


# Musculoskeletal pain is not clearly associated with the risk of anterior cruciate ligament reconstruction in adolescents

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## ABSTRACT

**Objectives** The purpose of this study was to investigate whether self-reported musculoskeletal pain (MSP) was associated with a future anterior cruciate ligament reconstruction (ACLR).

**Methods** In this population-based prospective cohort study, we included 8087 participants from the adolescent part of the Trøndelag Health Study (Young-HUNT) in Norway. The exposure was self-reported MSP from the Young-HUNT3 study (2006–2008), which was categorised into two MSP load groups (high MSP and low MSP) based on frequency and number of pain sites. The outcome was ACLRs recorded in the Norwegian Knee Ligament Register between 2006 and 2019. Logistic regression was used to investigate association between MSP load and ACLR, given as ORs with 95% CIs. All tests were two-sided and p values of  $\leq 0.05$  were considered statistically significant.

**Results** 8087 adolescents were included. We identified a total of 99 ACLRs, with 6 ACLRs (0.9%) in adolescents who reported high MSP load and 93 ACLRs (1.3%) among those who reported low MSP load. Adolescents reporting high MSP load had 23% lower odds of an ACLR (OR 0.77, 95% CI 0.31 to 1.91) compared with adolescents with low MSP load. However, the CIs were very wide.

**Conclusion** Self-reported high MSP load in adolescents was not associated with increased risk of future ACLR.

Although the number of participants was high, the relatively few cases of ACLR mean that we cannot be conclusive about the presence or absence of an association.

## INTRODUCTION

Musculoskeletal pain (MSP) is a globally common problem which affects individuals, families and societies.<sup>1,2</sup> There is an increasing prevalence of children and adolescents with MSP,<sup>3</sup> which often presents as multisite, persistent and idiopathic.<sup>4,5</sup> In addition, MSP in adolescence is associated with greater risk of chronic pain in adulthood.<sup>6</sup> Although the epidemiology, burden and treatment of MSP in adults has been the subject of considerable

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Musculoskeletal pain (MSP) and anterior cruciate ligament reconstruction (ACLR) are becoming increasingly common among adolescents, and both are suggested to have a large impact and long-term consequences on both individuals and society.

## WHAT THIS STUDY ADDS

⇒ To our knowledge, this is the first large population-based study to investigate the possible association between MSP and ACLR in adolescents.

⇒ Identifying risk factors and consequences of both MSP and ACLR is an important step towards a better understanding of these burdensome health challenges, as well as early detection and prevention.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study could give additional insight into future investigations looking at anterior cruciate ligament injuries and possible associations with MSP load, regardless of whether the participant has undergone reconstruction or not.

research, the same is not true for children and adolescents.<sup>2</sup> MSP may reduce muscle strength and have a dysfunctional effect on joint stability and control.<sup>7–9</sup> Neuromuscular control plays an important role in physical activity in daily life and sports,<sup>9,10</sup> which is a significant factor for the development of an active lifestyle for children and adolescents.<sup>2,10</sup> Furthermore, poor neuromuscular control has been suggested to be a contributor to acute injury of lower limb structures such as the anterior cruciate ligament (ACL).<sup>9</sup>

The number of ACL injuries are increasing among adolescents.<sup>11,12</sup> An injury as such often results in great discomfort and long-term consequences, and is associated with increased risk of knee instability, osteoarthritis, meniscal injuries and reduced quality of life.<sup>13,14</sup> For adolescents, an ACL injury

could contribute to reduced participation in sport, and some might require reconstructive surgery of the ligament (ACLR) to be able to return to sport.<sup>15</sup> Known risk factors for ACL injury include high level of physical activity, participation in team sports, female gender, weakness of knee flexors and hip adductors, dynamic valgus, muscle fatigue and a history of muscle, tendon, knee or ankle injuries.<sup>16–19</sup> Identifying risk factors and consequences of MSP and ACL injuries are important steps towards better understanding, as well as early detection and prevention.<sup>20</sup> Whether MSP might be a risk factor for ACL injury leading to an ACLR has, to our knowledge, not been explored. Thus, the purpose of this study was to investigate whether self-reported MSP is associated with the risk of a future ACLR in a population-based cohort of adolescents. We hypothesised that high MSP load would lead to increased risk of a future ACLR due to possible reduced neuromuscular control, which can potentially alter movement patterns and thereby increase the risk of an initial ACL injury.

## METHOD

### Study design

The current study is a population-based prospective cohort study.

### Setting

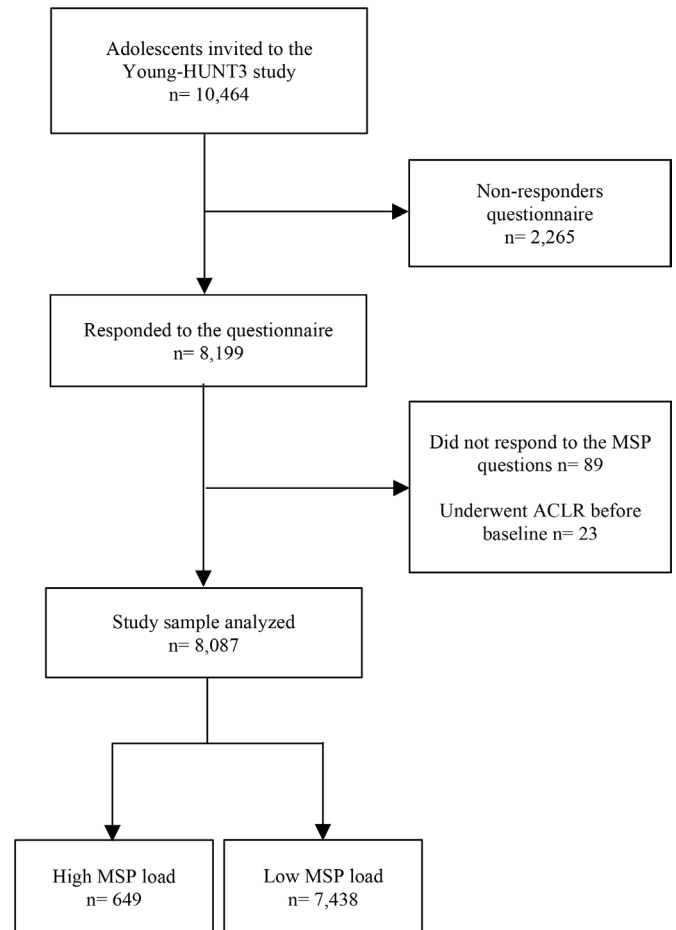
The adolescent part of the Trøndelag Health Study (Young-HUNT) is a large population-based study in Norway. From 2006 to 2008, all adolescent residents (age 13–19 years) of the Trøndelag county in Norway (n=10 464) were invited to participate in the third wave of the Trøndelag Health Study (Young-HUNT3). The Young-HUNT3 survey included self-reported questionnaires, structural interviews, clinical measurements and buccal smears.<sup>21</sup>

The Norwegian Knee Ligament Register (NKLR) was established in June 2004 to collect information on all ACLRs in Norway.<sup>22</sup> The compliance rate of hospitals reporting ACLRs to the NKLR is high (85.5%).<sup>23</sup> The NKLR also gathers information on pre-surgery Knee injury and Osteoarthritis Outcome Scores (KOOS) prior to and after ACLR.

### Study population

Our study included participants with baseline data on MSP from Young-HUNT3, and data on ACLR and KOOS scores registered in the NKLR between January 2006 and December 2019. MSP was measured once, and the follow-up period was the time from participation in Young-HUNT3 to the point of ACLR. Information from the NKLR was linked to the participants in the Young-HUNT3 study using their unique 11-digit personal numbers. Authors of this study had access to de-identified data received from HUNT, that is, they contained only ID numbers and no names or social security numbers.

All adolescents who participated in Young-HUNT3 and answered the questionnaire were initially included



**Figure 1** Flow chart. Flow chart of the study population in adolescent part of the Trøndelag Health Study, 2006–2008 (Young-HUNT 3). ACLR, anterior cruciate ligament reconstruction; MSP, musculoskeletal pain.

(n=8199). Further, adolescents who either failed to answer the questions concerning MSP (n=89) or had undergone an ACLR before baseline (n=23) were excluded. The study population comprised 8087 adolescents (figure 1).

The large sample of adolescents from the general population reduces the chances of selection bias, and the prospective design reduces the chances of confirmation bias and recall bias.

## Variables

### Exposure variable

To assess MSP, we used an item from the questionnaire where the respondent's reported frequency of MSP, unrelated to any known disease or acute injury, during the past 3 months. The response alternatives were: never/seldom, about once a month, once a week, several times a week and almost every day. The respondents reported the number of pain sites, which included pain in the neck/shoulder, left or right arm, upper back, lower back and left or right leg. Headache/migraine, chest and abdominal pain were excluded in the current study as they were not necessarily considered to represent MSP.<sup>24 25</sup> The question retrieved from the Young-HUNT3 study has

**Table 1** Definition of high and low load of MSP in the current study

MSP load group	Definition
High MSP load	Number of pain sites: $\geq 3$ sites of pain. Frequency: $\geq 1$ day per week.
Low MSP load	Number of pain sites: $< 3$ sites of pain. Frequency: $< 1$ day per week.

MSP, musculoskeletal pain.

been adapted from Mikkelsen *et al.*<sup>26</sup> and has shown good test–retest reliability for detecting occurrence of pain at least once a week as well as demonstrating good concurrent validity in comparisons with interviews.<sup>27</sup> Two MSP load groups were defined by a composite of *frequency of MSP* and *number of pain sites* (table 1). Frequent MSP was defined as experiencing pain, unrelated to any known disease or acute injury, in any of the abovementioned body sites  $\geq 1$  day per week during the past 3 months. The same cut-off has previously been used to define frequent MSP and chronic non-specific MSP in the same population of adolescents.<sup>28 29</sup> Multisite MSP was defined as having pain unrelated to any known disease or acute injury in  $\geq 3$  of the abovementioned body sites during the past 3 months.<sup>29 30</sup> From this, high MSP load was defined as a combination of frequent MSP and multisite MSP, and low MSP load was defined as adolescents who reported MSP  $< 1$  day per week and had  $< 3$  sites and used as the reference group in the analysis.

### Outcome variable

The main outcome of interest was ACLR after a primary ACL injury. Pre-surgery KOOS data was used as a descriptive estimate to investigate differences in knee-related pain and function between adolescents with high and low MSP load undergoing an ACLR.

### Confounders

The most common confounders associated with both ACLR and MSP were identified based on previous studies, and were age, gender, body mass index (BMI) and sport level.<sup>16 17 19 28</sup> Sport level was assessed by asking how often the respondents had performed different and/or multiple sports/activities during the past 12 months. The sport levels were categorised as level I, II or III based on the degree of knee joint load. This was done according to Moksnes *et al.*<sup>31</sup> who modified the original classification of Hefti *et al.*<sup>32</sup> to make it suitable for European sports.

### Statistical methods

A descriptive analysis was performed on baseline characteristics. Continuous variables were presented with means and SD, and categorical variables with counts and percentages. A Mann-Whitney U test was used to investigate the difference in pre-surgery KOOS subscores between the MSP load groups for those who had undergone an ACLR. Logistic regression was used to explore

the association between MSP and ACLR, and supplementary analysis was performed for adolescents reporting  $\geq 2$  and  $\geq 1$  pain location. The results were presented as unadjusted and adjusted ORs with 95% CIs. Adjustments were made for age, gender, BMI and sport level. P values  $\leq 0.05$  were considered statistically significant. All statistical analyses were performed using SPSS Statistics V.27.

## RESULTS

### Participants and descriptive data

In the study population of 8087 adolescents (table 2), 99 (1.2%) ACLRs were identified with 6 ACLRs (0.9%) in the high MSP load group and 93 (1.3%) in the group with low MSP load. The mean age at baseline was 15.9 years (SD 1.7) and 21.8 (SD 4.0) at ACLR. More girls (64.4%) than boys (35.6%) reported high MSP load at baseline. The mean time from injury to reconstruction was 12.7 months (SD 22.9) in the group with low MSP load, and 7.0 months (SD 7.1) in the group with high MSP load.

### Main results

#### The association between MSP and ACLR

No difference in odds for ACLR was found between the two MSP load groups. The group reporting high MSP load had 23% lower odds of a future ACLR (OR 0.77, 95% CI 0.31 to 1.91) compared with the group with low MSP load in the adjusted analysis (table 3), however this result was not statistically significant (figure 2).

### Other analyses

#### Pre-surgery KOOS scores

Adolescents with high MSP load reported lower mean KOOS scores prior to surgery in the sport and quality of life (QOL) categories (table 4), indicating a greater burden of symptoms. Only the difference in QOL was statistically significant, with lower mean scores reported among those with high MSP load (22.5, SD 7.1) compared with the group with low MSP load (38.3, SD 18.4) ( $p=0.028$ ).

#### Supplementary analyses for the association between high load of MSP and ACLR

The supplementary analysis of adolescents reporting  $\geq 2$  or  $\geq 1$  pain sites, with a frequency of  $\geq 1$  day per week during the past 3 months, revealed similar results as the main analysis, with no statistical difference between the groups. The group reporting  $\geq 2$  pain sites had 31% lower odds of a future ACLR (OR 0.69, 95% CI 0.37 to 1.31) compared with the group reporting  $\leq 1$  pain sites, and the group reporting  $\geq 1$  pain sites had 22% lower odds of a future ACLR (OR 0.78, 95% CI 0.48 to 1.25) compared with the group reporting no pain sites.

## DISCUSSION

The aim of this large population-based study of adolescents was to investigate whether self-reported MSP was associated with a future ACLR. The CIs were very wide, thus we cannot be conclusive of the presence or absence

**Table 2** Characteristics of the study sample

Variables	All (n=8087)	High MSP (n=649)	Low MSP (n=7438)
Age at baseline, years, (mean (SD))	15.9 (1.7)	16.0 (1.7)	15.9 (1.7)
Age at injury, years, (mean (SD))*	20.3 (4.1)	18.8 (6.6)	20.4 (3.9)
Age at reconstruction, years (SD)*	21.8 (4.0)	19.6 (6.5)	21.6 (3.7)
Gender, n (%)			
Female	4076 (50.4)	418 (64.4)	3658 (49.2)
Male	4011 (49.6)	231 (35.6)	3780 (50.8)
Body mass index, kg/m <sup>2</sup> (median (min–max))	21.5 (13.7–48.8)	22.2 (16.4–43.5)	21.5 (13.7–48.8)
Missing	592	57	535
Sport level, n (%)†			
I	4821 (59.6)	345 (53.2)	4476 (60.2)
II and III	1958 (24.2)	169 (26.0)	1789 (24.0)
Missing	1308 (16.2)	135 (20.8)	1173 (15.8)
Physical activity level, n (%)‡			
Low	1963 (24.3)	201 (31.0)	1762 (23.7)
Moderate	2796 (34.6)	190 (29.3)	2606 (35.0)
High	3236 (40.0)	248 (38.2)	2988 (40.2)
Missing	92 (1.1)	10 (1.5)	82 (1.1)

\*Numbers retrieved from Norwegian Knee Ligament Register.

†Sport level classified according to the degree of knee joint load. Level I: jumping, cutting and pivoting movements, Level II: lateral movements, Level III: straight ahead activities, no jumping or pivoting.

‡Physical activity level was assessed by asking the respondents how many times per week they performed sport/exercise at such an intensity that they were short of breath and/or sweaty. 4–6 times a week was defined as high level, 2–3 times a week as moderate and ≤1 time per week was defined as low level of activity.<sup>40</sup>

MSP, musculoskeletal pain.

of an association. We found a slightly higher distribution of ACLRs in the low MSP load group (1.3%) compared with the high MSP load group (0.9%).

Our main analysis showed 23% lower odds of having an ACLR among adolescents with high MSP load compared with low MSP load, but the wide 95% CI indicates

uncertainty about the direction of the odds. Hewett *et al* found an association between decreased neuromuscular stability and risk of ACL injury,<sup>9</sup> and MSP might have a dysfunctional effect on joint stability and control, as well as muscle strength.<sup>7,8</sup> However, our findings did not support the possible relationship between high MSP and

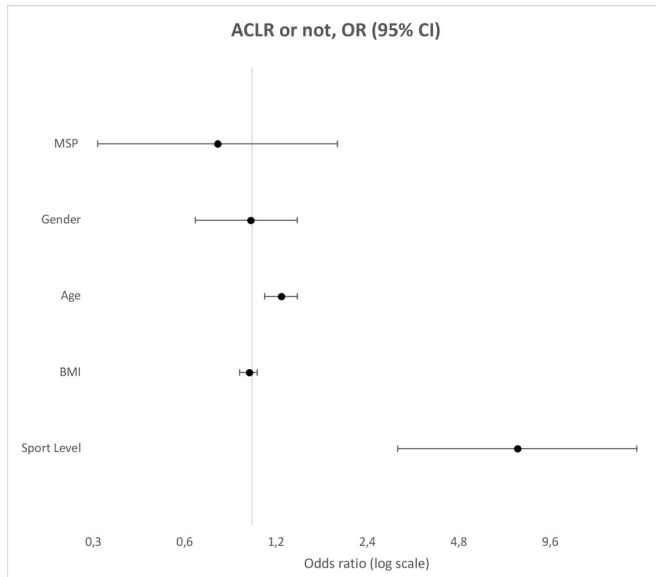
**Table 3** The association between high load of MSP and ACLR in a population-based sample of adolescents

	n	No. ACLRs	Unadjusted		Adjusted*	
			OR (95% CI)	P value	OR (95% CI)	P value
MSP						
High	649	6	0.74 (0.32 to 1.69)	0.47	0.77 (0.31 to 1.91)	0.57
Low	7438	93	1		1	
Gender (female)	4076	54	0.82 (0.55 to 1.23)	0.34	0.99 (0.65 to 1.41)	0.96
Male	4011	45	1			
Age	8087	99	1.12 (0.99 to 1.25)	0.056	1.25 (1.10 to 1.41)	0.001
Body mass index	7575	94	0.99 (0.94 to 1.05)	0.86	0.98 (0.91 to 1.04)	0.46
Sport level						
I	4821	89	7.35 (2.98 to 18.17)	<0.001	7.49 (3.02 to 18.53)	<0.001
II and III	1958	5	1		1	

\*Adjusted for gender, age, body mass index and sport level.

ACLR, anterior cruciate ligament reconstructions; MSP, musculoskeletal pain.





**Figure 2** Forest plot. The OR on log scale with 95% CI of musculoskeletal pain related to anterior cruciate ligament reconstruction. ACLR, anterior cruciate ligament reconstruction; BMI, body mass index; MSP, musculoskeletal pain.

risk of a future ACLR. Looking at the baseline characteristics, there was no statistically significant difference among the high and low MSP load groups regarding the level of sport, which has previously been shown to increase the risk of undergoing an ACLR.<sup>17</sup> Having high MSP load might lead to adolescents being more careful during activity and more reluctant to perform high impact loading and pivoting/twisting movements. We found a significant difference in the pre-surgery KOOS QOL among those who underwent ACLR, with the high MSP load group reporting more severe symptoms. The two groups showed no difference in pain symptoms immediately prior to ACLR surgery according to the KOOS subscale, which might suggest similar levels of pain but a difference in how much the pain affects the participants' daily lives. High MSP load might contribute to a negative orientation toward the pain experience, or

**Table 4** Pre-surgery KOOS score among ACLRs cases (n=99) according to MSP load groups

	Pre-surgery KOOS score (mean)	
	High MSP load	Low MSP load
Pain	77.8	78.5
ADL	88.8	86.2
Sport	29.0	49.2
QOL	22.5	38.3

Scores range from 0 to 100 with a score of 0 indicating extreme symptoms and 100 indicating no symptoms. ADL, activities of daily life; KOOS, Knee injury and Osteoarthritis Outcome Scores; QOL, quality of life.

pain catastrophising, which may have an adverse impact on pain coping behaviour and prognosis.<sup>33</sup>

We performed two separate analyses according to upper or lower body MSP and the association with a future ACLR in the initial stages of the study. The hypothesis was that MSP in the lower extremities would be associated with greater risk compared with MSP in the upper extremities, and that reduced neuromuscular control and/or ongoing lower limb injury might explain the association.<sup>19</sup> However, in the adjusted analysis both groups showed non-significant decreased odds. The analysis was later rejected due to small subgroups of adolescents with frequent MSP when divided into extremity groups.

It is possible that we underestimated the number of ACL injuries in the population by only looking at ACLRs. Operative treatment is often based on factors such as age, occupation and functional demands, significant instability, or number of injured structures.<sup>34 35</sup> Athletes and younger patients are more likely to undergo operative treatment.<sup>15 34 35</sup> The number of ACLRs reported in NKLR gives us insight into the number of ACL injuries, since a ligament reconstruction naturally presupposes a ligament injury. However, not every injury results in reconstruction, and this number may only represent the tip of the iceberg.<sup>36</sup> A recent population-based study in Finland reported that 67% of those hospitalised with ACL injuries underwent reconstruction,<sup>12</sup> and the NKLR reports that about half of all cruciate injuries in Norway result in an operation.<sup>23</sup> There has been an increased focus in Norway on the benefits of non-operative treatment measures to delay surgery in skeletally immature children and adolescents.<sup>37</sup> Although a low number of ACLRs might be seen as a positive factor from a clinical perspective, it might make it difficult for us to detect possible associations due to low statistical power. It is also possible that the two MSP load groups are too similar to detect any possible differences. In the current study, we did not have an excluding control group with adolescents with no MSP at all. In the group with low MSP load, 3142 adolescents (42.2%) reported that they had experienced pain in any of the seven pain sites 'never/seldom' during the last 3 months. In addition, the low MSP load group included adolescents with pain in multiple body sites, but who experienced pain less than once a week.

The MSP question asks about regional pain during the last 3 months unrelated to any known disease or acute injury. Although adolescents have shown to accurately recall and report pain experienced in a 3-month period,<sup>38</sup> the possibility of recall bias is still present. The question may also have been misunderstood, and it is possible that the reported pain could be linked to a specific event or injury. Furthermore, the fact that MSP is measured only once means that association but not causation can be inferred from this study. An average of 6.2 years between baseline and reconstruction allows the nature of MSP experienced (frequency/

number of sites) and/or factors other than MSP to impact the results. The combination of frequency and number of pain sites used in the definition of MSP load groups has previously been used by Skrove *et al* 2014<sup>29</sup> on the same study population (YHUNT3) to define chronic multisite pain. The chosen frequency of pain was used by Guddal *et al* on the same study sample,<sup>28</sup> and Hoftun *et al* defined chronic multisite pain as chronic non-specific pain in at least three locations in a previous Young-HUNT study.<sup>30</sup> Additional analysis was performed on adolescents reporting  $\geq 2$  or  $\geq 1$  pain sites with the purpose of investigating whether the chosen number of pain sites might have impacted the results. Both groups had shown similar results as the main analysis, with non-significant reduced odds of a future ACLR.

A strength of this study is the large study sample of adolescents from the general population with a high participation rate (78.4%), which reduces the chance of selection bias, in addition to the high compliance rate (85.5%) of hospitals reporting ACLRs to the NKLR.<sup>39</sup> Furthermore, the method of this study makes it transferable to other studies, both national and international. The prospective design allows us to assess the exposure before the outcome has occurred and reduces the chances of confirmation bias and recall bias.

## CONCLUSION

In this study, high MSP load in adolescents did not increase the risk of future ACLR. Although the number of participants in this study was high, the relatively few cases of ACLR mean that we cannot be conclusive about the presence or absence of an association.

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**Competing interests** None declared.

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**Patient consent for publication** Not applicable.

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**Data availability statement** Data are available upon reasonable request. Data may be obtained from a third party and are not publicly available. All data relevant to the study are included in the article or uploaded as supplementary information.

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