
Temporomandibular Joint Involvement is Associated with Quality of Life, Disability and High Disease Activity in Juvenile Idiopathic Arthritis.

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Temporomandibular Joint Involvement is Associated with Quality of Life, Disability and High Disease Activity in Juvenile Idiopathic Arthritis

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ABSTRACT

Objectives. To evaluate the demographic, disease activity, disability and health-related quality of life (HRQoL) differences between children with juvenile idiopathic arthritis (JIA) and their healthy peers, and between children with JIA with and without clinical temporomandibular joint (TMJ) involvement and its determinants.

Methods. This study is based on a cross-sectional cohort of 3343 children with JIA and 3409 healthy peers, enrolled in the Pediatric Rheumatology International Trials Organisation (PRINTO) health-related quality of life (HRQoL) study or in the methotrexate trial. Potential determinants of TMJ involvement included demographic, disease activity, disability and HRQoL measures selected through univariate and multivariable logistic regression.

Results. Clinical TMJ involvement was observed in 387/3343 (11.6%) JIA children. Children with TMJ involvement, compared to those without, more often had polyarticular disease course (95% versus 70%), higher Juvenile Arthritis Disease Activity Score (JADAS) (odds ratio (OR) 4.6), more disability and lower HRQoL. Children with TMJ involvement experienced clearly more disability and lower HRQoL compared to their healthy peers. The multivariable analysis, showed that cervical spine involvement (OR 4.6), disease duration > 4.4 years (OR 2.8), and having more disability (Childhood Health Assessment Questionnaire Disability Index >0.625) (OR 1.6) were the most important determinants for TMJ involvement.

Conclusion. Clinical TMJ involvement in JIA is associated with higher disease activity, higher disability and impaired HRQoL. Our findings indicate the need for dedicated clinical and imaging evaluation of TMJ arthritis especially in children with cervical spine involvement, polyarticular course and longer disease duration.
**Key words:** Juvenile idiopathic arthritis, Temporomandibular joint, Disease activity, Quality of life, Physical disability.

**Short title:** TMJ Arthritis in JIA
SIGNIFICANCE AND INNOVATIONS

- Clinical TMJ involvement is associated with high levels of disability, high disease activity and impaired quality of life in children with JIA.

- Clinicians should pay special attention to TMJ involvement in children with JIA and cervical spine involvement, polyarticular course and longer disease duration.

- Observations were based on 387 out of 3343 children with JIA, representing those with clinically evident TMJ involvement.
INTRODUCTION

Temporomandibular joint (TMJ) arthritis in childhood is recognized as a common problem in children with juvenile idiopathic arthritis (JIA), and may lead to reduced mouth opening and pain, as well as cranio-mandibular growth disturbances. The growth disturbances in childhood TMJ arthritis are different from arthritis in other joints because of the special anatomy of the TMJ with fibrous cartilage and the intraarticular condylar growth pattern [1]. Bilateral involvement may lead to micrognathia and dental malocclusion [2, 3], and unilateral involvement may lead to facial asymmetry [4]. TMJ arthritis may also hamper oral hygiene and lead to dental caries [5, 6].

Depending on the examination methods and study design used, the prevalence of TMJ arthritis varies in different JIA studies. Rheumatologists may not have the same awareness for TMJ as for other joints, and standardized examination of TMJ range of motion is challenging in small children. Tenderness is very subjective, and young children often do not report pain in even obviously swollen chronically inflamed joints. An overall TMJ prevalence of about 40-45% has usually been found using panoramic radiography [7, 8]. In two large series of children examined with magnetic resonance imaging (MRI), frequencies of about 39% and 43% were reported [9, 10]. In 47 patients followed longitudinally for 27 years, Arvidsson et al [11] reported a frequency of 70% when the adult JIA patients were examined with both computed tomography and MRI. Both lower and higher prevalence have been reported in clinical and radiologic studies [12, 13], and in particular with MRI [14, 15] higher prevalence of TMJ arthritis have been found. However, many TMJ studies are characterized by a low number of patients. There is a fact that MRI may detect TMJ arthritis in children with JIA without symptoms or clinical findings. However, contrast enhancement is also seen in healthy
children and adolescents [16, 17], thus the reliability of contrast-enhanced MRI to assess synovial inflammation is discussed [18], reflecting the complex diagnostics of the TMJ.

TMJ pain has a negative impact on health-related quality of life (HRQoL) in adult rheumatoid arthritis patients [19], and a high prevalence of temporomandibular disorders (TMDs) in adult JIA patients has also been reported [20]. TMDs in general, lead to reduced HRQoL in preadolescents [21]. Oro-facial symptoms are frequent, and are reported to influence daily life severely for almost a quarter of a series of children with JIA [22]. However, little is known about the effect of TMJ involvement on HRQoL and disability in children with JIA.

The purpose of the present study was to examine the difference in clinical characteristics, disease activity, disability and HRQoL in a large cohort of children with JIA with and without clinical TMJ involvement, to compare the results with those obtained in healthy peers, and to identify the factors that have the greatest influence on TMJ arthritis. The overall hypothesis was that children with JIA and TMJ involvement have distinctive clinical features when compared to children without TMJ involvement.
MATERIALS AND METHODS

Patients. This is a cross-sectional study based on data extracted from two studies of the Pediatric Rheumatology International Trials Organisation (PRINTO) [23]. The first relates to the HRQoL study which enrolled 3235 children with JIA and 3409 healthy controls to validate the translation of the Childhood Health Assessment Questionnaire (CHAQ) and Child Health Questionnaire (CHQ) into 32 different languages [24]. The second study was the PRINTO high dose of methotrexate (MTX) trial with 633 participants [25]; for the MTX trial only baseline data, with patients in high disease activity state, were enrolled. Children were classified as per the International League of Associations for Rheumatology (ILAR) criteria [26]. Children with psoriatic or enthesitis-related arthritis (ERA) were excluded.

Assessment of functional disability and HRQoL measures. The national version of the CHAQ questionnaire was completed by one of the parents or the child if aged > 9 years. The CHAQ is used to assess the patient’s ability to carry out daily life activities [24, 27] and the child’s ability to perform different functions grouped in eight domains (range 0-3): dressing, grooming, arising, eating, walking, hygiene, reach, grip, and activities. The CHAQ disability Index (CHAQ-DI) is calculated with a range from 0 (no or minimal physical disability) to 3 (very severe physical disability). A parent’s / patient’s reported global assessment of the child’s overall well-being in the previous week scored on a 0-10 cm visual analogue scale (PRglowVAS) (0 = very well and 10 = very poor) and parent’s / patient’s reported global assessment of the child’s pain in the previous week on a 0-10 cm VAS (0 = no pain and 10 = very severe pain) (PRpainVAS) were included.

The national language version of the parent’s administered 50 items version of the CHQ (also called CHQ-PF 50) was used to assess HRQoL of patients and healthy children. The CHQ is a
A generic self-administered instrument designed to capture the physical, emotional, and social components of health status of children 5 to 18 years of age which comprises 15 health concepts (range 0-100): global health (GGH), physical functioning (PF), role/social limitations - emotional/behavioral (REB), role/social limitations - physical (RP), bodily pain/discomfort (BP), behavior (BE), general behavior (GBE), mental health (MH), self-esteem (SE), general health perception (GH), change in health (CH), parent impact emotional (PE), parent impact time (PT), family activities (FA), and family cohesion (FC). CHQ comprises two summary measures based on US normative standard, the physical summary score (PhS) and the psychosocial summary score (PsS) (mean 50 ± SD 10). Higher scores in the scales indicate better HRQoL [28].

**Assessment of disease activity.** The JIA core set activity variables [29] were assessed: the number of joints with active arthritis (i.e. swelling within a joint, or limitation in the range of joint movement with joint pain or tenderness) [26, 29], the number of joints with limitation of motion (LOM), the physician global evaluation of disease activity on a 10 cm VAS, erythrocyte sedimentation rate (ESR), the CHAQ, the PRgloVAS, and the Juvenile Arthritis Disease Activity Score 71 (JADAS) [30-32].

**Assessment of TMJ involvement.** For this study we defined TMJ involvement as a clinical evaluation of TMJ arthritis based on the presence of TMJ pain or LOM, registered by the local pediatric rheumatologist in the PRINTO joint examination form. Jaw deviation during opening and maximal mouth opening capacity was not registered, but LOM was assessed according to standard pediatric rheumatology textbooks.
**Statistical analysis.** For clinical and demographic data, descriptive statistics was used such as median (1st – 3rd quartile), frequencies (percentage). Associations between TMJ and other disease characteristics were analyzed by chi-squared test for categorical variables, and Student’s t-test for continuous variables if reasonably normally distributed, otherwise Wilcoxon test was used. A p-value <0.05 was considered statistically significant. To identify factors differentiating JIA patients with or without TMJ involvement, univariate logistic regression was performed, using as exploratory measures the JIA core set, the CHAQ and the CHQ domains. Multivariable logistic regression was performed to identify factors independently associated with TMJ involvement. In both univariate and multivariable regression analyses the continuous variables were dichotomized as per Receiver Operating Characteristics (ROC) analysis. Statistical analysis was performed using the SAS software version 9.3 and the SPSS software version 21.

**Ethical considerations.** Approval from appropriate medical ethical committees and data authorities was obtained according to the requirements of each participating country.
RESULTS

Study population

Of the original two studies we enrolled 2715/3235 (84%) JIA patients from the HRQoL study, 628/633 (99%) from the MTX trial, and all 3409 healthy participants from the HRQoL study, in total 6752 subjects analyzed (Figure 1). Participants from the MTX trial had higher level of disease activity, disability and worse HRQoL when compared to the participants from the cross-sectional HRQoL study (Supplementary Table 1 and Supplementary Table 2). Of the 3343 JIA children included, 2278/3243 (70.2%) were female, and 1530 (45.8%) were diagnosed with persistent or extended oligoarthritis (Table 1).

Demographic and disease activity parameters

Demographic and disease activity characteristics and univariate analysis for the TMJ group and non-TMJ group are given in Table 1. Of the 387 children with clinical TMJ involvement (11.6% of the entire cohort), 75 (19.4%) had unilateral and 312 (80.6%) had bilateral TMJ involvement (Table 1). In the TMJ group there was a female predominance (75.5%) and longer disease duration, versus the non-TMJ group, but no statistically significant difference in age at onset (Table 1). Polyarticular disease course (extended oligoarthritis, polyarthritis RF positive or negative and systemic arthritis) was more common in the TMJ group (95.1%) compared to the non-TMJ group (70.0%), and a polyarticular RF positive or negative JIA category was reported in 50.9% of the children in the TMJ group compared to 31.7% in the non-TMJ group (Supplementary Figure 1). Disease activity measures as measured by the JADAS score, MDgloVAS, ESR, and number of active joints were significantly higher in the TMJ group compared to the non-TMJ group.
Disability and HRQoL

Disability and HRQoL are reported in Figure 2 and Figure 3 and the related descriptive statistics in Supplementary Table 2 and Table 3. Children with clinical TMJ involvement had more disability compared to children without TMJ involvement as measured by the eight CHAQ subscales, PRPainVAS, PRgloVAS and CHAQ-DI. As shown by the arrows in Figure 2, children with clinical TMJ involvement had scores more than 2 SD above the mean values of healthy controls in the domains dressing, eating, and activities.

All CHQ health concept and summary scores (PhS and PsS) in children with clinical TMJ involvement were significantly lower than in children without TMJ involvement except for BE and GBE. In addition children with clinical TMJ involvement had values more than 2 SD below the mean of healthy controls for the following health concepts; global general health (GGH), role limitations emotional/behavioral (REB), role limitations physical (RP), and bodily pain (BP).

Univariate analysis

In order to evaluate the association of disease activity, disability, and HRQoL with clinical TMJ involvement we report the results of the univariate analyses (OR and 95% CI) with continuous variables dichotomized as per ROC analysis in Table 1 and Table 2. A significant association with clinical TMJ involvement was found for extended oligoarticular, polyarticular, and systemic arthritis categories using the oligoarticular persistent category as a reference (OR range 6.7-9.8). Disease activity measures as measured by the JADAS score (OR=4.6), MDgloVAS (OR=2.7), ESR (OR=2.8), and number of active joints (OR=3.9) were significantly higher in the TMJ group compared to the non-TMJ group. Children with clinical
TMJ involvement had more frequently cervical spine involvement (OR 7.8) or upper limb involvement (data not shown).

All the CHAQ domains had higher scores in the TMJ group compared with the non-TMJ group, particularly for the domains reach (OR=5.5), difficulties concerning arising, grip, and activities (all with ORs > 3.5). In addition, the TMJ group had higher scores for CHAQ-DI (OR=4.1) compared with the non-TMJ group. The TMJ group also had higher scores compared to the non-TMJ group for PRgloVAS and for PRpainVAS (OR=3.1 and OR=2.7 respectively). An adverse impact on physical and psychosocial well-being was found in the TMJ group, with lower PhS (OR=3.2) and to a lesser extent PsS (OR=1.7) scores compared with the non-TMJ group. There were significantly lower scores for the specific CHQ health concepts concerning self-esteem (SE), global general health (GGH), bodily pain (BP), impact on general health (GH), family activity (FA), the parent’s emotions (PE), the child’s physical and emotional behavior (BE), and physical functioning in the TMJ group, with an OR between 2.0-2.9 (Table 2). A univariate analysis was performed for the same continuous variables dividing them into quartiles, and the results were overlapping (data not shown).

**Multivariable logistic regression**

In the final regression model we entered all variables which were found to be significantly associated with clinical TMJ involvement at the univariate analysis based on OR as follows: gender, disease duration, RF, cervical spine involvement, ESR, number of active joints, MDgloVAS, PRpainVAS, PRgloVAS, CHAQ-DI, PhS and PsS (CHQ). We excluded JIA categories, number of joints with pain in lower and upper limb, LOM, and swelling that were significant in the univariate analysis, but for whom there was collinearity with other variables entered in the model. The eight CHAQ domains and the 13/15 CHQ health concepts were excluded since they were collinear with the respective total scores the CHAQ-DI, PhS and
PsS (CHQ). In the final model, to control for the level of disease activity we also adjusted (adjusted OR) for the following measures: participation in the MTX trial, number of active joints, ESR, and RF. The multivariable analysis (Table 3) showed that cervical spine involvement (adjusted OR 4.6), disease duration >4.4 years, being female, and having higher CHAQ-DI were the most important determinants for TMJ involvement (OR 2.8-1.5).

DISCUSSION

The present study demonstrated an association between clinical TMJ involvement, disability, and HRQoL in children with JIA, and independent associations between TMJ and cervical spine involvement. We found a female predominance, longer disease duration, polyarticular course, and higher level of disease activity in the group with clinical TMJ involvement, and that the majority had bilateral involvement.

The strength of the present study is the large international cohort of 3343 children with JIA, with as many as 387 children with clinical TMJ involvement. In this cohort systemic arthritis is overrepresented compared to population-based JIA cohorts, and ERA and psoriatic arthritis are not included, but otherwise our cohort is representative of most JIA populations according to gender and JIA category distribution [9, 10, 13, 33, 34]. Moreover, the observed associations between clinical TMJ involvement and a number of disease variables are in accordance with studies based on radiologic TMJ involvement [7, 9].

An obvious weakness in the present study is the assessment of TMJ involvement. No data on imaging was available. Since recognizable swelling in the TMJ is rare, the general definition of arthritis could not be applied [26]. We are not aware of any TMJ studies in children with JIA that have used this general definition of arthritis. In line with other studies [7, 9, 15, 35], clinical TMJ involvement (whether active or not) in our study was based on the presence of TMJ pain and / or LOM. The observed low frequency of clinical TMJ involvement was
therefore not surprising. TMJ imaging and in particular MRI may detect TMJ abnormalities even in JIA children without any clinical symptoms or signs of TMJ arthritis.

However, in a recent study using the same criteria for assessing clinical TMJ involvement in JIA, Kirkhus et al [35] reported that contrast-enhanced MRI demonstrated TMJ arthritis in 85% of the children with clinical TMJ involvement. Mostly, they found a combination of synovitis (78%) and bone abnormalities (72%). This is also in accordance with others [15, 33]. Koos et al [15] found a specificity of 0.86 for TMJ pain and 0.83 for LOM when comparing with MRI-detected TMJ arthritis in children with JIA. Sensitivity of these clinical signs of TMJ involvement was however low [15]. We therefore anticipate that in the present study, the vast majority of the children with clinical symptoms actually had TMJ arthritis.

It must be emphasized that symptoms and signs in these joints are quite unspecific. We could expect that a minority, as discussed by Kirkhus et al [35], might have TMJ symptoms / signs due to myalgia or mechanical disorders such as disc displacement. MRI would have been highly valuable for differential diagnostics.

In the present study, we do not know to what extent dento-facial growth disturbances were registered. In other studies, approximately one third of children with JIA and TMJ arthritis have been observed with micrognathia [2, 3].

Children with JIA below the age of 7 years are reported to have almost no subjective TMJ dysfunction or symptoms [36]. They may not be able to give a precise description of their symptoms, and may develop severe facial growth disturbances apparently without previous symptoms [2]. With an average age at visit ≥10 years in the present study the majority should have been old enough to report symptoms. The subgroup with TMJ arthritis constituted a
rather large number of patients, although being only a small percentage of the whole series. Therefore, the present study can provide valuable characteristics of a large group of children with symptomatic TMJ involvement.

To our knowledge, no study has actually analyzed the relationship between TMJ involvement in children with JIA and HRQoL measures, although one study has reported an impact on the daily life activities [22]. Our results showed an association with increased pain, and difficulties in eating, arising, and reaching in univariate analysis, and being disabled measured by the CHAQ-DI in multivariable analyses compared to the non-TMJ group. The associations between TMJ involvement and impaired HRQoL are in agreement with studies on non-JIA children and young adult JIA patients, showing that TMD may lead to impaired oral health and influence daily life [21, 22, 37]. This is in accordance also with Leksell et al [22] who found that almost 80% of their JIA children reported pain from the TMJs or the face, and nearly a quarter was severely influenced by oro-facial pain in daily life. However, their findings were based on a small JIA cohort of 41 children and adjustment for disease severity was not performed. Leksell et al [22] studied general oro-facial symptoms, while the present study focused on clinical TMJ involvement. A high prevalence of TMD problems in adolescent and adult JIA patients is also reported by other authors [11, 20].

The present study show associations between clinical TMJ involvement and impaired HRQoL factors such as activity and physical and emotional wellbeing [38]. A lower self-esteem (SE of the CHQ) and eating difficulties (CHAQ) were significantly associated with clinical TMJ involvement in univariate analysis, but not in multivariable analysis. A lower self-esteem may be explained by craniofacial growth disturbances resulting in asymmetries and micrognathia, or related to high disease activity, since it is not significantly associated to clinical TMJ involvement in the adjusted analyses. However, several studies show a positive psychosocial effect in JIA patients after orthognatic surgery [39, 40].
The TMJ is important for many daily life activities such as eating, chewing, talking, and oral health [5, 37, 41]. Our results on eating problems in univariate analyses are in accordance with Leksell et al who report problems with eating and oral health among JIA patients aged 10-19 years compared to healthy controls [41]. Welbury et al [5] report significantly increased levels of poor oral hygiene and dental decay in children with JIA in general compared to controls. Ahmed et al [6] report about greater gingivitis score for the permanent teeth in the JIA children and greater TMJ dysfunction in JIA children compared to controls. Leksell et al however [41], believe the problems with eating and performing a good oral hygiene, are not only due to TMJ pain, but also due to medication and general disease activity. Adequate nutrition is essential for growth and general wellbeing in children with chronic inflammation. Eating difficulties is one of the eight domains in the CHAQ and one question is as follows; “Is your child able to: Cut his/her own meat?” This question probably mainly reflects problems with fine motor skills due to finger and wrist arthritis more than eating problems due to TMJ. CHAQ is therefore not a specific tool for assessing TMJ dysfunction. The newly developed questionnaire “Juvenile Arthritis Multidimensional Assessment Report (JAMAR)” may better explore eating difficulties and TMJ involvement in the question “Difficulties/limitations with bite into a sandwich or an apple” [42]. Also, a standardized protocol for a proper diagnostic and classification system of the TMJs in children with JIA, similar to, but shorter than the established and validated Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) [43, 44], is under development in the EuroTMjoint network. Jaw opening is also included in the pGALS (pediatric Gait, Arms, Legs, and Spine) screening tool for musculoskeletal examination in children [45].

In contrast to Cannizzaro and coworkers [9], we found longer disease duration in the TMJ group, but not significant differences between the two groups according to age at onset. Peak
onset of TMJ arthritis according to age and time after disease onset are best studied in prospective JIA cohorts with imaging.

In line with other studies, we found associations between TMJ involvement and upper limb involvement as well as higher ESR [7, 9]. We also found a significant association between TMJ and cervical spine involvement, and in contrast to Cannizzaro and coworkers, the association was confirmed in multivariable analysis adjusting for higher disease activity [7, 9].

Cervical spine arthritis is often based on clinical criteria such as cervical pain and stiffness. However, this could also be the result of myalgia, in the same way as clinical TMJ involvement may represent muscular pain instead of TMJ arthritis. The close proximity of the neck and masticatory muscles might partly explain this association.

Bilateral involvement was registered in 80.6% of the children with clinical TMJ involvement, in agreement with observations in adult JIA patients [11]. At the baseline radiographic examination of that longitudinal follow-up study by Larheim et al, about 60% of the children with TMJ arthritis were assessed with bilateral TMJ involvement [7]. This figure seems to be in accordance with most radiographic TMJ studies of JIA children [2, 11, 46, 47] but the occurrence of bilateral TMJ involvement seems to be higher when using MRI [10, 48, 49]. Children may have difficulties to distinguish whether there is pain in one or both TMJs.

There are some limitations in the present study. It was not designed to study TMJ arthritis specifically and no imaging was performed. Furthermore, pediatric rheumatologists and not trained dental specialists performed the TMJ examination. Since TMJ involvement is most common in children with polyarthritis, another limitation of our study is to distinguish clinical variables associated with TMJ involvement from associations with arthritis in any specific joint or polyarticular disease in general. Therefore, we have performed a multivariable
analysis adjusting for measures of high disease activity such as participation in the PRINTO Methotrexate trial, higher number of active joints, higher ESR, and being RF positive. However, other activity variables not adjusted for, may still have interfered with our analyses.

In conclusion, clinical TMJ involvement is associated with impaired HRQoL in JIA children. The prevalence of TMJ involvement is surely an underestimate of TMJ arthritis, but most children with clinically evident TMJ involvement were probably identified. Special attention should be payed to the TMJ in children with cervical spine involvement, polyarticular course, longer disease duration, physical disability and female gender. There is a need for an internationally accepted definition of TMJ arthritis whether based on clinical findings and/or imaging. Longitudinal TMJ studies with clinical assessment and imaging are warranted to identify early predictors of severe facial growth disturbances, treatment modalities and outcome over time.
Figure 1. Flow chart of the participants enrolled in the study

- **MTX TRIAL (23)**
  - N=633

- **HRQoL STUDY JIA PARTICIPANTS (24)**
  - n=3235
  - HEALTHY CHILDREN (n=3409)

- **DUPLICATED JIA PARTICIPANTS**
  - (n=517)

- **PARTICIPANTS ELEGIBLE FOR THE ANALYSIS (n=6760)**
  - MTX TRIAL (n=633)
    - CHILDREN WITH JIA (n=2718)
    - HEALTHY CHILDREN (n=3409)

- **EXCLUDED (n=6)**
  - Psoriatic Arthritis (n=3)
  - Enthesitis-related arthritis (n=4)
  - Patients without clinical examination (n=1)

- **PARTICIPANTS ANALYZED (n=6752)**
  - MTX TRIAL (n=628)
    - CHILDREN WITH JIA (n=2715)
    - HEALTHY CHILDREN (n=3409)
Figure 2. Mean and 95% confidence intervals for the Childhood Health Assessment Questionnaire (CHAQ) for children with and without clinical TMJ involvement. Vertical bars represent +2SD of the mean of healthy children. Higher scores indicate more disability. Arrows indicate the three CHAQ domains (Dressing, Eating, and Active) in which only JIA children with clinical TMJ involvement have scores >2 SDs of the mean of healthy children.
Figure 3. Mean and 95% confidence intervals of the 15 subscales (range 0–100) and the two summary scores (norm-based values with mean ± SD of 50 ± 10) of the Child Health Questionnaire (CHQ) for children with and without clinical TMJ involvement. Higher scores indicate better health. Vertical bars represent -2SD of the mean of healthy children. Arrows indicate the four CHQ health concepts (GGH, REB, RP and BP) in which only JIA children with clinical TMJ involvement have scores < -2 SDs of the mean of healthy children.
Table 1. Demographic and disease activity characteristics according to clinical TMJ involvement among 3343 children with JIA.

<table>
<thead>
<tr>
<th></th>
<th>With clinical TMJ involvement N=387</th>
<th>Without clinical TMJ involvement N=2956</th>
<th>Cut-off</th>
<th>Clinical TMJ involvement OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female*</td>
<td>292 (75.5%)</td>
<td>1986/2951 (67.3%)</td>
<td>1.5</td>
<td>(1.2 – 1.9)</td>
</tr>
<tr>
<td>Age at visit†</td>
<td>11.6 (8.5-14.9)</td>
<td>10.0 (6.5-13.6)</td>
<td>&gt;9.2</td>
<td>1.8 (1.4 – 2.3)</td>
</tr>
<tr>
<td>Age at onset‡</td>
<td>4.9 (2.3 – 8.3)</td>
<td>5.2 (2.5 – 8.8)</td>
<td>≤8.9</td>
<td>1.2 (0.9 - 1.5)</td>
</tr>
<tr>
<td>Disease duration†</td>
<td>5.1 (2.1 – 8.6)</td>
<td>3.2 (1.3 – 6.0)</td>
<td>&gt;4.4</td>
<td>2.2 (1.8 – 2.8)</td>
</tr>
<tr>
<td>JIA category*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent oligoarthritis</td>
<td>19 (4.9%)</td>
<td>887 (30.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended oligoarthritis**</td>
<td>78 (20.2%)</td>
<td>546 (18.5%)</td>
<td>6.7</td>
<td>(4.0 – 11.1)</td>
</tr>
<tr>
<td>Polyarthritis**</td>
<td>93 (24.0%)</td>
<td>585 (19.8%)</td>
<td>7.4</td>
<td>(4.5 – 12.3)</td>
</tr>
<tr>
<td>Syst. arthritis**</td>
<td>197 (50.9%)</td>
<td>938 (31.7%)</td>
<td>9.8</td>
<td>(6.1 – 15.8)</td>
</tr>
<tr>
<td>ANA*</td>
<td>142/368 (38.6%)</td>
<td>1057/2823 (37.4%)</td>
<td>1.1</td>
<td>(0.8 – 1.3)</td>
</tr>
<tr>
<td>RF†</td>
<td>43/377 (11.4%)</td>
<td>216/2831 (7.6%)</td>
<td>1.6</td>
<td>(1.1 – 2.2)</td>
</tr>
<tr>
<td>MTX study*</td>
<td>116 (30.0%)</td>
<td>512 (17.3%)</td>
<td>2.0</td>
<td>(1.6 – 2.6)</td>
</tr>
<tr>
<td>Disease activity variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JADAS score†</td>
<td>20.6 (11.1–30.3)</td>
<td>9.2 (3.2–17.9)</td>
<td>&gt;18.1</td>
<td>4.6 (3.7 – 5.8)</td>
</tr>
<tr>
<td>MDgloVAS†</td>
<td>4.2 (2.2 – 6.2)</td>
<td>2.3 (0.6 – 4.5)</td>
<td>&gt;2.6</td>
<td>2.7 (2.2 – 3.4)</td>
</tr>
<tr>
<td>ESR†</td>
<td>32.0 (18.0 – 52.0)</td>
<td>22.0 (11.0 – 41.0)</td>
<td>&gt;15.0</td>
<td>2.8 (2.1 – 3.7)</td>
</tr>
</tbody>
</table>

No of patients with
<table>
<thead>
<tr>
<th></th>
<th>259 (66.9%)</th>
<th>1044 (35.3%)</th>
<th>≥ 5.0</th>
<th>3.7 (3.0 – 4.6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of joints with swelling†</td>
<td>4.0 (1.0 – 12.0)</td>
<td>2.0 (0.0 – 5.0)</td>
<td>&gt;2.0</td>
<td>2.3 (1.8 – 2.8)</td>
</tr>
<tr>
<td>No of joints with pain†</td>
<td>7.0 (2.0 – 15.0)</td>
<td>1.0 (0.0 – 5.0)</td>
<td>&gt;5.0</td>
<td>4.5 (3.6 – 5.6)</td>
</tr>
<tr>
<td>No of joints with LOM†</td>
<td>13.0 (6.0 – 29.0)</td>
<td>2.0 (0.0 – 7.0)</td>
<td>&gt;4.0</td>
<td>8.9 (6.8 – 11.7)</td>
</tr>
<tr>
<td>No of active joints†</td>
<td>8.0 (3.0 – 17.0)</td>
<td>2.0 (0.0 – 6.0)</td>
<td>&gt;5.0</td>
<td>3.9 (3.1 – 4.8)</td>
</tr>
<tr>
<td>Cervical spine involvement*</td>
<td>239 (61.8%)</td>
<td>508 (17.2%)</td>
<td>7.8 (6.2 – 9.8)</td>
<td></td>
</tr>
</tbody>
</table>

*Values are number (percentage). Chi-Squared test is used for testing associations with TMJ (categorical variables) together with Student’s T-test and the Wilcoxon test (continuous variables). †Continuous variables are median (1st – 3rd quartile). Cut-off values for continuous variables were dichotomized as per ROC analyses. P-value is <0.05 for all variables. Age at onset and ANA are not statistically significant. The variables are known for >95% of the total participants, except for the following: ESR (90%), JADAS Score (89%). **JIA category versus persistent oligoarthritis used as a reference; TMJ = temporomandibular joint; JIA = juvenile idiopathic arthritis; ANA = antinuclear antibody; RF = rheumatoid factor; ESR = erythrocyte sedimentation rate; MDgloVAS = medical doctor global visual analogue scale; MTX = methotrexate; JADAS score = Juvenile Arthritis Disease Activity Score; LOM = limited range of motion.
Table 2. Disability and HrQoL measures for children with (n=387) and without clinical TMJ involvement (n=2956).

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Clinical TMJ involvement OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHAQ</strong>*</td>
<td></td>
</tr>
<tr>
<td>Dressing &gt;0.0</td>
<td>3.1 (2.4 – 3.9)</td>
</tr>
<tr>
<td>Arising &gt;0.0</td>
<td>3.7 (3.0 – 4.7)</td>
</tr>
<tr>
<td>Eating &gt;0.0</td>
<td>3.4 (2.7 – 4.2)</td>
</tr>
<tr>
<td>Walking &gt;0.0</td>
<td>2.6 (2.1 – 3.3)</td>
</tr>
<tr>
<td>Hygiene &gt;0.0</td>
<td>3.0 (2.4 – 3.7)</td>
</tr>
<tr>
<td>Reach &gt;0.0</td>
<td>5.5 (4.1 – 7.2)</td>
</tr>
<tr>
<td>Grip &gt;0.0</td>
<td>3.6 (2.8 – 4.4)</td>
</tr>
<tr>
<td>Active &gt;1.0</td>
<td>3.5 (3.3 – 5.6)</td>
</tr>
<tr>
<td><strong>CHAQ-DI</strong></td>
<td></td>
</tr>
<tr>
<td>&gt;0.6</td>
<td>4.1 (3.2 – 5.2)</td>
</tr>
<tr>
<td><strong>PRPainVAS</strong>*</td>
<td></td>
</tr>
<tr>
<td>&gt;1.8</td>
<td>2.7 (2.2 – 3.5)</td>
</tr>
<tr>
<td><strong>PRgloVAS</strong>*</td>
<td></td>
</tr>
<tr>
<td>&gt;2.2</td>
<td>3.1 (2.5 – 4.0)</td>
</tr>
<tr>
<td><strong>CHQ</strong>*</td>
<td></td>
</tr>
<tr>
<td>GGH ≤30.0</td>
<td>2.0 (1.6 – 2.5)</td>
</tr>
<tr>
<td>PF ≤72.2</td>
<td>2.9 (2.3 – 3.6)</td>
</tr>
<tr>
<td>REB ≤77.8</td>
<td>2.4 (1.9 – 3.0)</td>
</tr>
<tr>
<td>RP ≤66.7</td>
<td>2.4 (2.0 – 3.1)</td>
</tr>
<tr>
<td>BP ≤50.0</td>
<td>2.2 (1.7 – 2.7)</td>
</tr>
<tr>
<td>BE N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>GBE N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>MH ≤70.0</td>
<td>1.7 (1.3 – 2.1)</td>
</tr>
<tr>
<td>SE ≤70.8</td>
<td>2.0 (1.6 – 2.4)</td>
</tr>
<tr>
<td>GH ≤51.0</td>
<td>2.0 (1.6 – 2.5)</td>
</tr>
<tr>
<td>CH ≤25.0</td>
<td>1.6 (1.2 – 1.9)</td>
</tr>
<tr>
<td>PE ≤75.0</td>
<td>2.3 (1.7 – 3.0)</td>
</tr>
<tr>
<td>PT2 ≤77.8</td>
<td>1.9 (1.5 – 2.3)</td>
</tr>
<tr>
<td>FA ≤66.7</td>
<td>2.0 (1.6 – 2.5)</td>
</tr>
<tr>
<td>FC ≤30.0</td>
<td>1.7 (1.3 – 2.3)</td>
</tr>
<tr>
<td><strong>PhS</strong>*</td>
<td></td>
</tr>
<tr>
<td>≤35.1</td>
<td>3.2 (2.5 – 4.1)</td>
</tr>
<tr>
<td><strong>PsS</strong>*</td>
<td></td>
</tr>
<tr>
<td>≤50.3</td>
<td>1.7 (1.4 – 2.2)</td>
</tr>
</tbody>
</table>

*Cut-off values for the continuous variables were dichotomized as per ROC analyses; CHAQ-DI = child health assessment questionnaire disability index; GGH = global general health; PF = physical function; REB = role emotional behavior; RP = role physical; BP = Bodily pain; BE = behavior; GBE = general behavior; MH = mental health; SE = self-esteem; GH = general health; CH = change in health; PE = parental impact emotional; PT = parental impact time; FA = family activities; FC = family cohesion; PhS = physical score; PsS = psychosocial score. p-value is <0.05 for all variables except for BE and GBE that were not significant in the univariate analysis (i.e. N/A = not applicable).
Table 3. Disease activity, disability and HRQoL characteristics associated with clinical TMJ involvement adjusted for measures of high disease activity*

<table>
<thead>
<tr>
<th>Clinical TMJ involvement</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical joint involvement</td>
<td>7.8 (6.2 – 9.8)</td>
<td>4.6 (3.5 – 6.1)</td>
</tr>
<tr>
<td>Disease duration &gt;4.4 years</td>
<td>2.2 (1.8 – 2.8)</td>
<td>2.8 (2.1 – 3.8)</td>
</tr>
<tr>
<td>CHAQ-DI &gt;0.6</td>
<td>4.1 (3.2 – 5.2)</td>
<td>1.6 (1.2 – 2.3)</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>1.5 (1.2 – 1.9)</td>
<td>1.5 (1.1 – 2.1)</td>
</tr>
<tr>
<td>PRgloVAS &gt;2.2</td>
<td>3.1 (2.5 – 4.0)</td>
<td>1.3 (0.9 – 1.8)</td>
</tr>
<tr>
<td>CHQ PhS ≤35.1</td>
<td>3.2 (2.5 – 4.1)</td>
<td>1.2 (0.9 – 1.7)</td>
</tr>
<tr>
<td>CHQ PsS ≤50.3</td>
<td>1.7 (1.4 – 2.2)</td>
<td>1.2 (0.9 – 1.6)</td>
</tr>
<tr>
<td>PRPain VAS &gt;1.8</td>
<td>2.7 (2.2 – 3.5)</td>
<td>1.1 (0.8 – 1.6)</td>
</tr>
<tr>
<td>MDgloVAS &gt;26.0</td>
<td>2.7 (2.2 – 3.4)</td>
<td>0.9 (0.6 – 1.3)</td>
</tr>
</tbody>
</table>

*Multivariable logistic regression analysis adjusted for the following measures of high disease activity: MTX trial participation, number of active joints >5, erythrocyte sedimentation rate (ESR) >15, and RF positive. TMJ = temporomandibular joint; CHAQ-DI = child health assessment questionnaire disability index; MDgloVAS = medical doctor’s global assessment of disease activity; PRgloVAS = parent’s / patient’s reported global assessment of the child’s overall well-being in the previous week; PRPain VAS = parent’s / patient’s reported global assessment of the child’s pain in the previous week; CHQ = Child Health Questionnaire; PhS = physical summary score; PsS = psychosocial summary score.
REFERENCE LIST


