Y, Shen X, et al. A Review of the Extraction and Determination Methods of Thirteen Essential Vitamins to the Human Body: An Update from 2010. Molecules. 2018;23(6):1484. doi:10.3390/molecules23061484.

[39] Davidson ZE, Truby H. A review of nutrition in Duchenne muscular dystrophy. Journal of Human Nutrition and Dietetics. 2009;22(5):383-93. doi:10.1111/j.1365-277x.2009.00979.x.

[40] Elliott SA, Davidson ZE, Davies PS, Truby H. Accuracy of Parent-Reported Energy Intake and Physical Activity Levels in Boys With Duchenne Muscular Dystrophy. Nutrition in Clinical Practice. 2014;30(2):297-304. doi:10.1177/0884533614546696.

[41] Arikian A, Boutelle K, Peterson CB, Dalton J, Day JW, Crow SJ. Targeting parents for the treatment of pediatric obesity in boys with Duchenne muscular dystrophy: A case series. Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity. 2010;15(3). doi:10.1007/bf03325295.

[42] Food consumption survey, change in food consumption [Internet]. National Institute for Public Health and the Environment [cited 17 July 2020]. Available from: https://www.wateetnederland.nl/resultaten/voedingsmiddelen/verandering

[43] Haugen HA, Chan L-N, Li F. Indirect Calorimetry: A Practical Guide for Clinicians. Nutrition in Clinical Practice. 2007;22(4):377-88. doi:10.1177/0115426507022004377.