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A widening gap between boys and girls in musculoskeletal complaints, while growing up from age 11 to age 20 - the PIAMA birth Cohort study

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Abstract

Introduction: The adolescent years represent a key period for the development of musculoskeletal complaints (MSC) and the differences between boys and girls. We evaluated the prevalence and course of MSC and factors associated with MSC while growing up from age 11 to age 20.

Methods: Questionnaire-based data at age 11 ($n = 2{,}638$), age 14 ($n = 2{,}517$), age 17 ($n = 2{,}094$) and at age 20 ($n = 2{,}206$) from the ongoing Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort were analyzed. MSC refers to pain of lower back, upper- and/or lower extremities. A multivariable logistic regression analysis was used to evaluate a number of factors in relation to persistent pain (pain reported at three out of four measurements).

Results: Prevalence of MSC increased from 14.2% at age 11 to 22.1% at age 20 for boys, and from 17.4% at age 11 to 37.9% at age 20 for girls. Persistent pain was found among 5.1% of the boys and 16.5% of the girls. Being bullied, sleeping problems and tiredness during the day were significantly associated with persistent pain, in both boys and girls, while the latter two were more prevalent among girls. Self-reported (sports-) accidents, and among girls also early onset of puberty, were also

significantly associated with persistent pain, but lifestyle factors, such as physical activity and smoking, were not.

Conclusion: The prevalence of MSC increases during adolescence, with a widening gap between boys and girls. The factors associated with MSC are similar in boys and girls, though the prevalence of some of these differ by sex.

Significance: Measuring a group of youngsters 4 times between age 11 and 20 shows an increase in the percentage reporting musculoskeletal complaints (MSC) with a widening gap between girls and boys, with more pain among girls. Boys and girls do hardly differ with respect to factors associated with MSC, being mainly psychosocial factors and (sports) accidents.

1 | INTRODUCTION

Health problems characterized by musculoskeletal complaints (MSC) are the second most common cause of disability worldwide (Coenen et al., 2017; Fuglkjaer et al., 2017; Watson et al., 2002). Two aspects of MSC that have recently been the subject of several studies, are that the prevalence is already high at an early age (Hulsegge et al., 2011; Leino-Arjas et al., 2018; Perquin et al., 2000; Picavet et al., 2016), and that the prevalence in women/girls appears to be higher than in men/boys (Perquin et al., 2000). The adolescent years seem to be important for several reasons: the prevalence of MSC is already high in those years (Leino-Arjas et al., 2018), and adolescents with pain are more often absent from school (Cohen et al., 2010), experience more difficulties in friendships (Forgeron et al., 2010) and report a lower quality of life (Holley et al., 2017; Wurm et al., 2018). Also, the differences between men and women in prevalence may originate in adolescence: these years encompass the rapid physical and mental developments that may affect the way we experience and cope with health issues like pain, eventually affecting future adult life.

In general, MSC in children and adolescents have not been much studied (Kamper et al., 2016). A high prevalence is often found, but little is known about the course of pain during adolescent years (Coenen et al., 2017; Dissing et al., 2017; Picavet et al., 2016). We do not know whether those reporting pain in early adolescent years continue to report pain at later (adolescent) ages, or whether the high prevalences in adolescent years are the reflection of a more or less random phenomenon, now affecting one and then the other ('everybody will experience pain now and then'). Further insight into the development of MSC with individual repeated measurements seems relevant. In addition, not much is known about the factors associated with the development and the course of MSC (Hulsegge et al., 2011; Kamper et al., 2016). The experience of pain is influenced by physical, psychological and social factors (Kamper et al., 2016), and for MSC among children and adolescents, those include: a low socioeconomic status (SES), being overweight, smoking, physical inactivity, a sedentary lifestyle, mental health problems (Andorsen et al., 2017; Hulsegge et al., 2011; Pourbordbari et al., 2019) and sleep disturbances (Holley et al., 2017). A review on musculoskeletal pain summarized the literature as follows: low socioeconomic status and also negative emotional symptoms and smoking are associated with musculoskeletal pain, but overweight is not (Huguet et al., 2016). A recent review on prognostic factors for low back pain among adolescents mentioned that only older age and participation in competitive sports showed a consistent association with low back pain (Calvo-Munoz et al., 2018). These reviews showed that sex was not associated with onset of pain independently of other factors and that findings were inconsistent for persistent pain. So, the key to the sex differences in pain may be found in the differences in sensitivity for factors and/or differences in prevalence of these factors associated with MSC.

Using data from an ongoing birth cohort—the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study—we previously reported that the 1-year prevalence of MSC increased from 15.8% among 11-year-olds to 24.4% at the age of 14 (Picavet et al., 2016). These figures are within the range (4%–40%) of figures presented in a systematic review (King et al., 2011). Most studies, including ours, found that adolescent girls reported more MSC than adolescent boys (Gustafsson et al., 2018; Hulsegge et al., 2011; Jones & Macfarlane, 2005; Watson et al., 2002; Wurm et al., 2018).

Having extended the follow-up of the PIAMA birth cohort study with two measurement points since our previous report, the purpose of this article was to evaluate the prevalence, course and factors associated with MSC among adolescents, with a focus on the differences between boys and girls. We aimed to answer the following research questions: (a) What is the prevalence of MSC in adolescent boys and girls at the ages of 11, 14, 17 and 20 years, (b) What is the course of

MSC among boys and girls over that period, and (c) How do boys and girls with persistent MSC differ with respect to a number of health and life style factors?

2 | METHODS

This is a longitudinal study embedded in the ongoing PIAMA birth cohort study that has been described in detail elsewhere (Wijga et al., 2014). In brief, pregnant women were recruited from the general population through 52 antenatal clinics in three different regions of the Netherlands (North, Central and West). There were no exclusion criteria, but the study information and questionnaires were in Dutch, so that in practice non-Dutch speaking families were unable to participate. The baseline study population consisted of 3,963 children born to these women in 1996 or 1997. All participants gave written informed consent and the Medical Ethical Committees concerned gave approval.

2.1 | Musculoskeletal complaints

The presence of MSC was assessed by the question: 'Please indicate whether you experienced one of the following health problems in the past 12 months'. Three items pertaining to MSC were: 'long-lasting back complaints', 'long-lasting complaints of the upper extremities (neck, shoulder, elbow, wrist or hand), and 'long-lasting complaints of the lower extremities (hip, knee, ankle or foot). It was explicitly stated that 'long-lasting' refers to longer than one month. There were three response categories: 'no', 'yes, but no visit to the doctor' and 'yes, visit to the doctor'. The last two were combined into 'yes'. 'Having any MSC' was defined as having complaints in one or more of the three anatomical locations. Although the term 'complaints' was used in the questionnaire, we interpret this to be almost identical to 'pain', and use these terms interchangeably in this paper.

To evaluate the course of MSC over time, measurements at the four time points, corresponding to four ages, were used to distinguish five long-term pain patterns: never pain, persistent pain, development of complaints, a decrease in complaints and a varying course of complaints (Picavet et al., 2019). The pattern 'persistent pain' included all adolescents who reported at least one MSC in at least three out of four measurements. Adolescents who reported having no MSC at three or all four measurements, were assigned to the pattern '(almost) never pain'. 'Development of complaints' included those who reported no complaints at the first two measurement years followed by reporting of complaints at the next two. Adolescents reporting MSC at the first two measurements followed by no complaints at subsequent ones, formed the 'decrease in pain' pattern. 'A varying course of complaints' was assigned when MSC were variably reported. For 1895 participants, we had enough valid data points to classify them according to these long-term pain patterns between the age 11 and 20 years.

2.2 | Factors studied in association with MSC

The independent variables were sociodemographic factors, growth and development factors, psychosocial factors, lifestyle factors and (sports) accidents. For most characteristics we chose the measurements of these characteristics at age 14, because 11 was considered to be too young, at age 17 the number of missing values was higher than at the other ages, and age 20 was too old However, the variable 'attained height' was measured at age 20 and the variable 'early puberty' was assessed for girls based on data at age 11 and for boys at age 14.

The *sociodemographic factors were:* age, sex and educational level of the adolescent. In addition the educational level of the mother was included as measure for 'family lifestyle'. The highest completed educational level of the mother was divided into three categories: low education (primary school, lower vocational education, or lower secondary education, intermediate vocational education), intermediate education (higher secondary education) and higher education (higher vocational education or university degree). The educational level of the adolescent at age 14 was divided into two categories; low (practical and special education, lower secondary education) and high (higher secondary education and pre-university education).

As *growth and development factors*, pubertal status, being overweight and attained height were used. Pubertal status was measured at ages 11, 14 and 17, using the Pubertal Development Scale (Petersen et al., 1988). This scale consists of three general questions, respectively on growth spurt, body hair and skin changes, and two sex-specific questions: facial hair growth and voice changes for boys, and questions on breast development and menarche for girls. For each of these five items the response categories were: no development yet; development has barely begun; development is definitely underway; or development has already been completed. Sum scores [range 4–20] were divided by five to get a score between 1 and 4, with 1 referring to no development and 4 to a completed pubertal development. Classified as 'early puberty' were girls in the highest 25% at age 11, and boys in the highest 25% at age 14. We used a sex-specific definition of early puberty because pubertal development starts earlier in girls than in boys.

At age 14 parents were asked to report the measured weight (in kilogram) and height (in centimetres) of their child. Overweight (including obesity) was defined according to the

international age- and sex-specific cutoff points for children (a body mass index of >22.6 kg/m^2 for boys and >23.3 kg/m^2 for girls at age 14, for example; Cole et al., 2000). At age 20, the attained height was reported by the adolescents themselves. The sex-specific 20th percentile (175 cm for girls, 190 cm for boys) was used as cut-off point to divide the adolescents into the category tall versus not tall. Attained height can be seen as a growth indicator, and is also suggested as a risk factor for MSC, in particular for low back pain (e.g. Huguet et al).

Psychosocial factors included were overall mental health status, worrying, being bullied, sleeping problems, daytime tiredness/sleepiness and hyperactivity. To measure mental health status, the RAND Mental Health Inventory (MHI-5) (Berwick et al., 1991) was used. Data on five items with four response categories were rescaled to a score ranging from 0 to 100, where a higher score indicated a better mental health. A low score was defined as a score between 0 and 60 (Rumpf et al., 2001). Worrying was based on the item: 'Do you have problems that keep you busy day and night?' To assess bullying, children were asked if they had been bullied in the last 12 months with response options yes or no. Sleeping problems was a composed variable based on the frequency and duration of nighttime awakenings. The children who reported being awake sometimes or every night, or reported being awake for a while or a longer time, were categorized as having sleeping problems. Daytime tiredness/sleepiness was measured by the question 'How often are you tired or sleepy during the day?' with response options '(almost) never', 'occasionally, but on less than one day per week', 'on one day per week', 'on two days per week' or 'on three days per week or more'. Adolescents who reported being tired or sleepy on at least three days per week were defined as experiencing daytime tiredness/sleepiness. Hyperactivity was based on self-reporting of attention-deficit hyperactivity disorder or hyperactivity in the last twelve months, irrespective of having visited a doctor.

Lifestyle factors were physical activity, screen time and smoking. Physical activity was measured by several items. Children were classified as being moderately physically active when being active for at least 60 min a day on at least five days a week. Being vigorously physically active was defined as being physically active with heavy breathing and sweating for at least 30 min on at least two days per week. Screen time was used as an indicator of sedentary behavior and dichotomized as at least two hours per day versus less, at age 14, with screen time being watching television, using a (game)computer or tablet outside school hours. The WHO advice for youth between 4 and 17 years is a maximum of two hours a day (WHO, 2010). Smokers were defined as those who smoked at least one cigarette per month, at age 14.

'Accidents' was a composite variable based on the question if the children had accidents or injuries in traffic, during sports activities or physical education in the last twelve months. Response options were 'no', 'yes, no visit to the doctor' and 'yes, visit to the doctor'. The children, who answered 'yes' were categorized as having had an accident or injury.

2.3 | Statistical analyses

We used descriptive statistics to evaluate the MSC prevalence by age and sex. Sex differences in prevalence were assessed by logistic regression analyses and the differences are presented as difference in percentage points (absolute difference) and as the percentage difference in girls compared to boys (relative difference). Univariable and multivariable logistic regression analyses were then used to evaluate the associations of sociodemographic factors, growth and development factors, psychosocial factors, lifestyle factors and accidents with (the long-term course defined as) persistent pain, using (almost) never MSC as the reference category, and expressed as odds ratio's (OR). These analyses were also stratified by sex. We did not do these analyses for the other 'courses', because the numbers in these groups were very small (with exception of the complaints with a varying course). Statistical Analysis System (SAS), version 9.4, was used. Results were presented with 95% confidence intervals (CI). A p-value of $\leq .05$ was considered to be statistically significant.

3 | RESULTS

Questionnaires were completed by adolescents when they were 11 (n = 2,638), 14 (n = 2,517), 17 (n = 2,094), and 20 (n = 2,206) years old. For a total of 1,895 (970 girls and 925 boys) we were able to define the long-term course MSC pattern.

At age 14, 9.0% of the adolescents were classified as being overweight (Table 1). A MHI-5 score below 60 at age 14 was found among 12% of the adolescents. Almost one in five adolescents reported sleeping problems. In addition, 17.3% of the adolescents reported feeling tired/sleepy during the day. Approximately half of the adolescents reported being moderately physically active. Screen time of more than two hours a day was reported by 65%. At age 14, 4.5% reported to smoke at least one cigarette a month. Sex differences were in particular found for the psychosocial factors. Especially a MHI-5 score below 60 ($P_{♀}$ = 17%, $P_{♂}$ = 7%), worrying ($P_{♀}$ = 16%, $P_{♂}$ = 7%), sleeping problems ($P_{♀}$ = 26%, $P_{♂}$ = 12%) and daytime tiredness/sleepiness ($P_{♀}$ = 24%, $P_{♂}$ = 12%) were significantly more prevalent among girls than among boys.

TABLE 1 Characteristics of the study population

Sociodemographic characteristics	Total %	Girls %	Boys %
n (MSC selection)		970	925
Education			
Level of education child (14 years)			
High	63.6	67.0	60.2
Low	36.4	33.0	39.8
Level of education mother			
High	35.0	34.6	35.2
Intermediate	41.6	41.8	41.4
Low	23.5	23.7	23.3
Growth and development factors			
Early puberty (g11y, b14y)	25.8	24.9	26.7
Attained height (20 years)	22.9	24.5	21.0
Overweight (14 years)	9.0	7.4	10.5
Psychosocial factors (14 years)			
MHI-5 score less than 60	12.0	17.0	7.2
Worrying	11.9	16.4	7.3
Being bullied	15.5	15.8	15.3
Sleeping problems	18.6	25.5	11.8
Daytime tiredness/sleepiness	18.1	24.2	12.1
Hyperactivity	5.8	3.6	8.1
Lifestyle factors (14 years)			
Moderate physical activity (≥5 d/wk)	47.9	44.9	50.9
Vigorous exercise (≥2 d/pw)	67.3	64.3	70.2
Screen time (>2 h/d)	65.2	61.3	69.0
Smoking (>1/mo)	6.1	6.8	5.5
Accidents (14 years)	37.5	36.8	38.1

3.1 | Prevalence of MSC

The prevalence of any MSC increased gradually from age 11 to 20, with prevalences of 15.8%, 24.4%, 27.5% and 30.4% at ages 11, 14, 17 and 20 respectively (Table 2). The prevalence of MSC increased in both girls and boys, but the increase seemed steeper in girls: for girls from 17.4% at age 11 to 37.9% at age 20, and for boys from 14.2% at age 11 to 22.1% at age 20.

This age-related increase in prevalence was also found for the following anatomical sites considered separately: back complaints (from 2.7% to 16.2%) and upper extremity complaints (from 4.6% to 15.3%). The prevalence of lower extremity complaints remained relatively stable: 10.9% (age 11) 14.7% (age 14), 12.2% (age 17) and 11.8% (age 20). Also the reporting of complaints at more than one anatomical site increased with age, from 2.2% at age 11 to 10.5% at age 20. Sex differences were found for each of the three anatomical sites. At age 11, the prevalence of having at least one MSC was 3.2 percentage points greater in girls than in boys (17.4% vs. 14.2%). This difference increased to 15.8 percentage points at age 20. Expressed in relative terms, at age 11 the prevalence in girls was 23% greater than in boys, which increased to 71% at age 20.

3.2 | Course of MSC in the adolescent years

The majority (75.8%) of the adolescents reported no or only occasional pain over the 10-year period studied, and persistent pain was found among 10.9% (Table 3). In particular persistent pain was more prevalent among girls (16.5%) than among boys (5.1%).

3.3 | Factors associated with persistent MSC

With exception of the psychosocial factors, there were hardly any differences between the univariable and multivariable models evaluating the factors associated with persistent MSC (Table 4), indicating that these associations were largely independent of each other. We will therefore focus on the findings from the multivariable models.

Adolescents with lower education reported more often persistent pain than those with high educational level, both in girls [OR = 1.82 (1.05–3.15)] and boys [OR = 3.41 (1.49–7.76)] (Table 4). The education of the mother was not associated with MSC.

Of the growth and development factors only 'early puberty' was associated with persistent pain, in particular among girls [OR 2.41 (95% CI 1.41–4.09)].

Psychosocial factors showed strongly significant associations with having persistent MSC, in particular sleeping problems (OR = 2.29 (95% CI 1.46–3.59)), daytime tiredness/sleepiness (OR = 2.54, (95% CI 1.63–3.97)), and being bullied (OR = 2.38 (95% CI 1.50–3.76)). These associations were found in both girls and boys. The association of MHI-5 score less than 60, worrying and hyperactivity with persistent pain was high in the univariable model but changed to non-significant in all multivariable models.

Lifestyle factors, such as physical activity, were not associated with MSC, neither in boys nor in girls.

Self-reported accidents were significantly associated with having persistent MSC in boys as well as in girls [OR = 4.14 (95% CI 2.77–6.19)].

Two of the factors that were associated with MSC in both boys and girls showed sex differences in prevalence: sleeping problems ($P_{♀} = 26\%$, $P_{♂} = 12\%$) and daytime tiredness/sleepiness ($P_{♀} = 24\%$, $P_{♂} = 12\%$).

TABLE 2 Prevalence of musculoskeletal complaints by age and sex

Musculoskeletal complaints	Total (%)	Girls (%)	Boys (%)	Sex differences		
				Statistical significance[a]	Absolute difference	Relative difference
MSC at age 11 (n = 2,627)						
Back complaints	2.7	3.4	2.1	ns	1.3	62
Upper extremity complaints	4.6	6.3	3.0	**	3.3	110
Lower extremity complaints	10.9	11.3	10.5	ns	0.8	8
Two or more	2.2	3.0	1.4	**	1.6	114
Any MSC	15.8	17.4	14.2	*	3.2	23
MSC at age 14 (n = 2,517)						
Back complaints	9.3	12.2	6.3	**	5.9	94
Upper extremity complaints	7.6	9.4	5.9	**	3.5	59
Lower extremity complaints	14.7	18.4	11.0	**	7.4	67
Two or more	5.9	8.2	3.7	**	4.5	122
Any MSC	24.4	30.1	18.7	**	11.4	61
MSC at age 17 (n = 2086)						
Back complaints	13.7	16.8	10.3	**	6.5	63
Upper extremity complaints	12.8	18.6	6.5	**	12.1	186
Lower extremity complaints	12.2	16.4	7.8	**	8.6	110
Two or more	9.1	12.7	5.1	**	7.6	149
Any MSC	27.5	35.6	18.9	**	16.7	88
MSC at age 20 (n = 2,205)						
Back complaints	16.2	21.2	10.6	**	10.6	100
Upper extremity complaints	15.3	20.2	9.9	**	10.3	104
Lower extremity complaints	11.8	14.8	8.4	**	6.4	76
Two or more	10.5	14.6	5.9	**	8.7	147
Any MSC	30.4	37.9	22.1	**	15.8	71

[a]Statistically significant differences between boys and girls, *$p < .05$, **$p < .001$, using univariate logistic regression; ns = no statistically significant differences.

4 | DISCUSSION

MSC were common among adolescents and increased with age, with the prevalence showing an widening gap between boys and girls. Factors associated with persistent MSC in both sexes include educational level, being bullied, sleeping problems and daytime tiredness/sleepiness, while the latter two were more prevalent among girls than in boys. Of the growth and development factors, among girls early puberty was associated with having persistent MSC. Self-reported accidents were also associated with having persistent MSC, in boys as well as in girls.

The prevalence of MSC found in our study falls within the wide range (4%–40%) found in other studies (King

TABLE 3 Adolescent course of MSC: prevalences of long-term MSC patterns, Y = having MSC, *N* = no MSC

	Age 11	Age 14	Age 17	Age 20	Total (*N* = 1,895)	Girls	Boys
Persistent pain[a]	≥3 measurements *with* complaints				10.9%	16.5%	5.1%
Never pain[a]	≥3 measurement *without* complaints				75.8%	67.1%	85.0%
A decrease in complaints	Y	Y	N	N	1.2%	1.4%	0.9%
Development of complaints	N	N	Y	Y	4.8%	6.8%	2.6%
Complaints with a varying course[b]	Y	N	Y	N	7.3%	8.1%	6.5%
	Y	N	N	Y			
	N	Y	N	Y			
	N	Y	N	N			

[a]Only in the pattern 'persistent pain' and in the pattern 'never pain' one missing value was allowed.

[b]Adolescents with any pattern that did not meet the inclusion criteria of the other patterns.

et al., 2011). In the current study, the prevalence of MSC increased with age, in particular complaints of the back and complaints of the upper extremities. It has often been reported that the prevalence of MSC is higher in older adolescents than in younger ones (Coenen et al., 2017; Hagen et al., 2011; Jones & Macfarlane, 2009; Jussila et al., 2014), and the same is true for boys and girls (Gustafsson et al., 2018; Hulsegge et al., 2011; Jones et al., 2003; Leino-Arjas et al., 2018; Mikkelsson et al., 1998). We showed that the prevalence gap between boys and girls increased with adolescent age, both in absolute (in prevalence points) and in relative terms.

Possible explanations for these sex differences in MSC are that girls may be more sensitive to pain (Mogil, 2012), may be more willing to report MSC than boys, or may be more exposed to risk factors for MSC (Wijnhoven et al., 2006). The sex-related differences may also be associated with age dependent-hormonal changes during puberty, and we see that among girls early puberty is associated with increased risk of experiencing persistent pain. This corresponds with findings from other studies. For example, in the study by Kloven et al. (2017) an early menarche was associated with a significantly higher odds of chronic pain in adolescence. Also Hebert et al. (2019) showed that advanced puberty is associated with more spinal pain.

In addition, we studied the long-term course of MSC using predefined longitudinal patterns, and we observed that the prevalence of persistent MSC was more than three times higher among girls (16.5%) than among boys (5.1%).

Although the prevalence of MSC differed between boys and girls, we found that most factors showed similar associations in girls and boys. This holds for the level of education, being bullied, sleeping problems and daytime tiredness/sleepiness and accidents. Psychosocial factors have often been found to be associated with MSC (Jussila et al., 2014; Leino-Arjas et al., 2018; Mikkelsson et al., 1998; Paananen, Auvinen, et al., 2010; Picavet et al., 2016; van de Putte et al., 2006). Mikkelsson et al. (1998) and Gustafsson et al. (2018), for instance, also showed that daytime tiredness was associated with persistent pain. Our study showed that sleeping problems and daytime tiredness were both associated with MSC, but these may represent two sides of the same coin.

Self-reported accidents (sports injuries and traffic accidents) were also significantly associated with persistent MSC in our study, both in girls and in boys. A study among adolescents with musculoskeletal complaints visiting an emergency unit or orthopedic unit also mentioned that sports injuries were reported to be the primary cause of pain complaints (Holley et al., 2017). Guddal et al. (2017) showed that strength and extreme sports were associated with pain and that moderate physical activity might be protective. Physical inactivity has suggested to be a risk factor for back pain (Scarabottolo et al., 2017).

Surprisingly, for none of the lifestyle factors that we studied, an association with MSC was found. This is in contrast with other studies where for example smoking was significantly associated with MSC (Andorsen et al., 2017; Paananen, Auvinen, et al., 2010; Paananen, Taimela, et al., 2010).

Differences between boys and girls in the factors associated with MSC include early puberty (only among girls) and daytime tiredness/sleepiness, with the latter being associated with MSC in both sexes, but showing much stronger associations in boys than in girls. Some of the factors associated with MSC were much more prevalent among girls than among boys; this holds in particular for sleeping problems and daytime tiredness/sleepiness, which were reported by approximately one quarter of the girls compared to only 12% of the boys. Part of the differences in MSC prevalence between boys and girls is probably due to the higher prevalence of these risk factors among girls.

The focus of this paper was on the theme of sex differences and especially the use of data spanning the adolescent years between 11 and 20 years makes this study unique. The increasing gap between boys and girls is both due to more girls having persistent pain and more girls developing pain complaints as they grow up (6.8% vs. 2.6%). There is also a substantial group showing a varying pattern of complaints

TABLE 4 Factors associated with persistent musculoskeletal pain (with 'never pain' as reference), univariable (model 1) and multivariable (model 2)

	Persistent pain (Total population)		Persistent pain - Girls		Persistent pain - Boys	
Characteristics	**Model 1**	**Model 2[a]**	**Model 1**	**Model 2[a]**	**Model 1**	**Model 2[a]**
Sociodemographic characteristics						
Sex						
Boys	1.00	1.00				
Girls	**4.11 (2.92–5.78)**	**3.75 (2.40–5.87)**				
Level of education adolescent						
High	1.00	1.00	1.00	1.00	1.00	1.00
Low	**1.53 (1.14–2.07)**	**2.07 (1.34–3.22)**	1.41 (0.97–2.03)	**1.82 (1.05–3.15)**	**2.92 (1.60–5.33)**	**3.41 (1.49–7.76)**
Level of education mother						
High	1.00	1.00	1.00	1.00	1.00	1.00
Intermediate	0.96 (0.69–1.34)	0.85 (0.54–1.34)	0.95 (0.64–1.40)	0.85 (0.50–1.46)	1.00 (0.51–1.97)	0.86 (0.34–2.15)
Low	**1.52 (1.04–2.24)**	0.98 (0.55–1.74)	1.37 (0.86–2.18)	0.89 (0.44–1.79)	1.85 (0.87–3.95)	1.27 (0.45–3.58)
Growth and development factors						
Early puberty	**1.56 (1.13–2.15)**	**1.90 (1.23–2.93)**	**1.79 (1.21–2.65)**	**2.41 (1.41–4.09)**	1.39 (0.74–2.63)	1.16 (0.51–2.66)
Attained height (20 years)	1.13 (0.80–1.60)	0.88 (0.56–1.38)	1.03 (0.69–1.55)	0.96 (0.56–1.63)	1.12 (0.54–2.31)	0.70 (0.27–1.79)
Overweight	1.28 (0.75–2.17)	1.11 (0.57–2.18)	1.31 (0.64–2.67)	1.12 (0.46–2.74)	1.88 (0.80–4.43)	0.81 (0.26–2.52)
Psychosocial factors						
MHI-5 score less than 60	**3.13 (2.16–4.54)**	0.99 (0.55–1.80)	**2.19 (1.43–3.35)**	0.94 (0.48–1.84)	**3.74 (1.64–8.54)**	0.66 (0.15–2.91)
Worrying	**3.35 (2.32–4.83)**	1.35 (0.75–2.43)	**2.87 (1.89–4.37)**	1.58 (0.81–3.07)	2.15 (0.87–5.31)	0.83 (0.21–3.37)
Being bullied	**2.70 (1.93–3.79)**	**2.40 (1.52–3.81)**	**2.43 (1.60–3.68)**	**2.23 (1.26–3.95)**	**3.50 (1.85–6.63)**	**2.58 (1.12–5.93)**
Sleeping problems	**4.02 (2.91–5.56)**	**2.33 (1.48–3.67)**	**2.77 (1.90–4.04)**	**2.19 (1.30–3.70)**	**5.35 (2.75–10.40)**	**3.19 (1.26–8.06)**
Daytime tiredness/ sleepiness	**3.34 (2.41–4.63)**	**2.57 (1.64–4.02)**	**2.10 (1.42–3.08)**	**1.93 (1.13–3.29)**	**6.40 (3.38–12.12)**	**7.80 (3.15–19.31)**
Hyperactivity	**2.23 (1.31–3.82)**	1.50 (0.69–3.27)	**3.06 (1.38–6.79)**	0.91 (0.31–2.69)	**3.23 (1.43–7.31)**	3.07 (0.99–9.56)
Lifestyle factors						
Moderate physical activity (≥5 d/wk)	1.01 (0.75–1.35)	0.87 (0.58–1.30)	0.93 (0.66–1.32)	0.82 (0.51–1.30)	0.96 (0.53–1.74)	0.90 (0.40–2.00)
Vigorous exercise (≥2 d/wk)	0.85 (0.62–1.17)	0.77 (0.49–1.19)	0.78 (0.54–1.14)	0.70 (0.42–1.17)	0.85 (0.44–1.64)	1.09 (0.46–2.58)
Screen time (>2 h/d)	1.04 (0.76–1.42)	1.00 (0.66–1.52)	1.12 (0.78–1.61)	1.03 (0.63–1.67)	1.44 (0.72–2.87)	1.11 (0.46–2.66)
Smoking (>1/mo)	**2.07 (1.16–3.69)**	0.52 (0.21–1.26)	1.74 (0.89–3.41)	0.47 (0.17–1.30)	2.12 (0.61–7.30)	1.03 (0.16–6.60)
Accidents	**3.45 (2.55–4.68)**	**4.14 (2.77–6.19)**	**3.62 (2.52–5.21)**	**4.41 (2.74–7.07)**	**3.56 (1.93–6.57)**	**4.21 (1.86–9.52)**

[a]Adjusted for all selected factors presented in this table.

(8.1% among the girls and 6.5% among boys), which reflects the notion that a part of MSC 'comes and goes' and does not become chronic in a considerable number of cases. These findings emphasize that MSC represent a large variety of complaints that not only differ by site, frequency and severity but also by large differences in the development over the life course, in this case the adolescent years.

4.1 | Strengths and limitations

Strengths of the PIAMA birth cohort study are the large number of adolescents who participated, with 2,206 young adults having completed the questionnaire at age 20, and the long follow-up period from birth into adolescence with four measurement points for MSC in adolescence. Another strength is

the availability of data on a large range of factors that could be studied in association with MSC.

A limitation of the PIAMA birth cohort study is the relative limited information on MSC, with the questionnaires containing questions only on unspecified complaints pertaining to three anatomical locations (back, upper extremities and lower extremities). More detailed information on e.g. more specific pain sites, duration, intensity, frequency and specific medical conditions associated with MSC, may also be relevant to evaluate MSC in adolescent years, and studies focusing specifically on MSC should include these. In general, MSC and their additional characteristics can only be measured by self-report, which may be hampered by, for example, remembering issues or willingness to report issues, resulting in over- or underreporting. In order to avoid reporting of 'transient aches and pains' we made it explicit in the questionnaire that the MSC refer to long-lasting complaints lasting at least one month. The individual trajectories could only be based on four measurements and we do not have information on MSC before the age of 11 and in between the four measurement points.

Also, as a first exploration of factors that characterize subjects with the long term pattern 'persistent pain', we used factors measured at one time only (most at age 14). This might have led to missing the report of specific factors that may occur at a discrete time point such as an injury, and does not acknowledge that some of these factors might also change over time. Future studies could focus on how data obtained at different ages can best be combined to characterize subjects with different MSC patterns over the adolescent life course.

Another limitation refers to representativity issues, ethnicity, loss to follow-up and missing values. Most of the participants have native Dutch parents (93%), so adolescents with different ethnicity could not be studied separately, and extrapolation to those of non-Western ethnicity should be done with caution. In long term follow-up studies a certain amount of loss to follow-up and missing data cannot be avoided, in the present study 48% of the original study population was included in the analyses. It is known, also for the PIAMA study, that both non-response and loss to follow-up results in slightly higher number of participants of higher socio-economic status (SES) or educational level compared to the general population. For example, at the time of recruitment (prenatally) 23.5% of the participants had a low educated mother, which was reduced to 19% when the participants were 20 years old. It is expected that also the number of adolescents with lower education are slightly underrepresented in the study, which suggest that the presented MSC prevalences are an underestimation, because we found higher MSC prevalence among the lower educated. We do not expect that this has a large effect on the associations between factors and MSC or on the sex differences.

4.2 | Practical implications and future research directions

The notion that a substantial number of adolescents already report (long-lasting) MSC and that there is a large gap between boys and girls should be acknowledged in youth health care and prevention. Health care providers working with adolescents with MSC have limited evidence from research and their treatments are often based on recommendations based on research in adults (Kamper et al., 2016). A better knowledge of the onset and prevalence of MSC and the factors associated with MSC in adolescents may provide better opportunities to develop effective prevention and/or treatment interventions at an early age. In general, more research with larger samples is necessary to evaluate the different trajectories of pain and their risk factors. Currently, we cannot say anything about causality in the association between the factors studied and MSC, but it is relevant to know that all these factors often go together. Our suggestions for future research are to assess MSC at an earlier age, and gain more insight into the significance and implications of the strong association between psychosocial factors and MSC, in particular among girls. Psychosocial factors, including mental health problems, sleeping problems and day time tiredness, are significantly associated with MSC in this study (and many others). It is therefore important to acknowledge these in preventive interventions.

4.3 | Conclusion

In summary, this study showed that MSC are already common in adolescence and increase with age, with a widening gap between boys and girls. One in 20 boys reported persistent pain, versus one in six girls Similar risk factors were found for boys and girls, in particular being bullied, sleeping problems, daytime tiredness/sleepiness and accidents. Two of those risk factors—sleeping problems and daytime tiredness/sleepiness—are much more prevalent in girls than in boys and this may explain part of the MSC prevalence difference between boys and girls. Future MSC-related research and preventive interventions and/or treatments should focus on adolescent girls and on the role of psychosocial factors in adolescence.

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CONFLICTS OF INTEREST

None.

AUTHOR CONTRIBUTIONS

HSJP and AW developed the idea for this study. AvH and AW participated in data analyses. AW, UG, HAS and GHK participated in the data collection. All authors contributed to the writing of the manuscript, and approved the final version. None of the authors has conflicts of interest.

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