Assessment of orofacial symptoms in juvenile idiopathic arthritis: Validation of a consensus-based short patient questionnaire

Short title: Orofacial symptoms in JIA

Key Indexing Terms: Temporomandibular joint, juvenile idiopathic arthritis, pain, symptoms, questionnaire, outcome

Authors: Peter Stoustrup*, Hanna Rahimi, Marinka Twilt, Y. Ingrid Goh, Thomas Klit Pedersen, Troels Herlin, Lynn Spiegel; on Behalf of the Temporomandibular joint Juvenile Arthritis Work group (TMJaw).

Peter Stoustrup: DDS, PhD. Associate Professor of Orthodontics, Section of Orthodontics, Department of Dentistry and Oral Health, Aarhus University, Aarhus, Denmark. ORCID: 0000-0002-0903-6718

Hanna Rahimi: MD, Department of Paediatrics and Adolescent Medicine, Herlev and Gentofte Hospital, Copenhagen University Hospital, Herlev, Denmark

Marinka Twilt: MD, MSCE, PhD, Associate professor, Department of Pediatrics, Cumming School of Medicine, University of Calgary and Alberta Children's Hospital, Calgary, Alberta, Canada

Y. Ingrid Goh: PhD, Division of Rheumatology, The Hospital for Sick Children; Child Health Evaluative Sciences, SickKids Research Institute, Toronto, Ontario, Canada

Thomas Klit Pedersen: Consultant Orthodontist, Professor, PhD. Department of Oral and Maxillofacial Surgery, Aarhus University Hospital, Section of Orthodontics, Aarhus University, Denmark. ORCID: 0000-0002-7911-9180

Troels Herlin: Professor, MD, DMSci, Pediatric Rheumatology Clinic, Pediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark. ORCID: 0000-0002-6525-3207

Lynn Spiegel: MD, FRCPC, Associate Professor, Department of Pediatrics, University of Toronto, Division of Rheumatology, The Hospital of Sick Children, Child Health Evaluative Sciences, SickKids Research Institute, Toronto, Ontario, Canada.

*Corresponding author: pstoustrup@dent.au.dk, Section of Orthodontics, Aarhus University, Vennelyst Boulevard 9-11, 8000, Aarhus C

Funding: None

Conflicts of interest: None

Statement of ethics and consent:

Word count: 3500

Abstract

Objective. To develop, validate and test the performance of patient reported outcomes (PROs) in a short patient questionnaire (<5 min) to assess the multidimensional aspects of orofacial symptoms related to juvenile idiopathic arthritis (JIA) from ≥10 years.

Methods. The study was conducted by an interdisciplinary task force from the Temporomandibular joint Juvenile Arthritis Working Group (TMJaw). The project consisted of a multi-phased approach including: 1) Conceptual phase with online international survey of 167 healthcare workers, 2) item generation and drafting of preliminary questionnaire(s) (face validity), 3) cognitive script interview and probing (content validity, n=16 patients with JIA), 4) assessment of construct validity (convergence and divergence, n=53 patients with JIA), 5) test of reliability, 6) test of clinical performance and psychometric characteristics (n=95 patients with JIA).

Results. Seven PROs were included in the final patient questionnaire: (1) pain frequency, (2) pain intensity, 3) pain location, 4) jaw function, 5) specific questions related to symptoms and dysfunction, 6) changes in face and jaw pain since last visit, 7) changes in jaw function since last visit. Eighty percent of the patients were able to complete the questionnaire in less than 5 minutes.

Conclusion. We have developed and validated a short patient questionnaire to assess the multidimensional aspects of JIA-related orofacial symptoms. The PROs included in our questionnaire show acceptable validity and reliability. The questionnaire is applicable to routine monitoring of subjects with JIA, as well as future research studies.

Introduction

Involvement of the temporomandibular joint (TMJ) is a frequent complication of juvenile idiopathic arthritis (JIA) with a prevalence of 30-45%(1-3). The condition can lead to a diverse spectrum of symptoms including impaired function of the TMJ and facial muscles, joint destruction, and growth disorders of the mandible(1, 2, 4-11). TMJ involvement has an impact on quality of life, and orofacial signs and symptoms can persist well into adulthood(12-14). Persistent orofacial symptoms can lead to widespread multiregional distribution of facial pain with involvement of more than the TMJ area(14). Orofacial symptoms may originate from the presence of TMJ inflammation. However, orofacial symptoms and the presence of TMJ arthritis are poorly correlated(15, 16). In otherwise well-treated patients, symptoms can originate from mechanical dysfunction related to TMJ degeneration and dysfunction caused by previous TMJ inflammation(17).

The orofacial manifestations of JIA have received increasing attention over the last 10-15 years. Interdisciplinary consensus recommendations for orofacial assessment of patients with JIA were published in 2017 by the Temporomandibular joint Juvenile Arthritis Working Group (TMJaw, formerly known as euroTMJoint)(9). In 2020, these recommendations led to the publication of a validated short screening protocol for the orofacial examination in JIA focusing on TMJ function and facial morphology(18).

The purpose of the present study was to develop, validate and test the performance of patient reported outcomes (PROs) in a short patient questionnaire for the assessment of JIA-related orofacial symptoms in patients ≥10 years.

Material and Methods

The project was conducted by a clinical task force consisting of members from TMJaw, which is an international, interdisciplinary research network dedicated to improving the management of TMJ arthritis and its associated conditions. The initial TMJaw task force consisted of three orthodontists with special expertise in JIA, three pediatric rheumatologists, and two orofacial pain specialists, representing five different countries. The project outline consisted of a multi-phased approach including: 1) Conceptual phase, 2) item generation and drafting of preliminary questionnaire(s) (face validity), 3) cognitive script interview and probing (content validity), 4) assessment of construct validity (convergence and divergence), 5) test of reliability, 6) assessment of clinical performance and psychometric characteristics of the TMJaw patient questionnaire.

The current project is related to our previous work creating recommendations for a short clinical screening protocol for the orofacial examination in JIA(18). It complies with the standardized terminology for orofacial manifestations of JIA(19) with the following definitions: “TMJ arthritis”:

active inflammation in the TMJ; "TMJ involvement": abnormalities presumed to be the result of current or previous TMJ arthritis; and "TMJ symptoms": patient or parent-reported conditions related to TMJ arthritis or involvement.

1) Conceptual phase

An online international Delphi survey was conducted to study current practices related to the assessment of orofacial symptoms during the clinical examination of patients with JIA. The survey invitation was distributed to everyone included on the membership lists of the email driven Pediatric Rheumatology Bulletin Board and the TMJaw membership list. To enhance feasibility of the future patient reported outcome measures (PROMs), survey respondents were asked to indicate the maximum amount of time they felt patients would be willing to devote to completing PROMs.

2) Item generation and drafting of preliminary questionnaire(s)

Item generation was conducted by the task force. Eligible items for the patient questionnaire were identified from the interdisciplinary, consensus-based recommendations for monitoring orofacial health in JIA (9). To ensure high face validity, only items rated of "high importance" as PROs of JIA-related orofacial symptoms were considered eligible for the patient questionnaire (9). The items and their domains are illustrated in table 1.

A preliminary English version of the patient questionnaire was drafted. In addition, a comparable preliminary Danish version of the patient questionnaire was conducted using an internationally acknowledged approach for cross-cultural adaptation(20): 1) forward translation by two independent bilingual translators, 2) synthesis of the translation (Danish version), 3) back translation by two independent translators blinded to the original English version, and 4) consolidation of a pre-final version of the Danish questionnaire evaluated for semantic and conceptual equivalence.

3) Cognitive script interview and probing (content validity)

A researcher with expertise in TMJ arthritis (HR) conducted a series of probing interviews. The researcher was bilingual (English/Danish) and had not participated in the previous phases of the study. Participants for the probing interviews were recruited from the pediatric rheumatology out-patient clinics at The Hospital for Sick Children, Toronto, Canada and from the Regional Specialist Craniofacial Clinic (RSCC) at the Section of Orthodontics, Aarhus University, Denmark. Inclusion/exclusion criteria were: 1) A diagnosis of JIA according to the International League Against Rheumatism (ILAR) criteria(21), 2) experience of JIA-related orofacial symptoms within the past two weeks defined as pain > 5mm on a 0-100 mm visual analogue scale (VAS); or JIA-related orofacial dysfunction defined by difficulty performing tasks such as chewing, talking and reduced mouth opening, 3) age 10-18 years, and 4) ability to read and speak English or Danish.

In a one-on-one interview, participants were asked about the clarity of the content, meaning, wording, and intelligibility of items, and whether any items were missing. In addition, the participants rated the importance of each question on a 5-point double-anchored categorical scale (from 1 to 5, with 1 = not important to 5 = highly important for assessing TMJ symptoms in youth with JIA). The content validity ratio (CVR) was computed(22): Acceptable content validity was achieved if more than half the respondents rated an item as being important (CVR average score ≥ 4). A purposive recruitment of participants was done until a saturation of responses was achieved.

4) Assessment of construct validity (convergence and divergence)

Fifty-three eligible participants were recruited for a cross-sectional study of the construct validity of the questionnaire items (Toronto n=25, Aarhus n=28). A sample size calculation was performed prior to the initiation of the study. A sample size of 46-50 participants was found to be adequate for validation and reliability testing. Participants consisted of consecutive patients complying with the following inclusion criteria: 1) A diagnosis of JIA(21), 2) imaging or radiological evidence of TMJ arthritis/involvement(19), 3) age 10-18 years, and 4) ability to read and speak English or Danish. Exclusion criteria were: 1) A history of previous orofacial trauma or syndromes involving the orofacial area, and 2) patients with moderate to severe cognitive impairment or major psychiatric comorbid illnesses that could potentially affect the ability to understand and complete the questionnaires. Participants were recruited from the pediatric rheumatology out-patient clinics at The Hospital for Sick Children, Toronto, Canada and from the RSCC, Aarhus University, Denmark.

Eligible participants were asked to complete four different questionnaires: 1) The TMJaw orofacial symptom questionnaire. 2) The Patient-Reported Outcomes Measurement Information System (PROMIS®) Pain intensity Questionnaire(23): A 3-item questionnaire, using a 5-point scale that assesses the severity of respondents' pain. 3) The PROMIS® Pain Interference Questionnaire(24): An 8-item questionnaire that assesses how pain affects respondents' activities. 4) The Pediatric Quality of Life Inventory (PedsQL™) 3.0 Arthritis Module(25): A 22-item questionnaire that evaluates the severity of perceived problems of disease symptoms, daily activity limitations, treatments, worry/anxiety, and communication. Validated Danish and English versions were administered to Danish and English participants, respectively.

Convergent and divergent validity of the TMJaw symptom questionnaire was evaluated based on the following hypotheses:

H1: We expected moderate correlations (>0.5-0.75) between the TMJaw questionnaire items 1 and 2 ("pain frequency" and "pain intensity"), and the PROMIS® pain intensity questionnaire as they measure similar concepts.

H2: We expected low-moderate correlations (0.25-0.5) between the TMJaw questionnaire items 2 and 4 ("pain intensity" and "jaw function"), and the PROMIS® pain interference questionnaire since they measure some related and unrelated concepts.

H3: We expected low correlation (<0.25) between TMJaw questionnaire items 1, 2 and 4 ("pain frequency", "pain intensity" and "jaw function") and the PedsQL™, which measure unrelated concepts, providing discriminant validity.

5) *Test of reliability*

Participants were asked to complete an identical follow-up version of the TMJaw symptom questionnaire 2-24 hours after they completed the baseline version. The patients had not been informed about this duplicate completion when they completed the initial baseline version of the questionnaire.

In the test/retest of questionnaire item 3 (pain location) the outcome was assessed in a qualitative and dichotomous way. It was assessed if the patient was able to reproduce the markings on the face map with regards to distribution of the reported orofacial symptoms and anatomical structures; e.g. within the boundaries of TMJ and certain masticatory muscles (outcome yes/no).

Reliability was evaluated based on the following hypothesis:

H4: We expect stable correlation coefficients ($\geq$ 0.8) between identical TMJaw questionnaire items measured at the two time-points.

6) Clinical performance and psychometric characteristics

Knowledge about clinical performance is essential in the future process where the questionnaire is planned to be translated and cross-culturally tested in other languages. Assessment of questionnaire performance and psychometric characteristics was performed in consecutive patients with JIA and orofacial symptoms from the RSCC, Aarhus University, Denmark. Inclusion criteria for this phase were: 1) A diagnosis of JIA, 2) experience of JIA-related orofacial symptoms within the past two weeks defined as pain >5 mm on a VAS 0-100 mm scale; or JIA-related orofacial dysfunction defined by difficulty performing tasks such as chewing, talking and reduced mouth opening. To achieve a sufficiently high number of patients with orofacial symptoms, we also included patients from the primary Aarhus and Toronto cohorts used in phases four and five. Only patients complying with the inclusion criteria were used from the Aarhus and the Toronto cohorts.

To combine aspects of pain frequency and pain intensity into one outcome variable, we calculated the "pain index" composite variable by multiplying "pain frequency" (range 0-4) with the "pain intensity" VAS score (0-100 mm). The "pain index" is a validated outcome measure that has a range of 0-400 where a higher score indicates a higher degree of pain experience(14).

Statistics

Spearman correlation coefficients were used to test validity for ordinal data. Reliability parameters were assessed using Cohen's κ to assess reliability in categorical PROs (questionnaire items 1,3,5,6,7). Reliability in PROs with continuous variables (items 2 and 4) were assessed using intra-class correlation coefficient (ICC). Bland-Altman plots were used to assess 95% limits of agreement for continuous data. Descriptive statistics was used to assess clinical performance and psychometric characteristics of the questionnaire. The "floor and ceiling" effects were identified; for continuous outcome measure the "floor effect" was defined as the proportion of responses in the lower 10% of the response scale: for "pain intensity" and "jaw function" (VAS score ≤10 mm, on a 0-100 mm VAS) and "pain-index" (scores ≤40, when score range is 0-400). The ceiling effect was defined as the proportion of scores above 90% of the response scale: for "pain intensity" and "jaw function" (VAS score ≥ 90mm, on a 0-100 mm VAS) and "pain-index" (scores ≥360, when score range is 0-400). ICC/Cronbach's alpha was used to compare inter-item correlation in the psychometric characteristics between pain intensity, pain index, and jaw function.

Results

1) Conceptual phase

The Delphi survey was completed by 167 healthcare providers representing pediatric rheumatology, orthodontics, radiology, maxillofacial surgery, allied health professionals and others. The respondents to the online survey is identical to the group described in the previous related project. For details about the survey we refer to Stoustrup et al. (18). Based on survey responses, the task force indicated that the questionnaire should not take more than 5 minutes to complete.

2) Item generation and drafting of preliminary questionnaire(s)

The following seven items were included in the patient questionnaire for the description of JIA-related orofacial symptoms and dysfunctions within the last 2 weeks: 1) Assessment of frequency of orofacial pain 2) pain intensity 3) pain location 4) jaw function 5) orofacial symptoms 6) changes in face and jaw pain since the last visit, and 7) changes in jaw function since the last visit. The assessment of each outcome variable is described in Table 1.

3) Cognitive script interview and probing (content validity)

Sixteen subjects participated in the cognitive interviews (Toronto n=11, Aarhus n=5). Acceptable CVRs were achieved for all seven included items: Highest CVR scores were seen for item 1 ("pain frequency",

CVR=4.38, SD 0.5) and item 5 ("symptoms", CVR=4.38, SD 0.62). The lowest CVR score was seen for item 6 ("changes in face and jaw pain", CVR = 4.0, SD 0.55).

Ambiguities, misunderstandings, and missing items were addressed during the cognitive script interviews. The following items were raised by the participants: 1) lack of assessment of the psychosocial aspects of pain and dysfunction, 2) difficulties reporting "average" pain when symptoms fluctuate, and 3) inability to differentiate the intensity of symptomatic areas indicated on face map.

The interviews led to minor modifications to ensure conceptual equivalence between the English and the Danish version of the questionnaires.

4) *Assessment of construct validity (convergence and divergence)*

Table 2 describes the cohort characteristics of the participants for the construct validity testing and test of reliability (n=53). 18/53 (34%) of the patients complying with the inclusion for this phase of the study did not report any orofacial symptoms within the 2 weeks prior to the questionnaire completion. Table 3 displays the results of the construct validity tests:

H1 was fully accepted (convergent validity): The Spearman correlation coefficients for questionnaires items 1, 2 and 4 ranged from 0.53-0.74. This was within the expected ranges (0.50-0.75).

H2 was partially accepted (convergent validity): Moderate correlation coefficients were found between questionnaire items 1, 2 and 4 and the PROMIS® pain interference module, ranging from 0.52-0.66. We had expected a lower correlation ranging from 0.25-0.50.

H3 was fully accepted (discriminant validity): Negative correlations were found between questionnaire items 1, 2 and 4 and the PedsQL™ ranging from -0.56 to -0.70. We had anticipated a low correlation (<0.25).

The items in the English and the Danish versions of the TMJaw patient questionnaires showed comparable construct validity.

5) *Test of reliability*

Table 4 displays the results of the reliability testing:

H4 was partly accepted; 10/13 of the questionnaire items had a combined correlation coefficient ≥ 0.8 between identical TMJaw questionnaire items measured at the two time-points (Table 4). Items with a correlation coefficient Cohen's κ of <0.8 were assessment of "pain location" on the face map (κ =0.69), "changes in face and jaw pain" (κ =0.76), and "changes in jaw function" (κ =0.74).

Although the English version presented slightly lower reliability scores for some of the values, the items in the English and the Danish versions of the TMJaw patient questionnaire showed comparable reliability scores (Table 4).

6) Clinical performance and psychometric characteristics

A cohort of 95 patients with JIA-related orofacial symptoms was included for this phase. The cohort consisted of consecutive patients from the RSCC (n=60), and consecutive patients complying with the inclusion criteria from the initial cohorts from Toronto (n=19) and Aarhus (n=16) used in phases four and five. The mean age of the total cohort (n=95) was 14.3 years (SD 2.8 years). The distribution of the time frame from JIA onset to the completion of the questionnaire was: <1 year (n=4), 1-3 years (n=15), >3 years (n=76). The cohort distribution of JIA subcategories was: JIA oligoarticular persistent (n=36), JIA oligoarticular extended (n=16), JIA psoriatic arthritis (n=3), systemic arthritis (n=4), JIA polyarticular RF-negative (n=33), JIA polyarticular RF-positive (n=1), enthesitis-related arthritis (n=1), undifferentiated arthritis (n=1). The results of the clinical performance tests are displayed in Table 5. The psychometric properties of the questionnaire items are displayed in Table 6. Eighty percent of the cohort completed the questionnaire within the 5-minute time frame (Table 6). There were no significant inter-group differences between the Aarhus patients (n=76) and the Toronto patients (n=16) in terms of pain frequency, pain intensity, and pain index.

The study was conducted with approval from institutional and national ethics boards (REB Canada: 1000054678. Danish Data Protection Agency number: 1-16-02-16-16). Informed consent was obtained from all eligible patient before inclusion in the study.

Discussion

In this study, we have identified PROs of importance for the assessment of JIA-related orofacial symptoms. We have developed and validated the first interdisciplinary, consensus-based questionnaire to assess orofacial symptoms from JIA (online supplement S2). The questionnaire was developed in accordance with previously published consensus-based standards for terminology and the clinical orofacial examination in patients with JIA(9, 19). All included items in the questionnaire were rated of "high importance" in the 2017 interdisciplinary consensus-based recommendation for orofacial monitoring in JIA(9).

The patient questionnaire is intended as a standard assessment tool of orofacial symptoms for all JIA patients (≥10 years) and not only subjects with known TMJ involvement. Adjustments and future tests of reliability and validity are needed before a similar patient questionnaire can be distributed to children under 10 years of age. This work has been initiated by the TMJaw task force. The questionnaire items

are not intended as a diagnostic tool for TMJ arthritis. The presence of orofacial symptoms is a poor predictor of the presence of active TMJ arthritis (15, 16, 26). Contrast-enhanced magnetic resonance imaging (MRI) is considered the gold-standard to diagnose active TMJ arthritis(19). However, in combination with the short clinical examination protocol(18), we believe that this short patient questionnaire may serve as a feasible and standardized screening tool to inform the need for further diagnostic evaluation of orofacial conditions such as the presence of TMJ arthritis, TMJ and dentofacial deformity. Furthermore, it is a helpful tool to assess clinical status over time. Importantly, the questionnaire items are not unique to JIA-related orofacial symptoms as there is overlap with orofacial symptoms encountered in other temporomandibular dysfunction (TMD) subsets seen in 10-16% of the adolescent background population(5, 27, 28).

The items in the questionnaire can also be used as outcome measures in future interventional studies addressing management of JIA-related orofacial symptoms. They have previously been used in descriptive and interventional studies assessing JIA-related orofacial symptoms(5, 13, 14). This questionnaire does not address the psychological constructs of JIA-related orofacial symptoms. For this type of evaluation, we recommend to using specific validated questionnaires addressing (oral) health-related quality of life as a supplement to our questionnaire(29-31).

The process of identifying relevant questionnaire items has followed acknowledged standards for the development of PROMs in pediatric rheumatic diseases(32). The validation involved both English-speaking (Canadian) and Danish-speaking patients. The groups of Canadian and Danish patients were comparable in terms of age and disease duration (Table 1). TMJ intra-articular steroid injections and/or methotrexate were the most frequent management strategy in the Canadian cohort, whereas use of biologics was more frequent in the Danish cohort. Both cohorts included a proportion of patients that were off medication but still experienced orofacial symptoms secondary to sequelae of previous TMJ arthritis. In our assessment of content validity, construct validity and test of reliability, we found comparable performance of the questionnaire items in both groups indicating no presence of systemic bias or variation between the two groups. When testing the clinical performance and psychometric characteristics of the questionnaire items, we also involved both Canadian and Danish patients with JIA-related orofacial symptoms. The psychometric characteristics of the questionnaire items in the current study are in agreement with previous findings using comparable PROMs(3, 13, 14). We therefore feel confident, that the examined group in the present study represents the continuum that characterizes JIA-related orofacial symptoms.

There are some limitations that require further consideration.1). The 5-minute maximum duration was determined by healthcare providers rather than the patient end-user. 2). We acknowledge that correlations between “pain intensity” and “jaw function” and the PROMIS® pain interference questionnaire were greater than anticipated in the second construct validity hypothesis. The correlations

ranged from 0.52-0.66, whereas we had expected a lower correlation ranging from 0.25-0.50. 3) Future longitudinal studies are needed to assess the responsiveness to change of the questionnaire items. 4). It is also important to translate and cross-culturally adapt the questionnaire items to languages other than English and Danish. This process has already been initiated and future projects are planned to develop the questionnaire into multiple languages. 5). Another limitation is the decision to limit responses to patients 10 years of age and older. Additional work is needed to develop a questionnaire that can be either easily answered by younger individuals or by proxy.

Important strengths of the questionnaire are: 1) The careful multi-phased development and testing of questionnaire items in accordance with recognized standards and interdisciplinary consensus-based terminology. 2) The interdisciplinary approach involving relevant specialties and patient-input during the cognitive script interviews. 3) The brief time period required to complete the questionnaire. A majority of subjects (79.9%) were able to finish the questionnaire in ≤5 minutes. 4) The questionnaire items comply with the recent recommendation on patient-reporting in the 2022 interdisciplinary consensus-based recommendations for management of TMJ arthritis and the related orofacial manifestations of JIA (33).

In conclusion, we have developed and validated a short patient questionnaire to assess the multidimensional aspects of JIA-related orofacial symptoms. We recommend using this tool in combination with our previously published short orofacial screening protocol(18). Identification of symptoms is an important first step in the determination of appropriate management. We anticipate that this tool will be used for the clinical monitoring of individuals with JIA as well as in future studies addressing interventional outcomes.

Acknowledgement

We thank and acknowledge the work of Brian Feldman, MD, M.Sc., FRCPC and Jennifer Stinson RN-EC, PhD, CPNP for their assistance in the planning of the study. We acknowledge the work of Michel Steenks, DDS PhD, Willemijn van Bruggen, DDS PhD, and Bernd Koos DM PhD during the initial part of the project (item generation and drafting of preliminary questionnaire).

References

1. Cannizzaro E, Schroeder S, Müller LM, Kellenberger CJ, Saurenmann RK. Temporomandibular joint involvement in children with juvenile idiopathic arthritis. J Rheumatol. 2011;38:510-5.
2. Stoll ML, Sharpe T, Beukelman T, Good J, Young D, Cron RQ. Risk factors for temporomandibular joint arthritis in children with juvenile idiopathic arthritis. J Rheumatol. 2012;39:1880-7.
3. von Schuckmann L, Klotsche J, Suling A, Kahl-Nieke B, Foeldvari I. Temporomandibular joint involvement in patients with juvenile idiopathic arthritis: a retrospective chart review. Scand J Rheumatol. 2020;49:271-80.
4. Arvidsson LZ, Fjeld MG, Smith HJ, Flato B, Ogaard B, Larheim TA. Craniofacial growth disturbance is related to temporomandibular joint abnormality in patients with juvenile idiopathic arthritis, but normal facial profile was also found at the 27-year follow-up. Scand J Rheumatol.2010;39:373-9.
5. Fischer J, Skeie MS, Rosendahl K et al. Prevalence of temporomandibular disorder in children and adolescents with juvenile idiopathic arthritis - a Norwegian cross- sectional multicentre study. BMC oral health. 2020;20:282.
6. Fjeld MG, Arvidsson LZ, Smith HJ, Flatø B, Øgaard B, Larheim TA. Relationship between disease course in the temporomandibular joints and mandibular growth rotation in patients with juvenile idiopathic arthritis followed from childhood to adulthood. Pediatr Rheumatol Online J. 2010 22;8:13.
7. Stoustrup P, Glerup M, Bilgrau AE, et al. Cumulative Incidence of Orofacial Manifestations in Early Juvenile Idiopathic Arthritis: A Regional, Three-Year Cohort Study. Arthritis care res (Hoboken). 2020;72:907-16.
8. Stoustrup P, Traberg MS, Matzen LH, et al. Initial radiological signs of dentofacial deformity in juvenile idiopathic arthritis. Sci Rep. 2021;11:13142.
9. Stoustrup P, Twilt M, Spiegel L, et al. Clinical orofacial examination in juvenile idiopathic arthritis: International consensus-based recommendations for monitoring patients in clinical practice and research studies. J Rheumatol. 2017;44:326-33.
10. Twilt M, Schulten AJ, Nicolaas P, Dulger A, Suijlekom-Smit LW. Facioskeletal changes in children with juvenile idiopathic arthritis. Ann Rheum Dis. 2006;65:823-5.
11. Twilt M, Schulten AJ, Verschure F, Wisse L, Prahl-Andersen B, Suijlekom-Smit LW. Long-term followup of temporomandibular joint involvement in juvenile idiopathic arthritis. Arthritis Rheum. 2008;59:546-52.
12. Frid P, Nordal E, Bovis F, et al. Temporomandibular Joint Involvement in Association With Quality of Life, Disability, and High Disease Activity in Juvenile Idiopathic Arthritis. Arthritis Care Res. 2017;69:677-86.

13. Glerup M, Stoustrup P, Matzen LH, et al. Longterm Outcomes of Temporomandibular Joints in Juvenile Idiopathic Arthritis: 17 Years of Followup of a Nordic Juvenile Idiopathic Arthritis Cohort. J Rheumatol. 2020;47:730-8.
14. Rahimi H, Twilt M, Herlin T, et al. Orofacial symptoms and oral health-related quality of life in juvenile idiopathic arthritis: a two-year prospective observational study. Pediatr Rheumatol Online J. 2018;16:47.
15. Kristensen KD, Stoustrup P, Küseler A, Pedersen TK, Twilt M, Herlin T. Clinical predictors of temporomandibular joint arthritis in juvenile idiopathic arthritis: A systematic literature review. Semin Arthritis Rheum. 2016;45:717-32.
16. Muller L, Kellenberger CJ, Cannizzaro E, et al. Early diagnosis of temporomandibular joint involvement in juvenile idiopathic arthritis: a pilot study comparing clinical examination and ultrasound to magnetic resonance imaging. Rheumatology (Oxford). 2009;48:680-5.
17. Stoustrup P, Pedersen TK, Nørholt SE, Resnick CM, Abramowicz S. Interdisciplinary Management of Dentofacial Deformity in Juvenile Idiopathic Arthritis. Oral Maxillofac Surg Clin North Am. 2020;32:117-34.
18. Stoustrup P, Herlin T, Spiegel L, et al. Standardizing the Clinical Orofacial Examination in Juvenile Idiopathic Arthritis: An Interdisciplinary, Consensus-based, Short Screening Protocol. J Rheumatol. 2020;47:1397-404.
19. Stoustrup P, Resnick CM, Pedersen TK, et al. Standardizing Terminology and Assessment for Orofacial Conditions in Juvenile Idiopathic Arthritis: International, Multidisciplinary Consensus-based Recommendations. J Rheumatol. 2019;46:518-22.
20. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine. 2000;25:3186-91.
21. Petty RE, Southwood TR, Manners P, et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31:390-2.
22. Ayre C, Scally AJ. Critical Values for Lawshe's Content Validity Ratio: Revisiting the Original Methods of Calculation. Meas Eval Couns Dev. 2014;47:79-86.
23. Revicki DA, Chen W-H, Harnam N, et al. Development and psychometric analysis of the PROMIS pain behavior item bank. Pain. 2009;146:158-69.
24. Varni JW, Stucky BD, Thissen D, et al. PROMIS Pediatric Pain Interference Scale: an item response theory analysis of the pediatric pain item bank. J Pain. 2010;11:1109-19.
25. Varni JW, Seid M, Smith Knight T, Burwinkle T, Brown J, Szer IS. The PedsQL in pediatric rheumatology: reliability, validity, and responsiveness of the Pediatric Quality of Life Inventory Generic Core Scales and Rheumatology Module. Arthritis Rheum. 2002;46:714-25.

26. Rongo R, Alstergren P, Ammendola L, et al. Temporomandibular joint damage in juvenile idiopathic arthritis: Diagnostic validity of diagnostic criteria for temporomandibular disorders. J Oral Rehabil. 2019;46:450-9.
27. da Silva CG, Pacheco-Pereira C, Porporatti AL, et al. Prevalence of clinical signs of intra-articular temporomandibular disorders in children and adolescents: A systematic review and meta-analysis. J Am Dent Assoc. 2016;147:10-8.e8.
28. Graue AM, Jokstad A, Assmus J, Skeie MS. Prevalence among adolescents in Bergen, Western Norway, of temporomandibular disorders according to the DC/TMD criteria and examination protocol. Acta Odontol Scand. 2016;74:449-55.
29. Jokovic A, Locker D, Stephens M, Kenny D, Tompson B, Guyatt G. Validity and reliability of a questionnaire for measuring child oral-health-related quality of life. J Dent Res. 2002;81:459-63.
30. Rongo R, Ekberg E, Nilsson IM, et al. Diagnostic criteria for temporomandibular disorders (DC/TMD) in children and adolescents: an international Delphi study-Part 2-Development of Axis II. J Oral Rehabil. 2022;49:541-552.
31. Ruperto N, Ravelli A, Pistorio A, et al. Cross-cultural adaptation and psychometric evaluation of the Childhood Health Assessment Questionnaire (CHAQ) and the Child Health Questionnaire (CHQ) in 32 countries. Review of the general methodology. Clin Exp Rheumatol. 2001;19 Suppl 23:S1-9.
32. Brunner HI, Ravelli A. Developing outcome measures for paediatric rheumatic diseases. Best Pract Res Clin Rheumatol. 2009;23:609-24.
33. Stoustrup P, Resnick CM, Abramowicz S, et al. Management of orofacial manifestations of juvenile idiopathic arthritis: Interdisciplinary consensus-based recommendations. Arthritis Rheumatol. 2022. doi: 10.1002/art.42338. Online ahead of print.

Table 1: Questionnaire items. Patients are asked to report orofacial symptoms experienced within the last two weeks.

Questionnaire items	Outcome domain	Assessment of outcome
1) Pain frequency	TMJ and orofacial symptoms	Five ordinal outcomes: 0) Never, 1) Less than once a week, 2) Several times a week, 3) Several times a day, 4) All the time
2) Pain intensity	TMJ and orofacial symptoms	VAS 0-100 mm (0=no pain, 100=worst possible pain)
3) Pain location	TMJ and orofacial symptoms	Patient identification of pain locations on face map
4) Jaw function	TMJ dysfunction	VAS 0-100 mm (0=not affected, 100=severely affected)
5) Symptoms	TMJ symptoms and dysfunction	Seven questions (dichotomous outcome yes/no): 1) "I felt pain when I chewed", 2) "I avoided hard or chewy foods because it hurt my face or jaw", 3) "I felt pain when I opened my mouth wide (e.g. yawning)", 4) "I felt stiffness in my jaw muscles in the morning", 5) "I felt that my jaw got stuck in the open or closed position", 6) "I felt pain in my jaw when I talked for a long time", 7) "I felt clicking or popping from my jaw when I opened my mouth".
6) Changes in face and jaw pain	TMJ and orofacial symptoms	Four nominal outcomes: 1) no change, 2) improved (less pain), 3) worse (more pain), 4) cannot remember, Not applicable
7) Changes in jaw function	TMJ dysfunction	Four nominal outcomes: 1) no change, 2) improved (less pain), 3) worse (more pain), 4) cannot remember, Not applicable

Table 2: Cohort characteristics of participants for validity testing

Cohort characteristics	Danish group (n=28)	Canadian group (n=25)	Combined JIA group (n=53)
Gender, female	17 (61%)	23 (92%)	40 (76%)
Mean age at time of questionnaire completion years (SD, months)	13.7 Years (29 Months)	15.3 Years (30 Months)	14.5 Years (30 Months)
JIA subcategories, number			
Oligoarticular extended	10	5	15
Oligoarticular persistent	5	9	14
Polyarticular	9	9	18
Systemic	4	0	4
Psoriatic	0	1	1
Enthesitis related arthritis	0	0	0
Undifferentiated	0	1	1
JIA disease duration in years			
<1	1	4	5
1-3	4	4	8
>3	23	17	40
Current medical treatment at time of questionnaire completion			
No medication	9	6	15
NSAID	5	5	10
Methotrexate	7	16	23
Leflunomide	2	0	2
Systemic corticosteroid	1	0	1
Biologic	10	5	15
Combination of two drugs	4	5	9
Combination of three drugs or more	2	1	3
Previous intra-articular TMJ corticosteroid	0	17	17

Table 3: Construct validity testing (convergent and divergent validity). Spearman correlation coefficients

TMJaw questionnaire items	Convergent validity		Divergent validity
	Hypothesis 1: PROMIS® Pain Intensity module	Hypothesis 2: PROMIS® Pain interference module	Hypothesis 3: PedsQL™
Danish questionnaire results (n=28)			
Item 1 “Pain frequency”	0.73	0.62	-0.55
Item 2 “Pain intensity”	0.72	0.59	-0.51
Item 4 ”Jaw function”	0.53	0.51	-0.44
English questionnaire results (n=25)			
Item 1 “Pain frequency”	0.86	0.77	-0.88
Item 2 “Pain intensity”	0.81	0.75	-0.77
Item 4 ”Jaw function”	0.56	0.56	-0.67
Combined Danish and English questionnaire results (n=53)			
Item 1 “Pain frequency”	0.74	0.66	-0.70
Item 2 “Pain intensity”	0.73	0.62	-0.63
Item 4 ”Jaw function”	0.53	0.52	-0.56

Table 4: Test of reliability

Outcomes	**Danish questionnaire results, n=28 (95% CI)**	**English questionnaire results, n=25 (95% CI)**	**Combined Danish and English questionnaire results, n=53. (95% CI)**
TMJaw questionnaire items			
1) "Pain frequency" (Ordinal 5-point scale)	1.0	0.74	0.87
2) "Pain intensity" (VAS 0-100)	0.99 (0.98-1.0)	0.94 (0.87-0.97)	0.97 (0.95-0.98)
3) "Pain location" (Drawing on face map)	0.74	0.62	0.69
4) "Jaw function" (VAS 0-100)	0.97 (0.95-0.99)	0.98 (0.97-0.99)	0.98 (0.97-0.99)
5) "Jaw function" (Dichotomous outcomes; yes/no)			
- I felt pain when I chewed	0.86	0.76	0.81
- I avoided hard or chewy foods	1	0.73	0.85
- I felt pain when I opened my mouth wide (e.g., yawning)	0.92	0.84	0.88
- I felt stiffness in my jaw muscles in the morning	1	0.88	0.94
- I felt that my jaw got stuck in the open or closed position	0.84	1	0.91
- I felt pain in my jaw when I talked for a long time	0.79	0.91	0.85
- I felt clicking or popping from my jaw when I opened my mouth	1	1	1
6) "Changes in face and jaw pain" (4 nominal outcomes)	0.94	0.53	0.76
7) "Changes in jaw function" (4 nominal outcomes)	0.86	0.59	0.74

Table 5: Clinical performance of questionnaire items in subjects with juvenile idiopathic arthritis and self-reported orofacial symptoms (n=95).

Questionnaire items	Outcome
Pain frequency	
- Less than once a week	45%
- Several times a week	28%
- Several times a day	20%
- All the time	6%
Pain intensity*	
- Mean, (SD)	36 (25)
- Median (Percentiles: 10^{th}; 25^{th}; 75^{th}; 90^{th})	34 (0.6; 13;60;68)
Pain-index**	
- Mean (SD)	83 (84.4)
- Median (Percentiles: 10^{th}; 25^{th}; 75^{th}; 90^{th})	46 (6;16;135;210)
Pain location, region	
- TMJ	45%
- Masseter muscle	52.1%
- Temporalis muscle	7%
- other	18%
Jaw function*	
- Mean, (SD)	29 (28)
- Median (Percentiles: 10^{th}; 25^{th}; 75^{th}; 90^{th})	23 (0;0;55;71)
Symptoms	
- Pain when chewing	50%
- Avoidance of chewy food	41%
- Pain with mouth opening	63%
- Morning stiffness of TMJ or masticatory muscles	36%
- Locking of the jaw during function	32%
- Jaw pain when talking	28%
- Joint sounds (clicking/popping)	63%

*Visual analogue scale (VAS) from 0-100 mm **Pain-index (range 0-400) was calculated multiplying "pain frequency" (range 0-4) with the "pain intensity" VAS score (0-100 mm)

Table 6. Psychometric characteristics of the questionnaire items in subjects with juvenile idiopathic arthritis and self-reported orofacial symptoms (n=95)

Item	Psychometric characteristics
Response patterns,	
- Pain frequency (Item 1)	Positively skewed
- Pain intensity (Item 2)	Positively skewed
- Pain index (Intensity x frequency), (0-400)	Positively skewed
- Jaw functioning (Item 4)	Positively skewed
Floor effect (%),	
- Pain frequency (Item 1, score = 1, %)	43 (41/95)
- Pain intensity (Item 2; VAS score ≤ 10mm, %)*	21 (20/95)
- Pain index (Composite score ≤ 40, range 0-400, %)**	47 (45/95)
- Jaw function (Item 4) (VAS score ≤ 10mm, %)*	34 (32/95)
Ceiling effect (%),	
- Pain frequency (Item 1, score = 4, %)	6 (6/95)
- Pain intensity (Item 2; VAS score ≥ 90mm, range 0-100 mm, %)*	1 (1/95)
- Pain index (Composite score ≥ 360, range 0-400, %)**	0 (0/95)
- Physical functioning (Item 4) (VAS score ≥ 90mm, %)*	2 (2/95)
Inter-item correlation coefficient (ICC)	
- Pain intensity vs. jaw functioning	0.58
- Pain index vs. jaw function	0.65
Symptoms – jaw functions (Items 5)	
- Number of items reported by ≥ 50%	2/7
- Number of items reported by 30-49%	4/7
- Number of items reported by ≤ 30%	1/7
Time to complete questionnaire (%),	
- 1-2 minutes, (%)	21.6
- 3-5 minutes, (%)	58.3
- 6-9 minutes, (%)	16.7
- ≥ 10 minutes, (%)	3.3

*Visual analogue scale (VAS) from 0-100 mm **Pain-index (range 0-400) was calculated multiplying "pain frequency" (range 0-4) with the "pain intensity" VAS score (0-100 mm)