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Fatigue and pain in children and adults with multiple osteochondromas in Norway, a cross-sectional study

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ABSTRACT

Background: Multiple Osteochondromas (MO) is a rare skeletal disorder frequently needing orthopaedic surgery. High prevalence of pain has been reported, however fatigue has not previously been investigated.

Purpose: Our aims were to investigate prevalence of fatigue and pain in Norwegian children and adults with MO. Furthermore to compare prevalence of fatigue with reported prevalence in other groups and explore some factors that may contribute to fatigue in this population.

Methods: Questionnaire data was obtained from 11 children and 21 adults, approximately one third of the estimated MO population in Norway. Fatigue and pain was measured with validated instruments.

Results: Children with MO reported significantly higher fatigue than healthy children. Adults reported significantly higher fatigue than the general Norwegian population. Six of 11 children and 20 of 21 adults reported pain. Severe fatigue was more prevalent in persons with high age, high pain intensity and many pain locations; however none of these differences were significant.

Conclusion: High prevalence of fatigue was found in Norwegian children and adults with MO. Such findings have not been previously reported. Pain was prevalent in both children and adults. This implies that fatigue and pain warrant specific attention in clinical practice and further research regarding persons with MO.

Introduction

Multiple Osteochondromas (MO), also called Multiple Hereditary Exostoses (MHE), is a rare hereditary skeletal disorder frequently needing orthopaedic surgery (Jäger et al., 2007; Pacifici, 2017). MO has an incidence of approximately 1:50.000 (Jennes et al., 2009), and is characterized by multiple benign bony tumours (osteochondromas), most commonly occurring at the metaphysis of long bones, pelvis and ribs (Jennes et al., 2009). Osteochondromas can cause bony deformities, limb discrepancies, mild short stature, and compression of blood vessels, peripheral nerves and the spinal cord (Jäger et al., 2007; Payne et al., 2016; Pedrini et al., 2011). Surgical removal of osteochondromas may be necessary for several reasons, including reduced range of motion in joints, interference with growth and mobility, skeletal and muscular pain, compression of nerves, blood vessels and soft tissues and sometimes cosmetic reasons (Jäger et al., 2007; Payne et al., 2016). Many patients undergo several surgical operations throughout their lifetime. The most serious complication is the development of bone cancer (chondrosarcoma), with an estimated risk of 1–5% (Jennes et al., 2009; Pedrini et al., 2011). Chondrosarcoma almost never occur in children (Jennes et al., 2009).

Despite considerable symptoms and complications, there still are few studies on daily life limitations in MO patients. One qualitative study found that adults with MO perceive functional, psychological and social limitations in their daily living (Fraser and Porter, 2000). Goud et al. report that 53% of children with MO had problems at school (Goud et al., 2012). This correlates with our clinical experience where MO patients describe daily life limitations, fatigue and pain. Getting health professionals to address these problems is also described as challenging.

Lower health-related quality of life has been reported in both children and adults with MO, compared to general populations (Chhina et al., 2012; D'Ambrosi et al., 2017; Goud et al., 2012). High prevalence of pain has also been reported (D'Ambrosi et al., 2017; Darilek et al., 2005; Goud et al., 2012). According to Goud et al. (2012) 83% of adults and 63% of children with MO reported pain, with similar findings in another study by Darilek et al. (2005). The most common pain locations in these studies were the lower extremities, followed by shoulders/upper arms (Darilek et al., 2005; Goud et al., 2012). Research on general populations show that having multiple pain locations and high pain

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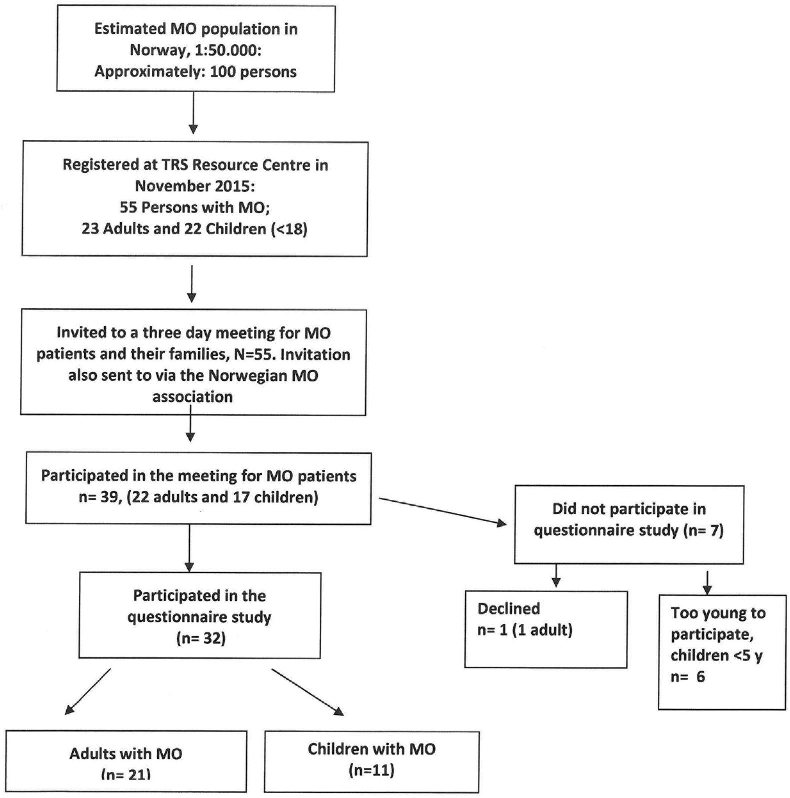

Fig. 1. Flowchart of inclusion of participants.

intensity have a large impact on how adults live with pain on a daily basis (Rustøen et al., 2005), and also affect work ability and quality of life (Rathleff et al., 2013). In adolescents multisite pain has been found as a risk factor for developing mental health problems (Echoff et al., 2017), sickness and use of social welfare benefits (Echoff et al., 2017b) and is associated with reduced quality of life (Rathleff et al., 2013). To our knowledge multiple pain locations in MO is investigated only by Darilek et al. (2005) who report that approximately half of their MO patients reporting pain had generalized pain, defined as pain in multiple locations in both sides of the body. They do not report number of pain locations, neither for children or adults. Two studies report moderate to high pain intensity, primarily in adult MO populations (D'Ambrosi et al., 2017; Darilek et al., 2005).

We have not found any studies investigating fatigue in children or adults with MO. There is a lack of consensus on how to define fatigue, both in adults and children. Our study is based on the following definition of fatigue in adults: "Extreme and persistent tiredness, weakness or exhaustion – mental, physical or both" (Dittner et al., 2004 p 157). A similar definition of fatigue in children emphasise that fatigue in children is multidimensional and also includes emotional aspects (McCabe, 2009).

Fatigue is prevalent in adults in general populations (Lerdal et al., 2005) and various diseases (Dittner et al., 2004), significantly impairs quality of life (Graham et al., 2011) and people's work ability (Ricci et al., 2007). Research on fatigue in children is limited (McCabe, 2009; Eddy and Cruz, 2007; Maher et al., 2015). High prevalence of fatigue is described in children both in general populations (Luntamo et al., 2012), children with chronic health problems (Eddy and Cruz, 2007) and physical disabilities (Maher et al., 2015). Fatigue has large impact on participation in daily activities and school (Eddy and Cruz, 2007; Maher et al., 2015; McCabe, 2009), and research indicate that fatigue is the factor most affecting children's quality of life (Eddy and Cruz, 2007; Gold et al., 2009).

Several studies have found strong associations between chronic pain and fatigue in children and adults, both in general populations and different patient groups (de Rooij et al., 2015; Gold et al., 2009; Landry et al., 2015; Luntamo et al., 2012; Pollard et al., 2006; Wong and Fielding, 2012). Landry et al. (2015) describe day-time fatigue as one risk factor for development of chronic pain. Further investigation of pain and fatigue in MO therefore seems warranted.

Our aims were to investigate prevalence of fatigue and pain in Norwegian children and adults with MO. Furthermore to compare prevalence of fatigue with reported prevalence in other groups and explore some factors that may contribute to fatigue in this population.

Methods

Design and participants

This cross-sectional study was performed at the TRS National Resource Centre for Rare Disorders (TRS) in Norway. TRS provides guidance and counselling on issues related to living with the diagnosis for several rare disorders, MO being one of them. TRS is not a diagnostic or treatment centre, but constitutes a supplement to Norway's public health services. Patients with MO all over Norway can contact TRS directly, without referral. Persons seeking services at TRS agree to being registered in an electronic database.

The study was planned in collaboration with The Norwegian MO association. In December 2015 TRS arranged a three day meeting for MO patients and their families. All patients registered at TRS at the time were invited to the meeting. Invitation was also sent to all members in the Norwegian MO association. The meeting was held at a location separate from TRS and included information on different aspects of living with the diagnosis.

An invitation to participate in the study, consent form and questionnaires were distributed during the meeting. Inclusion criteria were: Having a clinically confirmed diagnosis of MO. Only children > 5 years were included because self –report questionnaires on fatigue and pain for children, only were available from this age. Exclusion criteria were: Being unable to read and speak Norwegian. The inclusion process is described in Fig. 1.

Ethical considerations

Participation was voluntary and written consent was obtained for all participants. Parents asked their children if they wanted to participate and consented for children < 16 years. The information letter highlighted that participation or non-participation would have no consequences for further contact with TRS. Ethical approval was applied from the Data Protection Officer at Oslo University Hospital, who gave approval to use anonymous questionnaire data.

Questionnaire

In cooperation with the Norwegian MO organization, a questionnaire was designed including demographic questions, clinical variables and validated fatigue and pain instruments for children and adults.

Demographic and clinical variables

Age and gender were recorded. Other demographic variables were: Occupational status (working full time, part-time, studying, seeking jobs, on disability benefits or work rehabilitation benefits, part or full time), questions on clinical variables used in a previous MO study (Darilek et al., 2005): Osteochondroma-related surgeries (yes/no), number of operations (Check boxes: 0, 1–5, 6–10, 11–15, 16–20, > 20), body-location of operations (shoulders/scapulae, upper arms, forearms, hands/fingers, chest/ribs, pelvis, thighs/hips, calves, feet) and malignant development (chondrosarcoma) (yes/no).

Fatigue instruments

Fatigue in children and adolescents was measured with PedsQL Multidimensional Fatigue Scale (PedsQL MFS) (Varni et al., 2004; Crichton et al., 2015). The PedsQL MFS consists of 18 statements (eg. "I feel too tired to be with my friends"), and is divided into three areas: General fatigue, sleep/rest fatigue and cognitive fatigue. Age adjusted children report forms were used for age groups 5–7, 8–12 and 13–18 years. The questionnaire is scored on a scale from 0 (never) to 4 (almost always). A sum score is calculated for the whole scale (total fatigue) and for each area. Items are reverse-scored and linearly transformed to a 0–100 scale, so that higher scores indicate lower symptoms of fatigue (Varni et al., 2004). To analyze differences in prevalence of fatigue, we compared PedsQL MFS mean total fatigue score for our participants with reported mean scores for a) healthy children (Varni et al., 2012), b) other conditions reporting fatigue and chronic pain: Children with short stature (Varni et al., 2012), and rheumatoid arthritis (Varni et al., 2004).

Fatigue in adults was measured using Fatigue Severity Scale (FSS), developed to measure fatigue intensity and the impact on daily functioning (Krupp et al., 1989; Lerdal et al., 2005). FSS has nine items/statements, where each statement (eg. "Fatigue interferes with my work, family or social life") is rated on a 7- point response scale, ranging from 1 (completely disagree) to 7 (completely agree). A mean score is calculated for each person, range 1–7. Higher scores indicate higher levels of fatigue (Krupp et al., 1989). To assess prevalence of "severe fatigue", the following cut-off values were used: Non-fatigue = FSS mean score ≤ 4; borderline fatigue = FSS mean score > 4 and < 5; severe fatigue = FSS mean score ≥ 5 (Lerdal et al., 2005). To analyze differences in prevalence of fatigue, we compared FSS mean score for our participants with reported mean scores for a) the general Norwegian population (Lerdal et al., 2005) and b) other conditions reporting fatigue and chronic pain: Adults with rheumatoid arthritis (Mancuso et al., 2006) and cancer (Valko et al., 2015).

Pain instruments

Pain in children and adolescents was measured with PedsQL paediatric pain questionnaire (PedsQL PPQ) (Varni et al., 1987; Varni et al., 2005). Age adjusted children's report forms were used for age groups 5–7, 8–12 and 13–18 years (Benestad et al., 1996). PedsQL PPQ includes the following items: a) have pain/do not have pain now, b) worst pain intensity last seven days, measured with a VAS scale anchored with the pain descriptors "not hurting/no pain" with happy face at one end, and "hurting a lot/severe pain" with sad face on the other end, and c) pain drawing (front/back) marking body areas with pain now. To evaluate the presence of multisite pain we summed up the number of pain locations (NPL) (total of 11), and categorized these into three groups: Mild = "few pain locations" 1–3, moderate = "moderate pain locations" 4–6 and severe = "many pain locations" 7–11 (Rustøen et al., 2004).

Pain in adults was measured with: a) Presence of musculoskeletal pain last week; yes/no, b) pain intensity last week; marked on an 11-point Numeric Pain Rating Scale (NPRS) from 0 = "no pain" to 10 = "pain as bad as it can be" (Von Korff et al., 2000). A pain score of 1–3 indicates "mild pain", a score of 4–6 "moderate pain" and a score of 7–10 "severe pain" (Breivik et al., 2008), c) pain locations last week; marked on a pain-drawing (front, back, left and right side of the body) by checking boxes for 25 different body areas (Cleeland and Ryan, 1994; Margolis et al., 1988). Pain-locations were then divided into 11 areas (head, neck, shoulder/upper arms, elbow/forearms, wrist/hands, upper back, lower back, front chest, hips/thighs, knees/legs, ankles/feet). To evaluate the presence of multisite pain we summed up number of pain locations (NPL) (total of 11) and categorized them into three groups: Mild = "Few pain locations" 1–3, Moderate = "moderate pain locations" 4–6 and Severe = "many pain locations" 7–11 (Rustøen et al., 2004).

Data analysis

Data were entered into a customized database. All participants were given a number and a code list was made. After data entry was completed and checked, the code list was deleted and data anonymised. Data was then processed, using Statistical Package for the Social Sciences (SPSS, IBM; Armonk, NY) version 23.

Due to small sample sizes descriptive data are given as frequencies, percentages, medians and ranges. For comparison with mean values reported in other studies mean, standard deviation (SD), and mean difference with 95% confidence interval (CI) are reported. One sample's t-tests were used to compare mean fatigue scores to those reported for general populations and other patient groups.

To explore factors that may contribute to fatigue we analyzed associations between fatigue and other factors (gender, age, employment status, number of operations, pain intensity and number of pain locations). Prevalence of cancer was not included because of small numbers. Analysis of associations was only done for adults, due too few participants in the children group. To analyze bivariate associations between fatigue and other variables in adults, crosstabs and Fischer exact test were used due to small numbers. Fatigue scores (FSS) was dichotomized to two categories: Low fatigue = FSS score < 5, and severe fatigue = FSS score ≥ 5 (Lerdal et al., 2005). Variables on age, pain intensity and pain locations were dichotomized at median values. Number of MO-related surgeries was dichotomized in few surgeries < 6, and many surgeries ≥ 6. Employment status was dichotomized to show work capacity or not (with work capacity = working full time or part-time/studying/seeking jobs and not receiving disability benefits, reduced work capacity = receiving full or part time disability pension or work rehabilitation benefits). For all tests significance level was set at $p = \leq 0.05$.

Table 1
Demographic and clinical data on children (N = 11) and adults (N = 21) with multiple osteochondromas.

	Adults N (%)	Children N (%)
Occupation [a]		
Working full time	8 (38.1)	
Working part time	5 (23.8)	
Applying jobs	1 (4.8)	
Studying	1 (4.8)	
Disability benefits	6 (28.6)	
Work rehabilitation benefits	4 (19.0)	
Osteochondroma-related surgeries	20 (95.2)	9 (81.8)
Number of surgeries		
0	1 (4.8)	2 (18.2)
1-5	8 (38.1)	7 (63.6)
6-10	5 (23.8)	2 (18.2)
11-15	3 (14.3)	
16-20	3 (14.3)	
> 20	1 (4.8)	

[a] Two persons were part time on disability benefits and part time receiving work rehabilitation benefits, one was both studying and working part time.

One respondent had one FSS items missing. Missing items were replaced by the case substitution method that replaces missing values with the mean of the respondent's completed items (Polit and Beck, 2008).

Results

Demographic and clinical variables

Seventeen children and 22 adults participated in the meeting for MO patients and families. Written consent and questionnaire data were obtained from 32 persons, approximately one third of expected MO patients in Norway (Fig. 1). This included 11 children (7 boys and 4 girls, median age 10.7 years, range 6–16 years) and 21 adults (8 men and 13 women median age 37.1, range 21–67 years). Ten of 21 adults had challenges with work participation, being on disability or work rehabilitation benefits (Table 1). No participants were excluded.

Nine children and 20 adults reported having had at least one surgery for osteochondromas (Table 1). Most prevalent locations of osteochodroma-related surgeries in children were forearms, thighs/hips and feet, and in adults forearms, thighs/hips and calves (Fig. 2). Three adults reported having chondrosarcoma.

Fatigue

In children mean PedsQL MFS total score was 65.53 (SD 20.95) (Table 2), demonstrating significantly higher fatigue scores than reported for healthy children and similar fatigue values as reported for children with short stature and rheumatoid arthritis (Table 3). In adults FSS mean score was 5.6 (SD 1.12) (Table 2), demonstrating significantly higher fatigue scores than reported for the general Norwegian population, adults with rheumatoid arthritis and cancer (Table 3). Fifteen adults with MO (71%) reported severe fatigue (FSS ≥5) (Table 2).

Pain

Six of 11 children reported having pain now. Median worst pain intensity last week was 4.0 (0–9.5), median number of pain locations was 5 (Table 4). Most frequent reported pain locations were knees (6/6), ankles/feet (5/6) and shoulders/upper arms (3/6). Locations were evenly distributed on both sides of the body. Twenty of the 21 adults reported having had pain the last week (95%). Median pain intensity was 6.5 (2–9), and median number of pain locations was 5.5 (3–10) (Table 4). Most frequent pain locations were knees (18/20), shoulders/upper arms (16/20) and lower back (15/20). Locations were evenly distributed on both sides of the body.

Associations between fatigue, health-related and demographic variables

More women than men had severe fatigue. Severe fatigue was more prevalent in persons with high age, high pain intensity and many pain locations. However, none of these differences were significant (Table 5).

Discussion

Main findings

An important finding in this study is the high report of fatigue in children and adults with MO. To our knowledge this has not been reported previously. The study also supports previous findings of a high prevalence of pain in MO patients (D'Ambrosi et al., 2017; Darilek et al.,

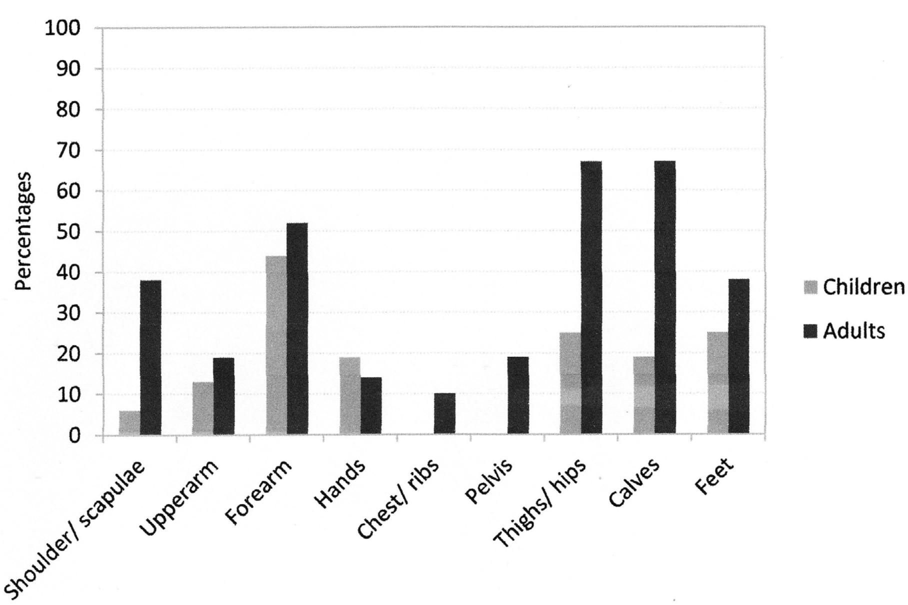

Fig. 2. Body-locations of osteochondroma-related surgeries in children (N = 11) and adults (N = 21) with multiple osteochondromas.

Table 2
Fatigue in children (N = 11) and adults (N = 21) with multiple osteochondromas.

	N (%)	Median (min-max)		Mean (SD)
Children, PedsQL Multidimensional fatigue scale				
Total fatigue		68.05	(29–97)	65.53 (20.95)
General fatigue		62.50	(25–100)	63.25 (25.47)
Sleep/rest fatigue		70.83	(25–96)	65.53 (24.73)
Cognitive fatigue		66.66	(38–100)	67.80 (17.69)
Adults, Fatigue severity scale (FSS)				
FSS total mean score		5.59	(3–7)	5.6 (1.12)
No fatigue (FSS ≤ 4)	3 (14.3)			
Borderline fatigue (FSS $^{>}$4 $^{<}$5)	3 (14.3)			
Severe fatigue (FSS ≥5)	15 (71.4)			

Table 3
Fatigue in children and adults with multiple osteochondromas, compared to reported findings in other groups.

	Mean PedsQL MFS total fatigue score (SD)	Mean difference	95% CI, mean difference	Independent samples *t*-test	
				t	*P* two-tailed
Current study (n = 11)	65.53 (20.95)				
Healthy children (n = 157) 0[b]	82.19 (12.27)	−16.66	−30.73, −2.58	−2.64	0.025[a]
Children with short stature (n = 29)[b]	71.56 (15.50)	−6.03	−20.11, 8.05	−0.95	0.362
Children with rheumatoid arthritis (n = 163)[c]	73.82 (21.93)	−8.29	−22.07, 5.79	−1.31	0.219
	Mean FSS score				
Adults, Current study (n = 21)	5.59 (1.12)				
General population (n = 1893)[d]	3.98 (1.31)	1.61	1.10, 2,12	6.57	≤0.001[a]
Rheumatoid arthritis (n = 122)[e]	4.20 (1.20)	1.39	0.88, 1.90	5.67	≤0.001[a]
Cancer (gliobastoma) (n = 65)[f]	3.90 (1.70)	1.69	1.18, 2.20	6.89	≤0.001[a]

[a] Significant.
[b] Varni et al., (2012).
[c] Varni et al., (2004).
[d] Lerdal et al., (2005).
[e] Mancuso et al., (2006).
[f] Valko et al., (2015)

Table 4
Prevalence of pain, pain intensity and pain locations in children (N = 11) and adults (N = 21) with multiple osteochondromas.

	N (%)	Median (min- max)		Mean (SD)
Children				
Pain now? Yes	6 (54.5)			
Pain intensity; worst pain last seven days (VAS 0–100 mm)		4	(0–9.5)	4.17 (3.50)
Number of pain locations (n = 6)[a]		5	(4–10)	6.33 (2.88)
Few pain locations (1–3 locations)[a]				
Moderate pain locations (4–6 locations)[a]	4 (66.6)			
Many pain locations (7–11 locations)[a]	2 (33.4)			
Adults				
Pain last week? Yes	20 (95)			
Pain intensity last week (NPRS range 0–10) (n = 20)[a]		6,5	(2–9)	6,1 (1.77)
Mild pain (score < 3)[a]	2 (10)			
Moderate pain (score 4–6)[a]	8 (40)			
Severe pain (score 7–11)[a]	10 (50)			
Number of pain locations (n = 20)[a]		5.5	(3–10)	6.05 (2.09)
Few pain locations (1–3 locations)[a]	1 (5)			
Moderate pain locations (4–6 locations)[a]	13 (65)			
Many pain locations (7–11 locations)[a]	6 (30)			

[a] Data only for individuals reporting pain intensity/locations.

2005; Goud et al., 2012).

Clinical description

The majority of our participants (20 adults and 9 children) reported that they had undergone osteochondroma-related surgeries. Three adults reported chondrosarcoma. Similar findings has been found in other MO populations (Darilek et al., 2005; Goud et al., 2012).

Fatigue

In this study Norwegian children with MO reported significantly higher fatigue than reported for healthy children (Varni et al., 2012) and comparable to reported fatigue levels in children with short stature (Varni et al., 2012) and rheumatoid arthritis (Varni et al., 2004). In other patient groups fatigue is reported to have major impact on children's life, affecting ability to participate in daily activities (Eddy and

Table 5
Bivariate Associations between fatigue and other variables in adults with Multiple Osteochondromas.

Categorical variables	Low fatigue FSS[a] score $^{<}$5 Number of persons	High fatigue FSS[a] score ≥5 Number of persons	Fischer exact (2 sided)
Gender (n = 21)			
Men	4	4	0.146
Women	2	11	
Age (n = 21)			
Age 20–37.1	5	6	0.149
Age 37.4–67	1	9	
Employment status (n = 21)[b]			
With work capacity	1	8	0.178
Reduced work capacity	5	7	
Number of operations (n = 21)			
Few operations ($^{<}$ 6)	1	8	0.178
Many operations (≥6)	5	7	
Pain intensity (NPRS) (n = 20)			
Low pain intensity (NPRS $^{<}$6)	3	4	0.613
High pain intensity (NPRS ≥ 6)	3	10	
Number of pain locations (n = 20)			
Few pain locations	2	3	0.291
Many pain locations	3	12	

Bivariate analyses of fatigue and other variables done by crosstabs and fisher exact test.
[a] FSS = Fatigue Severity Scale. NPRS = numeric pain rating scale.
[b] Employment status, recoded variable: With work capacity = not receiving disability benefits and working full time/part-time/studying/seeking jobs, n = 12. Reduced work capacity = receiving full or part time disability pension or work rehabilitation benefits n = 9.

Cruz, 2007; Maher et al., 2015). Our findings therefore indicate that addressing fatigue is important in children with MO.

Norwegian adults with MO reported significantly higher fatigue than reported for the general Norwegian population (Lerdal et al., 2005), patients with rheumatoid arthritis (Mancuso et al., 2006) and cancer (Valko et al., 2015). Seventy-one per cent of adults with MO reported severe fatigue (FSS ≥ 5), much higher than found in the general Norwegian population (22%) (Lerdal et al., 2005). Previous findings of reduced SF -36 vitality scores in MO patients (Chhina et al., 2012; Goud et al., 2012), support our findings of a high prevalence of fatigue in adults with MO.

Pain

Six of 11 children reported having pain. This is consistent with previous studies of children with MO (Darilek et al., 2005; Goud et al., 2012). The mean VAS pain intensity of 4.2 was higher than for children with rheumatoid arthritis (3.8) (Benestad et al., 1996). To our knowledge data on pain intensity has not been previously reported for children with MO. All six children reporting pain had moderate to many pain locations, indicating that pain was a serious problem.

Twenty of 21 adults reported pain in the preceding week, in line with previous findings of high pain prevalence and pain intensity in adult MO patients (Darilek et al., 2005; Goud et al., 2012). The mean pain intensity (NPRS 6.1) was higher than among persons with chronic pain in the general Norwegian population (NPRS 3.93) (Rustøen et al., 2004). Twenty of 21 adults with MO reported 4 or more pain locations. In comparison, a study of Norwegian persons with chronic pain found that 61% reported 4 or more pain locations (Rustøen et al., 2004). This supports findings that not only localized pain, but also multisite pain due to osteochondromas, is frequent in MO (Darilek et al., 2005).

Associations between fatigue, health-related and demographic variables

We found some differences regarding prevalence of severe fatigue in different health related and demographic variables in adults with MO. None of the differences were significant, but this may be due to the small sample size. Results should therefore be viewed with caution. There were more persons with high pain intensity and many pain locations who had severe fatigue. This coincides with studies of other patient groups, both children and adults, where pain has been found strongly associated with fatigue (Gold et al., 2009; de Rooij et al., 2015; Landry et al., 2015). Although we found no differences in fatigue severity related to number of operations or work capacity, this may influence the experience of fatigue, and should be explored in larger studies.

Many other factors may influence fatigue in persons with MO. Studies of other health conditions have shown that fatigue was significantly associated with lower physical activity (Maher et al., 2015) and restrict an individual‘s ability to compensate physically or mentally for functional impairment (Ricci et al., 2007). Persons with MO often have physical impairments (Jäger et al., 2007), and are substantially incapacitated in sports and physical activity (Goud et al., 2012). This may increase the risk of developing fatigue and disability. Sleep disturbances may also influence fatigue (Luntamo et al., 2012). Goud et al. (2012) found that 21% of children with MO reported sleeping problems due to pain. According to El-Metwally et al. (2007) day-time tiredness was one of the greatest risk factors for developing persistent pain. Psychological and emotional challenges have been reported in MO (Fraser and Porter, 2000; D'Ambrosi et al., 2017) and may encompass worry for disability and malignant development. Psychological variables may therefore also be relevant to investigate in association to fatigue.

Need for further research

This study found high prevalence of fatigue in Norwegian children and adults with MO, also compared to general populations and other patient groups. In line with other MO studies (Chhina et al., 2012; D'Ambrosi et al., 2017; Darilek et al., 2005; Goud et al., 2012) we found high prevalence of pain. As the study group was small our results cannot be generalized to the whole MO population. There is a need for further research on prevalence, possible causes and treatment for both fatigue and pain in children and adults with MO. Qualitative studies exploring the experience of living with pain and fatigue in persons with MO are needed.

Implications for clinical practice

This study supports other research findings reporting that MO may influence the patient's whole life (Fraser and Porter, 2000; Pacifici, 2017). As Fraser and Porter (2000) points out, it is important that health professionals ask MO patients about their problems and needs. Many MO patients will need repeated orthopaedic surgery. Orthopaedic nurses and surgeons are therefore important professionals in meeting them and recognising their problems. Several studies show that acceptance of the problem is an important factor in management of both fatigue and pain (Eddy and Cruz, 2007; Mathias et al., 2014; Thomas et al., 2015). In our clinical experience fatigue and pain are unpredictable and frustrating symptoms to live with, often invisible to others. Increased knowledge and acknowledgement of fatigue and pain as a common problem in MO may be valuable for patients living with MO. Therefore clinicians meeting adults and children with MO should inquire about fatigue and pain, investigate possible causes and plan interventions.

Limitations and strengths

This study has several limitations; small sample size and possible selection bias being the most important. However, as MO is a rare disorder, it should be noted that approximately one third of Norway's estimated MO patients participated. Recruiting persons with MO only from TRS may have resulted in selection bias. However, our sample may be more representative than samples recruited from specialized hospital clinics, as all persons with MO regardless of problems may use TRS. It is possible that collecting data at a patient meeting arranged by the resource centre may have influenced the results and that data collection in another setting, e.g. postal questionnaire may have given different results. However, other studies of MO patients show similar results on reduced vitality and high prevalence of pain and support our findings. Use of self-reported data can also imply a recall bias, however the use of standardized instruments relevant for children and adults is a strength and makes comparisons possible. Using self-report instruments with children can be challenging (Gallagher et al., 2010; Oulton et al., 2016) and it is possible that parents may have influenced their children's answers. However, research has shown that children are competent both to give consent and provide valid information about themselves (Danby and Farrell, 2005; Kim, 2016).

Conclusions

This cross-sectional study found high prevalence of fatigue in Norwegian children and adults with MO. Such findings have not been reported previously. As in other MO studies, pain was prevalent in both children and adults. A high proportion of the participants reported high pain intensity and many pain locations. This implies that fatigue and pain warrant specific attention in clinical practice and further research in MO.

Conflict of interest

The authors declare no conflict of interest.

Ethical statement

Participation was voluntary and written consent was obtained for all participants. Parents asked their children if they wanted to participate and consented for children < 16 years. The information letter highlighted that participation or non-participation would have no consequences for further contact with TRS. Ethical approval was applied from the Data Protection Officer at Oslo University Hospital, who gave approval to use anonymous questionnaire data.

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References

Benestad, B., Vinje, O., Veierød, M., Vandvik, I., 1996. Quantitative and qualitative assessments of pain in children with juvenile chronic arthritis based on the Norwegian version of the Pediatric Pain Questionnaire. Scand. J. Rheumatol. 25 (5), 293–299.

Breivik, H., Borchgrevink, P.C., Allen, S.M., Rosseland, L.A., Romundstad, L., Hals, E.K., Stubhaug, A., 2008. Assessment of pain. Br. J. Anaesth. 101 (1), 17–24. https://doi.org/10.1093/bja/aen103.

Chhina, H., Davis, J.C., Alvarez, C.M., 2012. Health-related quality of life in people with hereditary multiple exostoses. J. Pediatr. Orthop. 32 (2), 210–214. https://doi.org/10.1097/BPO.0b013e31823ee31c.

Cleeland, C.S., Ryan, K.M., 1994. Pain assessment: global use of the brief pain inventory. Ann. Acad. Med. Singapore 23 (2), 129–138.

Crichton, A., Knight, S., Oakley, E., Babl, F.E., Anderson, V., 2015. Fatigue in child chronic health conditions: a systematic review of assessment instruments. Pediatrics 135 (4), e1015–1031. https://doi.org/10.1542/peds.2014-2440.

D'Ambrosi, R., Ragone, V., Caldarini, C., Serra, N., Usuelli, F.G., Facchini, R.M., 2017. The impact of hereditary multiple exostoses on quality of life, satisfaction, global health status, and pain. Arch. Orthop. Trauma. Surg. 137 (2), 209–215. https://doi.org/10.1007/s00402-016-2608-4.

Danby, S., Farrell, A., 2005. Opening the research conversation. In: Farrell, A. (Ed.), Ethical Research with Children. Open University Press, Maidenhead, England, pp. 49–67.

Darilek, S., Wicklund, C., Novy, D., Scott, A., Gambello, M., Johnston, D., Hecht, J., 2005. Hereditary multiple exostosis and pain. J. Pediatr. Orthop. 25 (3), 369–376.

de Rooij, A., van der Leeden, M., de Boer, M.R., Steultjens, M.P., Dekker, J., Roorda, L.D., 2015. Fatigue in patients with chronic widespread pain participating in multidisciplinary rehabilitation treatment: a prospective cohort study. Disabil. Rehabil. 37 (6), 490–498. https://doi.org/10.3109/09638288.2014.923530.

Dittner, A.J., Wessely, S.C., Brown, R.G., 2004. The assessment of fatigue: a practical guide for clinicians and researchers. J. Psychosom. Res. 56 (2), 157–170. https://doi.org/10.1016/S0022-3999(03)00371-4.

Eddy, L., Cruz, M., 2007. The relationship between fatigue and quality of life in children with chronic health problems: a systematic review. J. Spec. Pediatr. Nurs. (JSPN) 12 (2), 105–114.

El-Metwally, A., Salminen, J.J., Auvinen, A., Macfarlane, G., Mikkelsson, M., 2007. Risk factors for development of non-specific musculoskeletal pain in preteens and early adolescents: a prospective 1-year follow-up study. BMC Muscoskelet. Disord. 8, 46. https://doi.org/10.1186/1471-2474-8-46.

Echoff, C., Straume, B., Kvernmo, S., 2017a. Multisite musculoskeletal pain in adolescence and later mental health disorders: a population-based registry study of Norwegian youth: the NAAHS cohort study. BMJ Open 7 (2), e012035. https://doi.org/10.1136/bmjopen-2016-012035. Feb 10.

Echoff, C., Straume, B., Kvernmo, S., 2017b. Multisite musculoskeletal pain in adolescence as a predictor of medical and social welfare benefits in young adulthood: the Norwegian Arctic Adolescent Health Cohort Study. Eur. J. Pain 21 (10), 1697–1706. https://doi.org/10.1002/ejp.1078. Epub 2017 Jul 6.

Fraser, M., Porter, D.E., 2000. Hereditary multiple exostoses: a qualitative study exploring families' and patients' perceptions of disease impact and self-expressed needs. J. Orthop. Nurs. 4 (3), 103–111.

Gallagher, M., Haywood, S.L., Jones, M.W., Milne, S., 2010. Negotiating informed consent with children in school-based research: a critical review. Child. Soc. 24 (6), 471–482. https://doi.org/10.1111/j.1099-0860.2009.00240.x.

Gold, J.I., Mahrer, N.E., Yee, J., Palermo, T.M., 2009. Pain, fatigue, and health-related quality of life in children and adolescents with chronic pain. Clin. J. Pain 25 (5), 407–412. https://doi.org/10.1097/AJP.0b013e318192bfb1.

Goud, A.L., de Lange, J., Scholtes, V.A., Bulstra, S.K., Ham, S.J., 2012. Pain, physical and social functioning, and quality of life in individuals with multiple hereditary exostoses in The Netherlands: a national cohort study. J. Bone Joint Surg. Am. 94 (11), 1013–1020. https://doi.org/10.2106/jbjs.k.00406.

Graham, C.D., Rose, M.R., Grunfeld, E.A., Kyle, S.D., Weinman, J., 2011. A systematic review of quality of life in adults with muscle disease. J. Neurol. Sep. 258 (9), 1581–1592. https://doi.org/10.1007/s00415-011-6062-5. Epub 2011 May 20.

Jennes, I., Pedrini, E., Zuntini, M., Mordenti, M., Balkassmi, S., Asteggiano, C.G., Wuyts, W., 2009. Multiple osteochondromas: mutation update and description of the multiple osteochondromas mutation database (MOdb). Hum. Mutat. 30 (12), 1620–1627. https://doi.org/10.1002/humu.21123.

Jäger, M., Westhoff, B., Portier, S., Leube, B., Hardt, K., Royer-Pokora, B., Krauspe, R., 2007. Clinical outcome and genotype in patients with hereditary multiple exostoses. J. Orthop. Res. 25 (12), 1541–1551. https://doi.org/10.1002/jor.20479.

Kim, C.-Y., 2016. Why research 'by' children? Rethinking the assumptions underlying the facilitation of children as researchers. Child. Soc. 30 (3), 230–240. https://doi.org/10.1111/chso.12133.

Krupp, L.B., LaRocca, N.G., Muir-Nash, J., Steinberg, A.D., 1989. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch. Neurol. 46 (10), 1121–1123.

Landry, B.W., Fischer, P.R., Driscoll, S.W., Koch, K.M., Harbeck-Weber, C., Mack, K.J., et al., 2015. Managing chronic pain in children and adolescents: a clinical review. PM &R 7 (11), S295–S315.

Lerdal, A., Wahl, A.K., Rustøen, T., Hanestad, B.R., Moum, T., 2005. Fatigue in the general population; A translation and test of the psychometric properties of the Norwegian version of the fatigue severity scale. Scand. J. Publ. Health 33 (2), 123–130.

Luntamo, T., Sourander, A., Santalahti, P., Aromaa, M., Helenius, H., 2012. Prevalence changes of pain, sleep problems and fatigue among 8-year-old children: years 1989, 1999, and 2005. J. Pediatr. Psychol. 37 (3), 307–318. https://doi.org/10.1093/jpepsy/jsr091.

Maher, C., Crettenden, A., Evans, K., Thiessen, M., Toohey, M., Watson, A., Dollman, J., 2015 Aug. Fatigue is a major issue for children and adolescents with physical disabilities. Dev. Med. Child Neurol. 57 (8), 742–747. https://doi.org/10.1111/dmcn.12736. Epub 2015 Mar 22.

Mancuso, C.A., Rincon, M., Sayles, W., Paget, S.A., 2006. Psychosocial variables and fatigue: a longitudinal study comparing individuals with rheumatoid arthritis and healthy controls. J. Rheumatol. 33 (8), 1496–1502.

Margolis, R.B., Chibnall, J.T., Tait, R.C., 1988. Test-retest reliability of the pain drawing instrument. Pain 33 (1), 49–51.

Mathias, B., Parry-Jones, B., Huws, J.C., 2014. Individual experiences of an acceptance-based pain management programme: an interpretative phenomenological analysis. Psychol. Health 29 (3), 279–296. https://doi.org/10.1080/08870446.2013.845667.

McCabe, M., 2009. Fatigue in children with long-term conditions: an evolutionary concept analysis. J. Adv. Nurs. 65 (8), 1735–1745. https://doi.org/10.1111/j.1365-2648.2009.05046.x.

Oulton, K., Gibson, F., Sell, D., Williams, A., Pratt, L., Wray, J., 2016. Assent for children's participation in research: why it matters and making it meaningful. Child Care Health Dev. 42 (4), 588–597. https://doi.org/10.1111/cch.12344.

Pacifici, M., 2017. Hereditary multiple exostoses: new insights into pathogenesis, clinical complications, and potential treatments. Curr. Osteoporos. Rep. 15 (3), 142–152. https://doi.org/10.1007/s11914-017-0355-2.

Payne, R., Sieg, E., Fox, E., Harbaugh, K., Rizk, E., 2016. Management of nerve compression in multiple hereditary exostoses: a report of two cases and review of the literature. Childs Nerv. Syst. https://doi.org/10.1007/s00381-016-3166-3.

Pedrini, E., Jennes, I., Tremosini, M., Milanesi, A., Mordenti, M., Parra, A., Sangiorgi, L., 2011. Genotype-phenotype correlation study in 529 patients with multiple hereditary exostoses: identification of "protective" and "risk" factors. J. Bone Joint Surg. Am. 93 (24), 2294–2302. https://doi.org/10.2106/jbjs.j.00949.

Pollard, L.C., Choy, E.H., Gonzalez, J., Khoshaba, B., Scott, D.L., 2006. Fatigue in rheumatoid arthritis reflects pain, not disease activity. Rheumatology (Oxford) 45 (7), 885–889. https://doi.org/10.1093/rheumatology/kel021.

Polit, D.F., Beck, C.T., 2008. Nursing Research. Generating and Assessing Evidence for Nursing Practice. Lippincott Williams & Wilkins, Philadelphia.

Rathleff, M.S., Roos, E.M., Olesen, J.L., Rasmussen, S., 2013. High prevalence of daily and multi-site pain – a cross-sectional population-based study among 3000 Danish adolescents. BMC Pediatr. 13 (1), 191. https://doi.org/10.1186/1471-2431-13-191.

Ricci, J.A., Chee, E., Lorandeau, A.L., Berger, J., 2007. Fatigue in the U.S. workforce: prevalence and implications for lost productive work time. J. Occup. Environ. Med. 49 (1), 1–10. https://doi.org/10.1097/01.jom.0000249782.60321.2a.

Rustøen, T., Wahl, A.K., Hanestad, B.R., Lerdal, A., Paul, S., Miaskowski, C., 2004. Prevalence and characteristics of chronic pain in the general Norwegian population. Eur. J. Pain 8 (6), 555–565. https://doi.org/10.1016/j.ejpain.2004.02.002.

Rustøen, T., Wahl, A.K., Hanestad, B.R., Lerdal, A., Paul, S., Miaskowski, C., 2005. Age and the experience of chronic pain: differences in health and quality of life among younger, middle-aged, and older adults. Clin. J. Pain 21 (6), 513–523.

Thomas, S., Kersten, P., Thomas, P.W., Slingsby, V., Nock, A., Jones, R., et al., 2015. Exploring strategies used following a group-based fatigue management programme for people with multiple sclerosis (FACETS) via the Fatigue Management Strategies Questionnaire (FMSQ). BMJ Open 5 (10), e008274. https://doi.org/10.1136/bmjopen-2015-008274.

Valko, P.O., Siddique, A., Linsenmeier, C., Zaugg, K., Held, U., Hofer, S., 2015. Prevalence and predictors of fatigue in glioblastoma: a prospective study. Neuro Oncol. 17 (2), 274–281. https://doi.org/10.1093/neuonc/nou127.

Varni, J.W., Burwinkle, T.M., Seid, M., 2005. The PedsQL as a pediatric patient-reported outcome: reliability and validity of the PedsQL Measurement Model in 25,000 children. Expert Rev. Pharmacoecon. Outcomes Res. 5 (6), 705–719. https://doi.org/10.1586/14737167.5.6.705.

Varni, J.W., Burwinkle, T.M., Szer, I.S., 2004. The PedsQL Multidimensional Fatigue Scale in pediatric rheumatology: reliability and validity. J. Rheumatol. 31 (12), 2494–2500.

Varni, J.W., Limbers, C.A., Bryant, W.P., Wilson, D.P., 2012. Assessment of fatigue in pediatric patients with short stature utilizing the PedsQL™ multidimensional fatigue scale. Child Health Care 41 (2), 162–181.

Varni, J.W., Thompson, K.L., Hanson, V., 1987. The Varni/Thompson Pediatrie Pain Questionnaire. I. Chronic musculoskeletal pain in juvenile rheumatoid arthritis. Pain 28 (1), 27–38.

Von Korff, M., Jensen, M.P., Karoly, P., 2000. Assessing global pain severity by self-report in clinical and health services research. Spine (Phila Pa 1976) 25 (24), 3140–3151.

Wong, W.S., Fielding, R., 2012. The co-morbidity of chronic pain, insomnia, and fatigue in the general adult population of Hong Kong: prevalence and associated factors. J. Psychosom. Res. 73 (1), 28–34. https://doi.org/10.1016/j.jpsychores.2012.04.011.