Oral health in children and adolescents with juvenile idiopathic arthritis

Caries, plaque, gingival bleeding, and oral health-related quality of life

Elisabeth Grut Gil

Thesis for the degree of Philosophiae Doctor (PhD)
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SCIENTIFIC ENVIRONMENT

In the course of the double competence program at the Department of Clinical Dentistry (IKO), University of Bergen (UIB), specializing in the discipline of orthodontics, this thesis was conducted during 2014-2022. Initially, the main supervisor was Professor Marit Slåttelid Skeie (IKO, UIB), and upon emeritus interchanged with Professor Keijo Luukko (IKO, UIB). Co-supervisors are Professor emeritus Marit Slåttelid Skeie (IKO, UIB and Center for Oral Health Services and Research Trondheim (TkMidt)), Professor Anne Nordrehaug Åstrøm (IKO, UIB), and Professor Karen Rosendahl ((Department of Radiology, University Hospital of North Norway (UNN) and Public Dental Health Competence Centre of Northern Norway Tromsø (TkNN)). The work of this thesis is part of the multicenter NorJIA study (The Norwegian JIA Study – Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis). The principal investigator (PI) is Professor Karen Rosendahl. NorJIA is a collaboration among universities (UIB, Norwegian University of Science and Technology, The Arctic University of Norway), university hospitals (Haukeland University Hospital, St. Olav's Hospital, UNN), and oral health centers (Oral Health Centre of Expertise in Western Norway-Vestland, TkMidt, TkNN) in Bergen, Trondheim, and Tromsø. The involved universities, university hospitals, oral health centers, and Norsk revmatikerforbund supported the current study in the data collection. The author's PhD program was financed by UIB (Faculty of Medicine) and the double competence program.

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ABBREVIATIONS

ACR	American College of Rheumatology
ANA	Antinuclear antibodies
Anti-CCP	Anti-cyclic citrullinated peptide
bDMARDs	Biologic disease-modifying antirheumatic drugs
BURG	Barne- og Ungdoms revmatiker gruppe
BW	Bitewing radiograph
BOP	Bleeding on probing
CHAQ	Childhood Health Assessment Questionnaire
Child-OIDP	Child Oral Impacts on Daily Performances
CI	Confidence interval
CI-S	Simplified Calculus Index
CRP	C-reactive protein
DI-S	Simplified Debris Index
dmf/DMF	Decayed, missing and filled
dmft/DMFT	Decayed, missing and filled teeth
ECOHIS	Early Childhood Oral Health Impact Scale
ESR	Erythrocyte sedimentation rate
FDI	World Dental Federation
GBI	Gingival Bleeding Index
HRQoL	Health-related quality of life
HLA	Human leukocyte antigen
ICC	Intra-class correlation coefficient
IKO	Department of Clinical Dentistry
ILAR	International League of Associations for Rheumatology
IRR	Incidence rate ratios
JIA	Juvenile Idiopathic Arthritis
MDgloVAS	Physician's global assessment of disease activity visual analogue scale
MTX	Methotrexate

NorJIA	The Norwegian JIA Study (Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis)
NSAIDs	Nonsteroidal anti-inflammatory drugs
OHI-S	Simplified Oral Hygiene Index
OHRQoL	Oral health-related quality of life
OR	Odds ratio
PDS	Public Dental Service
PI	Principal investigator
PRgloVAS	Patient/parent-reported global assessment of overall wellbeing visual analogue scale
QoL	Quality of life
REML	Restricted maximum likelihood
RF	Rheumatoid factor
RIM	Random intercept logistic model
RVE	Robust variance estimate
SC	Simple count
SE	Standard error
SES	Socioeconomic status
SD	Standard deviation
sDMARDs	Synthetic disease-modifying antirheumatic drugs
TMD	Temporomandibular disorder
TMJ	Temporomandibular joint
VAS	Visual analogue scale
VAS pain	Patient/parent-reported pain intensity visual analogue scale
WHO	World Health Organization

SUMMARY

Oral health in Norwegian children and adolescents with juvenile idiopathic arthritis (JIA) is undetermined. International studies report inconsistent findings, and high-quality research is called for. JIA encompasses a heterogeneous group of disease categories, and the distinct characteristics must be accounted for when evaluating this group of patients.

The main objective of this multicenter cross-sectional study was to explore whether the outcome variables caries, plaque, gingival bleeding, and oral health-related quality of life (OHRQoL) differ between young individuals with JIA compared to controls without JIA. Additionally, explore whether socio-behavioral and intraoral characteristics affect the outcomes and whether these covariates vary according to group affiliation on impacted OHRQoL. Multilevel modeling facilitated caries and periodontal exploration at surface-level and cluster effect measures. Association between JIA-specific features and the outcomes was evaluated. We hypothesized that young individuals with JIA have poorer oral health than their peers.

Participants, 4-16-year-olds with JIA (n=224) and their matched controls (n=224), were assessed, according to index-teeth and internationally acknowledged indices, during 2015-2018 by calibrated dentists. Pediatric rheumatologists evaluated JIA-specific characteristics, and socio-demographic, behavioral, and self-reported oral health information was collected through questionnaires and personal interviews. Adjusted mixed effects logistic regression showed a significant association between JIA status and plaque, and gingival bleeding, but not for caries. JIA status was significantly associated with impacted OHRQoL by application of negative binomial regression amongst the youngest (4-11 years) but not amongst the participants from 12 years; ordinary logistic regression did not show any significant associations in any age groups. Low maternal educational level was significantly associated with caries. Female adolescents (12-16 years) with JIA were more likely to report OHRQoL impacts. Surface-specific caries and plaque in the permanent dentition varied among the two groups. A trend of increased caries susceptibility on approximal surfaces (*i.e.*,

mesial) of permanent molars was apparent in the JIA group. Cluster effects warranted the application of multilevel modeling. Some JIA-specific features, often consistent with a more severe disease course, are suggested to increase susceptibility to impaired oral health.

In conclusion, the hypothesis of poorer oral health in young individuals with JIA compared to peers was confirmed for the periodontal outcomes but not for caries and OHRQoL measured by generic instruments. The potential of preventive strategies among young individuals with JIA is considerable; increased focus beyond the dental disciplines is needed to achieve the best possible outcomes.

SAMMENDRAG

Munnhelsen blant norske barn og unge med juvenil idiopatisk artritt (JIA) er ukjent. Internasjonale studier som fokuserer på munnhelsen hos denne pasientgruppen, viser motstridende resultater, samtidig som kvaliteten på forskningen som er utført spriker. JIA omfatter ulike sykdomskategorier med distinkte egenskaper, noe som medfører at forebyggende tiltak rettet mot denne pasientgruppen er avhengig av mer kunnskap.

Det overordnede målet med avhandlingen var å undersøke mulige forskjeller når det gjelder karies, plakk, gingival blødning og munnhelserelatert livskvalitet mellom unge individer med JIA og en kontrollgruppe uten JIA. I tillegg var delmål å vurdere om sosiale-, adferdsmessige - og munnhulefaktorer påvirket de observerte forskjellene i tannhelse, vurdere effekten av klynge data og evaluere variasjonen i karies og periodontale tilstander på flate-nivå. Et ytterligere delmål var å måle variasjoner i tannhelse etter JIA spesifikke karakteristika. Hypotesen var at unge individer med JIA har dårligere munnhelse og opplever dårligere munnhelserelatert livskvalitet enn jevnaldrende uten JIA.

Deltakerne, 4-16 år gamle med JIA (n=224) og matchete kontroller (n=224), fikk indekstenner undersøkt mellom 2015-2018 av kalibrerte tannleger ved hjelp av anerkjente måleinstrumenter. JIA-spesifikke karakteristika ble vurdert av barnerevmatologer, og sosiodemografiske, adferdsmessige og selv-rapporterte munnhelseopplysninger ble innsamlet ved hjelp av spørreskjema og intervju.

Flernivå analyser viste signifikant sammenheng mellom JIA status og plakk, og gingival blødning, men ikke for karies. Forskjeller mellom JIA- og kontrollgruppen med hensyn til munnhelserelatert livskvalitet var avhengig av type analyse og gav ikke entydige resultater. Lav utdanning blant mødre økte signifikant risikoen for karies. Jenter 12-16 år gamle med JIA hadde økt sannsynlighet for å rapportere om påvirket livskvalitet. Signifikant interaksjon mellom karies og plakk på flate-nivå og gruppetilhørighet ble påvist i det permanente tannsettet. Økt sannsynlighet for approksimal-karies (*i.e.*, mesial) var merkbar blant JIA gruppen i det permanente tannsettet. Klynge-effektene demonstrerte behovet for flernivå analyser. Visse JIA

spesifikke karakteristika, ofte forenelig med et mer alvorlig sykdomsforløp, indikerte økt risiko for påvirket munnhelse.

Det kan konkluderes med at hypotesen om dårligere munnhelse blant unge med JIA sammenlignet med jevnaldrende, bekreftes for de periodontale tilstandene, men ikke for karies og munnhelserelatert livskvalitet målt ved generiske instrumenter. Forebyggende tiltak har stort potensiale blant barn og unge med JIA; økt fokus er nødvendig på flere plan, også blant de som ikke er tannhelsepersonell, for å oppnå best mulig helse blant unge individer med JIA.

LIST OF PUBLICATIONS

This thesis is based on the following papers:

Paper I

Gil EG, Åstrøm AN, Lie SA, Rygg M, Fischer J, Rosén A, Bletsa A, Luukko K, Shi XQ, Halbig J, Frid P, Cetrelli L, Tylleskär K, Rosendahl K, Skeie MS.

Dental caries in children and adolescents with juvenile idiopathic arthritis and controls: a multilevel analysis.

BMC Oral Health. 2021 Aug 25;21(1):417.

Paper II

Gil EG, Åstrøm AN, Lie SA, Rygg M, Fischer J, Rosén A, Bletsa A, Luukko K, Shi XQ, Halbig J, Frid P, Cetrelli L, Tylleskär K, Rosendahl K, Skeie MS.

Dental plaque and gingival bleeding in adolescents with juvenile idiopathic arthritis and controls: a multilevel analysis.

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Paper III

Gil EG, Skeie MS, Halbig J, Jönsson B, Lie SA, Rygg M, Fischer J, Rosén A, Bletsa A, Luukko K, Shi XQ, Frid P, Cetrelli L, Tylleskär K, Rosendahl K, Åstrøm AN.

Oral health-related quality of life in 4-16-year-olds with and without juvenile idiopathic arthritis.

BMC Oral Health. 2022 Sep 6;22(1):387.

1. INTRODUCTION

1.1 Juvenile Idiopathic Arthritis (JIA)

1.1.1 General definition of JIA

"JIA is arthritis of unknown etiology that begins before the 16th birthday and persists for at least 6 weeks; other known conditions are excluded" (1). The mutually exclusive JIA categories according to the International League of Associations for Rheumatology (ILAR) are presented in Table 1.

1.1.2 Incidence and prevalence of JIA

Published incidence and prevalence estimates differ considerably worldwide, likely reflecting ethnicity, immunogenic susceptibility, environmental impacts, or underreporting in the developing world (2). The actual frequency is unknown; however, JIA is not rare. A systematic review of the prevalence and incidence of JIA by Thierry et al. (3) estimated pooled incidence and prevalence rates in Caucasians to be 8.3/100.000 and 32.6/100.000, respectively. The highest incidence rate (22.6/100.000) included in the review by Thierry et al. was from a Norwegian study by Moe et al. (4) in 1998. A possible north-south gradient in the incidence of juvenile arthritis in Europe has been suggested (5). According to the ILAR criteria, Nordic countries' overall incidence rate was 15/100.000 from 1997-2000 (6). The frequency proportion, age at onset, and sex ratio characterizing each category are presented in Table 1.

1.1.3 Etiology and pathogenesis of JIA

The cause of JIA is not known, but a multifactorial etiology is strongly indicated and probably varies according to the JIA category (2). The pathogenesis is not entirely understood, but the elemental pathological process in JIA is chronic inflammation controlled by the innate and adaptive immune system; products of activated T cells and macrophages compose the pathogenesis of synovitis (2). The suggested multifactorial influences contributing to the pathogenesis are immunopathogenic mechanisms, infection and immunizations, physical trauma, hormonal-,

psychological-, nutritional- and other environmental factors, and possible genetic susceptibility (2, 7, 8).

1.1.4 Manifestations of JIA

The signs and symptoms of JIA are diverse and can change throughout the course due to therapeutic effects and the progress of the underlying condition (9). Fatigue, anorexia, and weight loss may be seen in individuals with active JIA (2). An active joint inflammation manifests the cardinal signs of inflammation, including swelling, pain, heat, loss of function, and, more uncommonly, erythema; the distribution of affected joints is, to some extent, predictable according to the JIA category (2). Pain and joint stiffness may be apparent in active JIA, as well as with chronic JIA. Destructive changes in bone and cartilage may eventually occur in the pathogenesis of the joint. Typical features of the articular and periarticular inflammation of JIA in early and late disease are in order of advancement as follows: periarticular soft tissue change (synovitis, tendinitis, bursitis), periarticular bony change (bone edema, periostitis, growth disturbances, osteoporosis) and destructive change of bone and cartilage (erosive change of bone, joint space narrowing, bone fusion, malalignment) (10). The order may vary, and some features may be lacking or overlapping. Especially initial stages of JIA require sensitive diagnostic imaging techniques to detect inflammation early and prevent permanent sequelae. Another frequent complication of an inflamed joint is atrophy and weakness of muscles (2). Extraarticular manifestations typically involve ocular disease, most commonly uveitis, and generalized abnormalities of growth (2, 8).

Table 1. Classification of JIA according to the ILAR (1)

JIA categories	Freq.* (7)	Age at onset (7)	Presentation	♀♂ (7)	Excl. criteria **
Systemic Arthirits	4–17%	Through childhood	Arthritis and quotidian fever for at least 2 weeks plus one or more of the following: 1. Characteristic rash 2. Generalized lymphadenopathy 3. Enlargement of liver or spleen 4. Serositis	F=M	a, b, c, d
Oligoarthritis	27–56%	Early childhood, peak at 2-4 yrs.	Arthritis affecting one to 4 joints during the first 6 months of disease. Further characterized as: -Persistent: Affecting not more than 4 joints throughout the disease course -Extended: Affecting a total of more than 4 joints after the first 6 months of disease	F>>>M	a, b, c, d, e
Polyarthritis RF negative	11–28%	-Early peak: 2-4 yrs. -Late peak: 6-12 yrs.	Arthritis affecting 5 or more joints during the first 6 months of disease; a test for RF is negative.	F>>M	a, b, c, d, e
Polyarthritis RF positive	2–7%	Late childhood-adolescent	Arthritis affecting 5 or more joints during the first 6 months of disease; 2 or more tests for RF at least 3 months apart during the first 6 months of disease are positive.	F>>M	a, b, c, e
Psoriatic Arthritis	2–11%	-Early peak: 2-4 yrs. -Late peak: 9-11 yrs.	Arthritis and psoriasis, or arthritis and at least 2 of the following: 1. Dactylitis 2. Nail pitting or onycholysis 3. Psoriasis in a first-degree relative	F > M	b, c, d, e
Enthesitis Related Arthritis	3–11%	Late childhood-adolescent	Arthritis and enthesitis, or arthritis or enthesitis with at least 2 of the following: 1. The presence of or a history of sacroiliac joint tenderness and/or inflammatory lumbosacral pain 2. The presence of HLA-B27 antigen 3. Onset of arthritis in a male over 6 years of age 4. Acute anterior uveitis 5. History of ankylosing spondylitis, enthesitis related arthritis, sacroiliitis with inflammatory bowel disease, Reiter's syndrome, or acute anterior uveitis in a first-degree relative	M>>F	a, d, e
Un-differentiated Arthritis	11–21%		Arthritis that fulfills criteria in no category or in 2 or more of the above categories		

*Reported frequencies according to percentage of all JIA. Exclusions for each category: a. Psoriasis or a history of psoriasis in the patient or first-degree relative, b. Arthritis in an HLA-B27 positive male beginning after the sixth birthday, c. Ankylosing spondylitis, enthesitis-related arthritis, sacroiliitis with inflammatory bowel disease, Reiter's syndrome, or acute anterior uveitis, or a history of one of these disorders in a first-degree relative, d. Presence of IgM RF on at least two occasions at least three months apart, e. The presence of systemic JIA in the patient. Freq. = Frequency. Excl. = Exclusion. RF = Rheumatoid factor. HLA-B27=Human leukocyte antigen B27.

1.1.5 Management of JIA

JIA can not be cured, but disease control is more often accomplishable, particularly with the advanced modern therapeutic approaches (11-13). Objectives of disease treatment are remission, keeping comorbidities and adverse effects of drugs to a minimum, and achieving the best possible function, growth and development, quality of life (QoL), and social involvement (14). The advocated multidisciplinary care consists of a pediatric rheumatologist, nurse specialist, physical and occupational therapists, a social worker, and a psychologist working as a team with the child's or adolescent's primary care physician, moreover, in dialog with an orthopedic surgeon, ophthalmologist, nutritionist and dentist when needed (2). Pediatric radiologists' role in diagnosing and follow-up of JIA patients is also essential.

Pharmacological management

The principle of antirheumatic drugs is to suppress the inflammatory and immune response. Traditionally nonsteroidal anti-inflammatory drugs (NSAIDs) have been the first line agent (8). Local corticosteroid joint injections are effective in synovitis and may sometimes be part of first-line treatment (8). Systemic high-dose corticosteroid administration gives potent short-term effects, but long-term effects do not improve disease outcomes; in contrast, long-term use is associated with adverse effects such as growth suppression, osteoporosis, Cushing syndrome, and infection (2, 8). Synthetic disease-modifying antirheumatic drugs (sDMARDs), are indicated to be safe and effective, also when initiated early (2, 15). Methotrexate (MTX) is the most prescribed sDMARD for over 30 years (15, 16). In addition to being the second-line agent, MTX is sometimes also a first-line agent (2, 15). According to The National Health Service Commissioning Board England, MTX, on average, only induces total remission in 30-50% of patients; if activity persists, treatment with advanced biologic DMARDs (bDMARDs) is initiated (16).

sDMARDs target the immune system by interfering with essential pathways in the inflammatory cascade, whereas bDMARDs are very selective, targeting specific steps in the process (17). The first bDMARD approved for treatment in JIA was the anti-tumor necrosis factor-α agent: etanercept in 1999 (8, 11). Enhanced knowledge of the

immunological mechanisms of JIA pathogenesis facilitated the development of bDMARDs and has markedly improved disease outcomes over the past two decades (11).

1.1.6 Disease course and outcome of JIA

Appropriate early therapy is crucial for the disease course and outcome. Despite state-of-the-art approaches, the disease burden is still high. In the population-based Nordic JIA cohort, disease status 18 years after onset was evaluated, including participants diagnosed from 1997 to 2000 with a mean age of 24 years at follow-up ((standard deviations (SD) 1.7)) (18). According to the American College of Rheumatology (ACR) provisional criteria 2011 (19) they found 46% of the participants were in active disease (on the mild end of the scale), 10% were in remission on medication, 33% were in remission off medication, and 12% were in inactive disease not in remission (total n=329) (18). A Canadian longitudinal study also evaluated the disease status according to ACR provisional criteria (19). However, with a shorter follow-up period than the Nordic JIA cohort (median years: 5.6) and the population (n=247) was generally younger at follow-up (median age: 16.9); moreover, the participants were diagnosed in the biological era (2005-2010) (20). The Canadian study found that 27% of the participants were in active disease, 25% were in remission on medication, 47% were in remission off medication, and 1% were in inactive disease not in remission (20). These findings highlight the present long-term challenges of JIA in childhood and adulthood. With treatment, disease outcome varies to some extent according to the JIA category (2, 9, 21). In particular, oligoarthritis has been repeatedly associated with the highest attainment of clinically inactive disease and remission, with the lowest attainment in polyarthritis rheumatoid factor (RF)-positive (21-23). Other predictors (*e.g.*, gender and age at disease) are less evident (21-23). Despite objective indicators of low disease activity, poor scores according to patient-reported well-being and health-related quality of life (HRQoL) may be present, emphasizing the need for better comprehension of sociological mechanisms to capture the total impact of JIA and its treatment;

furthermore, such knowledge may facilitate better management and prediction of the outcome (9, 21, 24).

1.2 Oral health in children and adolescents with JIA

1.2.1 Definition of oral health

Reflecting the biopsychosocial view of health set forth by the World Health Organization (WHO) (25), the World Dental Federation's (FDI) definition of oral health is: "Oral health is multi-faceted and includes the ability to speak, smile, smell, taste, touch, chew, swallow and convey a range of emotions through facial expressions with confidence and without pain, discomfort and disease of the craniofacial complex" (26). The definition emphasizes oral health as an essential component of overall health and well-being and encompasses personal values, perceptions, and expectations. The complex interplay between determinants, the core elements of oral health, and the overall health and well-being are addressed by FDI (Figure 1) (27).

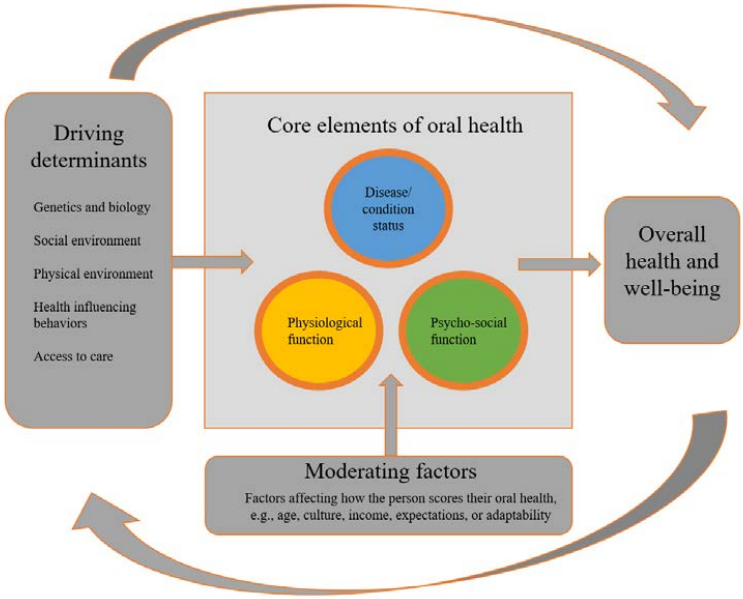

Figure 1. The framework for the World Dental Federation's oral health definition.
A PowerPoint presentation of the framework, available at https://www.fdiworlddental.org/fdis-definition-oral-health, forms the basis of the presented figure.

In this thesis, the term 'oral health' is used in conformity with FDI's definition and encompasses oral condition/disease and oral health-related quality of life (OHRQoL); the latter accords to the FDI's physiological- and psycho-social function elements.

1.2.2 Commonly experienced oral diseases and OHRQoL in children and adolescents

Dental caries

Dental caries is a biofilm- and diet-mediated, multifactorial, dynamic disease resulting in mineral loss of hard dental tissues due to disruption of the ecological balance between tooth minerals and oral microbial biofilms (28, 29).

White spots or initial caries can be detected clinically when sufficient mineral is lost. The process can be arrested or progress to more extensive destruction at this stage. Even initial physical cavities can be stopped depending on preventive actions, although the microbe retaining cavity will persist (28). A lesion in progress will eventually, without operative intervention, compromise the dental pulp. In the initial stages, caries is often asymptomatic. Toothache, on the other hand, is debilitating and can lead to loss of teeth. Infection and sepsis, a sequel to pulp involvement, can lead to severe systemic outcomes (28, 30). In any case, caries is associated with impaired OHRQoL in children, adolescents, and their families (31, 32).

Caries is a very common chronic disease; a meta-analysis of caries in primary and permanent dentition of children and adolescents worldwide between 1995-2019 revealed a prevalence of 46.2% and 53.8%, respectively (33). Corresponding results separately for Europe were 21.4% and 44.1%.

Gingivitis

Plaque-induced gingivitis is an inflammatory response of the gingival tissues due to the accumulation of dental plaque biofilm (34-36). It develops because of a disruption of the symbiosis between the microbial biofilm and the host immune-inflammatory response, and both local and systemic factors can affect the disease (34, 35). Gingivitis is generally painless, and unawareness of the condition is common, but symptoms such as bleeding, soreness, halitosis, swollen red gums, and reduced

OHRQoL can be reported (35, 36). Limited research has evaluated the impact of gingivitis on OHRQoL (36). In some of these studies, a high prevalence of gingivitis is proposed in adolescents; however, the effect on OHRQoL appears restricted, but the extent (bleeding on probing score) increases the impacts (36-39).

Considering gingival inflammation as a precursor for periodontitis (34) and the attribute of gingival inflammation to bacteremia following toothbrushing (40), preventive action is essential. Interpreting epidemiological prevalence data on clinical indicators of gingival inflammation is problematic due to variations in diagnostic criteria defining a gingivitis case (36).

1.2.3 Oral health-related quality of life

WHO defined QoL in 1995: "Individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (41). Four main considerations influence HRQoL: functional factors, psychological factors (appearance and self-esteem), social factors (*e.g.*, interaction with others), and experience of pain/discomfort; when orofacial aspects are subject to these considerations, OHRQoL is focused (42). Consequently, OHRQoL conveys the role of oral conditions or diseases on QoL by evaluating oral symptoms and functional and socio-emotional well-being. To capture the subjectivity and the multidimensions of oral health defined by FDI, OHRQoL needs to be evaluated. The importance of implementing OHRQoL in research is emphasized (43).

Various measurement tools exist. Generic OHRQoL instruments assess physical- and psycho-social consequences of diverse oral diseases and problems. In contrast, condition-specific OHRQoL tools capture subtle variance in distinct oral conditions (44). Continuous dentofacial and cognitive development challenges OHRQoL evaluation in young individuals (45). Consequently, age-dependent measures have been developed for self- or proxy-reporting children's and adolescents' OHRQoL (44). Among the indices providing self-reports, the most commonly employed indices are the Child Perceptions Questionnaire (CPQ) (46), the child version of Oral Impacts

on Daily Performances (Child-OIDP) (47), and the Child Oral Health Impact Profile (COHIP) (48); and for proxy-reporting, the Early Childhood Oral Health Impact Scale (ECOHIS) (49, 50). ECOHIS and Child-OIDP have been validated in a general local population of Norwegian children and adolescents (51). The Child-OIDP can be assessed in relation to both general and specific oral conditions (47).

1.2.4 The multilevel influences and determinants of children's and adolescents' oral health

The determinants and their complex interplay in the framework of the FDI's definition of oral health are well-grounded in widespread population health research (52-59). This research has also facilitated the development of the conceptual model by Fisher-Owens et al. (56), specifically targeting multilevel influences on young individual's oral health (individual, family, and community levels), in addition to the five essential domains of determinants of health (genetic and biological factors, the social environment, the physical environment, health influencing behaviors and access to care). Such conceptual frameworks are needed to fully understand children's and adolescents' oral health and prepare optimal research and public health intervention (56, 60-62).

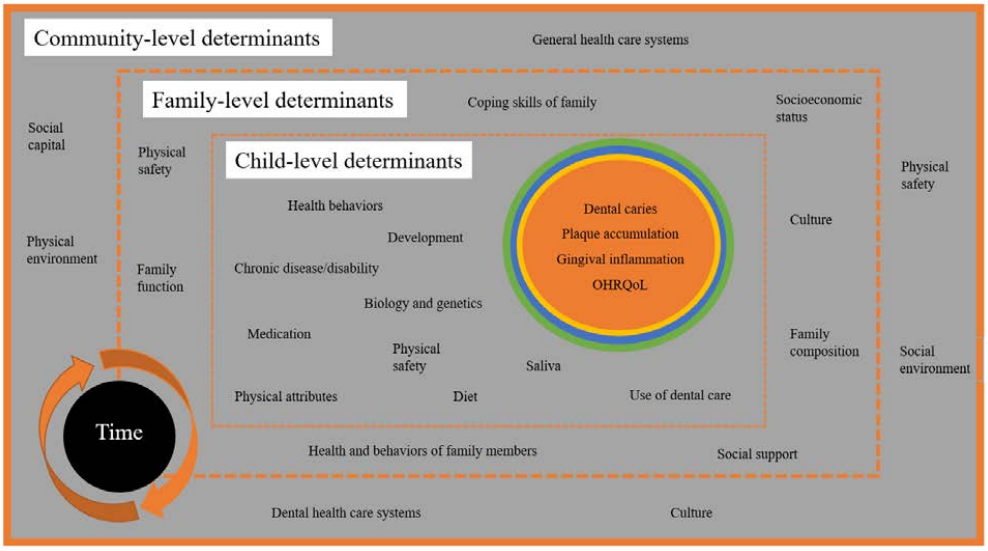

Figure 2. Illustration of the multilevel influences on a child's oral health. A figure in the article by Fisher-Owens et al. 2007 forms the basis of the presented figure (56).

Individuals with JIA constitute a particularly vulnerable group from an oral health perspective. In the following sections, I intend to describe influences on oral health in young individuals with JIA based on the model by Fisher-Owens et al. (56), which incorporates the key domains also included in the FDI's definition (Figure 2).

1.2.5 Community- and family-level determinants of oral health in young individuals with JIA

Community-level

At the community level, determinants are related to the quality of the neighborhood and community. Examples are the stability, safety, and cohesion of the neighborhood (social environment); and the local area's socioeconomic position (social capital) (56). Research has demonstrated community poverty in the United States as a predictor for delayed time to rheumatology care in newly diagnosed JIA after adjusting for social determinants such as insurance status and parental educational level (63). Norway is a wealthy nation with well-integrated public health services promoting general and oral health; at the community level, quality care is likely provided to JIA patients. However, specialties, the number of practitioners, and the collaboration between medical and dental care may vary locally (*e.g.*, geographically within Norway) and likely pose a difference in health care quality.

Family-level

At the family level, determinants are related to family composition, culture, and the health and behaviors of family members. Other determinants are the family's coping skills, family function, socioeconomic status (SES), and social support, which also have been demonstrated to impact the disease outcome of JIA (64, 65). Family-level determinants in oral health research on young individuals with JIA have gained insufficient attention. Considering caries, gingival health, and OHRQoL, only two studies in the last two decades have included such characteristics (66, 67). Both studies compared SES (education and income) between participants with JIA and controls, and parents reported higher income and educational level in the control group in the survey by Grevich et al.(66). In contrast, in the study by Santos et al. (67), the JIA group's parents had the highest education levels. Only Grevich et al.

(66) adjusted for SES characteristics when the dental indices were compared. The knowledge gap of family-level oral health determinants in children and adolescents with JIA is evident.

1.2.6 Individual-level determinants of oral health in young individuals with JIA

Biology and genetics

Temporomandibular joint (TMJ) involvement has been reported to occur in up to 87% of young individuals with JIA; the frequency reported in the literature varies according to the population studied and diagnostic measures applied (68, 69). TMJ arthritis may lead to significant craniofacial and dentoalveolar abnormalities, and deviations may cause temporomandibular disorder (TMD) (68, 70). TMJ involvement is indicated to impair HRQoL (71) and OHRQoL (72) in children and adolescents with JIA; TMJ pain influences daily life (73), and orofacial pain impairs their OHRQoL (74).

Susceptibility to periodontal disease in adolescents with JIA due to dysregulation of the immunoinflammatory response has been suggested in detail by Miranda et al. (75-77). *Porphyromonas gingivalis*, a pathogen associated with severe and aggressive forms of periodontitis, and antibody responses to the species, have been more frequently reported in supragingival plaque and blood serum in some subgroups of JIA (76, 78, 79). A higher abundance of oral salivary microbiota associated with chronic inflammation has been demonstrated (80). Some researchers speculate that the pathogenesis of JIA and gingivitis is contributed by the microbiota (66). The likelihood of periodontal disease (*i.e.*, probing depth >3.5 mm, indicating clinical attachment loss) is found to be increased in young patients with JIA expressing a specific human leucocyte antigen (HLA), and the authors propose a particular HLA supertype to be a common risk indicator for JIA and periodontitis in females (81). Periodontitis in JIA patients has been demonstrated to influence OHRQoL negatively (82). Whether other dental diseases, such as caries, impact OHRQoL specifically in children and adolescents with JIA has not been investigated.

Reduced bone mineral density in young individuals with JIA is documented in the literature and is multifactorial (*e.g.*, nutrition, medication, and a complication of the JIA disease) (83). Reduced alveolar bone density in adolescents with JIA has been indicated by intraoral radiographs (84). The authors discuss a possible association between osteoporosis and periodontal disease. However, the authors did not find any correlation between bone density and clinical indicators of periodontal disease but speculate rheumatological drugs improve clinical periodontal parameters and maybe camouflage a link between reduced bone density and periodontal inflammation (84).

Salivary abnormalities

Involvement of the salivary glands as a manifestation of JIA has been suggested (85, 86), and studies report altered salivary composition, increased peroxidase activity in saliva, and reduced salivary flow rate (85-89). Saliva is crucial in maintaining optimal oral health and salivary alterations may impair oral health (90).

Oral hygiene practices

TMD may contribute to increased plaque accumulation due to limited oral hygiene performance because of pain, restricted mouth opening, and altered masticatory function (88, 91). Functional disability due to the involvement of upper limbs may also sometimes complicate oral hygiene procedures (92). Hence, JIA patients may be prone to plaque-induced gingivitis and to caries. However, these risk factors are less apparent in modern times of enhanced strategies in JIA management improving disease course.

Diet

Poor oral hygiene combined with a disadvantageous diet: soft with free sugars of frequent intake, and candy offered by parents as consolation reported in young individuals with disabilities (93), as well as sugar-containing oral medication present risks for caries in individuals with JIA (94).

Medication

Sugar-containing medicines in JIA management have been an emphasized risk factor for caries (95). The development of sugar alternatives in pediatric drugs has probably

reduced this risk. However, the erosive and cariogenic potential of therapeutic NSAIDs and corticosteroid liquid preparations are still present (96). Antirheumatic drugs, such as various sDMARDs, particularly the commonly administered MTX, may cause side effects such as nausea, vomiting, and stomatitis (97, 98). In a recent study focusing on salivary gland involvement in children and adolescents with JIA, 14.3% of JIA patients reported occasionally vomiting due to MTX intake (85). These side effects may cause erosive wear and may negatively impact mood and, consequently, oral health behaviors associated with oral hygiene and dietary habits. Some authors focusing on periodontal health in JIA discuss the NSAID's property to decrease signs of gingival inflammation. In contrast, Grevich et al. (66) communicate NSAIDs predispose to bleeding by changing platelet function and possibly contributing to bleeding on probing (BOP). In a two-year follow-up study, periodontal conditions improved in adolescents with JIA; the authors interpret this as an effect of participants' antirheumatic drug use (77). Other authors have also indicated a reduction of periodontal inflammation in young individuals with JIA to be a sequela of pharmacologic therapy (84, 99). The effect of the drugs used in the treatment strategy of JIA on oral health is not clearly understood.

General health and well-being

A systematic qualitative review from 2022 concludes that young patients with JIA struggle with various issues, including psychological health, physical well-being, and QoL (100). To an unknown extent, these matters impact oral health in patients with JIA, considering the interplay between oral health, general health, and well-being.

1.2.7 Prevalence of oral diseases in children and adolescents with JIA

Oral manifestations of JIA are complex and encompass various symptoms. Some are well recognized (*i.e.*, TMD and malocclusion subsequent to TMJ involvement) compared to other conditions with apparent knowledge gaps and research demonstrating the absence of consensus. Findings in the literature diverge, especially concerning the prevalence of caries, plaque accumulation, and periodontal diseases. Our research group published a systematic review and meta-analysis on oral health among children and adolescents with JIA covering studies published from January

1998 to November 2018 (101). Salivary status and malocclusion were not considered in the review. The meta-analysis of dental caries found no difference in the mean of dmft/DMFT (decayed, missing and filled teeth) indices between individuals with JIA and controls without JIA. Concerning TMD and periodontal conditions, which could not fit for meta-analyses, these conditions were found to predominate in individuals with JIA. No studies focused on erosive wear and only one on enamel defects. Otherwise, the results of the systematic review found measures of dental maturation and OHRQoL not better nor worse amongst the individuals with JIA compared to controls.

A new literature search was performed to ensure updated information to this thesis. In contrast to the previous systematic review and meta-analysis (101), this literature search also included studies without a control group and the periods before 1998 and after November 2018. Results are presented in the following section (Tables 2 and 3).

1.2.8 The current state of knowledge concerning dental caries, oral hygiene, gingival inflammation, and OHRQoL in young individuals with JIA

Table 2 and 3 display studies (1985-2022) identified from an online literature search, with relevant findings, including clinical indicators of dental caries, oral hygiene, and gingival inflammation, as well as studies assessing OHRQoL by well-defined OHRQoL instruments in children and adolescents with JIA. A description of the search strategy is shown in Appendix I.

The studies of Miranda et al. (75-77) and Kobus et al. (88, 102) are based on the same study population. Most probably, this also applies to Polizzi et al. (82) and Isola et al.(72) (identical ethical research protocol and study period). All studies were of cross-sectional design, except for Miranda et al. 2006 (77) and Rahimi et al. (74) being longitudinal studies (2-year follow-up); however, in the study by Rahimi et al. (74), OHRQOL (the oral health indicator of relevance) was only assessed at 2-year follow-up. The age of the participants varied from 2-17 years, and the JIA sample size ranged from n=14 to n=149. Fifteen studies were conducted in Europe, nine in

South America, and one in the US and Russia. Twenty-two studies included a control group (without JIA), and five were without controls.

Of the studies including a comparison group, the studies reporting significantly more caries in individuals with JIA than their peers were published before the year 2005 (92, 94, 103, 104) (Table 2). Indicators of oral hygiene and gingival inflammation in individuals with JIA, compared to controls, were evaluated in 15 studies (66, 67, 75, 76, 84, 85, 87, 88, 91, 92, 94, 99, 103, 105, 106) and 17 studies (66, 67, 75-77, 84, 88, 91, 92, 94, 99, 102-106), respectively (Table 2). Plaque and gingival inflammation were significantly increased in individuals with JIA in five (66, 87, 91, 94, 105) and six (67, 91, 92, 94, 103, 104) of these studies, respectively.

Five studies evaluated OHRQoL in individuals with JIA (67, 72, 74, 82, 107) (Table 3). Two studies categorized the JIA patients according to TMJ involvement or periodontitis and compared the likelihood of impaired OHRQoL with reference to JIA patients without TMJ involvement and controls or JIA patients without periodontitis and controls (72, 82). Poorer OHRQoL was observed amongst participants with JIA and TMJ involvement and with periodontitis. OHRQoL was evaluated in individuals with JIA without stratification and compared to controls in the remaining two studies (67, 107). Santos et al. (67) found no difference in impaired OHRQoL among the two groups. Bucci et al. (107) discovered the controls to be more concerned about dental aesthetics than participants with JIA by evaluating the Dental Self-Confidence component of the Psychosocial Impact of Dental Aesthetics Questionnaire.

Table 2. Studies (n=22), from 1985-2022, including clinical indicators of dental caries, oral hygiene, and gingival inflammation in children and adolescents with JIA, identified from an online literature search.

Study	Country	Sample size	Age (yrs.)	Findings of relevance
Storhaug & Holst 1987 (108)	Norway	128 JIA	7-16	-DMFT[a] =8.31 (unadjusted)
Siamopoulou et al. 1989 (104)	UK (British journal of rheuma-tology)	16 JIA 83 No JIA	6-14	-DMFI: JIA=6.0, No JIA=3.2 -GI: JIA=1.0, No JIA=0.6
Miranda et al. 2003 (75)	Brazil	32 JIA 24 No JIA	Adol.	-VPI>0: JIA=54%, No JIA=44% -GBI>0: JIA=30%, No JIA=29%
Welbury et al. 2003 (94)	UK	149 JIA 149 No JIA Adults included in the sample (61 pairs)	2–17	-dmft/DMFT[b] dmft 0-11 years: JIA=1.46, No JIA=0.56* -DMFT 6-11 years: JIA=0.28, No JIA=0.33 -DMFT 12-17 years: JIA=2.34, No JIA=2.16 (*considering decay separately) -0-11years: GI: JIA=2.28, No JIA=0.92* PI: JIA=3.65, No JIA=1.50* OCI: JIA=32.04, No JIA= 36.86* -12-17 years: GI: JIA=3.50, No JIA=2.03* PI: JIA=4.27, No JIA=2.20* CI: JIA=30.09, No JIA= 35.33*
Ahmed et al. 2004 (92)	UK	55 JIA 55 No JIA	4–16	-dmft[a]: JIA=2.0, No JIA=3.2 (*considering decay separately) -DMFT[a]: JIA=1.8, Ctr.=2.1 (*considering decay separately) -Modified PCR: JIA=58.1, No JIA=48.7 -Simplified GI: JIA=39.9, No JIA=23.5*
Savioli et al. 2004 (103)	Brazil	36 JIA 13 No JIA	4–20	-DMFT[a]: JIA w/2-8 affected joints superior limbs (n=18) =6.72 No JIA=3.6, polyarticular JIA RF+=6.6 (*compared to No JIA) -PI: JIA w/2-8 affected joints superior limbs (n=18) =62.7, No JIA=42.4 -GBI: JIA w/2-8 affected joints superior limbs (n=18) =27.7, No JIA=4.07*
Miranda et al. 2005 (76)	Brazil Sweden	38 JIA 29 No JIA	Adol.	-VPI>0: JIA=55%, No JIA=47% -GBI>0: JIA=47%, No JIA=33%
Miranda et al. 2006 (77)	Brazil	18 JIA 14 No JIA	Adol.	-Baseline: VPI>0: JIA=54.6%, No JIA=46.9%, GBI>0 JIA=29.1%, No JIA=33.8%. -2 years follow-up: VPI>0: JIA=39.4%, No JIA=34.9%, GBI>0: JIA=41.6%, No JIA=38.9%
Reichert et al. 2006 (105)	Germany	78 JIA 75 No JIA	Adol.	-API: JIA=64.6%, No JIA= 49.9% * -Modified SBI: JIA=35.3%, No JIA=29.0%
Leksell et al. 2008 (91)	Sweden	41 JIA 41 No JIA	Adol.	-DMFS n of lesions: JIA=63, No JIA=50 (enamel caries included) -Sites w/plaque: JIA=32%, No JIA=19% * -Sites w/calculus: JIA=11%, No JIA=5% * -BOP: JIA=26%, No JIA=14% *
Silva et al. 2012 (84)	Brazil	16 JIA 11 No JIA	Adol.	-VPI>0: JIA=17%, No JIA=22% -GBI>0: JIA=9%, No JIA=36% *

Feres de Melo et al. 2014 (87)	Brazil	36 JIA 36 No JIA	6–12	-DMFT [a]: JIA=3.00, No JIA=2.93 -OHI-S: JIA=1.8, No JIA=1.49 * -GI: JIA=0.33, No JIA=0.30
Santos et al. 2015 (67)	Brazil	14 JIA 15 No JIA	6–14	-dmft: JIA=0.6, No JIA=4.4 * -DMFT: JIA=2.4, No JIA=3.3 -OHI-S: JIA=2.1, No JIA=2.2 -GBI: JIA=10.9, No JIA=1.4 *
Pugliese et al. 2016 (106)	Brazil	35 JIA 35 No JIA	Adol.	-DMFT: JIA=1.0, No JIA=2.0 -PI: JIA=66.6, No JIA=58.9 -GI: JIA=0 No JIA=1.0 -GBI: JIA=12.9, No JIA=15.8
Kobus et al. 2017 (88)	Poland	34 JIA 34 No JIA	6–18	-dmft[a]: JIA=3.6, No JIA=3.7 -DMFT[a]: JIA=6.21, No JIA=5.71 -GI: JIA=0.25, No JIA=0.24 -OHI-S: JIA=0.95, No JIA=0.85
Maspero et al. 2017 (99)	Italy	40 JIA 20 No JIA	Adol.	-FMPS: JIA w/etanercept=48%, JIA w/ other drugs=37%, No JIA=20% -FMBS: JIA w/etanercept=5%, JIA w/ other drugs=5%, No JIA=9%
Romero-Sanchez et al. 2017 (79)	Colombia	51 JIA	Adol.	-PI (median): Polyarticular JIA=33 (median), enthesitis-related arthritis JIA (ERA)=50, Other JIA (oligoarticular, psoriatic, undifferentiated, systemic arthritis) = 44 -GI (median): Polyarticular JIA =13, ERA JIA=23, Other JIA=5 -BOP (median): Polyarticular JIA=22, ERA JIA= 40, Other JIA=28
Grevich et al. 2019 (66)	US	85 JIA 62 Dental patients no JIA 11 Healthy controls	Adol.	-DMFT[a]: JIA=1.40, Dental=2.76, Healthy controls=0 -PI: JIA=0.592 (*compared to healthy), Dental=0.78, Healthy controls=0.22 -GI: JIA=0.37 (*compared to dental), Dental=0.63, Healthy controls=0.32 -BOP: JIA=0.17, Dental=0.08, Healthy controls=0.09
Kobus et al. 2019 (102)	Poland	34 JIA 34 No JIA	6-18	-PBI: JIA=0.2, No JIA=0.25
Galkina et al. 2020 (89)	Russia	60 JIA	Adol.	-DMF: JIA duration<6yrs.= 3.5, JIA duration>6yrs.=5.94 * -PMA: JIA duration<6yrs.= 10.78%, JIA duration>6yrs.=6.72% *
Merle et al. 2020 (109)	Germany	59 JIA	Adol.	-dmft/DMFT [a]: JIA=2.6 -PBI: n JIA PBI≤2=29, n JIA PBI≥3=39
Defabianis et al. 2021 (85)	Italy	56 JIA 28 No JIA	4-15	-n carious lesions>0: Oligoarticular (n=28) =8, Polyarticular (n=28) =10, No JIA= 8 -FMPS: Oligoarticular (n=28) =52.1, Polyarticular(n=28) =49.7, No JIA= 46.2

Results are reported as mean if there is no other explanation. *Statistically significant difference ($p<0.05$), [a]According to World Health Organization (WHO), [b]According to British Association for the Study of Community Dentistry (BASCD) criteria, Adol.=adolescents, dmft/DMFT=decayed, missed, filled primary/permanent teeth, VPI=Visible Plaque Index, GBI=Gingival Bleeding Index, GI=Gingival Index, PI=Plaque Index, OCI=The Oral Cleanliness Index (Turesky plaque scoring), PCR=Plaque Control Record by O'Leary, API=Approximal Plaque Index, SBI=Sulcular Bleeding Index, BOP=Bleeding on Probing, OHI-S=Simplified Oral Hygiene Index, FMPS=Full-Mouth Plaque Score, FMBS=Full-Mouth Bleeding Score, PBI=Papilla Bleeding Index, PMA= PMA-Index modified by Parma. Three studies (80, 110, 111) conducted by our research group are not included in the introduction chapter of this thesis (but identified in the literature search undertaken in 2022).

Table 3. Studies (n=5), from 1985-2022, including subjective indicators of OHRQoL in children and adolescents with JIA, identified from an online literature search.

Study	Country	Sample size	Age (yrs.)	OHRQoL
Santos et al. 2015 (67) [a]	Brazil	14 JIA 15 No JIA	6–14	-SF:13-B-PCPQ: JIA=7.4, No JIA=8.3
Rahimi et al. 2018 (74)	Sweden	113 JIA	Adol.	-CPQ($_{11-14}$), Emotional well-being items (11 items): JIA w/orofacial symptoms and OHRQoL impacts>0: 27.4%-93.5% (range) JIA w/no orofacial symptoms and OHRQoL impacts>0: 86.3%-100% (range) -CPQ($_{11-14}$), Social well-being items (18 items) JIA orofacial symptoms with OHRQoL impacts>0: 45.2%-100% (range) JIA no orofacial symptoms with OHRQoL impacts>0: 60.8%-100% (range)
Bucci et al. 2019 (107)	Italy	50 JIA 80 No JIA	Adol.	-PIDAQ, Aesthetic Component: JIA=4.20, No JIA=4.96 -PIDAQ, Psychosocial Impact: JIA=11.34, No JIA=10.44 -PIDAQ, Dental Self-Confidence: JIA=10.18, No JIA=7.67 *
Isola et al. 2019 (72)	Italy	62 JIA 35 No JIA	8-17	-CPQ($_{11-14}$), JIA w/TMJs involvement (n=32), compared to JIA without TMJ and no JIA: Oral symptoms OR=2.4 (95% CI: 1.6–4.5) * Functional limitations OR=3.7 (95% CI: 2.1–4.8) * Emotional well-being OR=2.2 (95% CI: 1.4–3.1) Social well-being OR=2.3 (95% CI: 1.3–2.9)
Polizzi et al. 2020 (82)	Italy	60 JIA 33 No JIA	8-17	-CPQ($_{11-14}$), JIA w/periodontitis (n=30), compared to JIA without periodontitis and no JIA: Oral symptoms OR=2.3 (95% CI: 1.6–4.2) * Functional limitations OR=3.7 (95% CI: 2.1–4.8) * Emotional well-being OR=2.2 (95% CI: 1.4–3.1) Social well-being OR=2.3 (95% CI: 1.3–2.9)

Results are reported as mean if there is no other explanation. *Statistically significant difference ($p<0.05$), [a] The study also includes clinical indicators of oral health and are presented in Table 2, Adol.=adolescents, SF:13-B-PCPQ = Short form of the Brazilian Parental-Caregiver Questionnaire (component of the Child Oral Health-related Quality of Life measure), CPQ($_{11-14}$)=Child Perception's Questionnaire, PIDAQ=Psychosocial Impact of Dental Aesthetics Questionnaire

The updated literature search generated limited new knowledge concerning caries. In 2020, Merle et al. (109) published results from an extensive oral examination including 59 participants with JIA; they highlighted high levels of caries experience and gingival bleeding in German adolescents with JIA. However, the interpretation of the result is challenged due to the lack of a comparison group. Compared to controls, individuals with JIA stand out in increased plaque and gingival inflammation findings; however, results are not homogenous. OHRQoL in young individuals with JIA has gained relatively more focus in the last few years. The likelihood of impaired OHRQoL amongst JIA patients with additional oral health burden (TMJ involvement,

orofacial symptoms, and periodontitis) is indicated (72, 74, 82), whether specific JIA features (such as disease activity, duration and medication use) increase the risk remain unexplored. Evaluation of oral health determinants in research focusing on young individuals with JIA is limited. However, a study published in 2019 by Grevich et al. (66) included socio-demographic covariates of oral health in the regression analyses (age, gender, race, household income, and parental education). The impact of socio-behavioral covariates on OHRQoL remains unexplored.

1.3 Rationale and justification

Caries of young individuals with JIA has not been investigated in Norway since 1989 (108, 112). Research on this group's periodontal status and OHRQoL has not been performed in a Norwegian population. The advanced modern JIA treatment strategies, constantly evolving, warrant up-to-date research on oral health among young individuals with JIA. In international studies, findings on oral health status in young individuals with JIA contradict, and high-quality research has been called for (101). Adequate sample size, comprehension of oral health-related covariates, and robust statistical analyses are essential to increase knowledge on the subject. Oral health plays a pivotal role in general health and QoL (113-115). Oral diseases, which in most cases are preventable, should not be of additional burden to the general health and the orofacial problems children and adolescents with JIA experience. Optimal preventive oral health intervention relies on identifying at-risk groups and awareness of how oral health discriminates between them. JIA encompasses a heterogeneous group of disease categories, and distinct characteristics must be accounted for when evaluating this group of patients.

2. AIMS

2.1 Overall aim

This thesis aimed to provide knowledge about clinical and subjective oral health status and associated factors among Norwegian children and adolescents with JIA compared to controls without JIA. We also aimed to investigate associations between disease-specific features and oral health status among participants with JIA.

2.2 Specific objectives

Paper I

- Explore whether caries is more prevalent among children and adolescents with JIA compared to matched controls.
- Independent of JIA/control group, examine the presence of caries according to socio-behavioral and intraoral (within mouth) characteristics and the extent to which surface-specific caries varies between and within individuals.
- Furthermore, assess whether surface-specific caries varies according to JIA/control group and dentition (primary/permanent molars).
- Finally, and specifically for patients with JIA, investigate whether clinical features such as JIA category, age at onset of JIA, disease duration, use of medication, or remission status associate with the presence of caries.

Paper II

- Explore whether plaque and gingival bleeding are more frequently experienced by adolescents with JIA as compared to matched controls without JIA.
- Additionally, explore whether surface- and site-specific periodontal outcomes vary between the two groups.
- Finally, and specifically for participants with JIA, investigate possible associations between disease-specific features and the periodontal outcome variables.

Paper III

- Investigate whether OHRQoL, assessed by the ECOHIS and Child-OIDP scale, differs between children and adolescents with JIA compared to controls without JIA, while adjusting for socio-demographic-, behavioral- and oral health-related covariates.
- Furthermore, to explore whether socio-behavioral and oral health-related covariates of OHRQoL vary according to group affiliation.
- Finally, specifically for individuals with JIA, to investigate whether disease-specific features associate with OHRQoL.

2.3 Working hypothesis

The principal hypothesis is that children and adolescents with JIA have more caries, plaque, gingival bleeding and impaired OHRQoL than controls without JIA.

3. MATERIAL AND METHODS

The papers in this thesis originate from baseline data of the Norwegian JIA Study (NorJIA)[1] (http://www.norjia.com/). NorJIA, registered at ClinicalTrials.gov (No: NCT03904459), is a prospective longitudinal multicenter study performed from April 2015 to October 2020 focusing on temporomandibular involvement, oral health, uveitis, bone health, and QoL in children with JIA. NorJIA baseline data collected from April 2015 to August 2018 addressing oral health and OHRQoL in JIA children and adolescents constitute the study presented in this thesis.

3.1 Study population

All individuals with JIA referred to the university hospitals involved in the NorJIA study (University Hospital of North Norway, St. Olav's Hospital, Haukeland University Hospital) were invited to participate (except for patients living in Nordland and Rogaland, two counties within the area of accountability of the universities, illustrated in Figure 3). Inclusion criteria were children or adolescents (4–16 years old) diagnosed with JIA by a pediatric rheumatologist at the university hospitals in conformity with specifications by the ILAR (1). Individuals without JIA (hereafter referred to as 'controls') were recruited at Public Dental Service (PDS) clinics. The exclusion criterion was the lack of written informed consent.

3.2 Study area

Norway constitutes five major geographical regions (Figure 3). The university hospitals in western, central, and northern Norway were involved in the study, encompassing three out of four existing regional pediatric rheumatology centers in Norway. The fourth regional center (eastern- and southern Norway) is located in Oslo. The oral health examination of the participants with JIA took place at the three oral health centers of expertise in the same city as the regional pediatric

[1]The Norwegian JIA Study – Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis.

rheumatology centers. The controls were examined at seven PDS clinics, presenting rural and urban areas near the respective pediatric rheumatology centers.

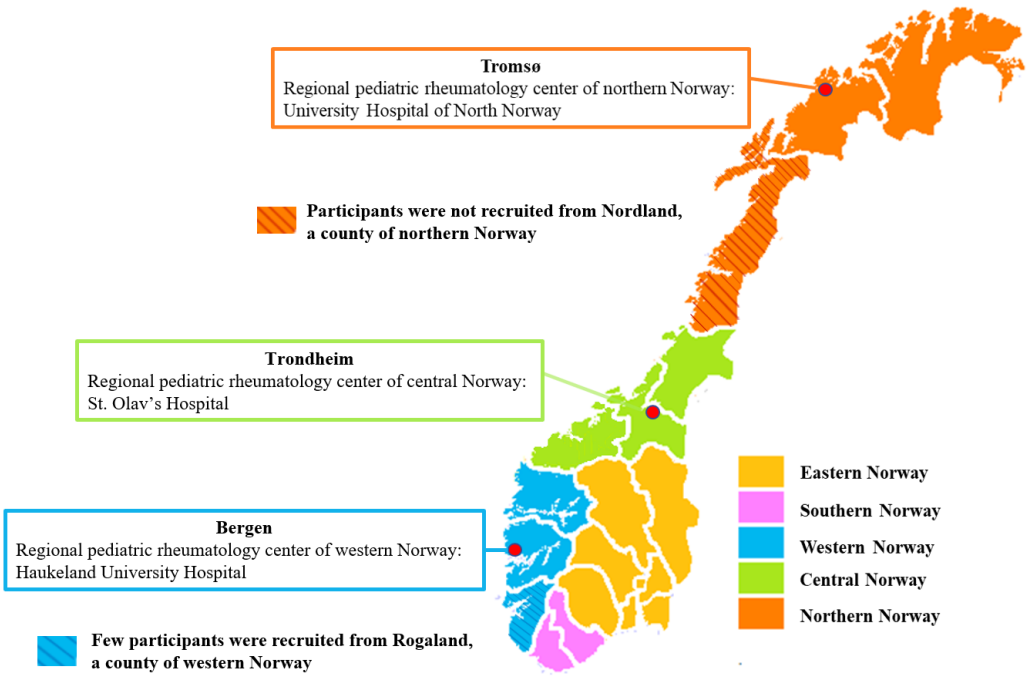

Figure 3. The five major geographical regions of Norway and location of the three regional pediatric rheumatology centers involved in the study. An illustration available on wikipedia.org forms the basis of the presentation of the geographical regions of Norway.

https://en.wikipedia.org/wiki/Regions_of_Norway (03.03.2022).

3.3 Study design

This baseline study has a comparative cross-sectional study design. Individuals with JIA receiving the oral health examination were matched 1:1 with controls according to sex, age, center site, and mothers' country of origin (western or non-western origin). Participants were continuously recruited throughout the study period and

constitute a census of children /adolescents with JIA in three out of five geographical regions in Norway.

3.4 Participants

A total of 360 individuals with JIA were invited to participate, of whom 228 were included and had a medical examination. Four of these participants did not undergo the oral examination. The oral examination was performed within a month after the medical examination. Controls were contacted based on a suitable planned oral health check, and 224 were enrolled. The controls received two cinema tickets as incentives for participating in more time-consuming appointments than usual at dental checkups.

A flow diagram of the enrolment of participants in the NorJIA study is shown in Figure 4.

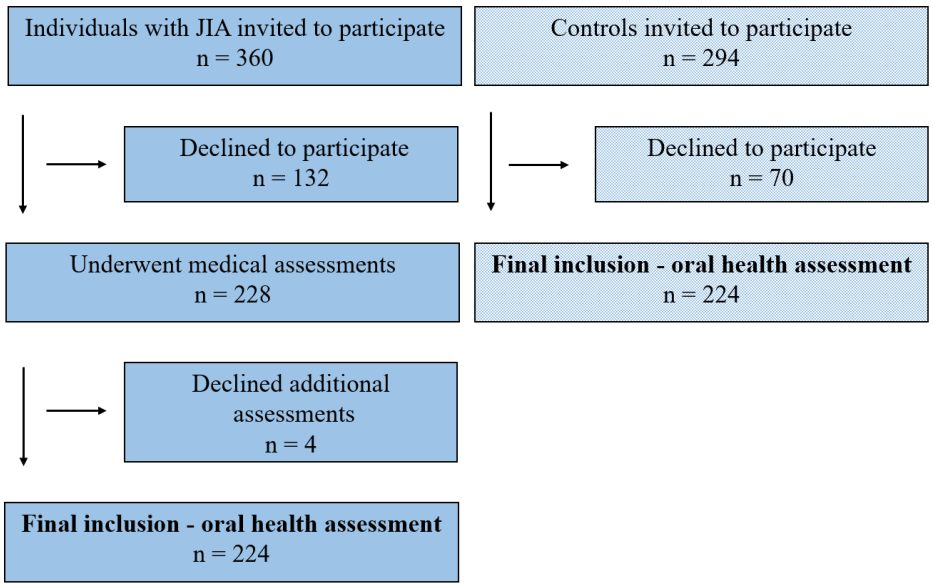

Figure 4. Flow diagram of the enrolment of individuals with JIA and controls in the NorJIA study.

3.5 Data collection

3.5.1 Questionnaires

Self-administered questionnaires provided information about socio-demographic characteristics, oral health-related behaviors, and self-reported oral health. The questionnaires were distributed either in printed form during the medical or oral examination or via the internet. Caregivers completed the questionnaire if the participant was under 12 years. The questionnaire given to participants 12 years and older was slightly different (both versions are included in Appendix II). The variables included in this study are presented in Table 4. Dichotomized variables were constructed. Several questionnaire items had numerous response categories; the categories originally coded and re-coded for analyses are available in Paper I-III (supplementary files).

Table 4. Overview of questionnaire variables included in this study

Socio-demographic variables	Behavioral variables	Self-reported oral health indicators	Explicitly for participants with JIA
• Educational level of caregivers • Number of caregivers in the household • Mother's country of origin • Toothbrushing frequency • Tooth flossing frequency	• Fluoride content in the choice of toothpaste • Age when toothbrushing started* • Cordial/milk in a bottle after the age of 1 year* • Drinks or food offered or available in bed in the evening/during the night*	• Gingival bleeding during toothbrushing • Pain or discomfort during toothbrushing • Frequency of intraoral ulceration(s) • Perception of dry mouth	• Oral health education in relation to the JIA diagnosis**

* Included in the questionnaire given to participants <12 years
** Concerned if the participants had received information about the importance of good oral health in relation to the JIA diagnosis. If so, they were to specify the health profession of the communicator (Paper II)

Another questionnaire, ECOHIS (49), was used to assess OHRQoL in participants 4-11 years old. ECOHIS intends to capture the child and family's OHRQoL by referencing the child's life experience of problems with teeth, mouth or jaws, and dental treatment. ECOHIS consists of thirteen items, composing the child impact section (first nine items: symptoms of pain, difficulty drinking, difficulty eating, difficulty pronouncing words, missed daycare/preschool/school, trouble sleeping, being irritable or frustrated, avoided smiling or laughing, avoided talking) and the family impact section (last four items involve family members: been upset, felt guilty, taken time off work, implications financially). Each item, assessed initially as never=0 to very often=5, was dichotomized (0=not affected, including the original category 0 and 1=affected, including the original categories 1-5), and the Child impact- and Family impact scores were calculated by summarizing the dummy variables. Calculating the ECOHIS total score was done by summarizing the Child and Family impact scores. The Child and Family impact scores were dichotomized into 0=no impacts and 1=1-9, or 0=no impacts and 1=1-4 impacts, respectively. The ECOHIS total score was dichotomized into 0=no impacts and 1=1-13 impacts. Participants with two or more items of the ECOHIS unanswered were excluded from the analysis. The response category "I do not know" was coded as missing and not considered in the analyses. Evaluation of self-reported oral health and satisfaction with the appearance of teeth (global measures) were included as separate items in the questionnaire. The variables and response categories of ECOHIS, originally coded and re-coded for analyses, are available in Paper III.

3.5.2 Personal interview

Among participants 12-16 years, OHRQoL was assessed by face-to-face interview using the Child-OIDP frequency inventory. OIDP was initially constructed for adults (116) and later modified for 12-year-olds into a child version: the Child-OIDP (47). One of the dentists conducted the interview in the dental office before the oral examination. This OHRQoL tool considers difficulty performing eight daily activities (eating, speaking, cleaning teeth, smiling-laughing-and showing teeth without embarrassment, sleeping and relaxing, emotional balance, social contact, and

schoolwork) due to problems with mouth or teeth during the past three months. Every eight items, assessed initially never=0 to every day/almost every day=3, was dichotomized (0=not affected, including the original category 0 and 1=affected, including the original categories 1-3). Participants with two or more items of the Child-OIDP unanswered were excluded from the analysis. The dummy variables were summarized, forming the Child-OIDP simple count (SC) score. The Child-OIDP SC score was dichotomized into 0=no impacts and 1=1-8 impacts. Evaluation of self-reported oral health and satisfaction with the appearance of teeth (global measures) were also included in the interview.

The variables and response categories of Child-OIDP, as originally coded and re-coded for analyses, are available in Paper III.

3.5.3 Medical examination of the participants with JIA

Experienced pediatric rheumatologists examined the participants with JIA. JIA-specific variables included in this study were JIA category, age at JIA onset, disease duration, medication, disease (activity/remission) status, self-reported physical disability, physician's global assessment of disease activity visual analogue scale (MDgloVAS) (117), and patient/parent-reported global assessment of overall well-being visual analogue scale (PRgloVAS) (117) and patient/parent-reported pain intensity visual analogue scale (VAS pain) (117). Specification of the JIA category was according to the ILAR classification criteria (1). Record of disease status on the day of the visit was according to Wallace et al. (118) and the American College of Rheumatology (ACR) provisional criteria (19), where inactive disease (on or off medication) included no active arthritis, no fever, no generalized lymphadenopathy, no splenomegaly, no serositis, no rash as a result of JIA, no active uveitis, normal levels of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), no morning stiffness exceeding 15 minutes, and MDgloVAS = 0.

The definition of clinical remission on medication was six continuous months of inactive disease on medications, and the definition of remission off medication was twelve continuous months of inactive disease and no anti-rheumatic medication

(118). Previous and ongoing medication was registered and categorized into the following groups: 1) sDMARDs nor bDMARDs, 2) sDMARDs, but no bDMARDs, and 3) bDMARDs (with or without sDMARDs). Each group was mutually exclusive. Categorization of the JIA cohort was also by groups using or not using systemic steroids. All groups were registered according to ongoing medication or ever used; the last included both previously used and ongoing medication. A measure of self-reported physical disability was by the validated patient/parent-reported disease-specific childhood health assessment questionnaire (CHAQ) (0=no difficulty and 3=unable to perform) (119, 120). The visual analogue scales measures were on a 21-numbered circle VAS (0=minimal impact, 10=maximal impact). The caregiver reported the self-reported background variables, PRgloVAS, VAS pain, and CHAQ if the child were below nine years, otherwise by the patient. All JIA-specific variables were categorized, and the coding is available in Paper I-III.

The following blood tests were taken at onset or during follow-up of all participants with JIA at each center and included in this study; human leukocyte antigen B27 (HLA-B27), antinuclear antibodies (ANA), RF, and anti-cyclic citrullinated peptide (anti-CCP). ANA was measured using immunofluorescence on HEp-2 cells. Methods and reference values for RF, anti-CCP, and HLA-B27 varied slightly between and within each center. Therefore, each physician reported the results of ANA, RF, and anti-CCP as positive or negative according to the reference values of their local laboratory. For ANA, RF, and anti-CCP, a positive result required two positive tests taken at least three months apart. At each study visit, the following additional blood tests were taken and analyzed locally at the study centers: CRP with reference value <5 mg/l at all study centers, ESR with slightly diverging reference values at the different centers and according to age and gender. We chose to use CRP <5 mg/l and ESR <20 mm/hour as the cut-off values in the analyses.

3.5.4 Training and calibration

Experienced dentists located at the different center sites were trained and calibrated by a professor in pediatric dentistry (MSS). Seven trainee examiners participated in

the training and calibration[2]. Before the study, the trainee examiners underwent a theoretical course focusing on descriptions and examination instructions, and insecurities were discussed until clarity. The formulation of personal interview questions was standardized to facilitate consistency of the interview (Child-OIDP). In-depth consideration of the modifications of the periodontal indices and the advised angulation of 60 degrees of the periodontal probe according to the tooth's longitudinal axis were studied (121). To illustrate the force to apply on probing the upper part of the gingival sulcus to determine gingival bleeding, the trainee examiners practiced with a dental probe on a digital letter scale (Wedo Package Scale Paket 50 Plus). Evaluation of caries followed the five-graded caries diagnosis system (122). According to caries, the trainee examiners evaluated dental bitewings (BW) and clinical pictures of teeth with and without caries in the training session. MSS gave specific feedback to the findings. Before and during the study period, four sessions with exercises were done (Test Caries 1, 2, 3, 4). As part of the calibration sessions, 71 schoolchildren with primary and permanent teeth were examined for caries. Also, BW (n=21) of both primary and permanent teeth contributed to this calibration material, as well as extracted teeth (n=9). Comparing results by the trainee examiner and a specialist in pediatric dentistry ("expert reference") lays the foundation of Test Caries 1. Test Caries 2 is an inter-examiner evaluation between the examiners, Test Caries 3 is an intra-examiner assessment with an interval between, and Test Caries 4 again compares the results by the examiners and an expert reference.

The examiners were given plastic-coated instruction sheets (to accompany the examinations of the participants throughout the study) with the standardized questions of the Child-OIDP items, illustrations and descriptions of the modified versions of the periodontal indices, and the description of the caries diagnosis system with associated photographs.

[2] The method section of Paper I-III describes five calibrated dentists examining the participants. The correct number is six (as opposed to n=5), as two of the seven calibrated dentists formed a unit by examining the participants together.

3.5.5 Oral health examination

The oral examination with BWs was performed in a dental unit under standard lighting using a plain mouth mirror and appropriate clinical explorer. Oral hygiene was evaluated prior to the other variables; after the periodontal evaluation, index teeth were, if necessary, professionally cleaned.

A structured clinical oral examination of various oral diseases and conditions were performed. The oral assessments and index teeth were determined by age on the day of the medical examination; accordingly, three different registration protocols were applicable (4-6 years, 6-9 years, and ≥10 years). The protocol for participants ≥10 years, available in Appendix III, includes the relevant clinical oral health variables in this study.

The participants underwent caries assessment based on BW combined with a visual inspection. According to a detailed five-graded diagnostic tool (122), surfaces were registered as decayed, missing, or filled (dmf/DMF). Grades 1–2 denoted enamel lesions and grades 3–5 dentin lesions. Definition of missing teeth was teeth extracted or indicated for extraction due to caries. BW was taken from the age of 5 years if there was intermolar contact. In the case of fixed orthodontic appliances, BW were excluded, and only visual inspection of occlusal surfaces was performed. Index teeth were molars (at younger than ten years, primary second molars, and permanent first molars at ten years and older). These index teeth were selected to attain comparability concerning the dentition's shedding/eruption stages among the participants. The variable dental caries was dichotomized (dmf/DMF>0 or dmf/DMF=0).

Examiners evaluated oral hygiene and gingival bleeding in participants 10-16 years according to modified versions of the Simplified Oral Hygiene Index (OHI-S) (123) and Gingival Bleeding Index (GBI) (124). Index teeth were the first permanent molars and one incisor in the upper- and lower jaw. OHI-S consists of the simplified Debris Index (DI-S) and the simplified Calculus Index (CI-S). Registration of oral hygiene was modified as subgingival calculus was not recorded (only supragingival calculus). Partially erupted teeth did not get an oral hygiene score, and fixed

orthodontic appliances were an exclusion criterion. The tooth was evaluated by running an explorer nr. 23 (Shepherd hook) along the tooth surface and scored according to the extent of plaque covering the surface, ranging from no presence (score 0) to more than 2/3 of the tooth surface covered with plaque (score 3). DI-S and CI-S were calculated by dividing the sum of scores of the examined surfaces by the total number of examined surfaces. OHI-S was calculated by summarizing DI-S and CI-S. At least two of the six surfaces needed to be scored to calculate the indices. Examiners evaluated the same index teeth corresponding to OHI-S to assess gingival bleeding. Modification of GBI was as follows: horizontal movement of the probe on the surface was substituted; instead, implementation of a vertical movement at three sites on the respective surface (mesial, medial, and distal). Probing the orifice of the gingival crevice was done with a WHO periodontal measuring probe with a 0.5 mm ball tip. A positive finding was scored if bleeding occurred within 10 seconds after probing. GBI was calculated by dividing the sum of bleeding sites by the number of sites examined, expressed as a percentage. Plaque and gingival bleeding variables were dichotomized (OHS-I>0 or OHS-I=0, and GBI>0 or GBI=0, respectively).

Other clinical characteristics of the oral cavity were fissure of lip or corner of the lip, gingival ulcers with discontinuation of the epithelium of at least 3 mm, buccal ridging, tongue indentation, buccal gingival hyperplasia (buccal side of the lower and upper anterior teeth), and potential mouth dryness (by evaluating if dental mirror sticks to buccal mucosa). These variables were dichotomized as present (=yes) or not present (=no).

A flow diagram of the oral health indices in this study, according to the papers, age, and the number of participants included in the two groups, is shown in Figure 5.

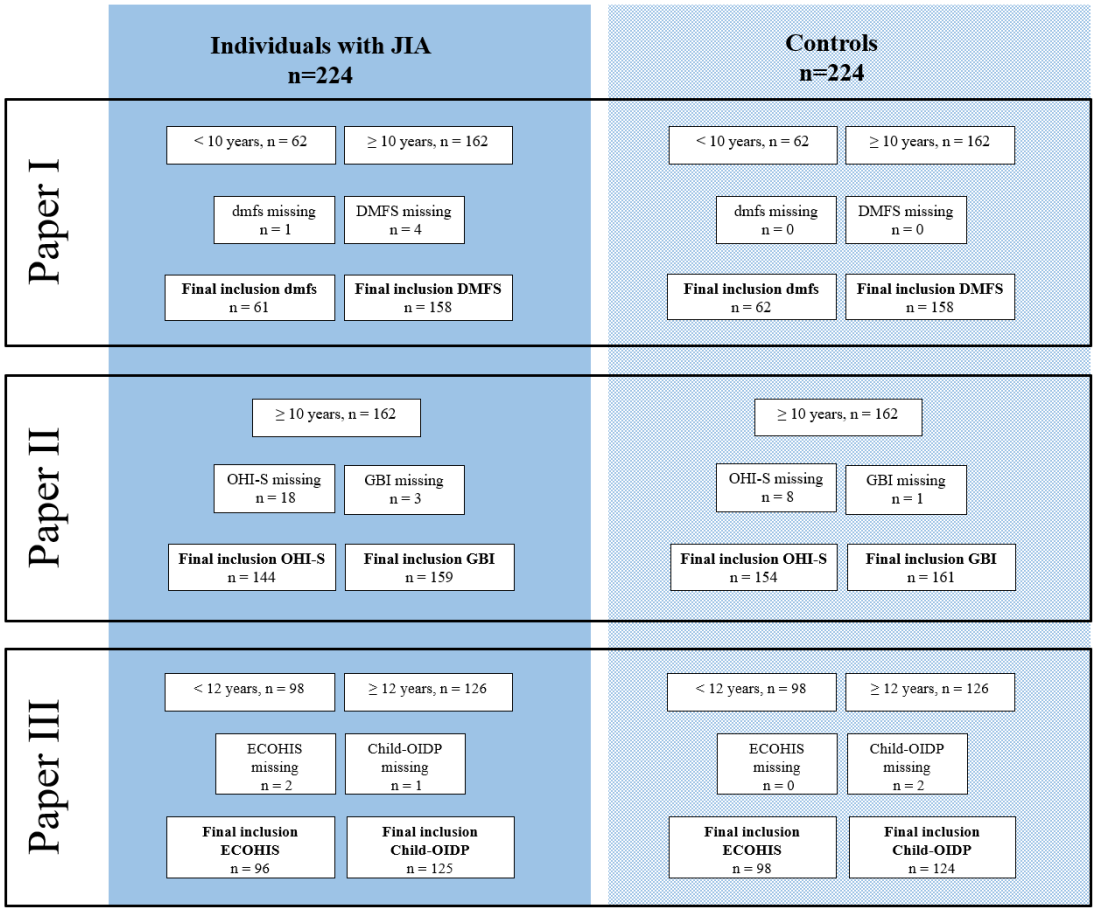

Figure 5. Flow diagram specifically for the oral health indices, according to the papers, age, and the number of participants included. Paper II also included "Other clinical characteristics of the oral cavity" (fissures, ulcers, buccal ridging, tongue indentation, gingival hyperplasia, mouth dryness). Description of participants missing: In Paper I, temporary misinterpretation of study instructions resulted in missing material. In Paper II, oral hygiene was not evaluated in the case of fixed orthodontic appliances, and evaluation of gingival bleeding was not performed in participants with an anamnesis indicating precaution concerning manipulation of gingival tissue. In Paper III, participants with two or more unanswered items of the OHRQoL inventories were excluded from the analysis.

3.6 Data analysis and statistical methods

Data were analyzed using SPSS version 25.0 (IBM Corp. Released 2013, IBM SPSS Statistics for Windows, Armonk NY: IBM Corp) and STATA version 16 (Stata Corp LP, College Station, TX). P-values less than 5% were considered statistically significant. Table 5 shows an overview of outcome- and exposure variables, and statistical tests/methods applied in Paper I-III.

3.6.1 Summary of the statistical tests and methods

Linear weighted Cohen's kappa was used to assess inter- and intra-rater reliability for the caries measurements. The internal consistency reliability of the OHRQoL inventories was assessed using Cronbach's alpha. Mean and standard deviation (SD) described continuous demographic variables. For the categorical variables, frequencies and percentages were reported using cross-tabulation, and Chi-squared tests were applied to test the differences between individuals with JIA and the control group. Two-sample t-tests were applied to test the difference in the aggregated indices OHI-S and GBI between participants with JIA and controls. Linear regression models with robust variance estimates (RVE) explored the mean difference (beta) between the matching pairs in the aggregated indexes OHI-S and GBI. Logistic regression analyses with RVE, reporting odds ratio (OR) and 95% confidence interval (CI), were applied with ECOHIS total score and Child-OIDP SC score as binary outcome measures. Negative binomial regression with RVE, reporting incidence rate ratios (IRR) with 95% CI, was implemented as a supplementary analysis with ECOHIS and Child-OIDP SC total scores as count variables. McFadden's R^2 was applied as a measure for the goodness of fit of the logistic regression models in Paper III. Two-way interactions were tested between group affiliation and the socio-behavioral- and oral health-related variables on ECOHIS and Child-OIDP. The multilevel models (Paper I and II) are described in the following section.

Table 5. Overview of outcome- and exposure variables and statistical tests/methods applied in Paper I-III

	Paper I	Paper II	Paper III
Main outcome variable(s)			
	Dental caries * (binary)	OHI-S, GBI * (binary and continuous)	ECOHIS, Child-OIDP (binary and continuous)
Main exposure variable			
	Group affiliation (JIA/control)	Group affiliation (JIA/control)	Group affiliation (JIA/control)
Exposure variables			
Socio-demographic variables	• Educational level of caregivers • Numbers of caregivers in the household	• Educational level of caregivers • Numbers of caregivers in the household	• Educational level of caregivers • Numbers of caregivers in the household
Behavioral variables	• Toothbrushing frequency • Tooth flossing frequency • Fluoride content in the choice of toothpaste	• Toothbrushing frequency • Tooth flossing frequency	• Toothbrushing frequency • Tooth flossing frequency
Self-reported oral health indicators	• Gingival bleeding during toothbrushing • Pain or discomfort during toothbrushing	• Gingival bleeding during toothbrushing • Pain or discomfort during toothbrushing • Frequency of intraoral ulceration(s) • Perception of dry mouth	• Gingival bleeding during toothbrushing • Pain or discomfort during toothbrushing
Clinical oral health indicators			• Dental caries
JIA-specific variables	• JIA category • Age at JIA onset • Disease duration • Medication • Disease status • CHAQ hygiene item: Toothbrushing • MDgloVAS • PRgloVAS	• JIA category • Age at JIA onset • Disease duration • Medication • Disease status • CHAQ hygiene item: Toothbrushing • MDgloVAS • PRgloVAS • Various blood tests	• JIA category • Age at JIA onset • Disease duration • Medication • Disease status • CHAQ • MDgloVAS • PRgloVAS • VAS pain
Statistical tests/methods			
	• Descriptives • Cohen's kappa • Chi-squared tests • Mixed-effects logistic regressions • Intra-class correlation • Akaike information criterion • Scheffe post-hoc test • Interactions	• Descriptives • Chi-squared tests • T-test • Linear regression with robust variance estimates • Mixed-effects logistic regressions • Intra-class correlation • Interactions	• Descriptives • Cronbach's alpha • Chi-squared tests • Logistic regression with robust variance estimates • Negative binomial regression with robust variance estimates • Interactions • McFadden's R^2

*The outcomes were evaluated at multiple levels (site, surface, tooth). Oral-specific variables (jaw, right/left, anterior/posterior) were also assessed in reference to the outcomes. CHAQ=Childhood Health Assessment Questionnaire. MDgloVAS=physician's global assessment of disease activity. VAS pain=patient/parent-reported pain intensity. PRgloVAS= Patient/parent-reported global assessment of overall wellbeing.

3.6.2 Clustered data

The data for the presence of caries ($d_{1\text{-}5}fs/D_{1\text{-}5}FS>0$), plaque (OHI-S>0) and gingival bleeding (GBI>0) had a clustered hierarchical structure. Plaque had a 2-level structure with measures on surfaces/teeth (level 1) clustered within individuals (level 2). Gingival bleeding and caries had a 3-level structure with sites/surfaces (level 1) clustered within teeth (level 2) and teeth clustered within individuals (level 3). In Paper I and II, mixed-effects logistic regressions, reporting OR with 95% CI, were applied to account for and to measure the clustering of clinical data. Multilevel modeling corrects for clustering and provides accurate standard errors, hence more precise CI and significance tests (125). Furthermore, intra-class correlation coefficients (ICC) for individual and teeth is calculated. Consequently, random intercept logistic models (RIM) were applied.

The formulas estimated (using restricted maximum likelihood (REML)) for the 3-level data, using mixed-effects (random intercept) logistic regression were:

$$logit\left(P\left(Y_{ijk}=1\right)\right)=\beta_0+\beta_1^T X_{ijk}+\beta_{0i}+\beta_{0ij}+e_{ijk}$$

$$Y_{ijk}\sim Binomial(n_i,p_i)$$

$$\beta_{0i}\sim N(0,\sigma_v^2)$$

$$\beta_{0ij}\sim N(0,\sigma_u^2)$$

$$icc_v=\frac{\sigma_v^2+\sigma_u^2}{\sigma_v^2+\sigma_u^2+\pi^2/3}$$

$$icc_u=\frac{\sigma_u^2}{\sigma_v^2+\sigma_u^2+\pi^2/3}$$

The multilevel models account for clustering of caries and gingival bleeding data for sites/surfaces (k) within teeth (j) and within individuals (i). icc_u is the intra-class

correlation for the measurements clustered within teeth, while icc_v is the intra-class correlation for the measurements of the teeth clustered within individuals.

As the outcome variable, the presence of caries ($d_{1\text{-}5}fs/D_{1\text{-}5}FS>0$) is binary; the variance in the presence of caries data was too small to estimate intra-class correlation within teeth ($icc_u = 0$); hence caries data on tooth level (j) was not accounted for in the analyses.

The formulas estimated for the 2-level data, using mixed-effects logistic regression:

$$logit\left(P\left(Y_{ij}=1\right)\right) = \beta_0 + \beta_1^T X_{ij} + \beta_{0i} + e_{ij}$$

$$Y_{ij} \sim Binomial(n_i, p_i)$$

$$\beta_{0i} \sim N(0, \sigma_v^2)$$

$$icc_v = \frac{\sigma_v^2}{\sigma_v^2 + \pi^2/3}$$

The multilevel models account for the clustering of plaque data for surface/teeth (j) within individuals (i). icc_v is the intra-class correlation for the measurements of the teeth clustered within individuals.

The effect of dependency at the individual level (caries, plaque, and gingival bleeding) and tooth level (gingival bleeding) was assessed by calculating ICCs by applying the described formulas. The ICCs demonstrate variations between clusters as a proportion of the total variance. ICC varies between 0 (implying the respective variable is independent within teeth/individuals) and 1 (implying no variation of the respective variable within teeth/individuals, *i.e.*, all variation is between clusters (teeth/individuals)). The post-hoc test was applied by Scheffe's method to adjust significance levels in multiple comparisons in the multilevel mixed-effects logistics regressions. Two-way interactions were tested between surface and group affiliation on the presence of caries, plaque, or gingival bleeding and between site and group affiliation on the presence of gingival bleeding.

RVE were applied in Paper II-III, using the option "cluster(match)" or "cluster(id)" (defining the clusters) to secure robust standard errors (SE). In paper II, SE was corrected according to the matching pairs. The variance (SD) was refined in the regression analyses in paper III, considering the whole study population and the JIA-specific analyses.

3.6.3 Selection of covariates in the multiple variable regression analyses

The multivariable regression analyses in Paper I-III included the main exposure variable (group affiliation), adjusted for potential confounding variables in terms of covariates that were statistically significantly associated with group affiliation and/or the respective main outcome variable in the unadjusted analysis. The analysis specifically for participants with JIA was not adjusted in Paper I. Whereas, in Paper II and III, separate adjustments of the covariate's age and gender; additionally, in Paper II, separate adjustments of the mother's and father's educational level were performed.

3.6.4 Sample size calculation

The sample size calculation for this study is based on the estimation of caries and in accordance with the studies by Welbury et al. (94) and Leksell et al. (91). Welbury et al. (94) reported a mean dmft of 1.46 in the JIA group and a mean dmft of 0.56 in the control group, with corresponding SD of 2.58 and 0.96, respectively. Leksell (91) provided information on caries prevalence ($D_{3\text{-}5}MF>0$) in first permanent molars of 48.8% (20/41) in the JIA group and 26.8% (11/41) among the controls upon request (the published article did not include results suitable for sample size calculation). Results used for sample size calculations did not consider enamel caries (only caries at dentine level). The significance level was 5%, and the statistical power was 80%. The estimated sample size for the primary dentition assuming a two-sample t-test, was 75 participants in each group. The estimated sample size calculated assuming a chi-square test for the permanent dentition was 76 participants in each group. The suggested numbers of participants for the primary and permanent dentitions implied 182 participants in each group (JIA/controls), considering a dropout rate of 20% (missed/canceled appointments).

3.7 Ethical approval and considerations

The NorJIA study was approved (2012) by the Regional Committees for Medical and Health Research Ethics (2012/542/REC), Rogaland, Vestland (West). Also, prior to the study, approval was received by the chairs of different County Dental Health Authorities, at different Oral Health Centre of Expertise, and the three pediatric university departments.

The ethical considerations were in accordance with the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects (126) and the Norwegian Health Research Act (127). Children and adolescents constitute a vulnerable group, and if involved in research, they are especially entitled to protection. According to the United Nations Convention on the Rights of the Child (Articles 3 and 12) (128) and the Constitution of the Kingdom of Norway (§104) (129), the best interest of a child shall be the foundation of all actions involving children. Furthermore, children shall be allowed to be heard, and their views shall be emphasized according to their age and maturity. In research involving children and adolescents, their specific needs and interests must be secured by adapted practices compared to the standards provided to the adult population. Written informed consents (Appendix IV) was obtained according to the Norwegian Health Research Act (127). The autonomy of the 4-11-year-olds involved in the papers of this thesis required parents' or guardians' written informed consent to be able to participate. Amongst the 12-16-year-olds, written informed consent was obtained by the parents or guardians in supplement to written informed consent by the participants themselves; if the adolescents did not want their parents or guardians to be informed, this was abided by. Age-adapted information about the study was provided, also including information about the consequences of participation, information about participation being voluntary, and the possibility of withdrawal at any time without the need for justification, with a clarification of the withdrawal not to have any negative impact on future collaboration with the health-care system.

4. SUMMARY OF RESULTS

4.1 Sample characteristics

The response rate among the individuals with JIA was 63.3% (228/360) and 76.2% (224/294) among the controls. The mean age of the 132 eligible individuals with JIA who declined participation was 10.5 (SD=3.5) years (*vs.* 12.0 (SD=3.2) years among the participants (p<0.001)). The proportion of females was slightly lower amongst the individuals with JIA who declined participation compared to the participants with JIA (58.3% *vs.* 59.2%, p=0.027).

The socio-demographic distribution of the participants is shown in Table 6. Among the 224 pairs, 211 (94.2%) of the pairs were matched to the mother's background of origin (for ten individuals, the family name was evaluated). For 14 participants with JIA, the period from the medical to the dental examination exceeded one month (median of 1.13 months (minimum; 1.1, maximum; 3.7).

Table 6. Socio-demographic distribution among the participants in this study, according to group affiliation

Socio-demographic characteristics	JIA n=224	Controls n=224	p-value
Females, n (%)	133 (59.4)	134 (59.8)	0.923
Age (years), mean (SD)	12.02 (3.2)	12.01 (3.2)	0.974
Maternal education > high school, n (%)	137 (64.6)	153 (73.9)	0.039
Paternal education > high school, n (%)	88 (42.1)	117 (57.4)	0.001
Single caregiver household, n (%)	44 (20.4)	35 (15.8)	0.210

There were no participants with major medical comorbidities such as congenital facial anomalies, skeletal dysplasia, or malignancies in the study population. Table 7 shows concomitant diagnoses and medication use among the participants considered potential oral health risk factors.

Table 7. Concomitant diagnoses and medication use amongst individuals with JIA (n=224) and the controls (n=224) considered potential oral health risk factors.

	JIA, n	Controls, n
Allergy and/or asthma (on medication)	13	7
Autism spectrum disorder	0	1
Neurodevelopmental disability (sensory and motor disability)	1	0
Psychiatric conditions (on psychotropic medications) (Attention Deficit Hyperactivity Disorder (ADHD), depression and insomnia)[3]	4	2
Coeliac disease	5	0
Diabetes*	3	0
Down syndrome	2	0
Epilepsy**	1	1
Hypothyroidism***	2	0

The caregiver or participant recollected the information. The table does not include previous diagnoses, intermittent medication use, previous medication use, medication administered by eye droplets, or medications used in the treatment strategy of JIA (*e.g.*, antiemetic). *Insulin use. **No use of medication. ***Levothyroxine use.

Disease-specific characteristics of the participants with JIA (n=224) are shown in Table 8. Figure 6 shows the frequency distribution of the various JIA categories. Table 8 and Figure 6 are a supplement to the published papers of this thesis.

[3] The papers included in the thesis missed to impart one participant (≥10 years) in each study group on psychotropic medication. Correct number of individuals with JIA is 4 (as opposed to n=3) and among controls 2 (as opposed to n=1). Also, the papers did not impart medications administered by eye droplets as not considered.

Table 8. Disease-specific characteristics of the individuals with JIA receiving the oral health examination (n = 224).

Disease-specific characteristics	n	Values
Age at examination [a], median years, (IQR)	224	12.0 (9.4-14.7)
Age at disease onset, median years, (IQR)	224	6.4 (2.3-10.4)
Disease duration [a], median years, (IQR)	224	5.7 (2.7-8.3)
Not in remission off medication [b], n (%)	224	195 (87.1)
DMARDs, ongoing, n (%)	224	148 (66.1)
DMARDs, ever used, n (%)	224	171 (76.3)
Systemic steroids [c], ongoing, n (%)	224	4 (1.8)
Systemic steroids [c], ever used, n (%)	224	48 (21.4)
MDgloVAS>0, n (%)	224	80 (35.7)
MDgloVAS [d], mean (±SD)	80	1.4 (±1.1)
VAS pain>0, n (%)	219	137 (62.6)
VAS pain [e], mean (±SD)	137	3.2 (±2.1)
PRgloVAS>0, n (%) [4]	219	159 (72.6)
PRgloVAS [f], mean (±SD)	159	3.0 (±2.2)
CHAQ total score>0, n (%)	218	127 (58.3)
CHAQ total score [g], mean (±SD)	127	0.6 (±0.5)

IQR=inter-quartile range (25th-75th percentile). DMARDs = disease-modifying anti-rheumatic drugs, including both synthetic DMARDs (methotrexate, hydroxychloroquine, mycophenolate mofetil, and cyclosporine) and biologic DMARDs (etanercept, infliximab, adalimumab, tocilizumab, golimumab, certolizumab, abatacept, and rituximab). SD = standard deviation. MDgloVAS=physician's global assessment of disease activity visual analogue scale (VAS). VAS pain=patient/parent-reported pain intensity VAS. PRgloVAS= Patient/parent-reported global assessment of overall wellbeing VAS. All VAS scales were measured on a 21-numbered circle VAS 0-10 cm (0 = no pain, 10 = maximum pain). CHAQ=Childhood Health Assessment Questionnaire (0=no disability, 3=maximum disability). [a] Based on the day of the oral health examination. [b] Disease activity according to Wallace (118) and the American College of Rheumatology provisional criteria (19). [c] Systemic steroids include oral or intravenous corticosteroids. [d] Mean MDgloVAS of 80 participants assigned VAS>0. [e] Mean VAS pain of 137 participants reporting VAS>0. [f] Mean PRgloVAS of 159 participants reporting VAS>0. [g] Mean CHAQ total score of 127 participants reporting CHAQ>0.

[4] In Paper I and II, PRgloVAS is presented as a dichotomous variable; PRgloVAS>0 or PRgloVAS=0. The variable was, in fact, incorrectly dichotomized as PRgloVAS>1 or PRgloVAS≤1. Repeated analyses did not differ significantly with the correct categorizing of the variable (PRgloVAS>0 or PRgloVAS=0).

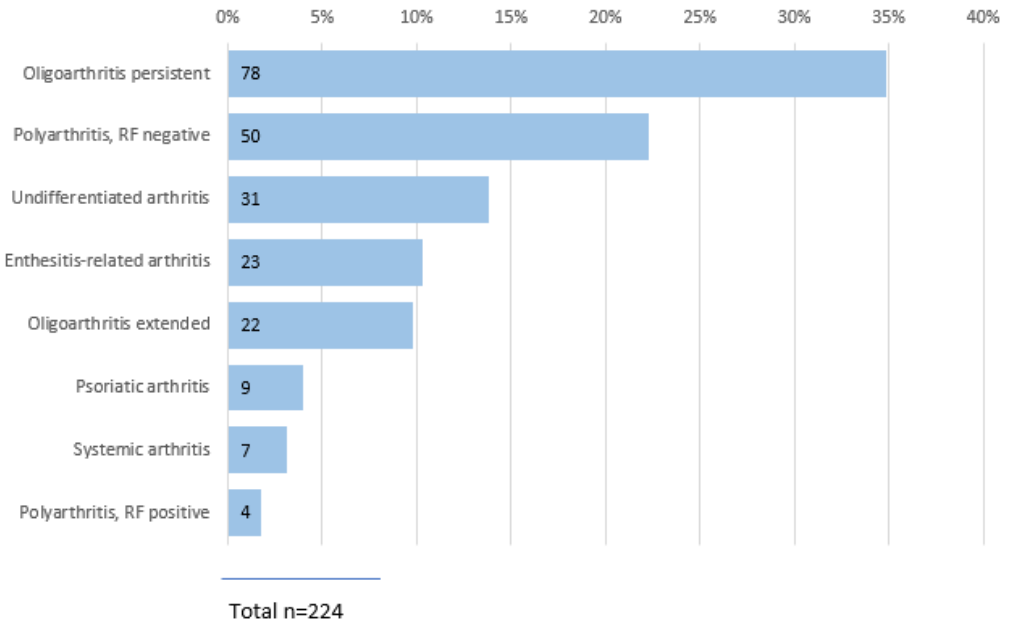

Figure 6. Number and percentage distribution of the different JIA categories according to the total sample of participants with JIA (n=224).

4.2 Paper I

Dental caries in children and adolescents with Juvenile Idiopathic Arthritis and controls: a multilevel analysis

The aims were to: explore whether caries is more prevalent among children and adolescents with JIA compared to matched controls; independent of JIA group examine the presence of caries according to socio-behavioral and intraoral (within mouth) characteristics and the extent to which surface-specific caries varies between and within individuals; assess whether surface-specific caries varies according to JIA group and dentition (primary/permanent molars); specifically for patients with JIA, investigate whether clinical features such as JIA category, age at onset of JIA, disease duration, use of medication, or remission status associate with the presence of caries.

The calibration process resulted in weighted Cohen's kappa values of 0.61 (Test Caries 1), 0.61 (Test Caries 2), 0.91 (Test Caries 3), and 0.65 (Test Caries 4).

No statistically significant difference in caries prevalence between individuals with JIA and controls was found [5]. The occlusal surface was most prone to caries in the primary and permanent dentitions (Figure 7).

Adjusted analyses showed no statistically significant association between JIA status and the presence of caries (OR=1.02, 95% CI: 0.62–1.66). A lower maternal educational level was associated with the presence of caries, independent of JIA group affiliation (OR=2.07, 95% CI: 1.24–3.46, p=0.01). Also, independent of group affiliation, compared to the buccal surface (primary and permanent dentition combined), the occlusal and mesial surfaces had statistically significantly higher odds of caries (OR=5.06, 95% CI: 3.76–6.83 and OR=1.66, 95% CI: 1.21–2.29, respectively), and the distal and lingual surfaces had statistically significantly lower odds of caries (OR=0.40, 95% CI: 0.27–0.61 and OR=0.63, 95% CI: 0.43–0.91, respectively). In the multilevel model (presence of caries in primary and permanent dentition independent of group affiliation) with no covariates, the ICC at individual level was 0.52, and in the adjusted analysis, the ICC was 0.56. The ICCs were statistically significant ($p<0.01$).

There was a robust trend for increased risk of mesial approximal caries (mesial surfaces compared to the buccal surfaces) in the permanent molars of the JIA group compared to the control group. Analysis showed a significant interaction between the surfaces in the permanent dentition and group affiliation (JIA/control group) ($p<0.01$) on the presence of caries. In contrast, the corresponding interaction was nonsignificant in the primary dentition (p=0.66).

With the primary and permanent teeth combined, no statistically significant associations were found between the JIA-specific variables and caries. However,

[5] In the published paper, caries prevalence at the individual level did not take into account the five participants not receiving the caries examination (analyses included 219 individuals with JIA, not 224); in addition, a small error in the calculations was observed. Consequently, the results concerning caries experience in one or more first permanent molars were at $D_{1\text{-}5}F$-level; 52.9% (83/157) (as opposed to 82/162 in the published article) amongst individuals with JIA and 50.6% (82/162) (as opposed to 81/162) amongst the controls. At $D_{3\text{-}5}F$-level the corresponding figures were 36.9% (58/157) (as opposed to 57/162) and 30.2% (49/162) (as opposed to 46/162), respectively. In the primary dentition, incorrectness in calculations only applied to the $d_{3\text{-}5}f$-level in one or more primary second molars: 8.2% (5/61) (as opposed to 4/61) amongst individuals with JIA and 12.9% (8/62) (as opposed to 7/62) amongst the controls.

analyzing the dentitions separately, the category oligoarthritis extended (n=8) had statistically significant higher odds for caries compared to oligoarthritis persistent (n=22) in the primary dentition (OR=20.82, 95% CI: 1.57–275.42)[6]. As for the permanent dentition, the category polyarthritis RF negative (n=33) had statistically significant higher odds for caries compared to oligoarthritis persistent (n=55) (OR=2.48, 95% CI: 1.13–5.45). Also, in the primary dentition, individuals assessed with MDgloVAS score>0 (n=21) had statistically significantly higher odds for caries (OR=5.78, 95% CI: 1.04–32.28) than individuals with MDgloVAS score=0 (n=40). No strong conclusions concerning associations between the presence of caries and JIA-specific features can be drawn because of the low number of participants in some categories.[7]

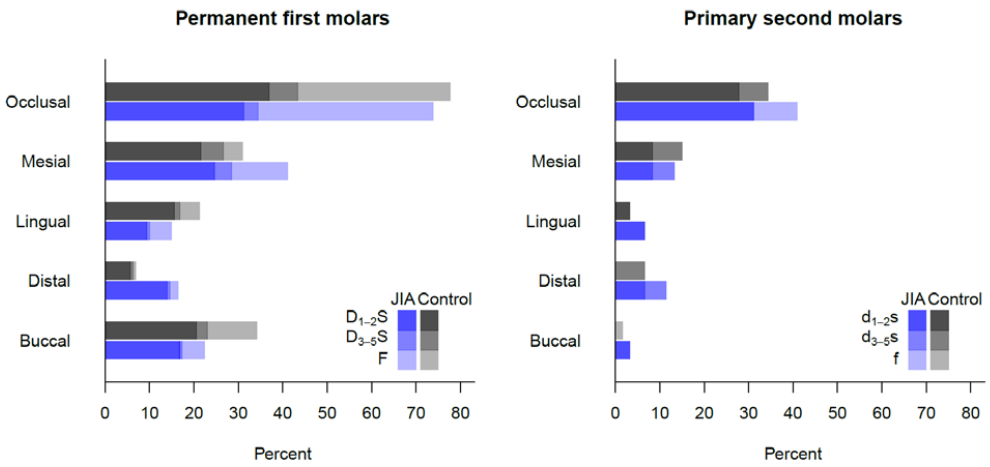

Figure 7. Distribution of $d_{1\text{-}5}fs$ and $D_{1\text{-}5}FS$ indices according to tooth surface separately for participants with and without JIA.

[6] No participants (<10 years) diagnosed with Enthesitis-related arthritis (n=2) experienced caries in the primary dentition ($d_{1\text{-}5}fs$); hence the participants diagnosed with Enthesitis-related arthritis were excluded in the multilevel model regressing the presence of caries in the primary dentition on JIA category. The published Paper (Paper I) missed imparting this information.

[7] In the analyses of the self-reported global disease-specific impact on well-being, PRgloVAS was mistakenly dichotomized as VAS>1 or VAS<1, not VAS>0 or VAS=0, as presented in Paper I. By analyzing the variable according to correct categorization, result do not vary of significance compared to results published.
(With reference to VAS<1, OR for VAS>1 is 1.24 (95% CI: 0.67-2.29), p=0.488 *vs.* with reference to VAS=0, OR for VAS>0 is 0.92 (0.46-1.81), p=0.797)

4.3 Paper II

Dental plaque and gingival bleeding in adolescents with juvenile idiopathic arthritis and controls: a multilevel analysis

The aims were to: explore whether plaque and gingival bleeding are more frequently experienced by adolescents with JIA compared to matched controls without JIA; explore whether surface- and site-specific periodontal outcomes vary between the two groups; specifically for participants with JIA investigate possible associations between disease-specific features and the periodontal outcome variables.

Plaque and gingival bleeding were more frequently experienced in JIA individuals than in controls without JIA. The modified OHI-S score in the two groups was statistically significantly different, with a mean score of 0.69 (SD 0.39) amongst individuals with JIA and 0.57 (SD 0.42) amongst the controls. The OHI-S score had a beta (mean difference between individuals with JIA and controls) of 0.12 (95% CI: 0.03 –0.21) (p=0.010). The mean percentage score of the modified GBI showed a significantly higher value in individuals with JIA than in controls (17.72 (SD 16.83) *vs.* 12.56 (SD 14.32), p=0.004). The GBI score had a beta of 5.16 (95% CI: 1.67–8.66) (p=0.004).

Adjusted analyses showed a statistically significant association between JIA status and OHI-S>0 (OR=2.33, 95% CI:1.47–3.67) and between JIA status and GBI>0 (OR=1.54, 95% CI:1.10–2.16).

In the multilevel model with OHI-S>0 as the outcome variable (independent of group affiliation), the ICC at the individual level with no covariates was 0.32. In the adjusted analysis, the ICC was 0.45. Corresponding ICC with GBI>0 as outcome variable were 0.29 and 0.30, respectively. The ICC at tooth level with GBI>0 as the outcome variable (independent of group affiliation) was 0.43 with no covariates. In the adjusted analysis, the corresponding ICC was 0.41. The ICCs were statistically significant (p<0.001).

There was a significant interaction between surface and group affiliation ($p<0.001$) on OHI-S>0. In contrast, the interaction between surface and group affiliation, and site and group affiliation, on GBI>0 were nonsignificant ($p=0.351$ and 0.27, respectively). Figure 8 and Figure 9 depict the prevalence (with error bars) of OHI-S>0 at the surface level and GBI>0 at the site level, separately for participants with and without JIA.

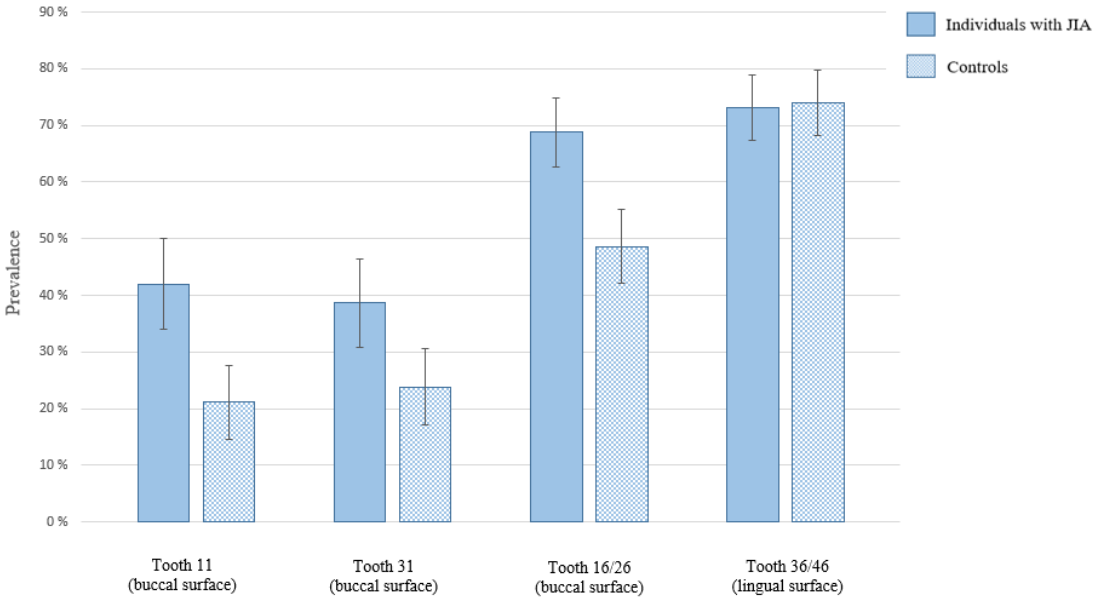

Figure 8. Percentage (95% CI represented as error bars) of plaque or calculus (OHI-S > 0) at surface level among participants with JIA and controls.

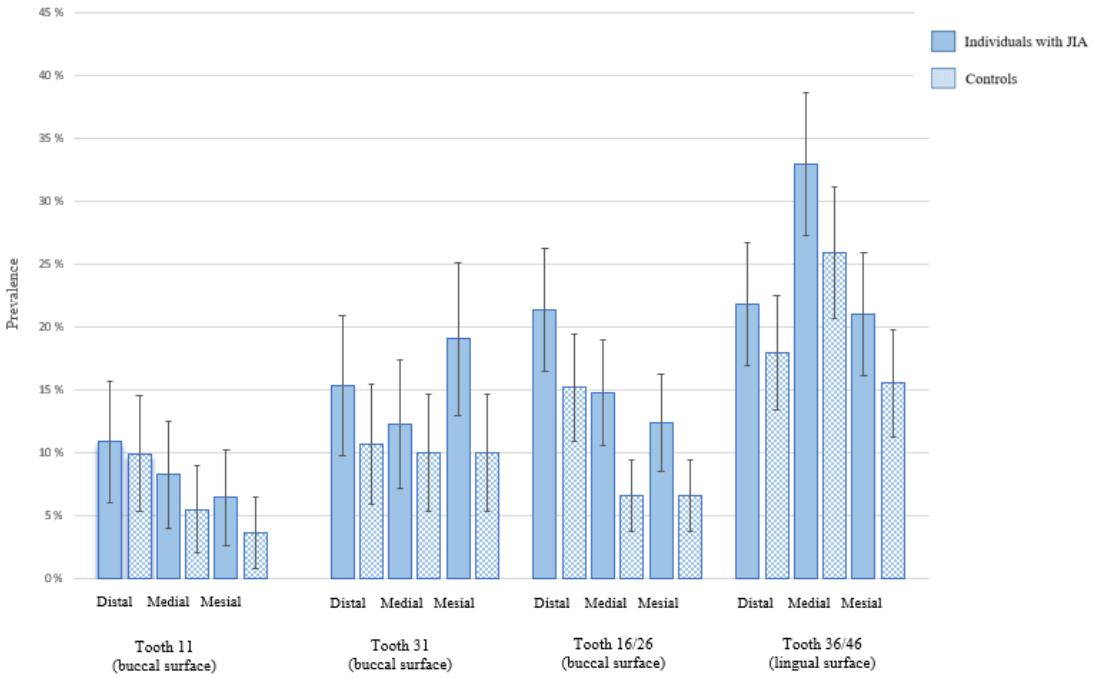

Figure 9. Percentage (95% CI represented as error bars) of gingival bleeding (GBI>0) at site level among participants with JIA and controls.

Adjusted analyses showed statistically significantly higher odds of OHI-S>0 in individuals with systemic arthritis (n=5) than in individuals with oligoarthritis persistent (n=50) (OR=5.20, 95% CI: 1.07 –25.32). According to the CHAQ hygiene item Tooth brushing, participants reporting difficulties with tooth brushing (n=7) had a statistically significantly higher odds of GBI>0 than participants reporting no difficulties (n=148) (OR=2.92, 95% CI: 1.14 –7.45).

No conclusions can be made due to the small number of participants in some categories. Individuals aged>6 years at JIA onset (n=94) had a statistically significantly higher odds of plaque OHI-S>0 in the adjusted analysis compared to individuals aged≤6 years at JIA onset (n=50) (OR = 1.80, 95% CI: 1.08 –3.00). [8]

[8] In the analyses of the self-reported global disease-specific impact on well-being, PRgloVAS was mistakenly dichotomized as VAS>1 or VAS<1, not VAS>0 or VAS=0, as presented in Paper II. By analyzing the variable according to correct categorization, results do not vary in significance compared to published results.

4.4 Paper III

Oral health-related quality of life in 4-16-year-olds with and without juvenile idiopathic arthritis

The aims were to: investigate whether OHRQoL, assessed by the ECOHIS and Child-OIDP scale, differs between children and adolescents with JIA compared to controls while adjusting for socio-demographic-, behavioral- and oral health-related covariates; explore whether socio-behavioral and oral health-related covariates of OHRQoL vary according to group affiliation; specifically for individuals with JIA, investigate whether disease-specific features associate with OHRQoL.

Internal consistency reliability of the ECOHIS total score in terms of Cronbach's alpha was 0.87 in participants with JIA and 0.79 in the control group, corresponding results for Child-OIDP SC score were 0.83 and 0.79. The ECOHIS family impact score>0 was more frequently reported among participants with JIA (45.8% *vs.* 25.5%, $p<0.05$). The Child-OIDP SC did not differ significantly between the adolescents with and without JIA. However, a pattern of more frequent impacts was observed in the JIA group compared to the controls.

Analyses regressing impacts of the OHRQoL inventories (ECOHIS total score>0, Child-OIDP SC score>0) on JIA status while adjusting for socio-, behavioral and clinical covariates showed no statistically significant association between JIA status and impaired OHRQoL (OR=1.95, 95% CI: 0.94–4.04 and OR=0.99, 95% CI: 0.46–2.17, respectively) by ordinary logistic regressions. However, adjusted negative binomial regressions showed a statistically significant increased incidence rate ratio of negatively impacted ECOHIS among participants with JIA compared to controls (IRR=1.61, 95% CI: 1.16–2.23).

Independent of group affiliation, adjusted regression analyses showed statistically significant higher odds of impaired OHRQoL (ECOHIS total score>0) among 4-11-year-olds with caries ($d_{1\text{-}5}ft/D_{1\text{-}5}FT>0$) compared to peers without caries ($d_{1\text{-}5}ft/D_{1\text{-}}$

(Adjusted analyses with OHI-S as outcome variable: With reference to VAS<1, OR for VAS>1 is 0.86 (95% CI: 0.52-1.40), p=0.534 *vs.* with reference to VAS=0, OR for VAS>0 is 0.80 (0.46-1.40), p=0.431.
Adjusted analyses with GBI as outcome variable: With reference to VAS<1, OR for VAS>1 is 0.98 (95% CI: 0.64-1.50), p=0.924 *vs.* with reference to VAS=0, OR for VAS>0 is 1.02 (0.64-1.65), p=0.925)

$_5$FT=0) (OR=3.39, 95% CI: 1.40–8.22). Adolescents reporting pain or discomfort during toothbrushing showed statistically significantly higher odds, and adolescents reporting low maternal educational levels showed statistically significantly lower odds of impaired OHRQoL (Child-OIDP SC score>0) (OR=7.76, 95% CI: 3.09–19.50 and OR=0.32, 95% CI: 0.13–0.82, respectively).

No inequalities in OHRQoL related to socio-behavioral and health-related characteristics were observed between the two groups. But there was a statistically significant interaction between group affiliation and gender on impaired OHRQoL (Child-OIDP SC score>0) among the adolescents. Stratified regression analyses showed that females had a higher odd ratio of having a Child-OIPD SC score>0 than males among participants with JIA (OR=6.12, 95% CI: 2.29–16.30, p<0.001). The corresponding association in the control group was not statistically significant (OR=1.23, 95% CI: 0.52–2.90).

Adjusted analyses, specifically targeting the 4-11-year-olds with JIA showed associations between impaired OHRQoL (ECOHIS total score>0) and ongoing and ever-used bDMARDs (OR=7.59, 95% CI: 1.77–32.67, p=0.006 and OR=9.20, 95% CI: 1.93–43.97, p=0.005). Adolescents categorized 'not oligoarthritis persistent'[9] showed a statistically significant higher odds of having Child-OIDP SC>0 than participants in the JIA category oligoarthritis persistent by adjusted analyses (OR=6.29, 95% CI: 1.83–21.63). Also, adolescents with continued activity or flare of the disease had a statistically significant higher odds of having Child-OIDP SC>0 than participants with inactive or disease in remission (OR=3.01, 95% CI: 1.15–7.89). The same applied to self-reported pain (VAS pain>0), compared to no pain (VAS pain=0) and self-reported physical disability (CHAQ>0), compared to no disability (CHAQ=0) (OR=4.39, 95% CI: 1.20–16.14 and OR=4.21, 95% CI: 1.40–12.68, respectively).

[9] The category 'not oligoarthritis persistent' comprises the JIA categories oligoarthritis extended, polyarthritis RF positive and RF negative, psoriatic arthritis, and enthesitis-related arthritis.

5. DISCUSSION

This section considers the methodological aspects of this study, followed by a discussion of Paper I-III's main findings and implications for oral health intervention and future research in children and adolescents with JIA.

5.1 Methodological considerations

5.1.1 Study design

This study might be classified as an epidemiological study of comparative cross-sectional design. Cross-sectional studies are observational, and all variables of interest are measured at a single point in time. Usually, cross-sectional studies are descriptive and performed to support public health planning by estimating the prevalence of the outcome for a given population and generating hypotheses for future research, requiring relatively limited resources (130). Observational studies can also be analytical, and a key feature is a comparison group (131). Including a comparison group in the present study facilitates hypothesis testing and exploring associations between risk factors and oral health. However, cross-sectional studies are limited in drawing valid inferences about cause and effect because single-point measures restrict knowledge of how the variables reflect the past. For that reason, causal relationships between exposures and outcomes cannot be established in this study (130).

5.1.2 Internal validity

Internal validity refers to the extent a study is free from bias or systematic errors (132). There are three broad categories of bias in epidemiologic studies: selection bias, information bias, and confounding (133).

Selection bias (systematic error)

Distortion of an association between exposure and outcome due to the procedures used to select individuals (into study or analysis) is defined as selection bias (133). Selection bias, threatening this study's validity (internal and external), was minimized by inviting all children and adolescents diagnosed with JIA affiliated to the regional

pediatric rheumatology centers involved in this study (census). Two cinema tickets were given to the controls as an incentive for participation to minimize the selection bias. However, the effect incentives have on the quality of the response (*e.g.*, questionnaire) is not well known (134).

Information bias (systematic error)

Information bias, error in collected information, was attempted to be reduced in the clinical act of data measures by thorough standardization of the examination protocols and by implementing well-established and internationally acknowledged indices. The instruments employed to measure the outcome variables in this study are widely used diagnostic tools (47, 49, 122-124). 10% of the data input was rechecked to control acceptable quality in data entry.

Information bias in the clinical oral health outcomes

The caries diagnostic tool (122) collected by dmf/DMF-Index is a well-known and used index for caries measures in epidemiological studies (135). The applied five-graded caries diagnostic tool (122) may be subject to misclassification, and calibration was therefore addressed. OHI-S and GBI are also frequently used epidemiological indices. They are rather easy to conduct and have acceptable reproducibility, especially scoring criteria of GBI are simple to interpret and are considered to be relatively insensitive to examiner variability (136, 137). This study is part of an extensive oral examination. The periodontal indices (OHI-S and GBI) were modified, and only index teeth were evaluated to avoid exhausting the participants and to account for various shedding and eruption stages. This complicates comparisons with other studies and the accuracy at individual level is reduced when practicing partial mouth protocols. Index teeth susceptible to caries were selected to secure sensitivity (138, 139). The simplified version of OHI is a shortfall of the high degree of sensitivity compared to the original index (12 teeth/surfaces are scored, as opposed to six); however, reasonable sensitivity is demonstrated (123). The literature emphasizes the need for full-mouth protocols to evaluate a gingivitis case, and by assessing index teeth, this study only provides site prevalence of gingivitis (36). However, a full-mouth protocol was not accomplishable

in this study considering time sources available. Another source of information bias was the examiners' non-blinding, which might have introduced observer bias and increased the possibility of misclassification (140).

Information bias in the self-reported oral health outcomes

Child-OIDP mainly focuses on behaviors that are easier to measure reliably than thoughts and symptoms. ECOHIS provides proxy reports (*i.e.*, informants are a parent or a caregiver), and originally, the target group of ECOHIS was preschool children (49). The accuracy of proxy reports, especially in older children, is uncertain. The literature points to various levels of agreement of the OHRQoL reported by the parent and the child. There is a tendency for parents to underestimate children's OHRQoL impacts, possibly due to restricted knowledge of the parent concerning children's social and emotional well-being (141). A consensus exists of children reliably communicating their health and experiences around age six; however, OHRQoL measures adapted for child self-reports in preschool children exist (*i.e.*, Michigan-OHRQoL and SOHO-5) (142). The OHRQoL inventories employed are translated to Norwegian and validated in a general local population of Norwegian children and adolescents, 4-11-years-olds for ECOHIS and 12-18-years-olds for Child-OIDP (14). In the present study, ECOHIS and Child-OIDP demonstrated discriminant- and construct validity, indicating satisfactory psychometrical properties of both instruments among children and adolescents with JIA in this study population. Internal consistency reliability of the OHRQoL inventories (*i.e.*, the consistency of results across the items of the inventory) was assessed by Cronbach's alpha, yielding satisfactory internal consistency of the results (143).

A standardized questionnaire was used to gather socio-behavioral and subjective clinical information. The phrasing of these questions was adapted to the target population's vocabulary; the items utilized were not apparently leading and did not concern the participant's attitudes or viewpoints; instead, easy questions were mainly directed at behaviors or perceptions of oral health. Recall bias may be present in the self-reported oral health outcomes, depending on the ability of the participants to

recall past events. The time aspect of ECOHIS includes the child's entire life experience of dental problems and dental treatments; Child-OIDP recalls the adolescent's past three months concerning difficulties performing daily activities. Due to subject non-anonymity, social desirability bias (*i.e.*, under-report socially undesirable and over-report more desirable attributes) may have accompanied the responses. The personal interview (Child-OIDP) was probably more subject to underreporting bias than the self-reported questionnaires distributed either in a printed form during the examination or via the internet (140).

Confounding

Confounding means distortion or confusing, mixing of an association, and occurs when a factor associates with (or causes) both exposure and outcome and is not on the causal path between them; the effect of the exposure on an outcome is, therefore, influenced by other variables and leads to bias (133, 144). As part of the study design, individual matching of the participants with JIA and the controls initially accounted for potential confounding factors. Analyses in Paper I-II revealed a weak correlation between the matching pairs, indicating the background variables sex, age, center site, and background-origin (western/non-western) were not sufficient matching variables for caries and the periodontal outcomes. However, matching 'harmonized' the data and allowed fewer potential confounding variables to be included in the adjusted analyses. Multiple variable regression analyses employed in this study further accounted for possible confounding factors. The selection of possible confounding variables in the multiple variable regression analyses was broadly statistic-based with an applied significance criterion ($p\text{-value}<0.05$) for the association between the possible confounding variable and the respective oral health outcome and/or for the association between the possible confounding variable and the main exposure, the group affiliation. The adjustment-variable selection approaches are usually backgrounded knowledge or statistics-based, with associated strengths and shortcomings (145, 146). Oral health research is complex due to the multifactorial nature and the dynamic multilevel interplay between them (56). Within the limits of this study, confounding factors are well controlled for, but assuredly hidden factors

associated with the outcomes have not been evaluated. Thus, we cannot rule out the possibility of unadjusted confounding in our data.

Reliability

The internal validity relies on the reliability of the data collected. Reliability refers to the extent of consistency exhibited for repeated measurements under similar conditions (147). Extensive training and various sessions of calibration of the dentists collecting clinical data facilitated good reliability of the data. Inter- and intra-examiner analyses were also performed to ensure the caries measures used in the study had a high degree of consistency. Inter-examiner (Cohen's kappa value of 0.61) and intra-examiner (Cohen's kappa value of 0.91) tests showed a "substantial" and "almost perfect" strength of agreement, respectively (148). An evaluation of the examiner's ability to repeat the measures of an expert reference was conducted in two sessions, demonstrating "substantial" repeatability (Cohen's kappa value of 0.61 and 0.65) (148). As deposits are manipulated, repeated measurements of the hygiene level by running an explorer along the tooth surface to determine examiner repeatability are challenged by subsequently lower plaque scores (149). Similarly, repeated probing of the gingival sulcus may lead to gingival irritation and result in increased scores in subsequent measures (147). Consequently, a test of repeated measurements was not conducted for the periodontal indices; instead, thorough standardization of the indices and practicing the force to apply while determining gingival bleeding (digital letter scale).

5.1.3 External validity

External validity refers to the extent results of the study are representative of the population from which the study participants emanate; internal validity is a prerequisite for the study's external validity (132). This study's representativeness is based on the population of children and adolescents with JIA referred to three (northern, central, and western Norway) out of four existing regional pediatric rheumatology centers in Norway.

Possible impairment of the generalizability should not be ignored due to non-response. Considering the response rate among the individuals with JIA (63.3%), we estimated slight but statistically significant differences in age and sex between the nonparticipants and the participants with JIA. Age and gender disparities in pediatric oral health may occur (150), and the study results may have differed in case of a higher response rate. The response rate among the controls was acceptable (76.2%) (151).

5.1.4 Hierarchical data and cluster effect

Random errors are variations in measured data due to chance. In a study free from bias, two types of random errors can arise during hypothesis testing: type I and type II errors (152). The statistical measure, p-value, is used to accept or reject the null hypothesis (133). The p-value is a standardized measure of how well the observed data fit the null hypothesis (153). Type I error declares a difference or relationship (rejecting the null hypothesis) when there is no difference or relationship (false-positive) (154). In dental research, the clustered observations within the same subject is often not accounted for, and type I error may increase (155). Standard statistical methodology, not accounting for the cluster effects within the same individual, treats the data as independent observations; data is handled as if the sample size is more powerful than the real effective size. Clustering effects occurred in the data of Paper I-II, since measures from multiple sites/surfaces and multiple teeth from each participant were analyzed. Multilevel modeling was applied to adjust for the independency in measures arising from clustering (of sites/surfaces within teeth, and teeth within subject) and to provide accurate standard errors, hence more precise CI and significance tests (156). Clustering is a common finding in oral health research and must be resolved; however, shortcomings in accounting for clustering effects are evident in published studies in leading dental specialty journals (157). Applying the RIM resulted in optimal data exploration, and the REML method also account for randomly missing data, further strengthening the statistical power. Type II error declares no difference or relationship (failing to reject the null hypothesis) when there is a difference or relationship (false-negative), and the likelihood of type II error

increases if the sample size is too small (154). In a clustered sample (*i.e.*, individuals clustered within the study population), a higher sample is needed to account for the independence of the individuals within the study population. In Paper I and II, a weak correlation between the matching pairs was revealed, and potential cluster effects between the individuals within the study population were negligible with reference to caries and periodontal outcome variables. Caries figures were the basis for the sample size calculation in this study. No extra sample size calculations were performed for the periodontal and OHRQoL outcomes (Paper II-III), as related studies with a similar target group and outcome measures were lacking.

5.2 Discussion of the main results

Some findings in this thesis call for action by intervention and future research in young individuals with JIA and are discussed in the following subsections.

5.2.1 Participants with JIA are more vulnerable to plaque and gingival bleeding but not to caries and impaired OHRQoL compared to controls without JIA

The principal hypothesis of this thesis, "children and adolescents with JIA have poorer oral health status than controls without JIA," was confirmed for plaque and gingival bleeding but not for caries and OHRQoL. However, according to the ECOHIS, this conclusion is unsure since the adjusted binomial regression analyses showed an increased risk of impaired ECOHIS scores amongst the 4-11-year-olds with JIA compared to controls. The result of JIA patients being more susceptible to plaque accumulation and gingival bleeding is in line with other studies reporting a more frequent occurrence of plaque (87, 91, 94, 105, 158) and gingival bleeding (66, 67, 91, 92, 94) in children and adolescents with JIA compared to healthy peers. The present study evaluated aggregated periodontal patient-level measures, and mixed-effect logistic regressions verified the results, providing a well-founded basis for confirming the hypothesis. SES, including parental educational level, has been shown to predict adolescents' oral health behaviors (159). In this study, parental educational

level was found to be lower among the participants with JIA than in the controls. Only maternal educational level was associated with gingival bleeding and included as a possible confounding factor in the adjusted analyses; however, adjusted analyses did not affect the association between JIA group status and gingival bleeding. There are likely other possible confounding factors in the relation between JIA group status and the periodontal outcomes of social and behavioral character not comprehended in this study. *E.g.*, JIA children experience psychological difficulties (100, 160), hampering their self-esteem (160), which is an identified protective factor to oral health behaviors in children (161). Although, the self-reported frequency of brushing and flossing teeth was similar between the two groups, it is reasonable to uphold plaque-induced gingivitis as an explanation for interpreting increased gingival bleeding among the participants with JIA. However, a NorJIA-study by Frid et al.(80) analyzed the salivary oral microbiome of some participants included in this study (n JIA=59, n controls=34). A higher abundance of microbiota associated with chronic inflammation was identified among the participants with JIA, and it was suggested that this occurred due to dysbiosis of the salivary microbiome in JIA. Grevich et al. (66) have suggested microbiota as a potential contributing factor to JIA's disease pathogenesis and gingival bleeding among adolescents with JIA. Another NorJIA-study by Cetrelli et al. (162) investigated the vitamin D status and its possible relation with clinical indicators of oral health among the participants with JIA included in this study (n=221). Results demonstrated an association between serum Vitamin D insufficiency and gingival bleeding. Nutrition, including vitamin D, plays a valuable immunomodulatory role (163). Individuals with JIA are perhaps more at risk of gingival bleeding due to less resistance to a disrupted symbiosis between the biofilm and host immune-inflammatory response, known to cause gingivitis (34). Some studies report significantly more findings consistent with periodontitis (75, 76, 91, 105) in adolescents with JIA compared to healthy peers. Gingival inflammation is considered a precursor of periodontitis; hence managing gingivitis is a critical primary prophylactic strategy for periodontitis and progressive attachment loss around teeth (34). A meta-analysis from 2011 (40) "showed that plaque accumulation and gingival inflammation scores significantly increased the prevalence of

bacteraemia following toothbrushing". Considering the immunocompromised state of many young individuals with JIA on immunomodulatory treatment, this thesis demonstrates the need for improved oral hygiene among individuals with JIA to maintain good oral health, control plaque-induced gingivitis and prevent periodontitis.

This thesis observed no difference in caries prevalence between individuals with JIA and controls, and no association between group affiliation and the presence of caries was found after adjustment for possible confounding factors. There has been an overall decline in caries among children in many developed countries (164). This trend is also evident in the literature focusing on dental caries in young individuals with JIA; older studies (before the 21st century) report a high prevalence of caries among individuals with JIA (104, 108, 112, 165), whereas the majority of studies performed in the 21st century, including a comparison group without JIA, report no significant difference in caries experience (66, 87, 88, 91, 103, 106). The new era of bDMARDs and the swift toward more early aggressive therapeutic approach the recent years have demonstrated a reduction of the detrimental effects of the disease (12), hence a plausible contributing factor of comparable caries status between participants with JIA and controls. In the present study enamel caries was included. Initial caries lesions have been scarcely evaluated in individuals with JIA (91). By only scoring dentine lesions, the caries prevalence will become underestimated, and evaluating enamel caries can illustrate the potency of preventive actions; the predominance of enamel lesions in this study demonstrates the potential of preventive dental strategies. Independent of group affiliation, low maternal educational level was associated with the presence of caries. Despite government-sponsored dental services often providing regular free dental checkups for children and adolescents in Nordic countries, low SES is an acknowledged risk factor for caries (166-168).

Concerning OHRQoL, the proportions of individuals confirming impacts according to ECOHIS and Child-OIDP scores tended to be consequently higher among participants with than without JIA, but neither scale score varied by group affiliation in the adjusted logistic regression analyses. However, adjusted binomial regression

analyses showed an increased risk of impaired ECOHIS scores amongst the 4-11-year-olds with JIA compared to controls. It should be emphasized that sample size calculation based on OHRQoL as an outcome has not been employed; hence the analyses on OHRQoL might be underpowered, increasing the risk of Type II errors. The OHRQoL inventories aim to capture the physiological- and psycho-social function of oral diseases and is one dimension included in the concept of oral health (26). Among previous studies focusing on OHRQoL in young individuals with JIA, different OHRQoL instruments are employed, socio-demographic- and behavioral covariates are not accounted for, and the participants were categorized according to other clinical indicators of oral health (*e.g.*, JIA+TMJ arthritis, JIA+periodontitis) (67, 72, 82, 107). This complicates comparison with the present findings. This study found caries associated with impaired ECOHIS in adjusted analyses independent of group affiliation. However, no difference in caries prevalence between the two groups was found. As documented in separate NorJIA studies, we know that the individuals with JIA included in this study were more prone to TMD and gingival bleeding than the controls (111, 169). Also, we know TMJ involvement among the study group was relatively frequent and may have compromised facial growth and affected the occlusal development (unpublished NorJIA data). Insufficient power in the analyses or the inability of the generic instruments to identify or distinguish between the levels of TMD symptoms, gingival bleeding, and plausible malocclusions may be why OHRQoL did not discriminate significantly between the individuals with JIA and controls in this study; conversely, the described oral conditions simply did not impact the participant's OHRQOL. Including these clinical indicators of oral health (TMD, TMJ involvement, malocclusion) would strengthen the understanding but was not an objective of the paper. An objective was to explore whether socio-behavioral and oral health-related covariates of OHRQoL vary according to group affiliation. Adjusted analyses did not reveal significant interactions (between socio-behavioral/oral health related characteristics) and group affiliation on OHRQoL suggesting that inequalities in OHRQoL related to socio-behavioral and oral health-related characteristics did not differ by group affiliation in this study. However, female adolescents with JIA were more likely than males to

report oral impacts; the corresponding association in the control group was nonsignificant, demonstrating more gender variation in oral health in the JIA group. Perhaps females are more conscious of problems and appearance (170, 171). Why this gender difference is more apparent in the JIA group may rely on symptoms of pain and depression, known to impact their QoL, are common (172-174). Furthermore, although conflicting, literature indicates that such symptoms are more frequently expressed in females than males, and this trend seems to emerge in their adolescent years (175-180).

5.2.2 Surface-specific caries and plaque varied according to group affiliation

Multilevel modeling facilitated the detection of surface-specific patterns of caries, plaque, and gingival bleeding, independent and dependent on group affiliation. Surface-specific exploration of oral health outcomes in young individuals with JIA is a valuable contribution as it has not been conducted before.

Surface-specific caries in the permanent dentition differed significantly according to group affiliation. A robust trend for increased risk of mesial caries (compared to buccal) in the permanent molars of the JIA group was demonstrated. Effective preventive strategies, *e.g.*, fissure sealants, do not apply to approximal lesions; preventing progression of these lesions demands continuous effort from the patient (*e.g.*, tooth flossing). Approximal composite restorations are associated with increased caries of adjacent surface (181) and future periodontal attachment loss as observed in adults (182). Preventive actions to avoid interproximal invasive procedures among individuals with JIA are stressed.

In this study, molars presented a higher risk of plaque than anterior teeth for both groups. This accords with previous studies assessing regional differences in plaque accumulation within the dentition among young adults in a total absence of oral hygiene and if the participants performed oral hygiene without special instructions (183, 184). Still, only the control group had an increased risk of plaque in the mandible compared to the maxilla, a previously demonstrated pattern in a general

population (183-185). Surface-specific exploration illustrated a substantially higher proportion of plaque on the buccal surface of first permanent molars in the maxilla in participants with JIA (Figure 8). Poorer oral hygiene in young individuals with JIA compared to healthy peers is typically linked to limited oral hygiene ability due to upper limb dysfunction and pain (91, 94). The advancement of therapeutic strategies in JIA management has considerably improved the outcome of JIA disease in recent years (12). This implies joint dysfunction is no longer such an apparent explanation for poorer oral hygiene. In addition to oral hygiene procedures, other host factors may contribute to the amount of plaque accumulation, *e.g.*, diet, composition and amount of saliva, inflammation of the gingiva, the effect of chewing and soft tissue movements, and the microbial composition of the biofilm itself (185, 186). Salivary abnormalities (*i.e.*, composition and flow) in children and adolescents with JIA are described in the literature (85-89, 104, 187). High concentrations of various salivary matrix metalloproteinases, correlated to OHI-S and clinical indicators of gingival bleeding, are postulated to be caused by reduced saliva production as a sequela of the JIA disease (102). Considering the crucial role saliva plays in dental plaque formation (188), the proximity of the orifice of the parotid duct to the buccal surface of the first molars may be a postulation of considerably higher proportions of plaque in the JIA group on this surface in this study. The surface-specific plaque distribution differed significantly between the two groups, and one might speculate biological host variations contribute to the differences in distribution and amount. Plaque's nature fluctuates, and only longitudinal studies can reveal such connections.

5.2.3 Certain JIA-specific features seem to increase JIA individual's susceptibility to impaired oral health

Most studies focusing on oral health among children and adolescents with JIA include a description of disease-specific characteristics, *e.g.*, JIA category, anti-rheumatic medication, functional impairment, activity, and the onset of the disease. However, few studies further assess the relationship between oral health outcomes and disease-specific characteristics (101).

In this study, participants diagnosed with oligoarthritis extended and polyarthritis RF negative were more likely to have caries in the primary and permanent dentition, respectively, than participants with persistent oligoarthritis. Savioli et al. (103) also found that participants with polyarthritis RF negative had higher caries experience compared to controls without JIA. Although samples in the subgroups are limited, hindering conclusions, a trend toward increased caries in subgroups consistent with a more severe disease course is apparent. This trend was substantiated by a positive association between the MDgloVAS and the presence of caries in the primary dentition. Pugliese et al. (106) also found MDgloVAS to be positively correlated with caries experience in female adolescents. Analyses in this study showed no statistically significant associations between the JIA-specific variables and caries primary and permanent teeth combined. In light of the differences in the dentitions (*i.e.*, primary teeth are more prone to caries than permanent teeth) (189), the merit of implementing both dentitions in research exploring caries in young individuals with JIA is accentuated.

Small numbers in subcategories of the disease-specific features also prevented conclusions related to plaque and gingival bleeding. However, the increased likelihood of plaque in participants more than six years at JIA onset, compared to younger age at JIA onset, should be noted. Some studies propose mechanisms of JIA disease to differ according to age at onset (190), but it is hard to make any presumption concerning this finding. One might anticipate a difference in JIA disease duration or age between the participants in the corresponding dichotomized categories (≤ 6 years or > 6 years at JIA onset). Additional analyses revealed a statistically significant difference in mean years of disease duration of the participants in the two categories (10.7 years *vs.* 3.5 years, $p<0.001$), in contrast, the mean age revealed no difference (13.5 years *vs.* 13.7 years, $p=0.522$) (data not presented elsewhere). Disease duration may have an impact on oral hygiene.

Clinical and self-reported JIA-specific features, consistent with a more severe disease course, were found to negatively affect OHRQoL amongst the 12-16-year-olds in this study. OHRQoL is related to HRQoL (191, 192), and the association between self-

reported variables and OHRQoL was anticipated. Also, amongst the youngest participants with JIA (4-11-year-olds), a more severe disease course as indicated by ongoing and ever-used bDMARDs associated with impaired OHRQoL. Condition-specific Child-OIDP is demonstrated to have better discriminative properties than generic Child-OIDP (193, 194). The generic instruments may have failed to identify the impacts of JIA-specific features on OHRQoL. Condition-specific measures, specific with regard to oral problems frequently assessed in individuals with JIA, would probably provide a fuller OHRQoL profile of the participants with JIA. The CIs of the regression analyses were not precise, pointing to inadequate power, and larger sample sizes in JIA subgroups are warranted in research focusing on OHRQoL amongst young individuals with JIA.

5.2.4 Summary of the discussion

State-of-the-art analyses using multilevel modeling provided solid results and novel knowledge of site-and surface-specific caries and periodontal outcomes. Often consistent with a more severe disease course, sub-groups within the JIA group demonstrated susceptibility to poorer oral health. According to the logistic regressions, no statistically significant increased risk for impaired OHRQoL was found in the participants with JIA. However, in this study, we used a generic OIDP measure, and it is possible that a condition-specific OIDP instrument could have discriminated more strongly between participants with JIA and controls.

Young individuals with JIA need special oral health care. In this study population, approximately 30% of JIA participants or their caregivers reported that they had received information about the importance of good oral health in relation to the JIA diagnosis (among participants ≥10 years; 43/149, 28.9% (Paper II) and among participants 4-16 years 63/209, 30.1% (data not reported elsewhere)). As part of the intervention, JIA patients and their caregivers need well-ordered information about susceptibility to and how the progression of approximal caries, plaque, and gingival inflammation is prevented. Various channels should distribute this; oral health-, medical professionals, and patient organizations. Dental checkup intervals are determined by each person's risk of oral disease. Oral health professionals must be

aware of JIA patients' fluctuating disease course and, for many, the immunosuppressant state.

JIA is not one disease but rather an umbrella term for a heterogeneous group of disease categories with chronic inflammatory arthritis as a common finding. As treatment options steadily increase and the ultimate treatment goal is remission, the heterogeneity of disease categories requires more individualized and optimized treat-to-target strategies. As remission on medication becomes an accessible goal for many children and adolescents with JIA, more focus is switched to drug safety, adverse events, and risk of infection. Oral health may play an important role in the risk and protection of infection, and future research should address disease activity, drug exposure, and its relation to oral health status in homogeneous JIA groups. The objective of disease management includes achieving the best possible QoL and social involvement; hence monitoring HRQoL is important and should also include OHRQoL as oral health is an essential part of general health. Furthermore, studies directing host variation concerning immune response, microbial diversity, nutrition, and salivary gland involvement are needed to increase knowledge of the susceptibility to periodontal disease among individuals with JIA.

6. CONCLUSIONS

This study has shown:

- Individuals with JIA are at increased risk of plaque and gingival bleeding, but not caries, compared to controls without JIA. Adjusted logistic regression analyses revealed no statistically significant risk of impaired OHRQoL amongst participants with JIA; however, amongst 4-11-year-olds with JIA, adjusted binomial regressions revealed a significantly increased likelihood for impaired OHRQoL.
- Low maternal educational level was associated with the presence of caries independent of group affiliation.
- The socio-behavioral and clinical distribution of OHRQoL did not vary across participants with and without JIA. The only exception was that in the JIA group, females were significantly more likely than males to report oral impacts according to Child-OIDP, whereas in the control group, the corresponding association was nonsignificant.
- Surface-specific distribution of caries and plaque differed significantly between the two groups in the permanent dentition.
- Certain JIA-specific features, often related to a more severe disease course were positively associated with caries, plaque, gingival bleeding, and impaired OHRQoL.
- The outcome variables caries, plaque, and gingival bleeding were highly dependent within individuals (ICCs with covariates were 0.56, 0.45, and 0.30, respectively) and for gingival bleeding also within teeth (ICC with covariates was 0.41).
- The application of mixed-effects models was crucial given the statistically significant ICCs calculated in this study.

7. FUTURE PERSPECTIVES

In the light of the knowledge brought forth in this thesis, I would like to address the following:

- Awareness of the importance of oral health care in individuals diagnosed with JIA amongst users (caregivers and patients) and health care personnel should be increased:

  Results will be published on our study projects website, http://www.norjia.com/, which is open to the scientific community and users. The results will be imparted to the users through regular user courses held at the departments of pediatrics and to the user representatives from The Norwegian organization for children and youth with rheumatism (Barne- og Ungdoms revmatiker gruppe (BURG)), which is part of the Norwegian Rheumatism Association (Norsk revmatikerforbund) in Norway. Representatives from BURG have already supported and participated in the planning of the NorJIA study. For health personnel specifically: Clinicians and researchers are reached through papers in scientific journals and congress presentations internationally and nationally.

- Employment of a condition-specific OHRQoL inventory, targeting oral problems frequently present in individuals with JIA, might provide a more comprehensive OHRQoL profile for young individuals with JIA; also, it may discriminate better between OHRQoL of individuals with and without JIA.

- Future research should focus on longitudinal studies with adequate sample sizes in more homogeneous JIA groups, and covariates of oral health should be implemented in the oral health analyses. Studies targeting host variation; in specific immune responses, microbial diversity, nutrition, and salivary gland involvement are needed to increase the understanding of JIA patients' susceptibility to periodontal disease.

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ORIGINAL PAPERS

Paper I

I

Dental caries in children and adolescents with juvenile idiopathic arthritis and controls: a multilevel analysis.

Gil EG, Åstrøm AN, Lie SA, Rygg M, Fischer J, Rosén A, Bletsa A, Luukko K, Shi XQ, Halbig J, Frid P, Cetrelli L, Tylleskär K, Rosendahl K, Skeie MS**.**

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RESEARCH

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Dental caries in children and adolescents with juvenile idiopathic arthritis and controls: a multilevel analysis

Elisabeth G. Gil[1*], Anne N. Åstrøm[1], Stein Atle Lie[1], Marite Rygg[2,3], Johannes Fischer[1], Annika Rosén[1,4], Athanasia Bletsa[5,1], Keijo Luukko[1], Xie-Qi Shi[1,6], Josefine Halbig[7,8], Paula Frid[9,7,8], Lena Cetrelli[10,2], Karin Tylleskär[11], Karen Rosendahl[12,8] and Marit S. Skeie[1,10]

Abstract

Background: Optimal utilization of dental caries data is crucial in epidemiological research of individuals with juvenile idiopathic arthritis (JIA). The aims were to: explore whether caries is more prevalent among children and adolescents with JIA compared to controls; examine presence of caries according to JIA group, socio-behavioral and intraoral characteristics, and the extent to which surface-specific caries varies between and within individuals; assess whether surface-specific caries varies according to JIA group and dentition; and investigate whether disease-specific clinical features of JIA are associated with presence of caries.

Methods: In this comparative cross-sectional study, calibrated dentists examined index teeth (primary 2. molars, 1. permanent molars) of 4–16-year-olds with JIA (n = 219) and matched controls (n = 224), using a detailed caries diagnosis system (including enamel caries). JIA-specific characteristics were assessed by pediatric rheumatologists and socio-behavioral information collected by questionnaires. Multilevel mixed-effect logistic regressions reporting odds ratios (OR) with 95% confidence interval (CI) were applied (caries at surface level as outcome variable). Potential confounders were adjusted for, and the effect of dependency of surface-specific caries data was estimated by calculating intra-class correlation coefficients (ICC).

Results: At individual level, no significant difference in caries prevalence was found between individuals with JIA and controls, regardless of inclusion of enamel caries. Proportion of enamel lesions exceeded dentine lesions. JIA was not associated with presence of caries, but in both groups, low maternal educational level was associated with presence of caries (OR: 2.07, 95% CI: 1.24–3.46). Occlusal and mesial surfaces, compared to buccal surfaces, had generally higher OR according to presence of caries than distal and lingual surfaces (ICC = 0.56). Surface-specific caries in the permanent dentition differed significantly according to group affiliation. Some JIA disease-specific variables were suggested to associate with presence of caries.

Conclusions: No overall difference in caries prevalence between individuals with JIA and controls was observed, but for both groups, low maternal educational level and tooth surface associated with presence of caries. Associations

*Correspondence: elisabeth.gil@uib.no
[1] Department of Clinical Dentistry, The Faculty of Medicine, University of Bergen, Årstadveien 19, 5009 Bergen, Norway
For the NorJIA (Norwegian JIA Study – Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis)
Full list of author information is available at the end of the article

between JIA disease-specific variables and presence of caries cannot be excluded. Due to predominance of enamel lesions, the potential of preventative dental strategies is considerable.

Keywords: Adolescent, Child, Dental care for children, Dental caries, Oral health, Juvenile idiopathic arthritis, Multilevel analyses

Background

Juvenile idiopathic arthritis (JIA) is the most common chronic arthritis disease in children and adolescents and is an important cause of short and long-term disability [1]. JIA is not a single disease, but a term that encompasses all forms of arthritis of unknown etiology, starting before the age of 16 and persisting for at least 6 weeks [2]. The prevalence and incidence rates of JIA varies across populations. A prevalence of 32.6/100,000 children and an incidence rate of 8.3/100,000 children per year has been estimated for Caucasians [3]. High incidence rates in northern European countries have been reported, and in Northern and Central Norway, an incidence rate of 23/100,000 children per year have been demonstrated [4, 5].

A recent systematic review and meta-analysis by our research team focusing on caries and other oral health conditions among children and adolescents with JIA, found no significant difference in mean dmft/DMFT (decayed/missing/filled teeth) between the groups with and without JIA [6]. This finding contrasts previous reviews by Walton et al. [7] and Synodinos et al. [8], reporting a high prevalence of caries among children and adolescents with JIA. Improved medical and effective overall treatment of JIA [9, 10], especially in countries with well-established health care services, have presumably reduced some of the prevailing dental caries risk factors associated with this disease. Also, development of current alternative sweeteners and sugar alternatives in pediatric drugs in general [11] may have reduced the risk for future caries development and explains why caries prevalence in young individuals with JIA in recent years have become comparable with those of the general population. However, children and adolescents with JIA face additional challenges associated with caries development. For example salivary alterations and reduced salivary flow rate have been reported [12, 13], which may reduce the protective role of the saliva and lead to poor oral hygiene [13]. Additionally, antirheumatic medication such as different synthetic disease-modifying antirheumatic drugs (sDMARDs), especially the commonly used Methotrexate, may cause side-effects like nausea, vomiting and stomatitis [14, 15], presumably constituting a negative impact on oral health behaviours associated with oral hygiene and dietary habits.

Insufficient sample sizes [6] and non-optimal utilization of data [16] are common challenges in caries epidemiology concerning children and adolescents with JIA. The aggregated dmf/DMF index does not account for the hierarchical structure of the data with surfaces clustered within teeth and teeth clustered within individuals. Applying data on tooth and surface level require adjustment of the clustered nature of the data. Neglecting to adjust for clustering may result in smaller standard errors and increased likelihood of falsely rejecting the null hypothesis (Type I error) [17]. Hence, multilevel modelling in the analysis of surface-specific caries is needed.

There is a need for more high-quality studies with sufficient sample sizes and better exploitation of caries data, to fill the knowledge gaps concerning caries status among children and adolescents with JIA and to assess whether rheumatological characteristics are associated with caries. The aims of this study were to explore whether caries is more prevalent among children and adolescents with JIA compared to matched controls. Independent of JIA group, we also examined the presence of caries according to socio-behavioral and intraoral (within mouth) characteristics and the extent to which surface-specific caries varies between and within individuals. Furthermore, we assessed whether surface-specific caries varies according to JIA group and dentition (primary/permanent molars). Finally, and specifically for patients with JIA, we investigated whether clinical features such as JIA category, age at onset of JIA, disease duration, use of medication, or remission status were associated with the presence of caries.

Methods

Study design

This comparative cross-sectional study is based on baseline data from NorJIA,[1] a prospective longitudinal multicenter study performed in the period 2015–2020 and registered at ClinicalTrials.gov (No: NCT03904459). Inclusion criteria were children or adolescents (4–16 years old) diagnosed with JIA by a pediatric rheumatologist according to the criteria by the International League of Associations for Rheumatology (ILAR) [2].

[1] The Norwegian JIA Study – Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis (JIA).

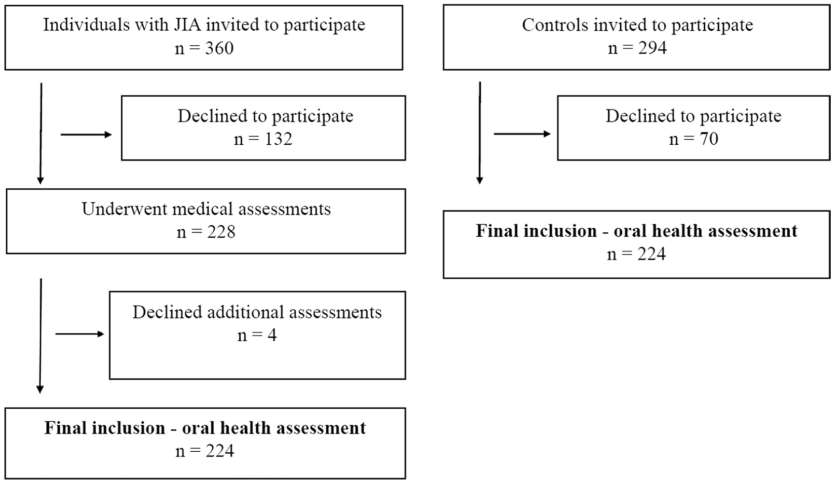

Fig. 1 Participant flow diagram of children and adolescents with juvenile idiopathic arthritis (JIA) and controls

Exclusion criterion was lack of written informed consent. There were no participants with major medical comorbidities such as congenital facial anomalies, skeletal dysplasia, or malignancies in the study population. The medical and caries data for the present sub-study were collected between April 2015 and August 2018. To validate acceptable entry of data, 10% of the data input was rechecked.

Sample size calculation

The sample size calculation is presented in Additional file 1.

Participants

A total of 360 individuals with JIA were invited to participate, 228 underwent a medical examination, and a total of 224 were included in the final oral health examination (Fig. 1). The participants were recruited from three university hospitals located in western, central, or northern Norway. The participants with JIA were matched 1:1 with a control group according to sex, age, center site, and mothers' country of origin (western or non-western origin). The controls were recruited from seven Public Dental Service (PDS) clinics and did not have JIA and substantially no other chronic diseases (Additional file 2, Table S1). The participants with JIA and their matched controls originated from the same geographical areas (western, central, or northern Norway). The PDS clinics were localized in both rural and urban areas. The controls had their appointments combined with planned regular oral health checks and received two cinema tickets as incentives for participation. The oral health examination was comprehensive, but subsequently this sub-study was restricted to only cover caries disease.

Questionnaires and construction of variables

All participants (and/or caregivers, as appropriate) were asked to complete a questionnaire concerning sociodemographic and behavioral characteristics. The questionnaire version given to participants under the age of 12 years was slightly different than the version given to those 12 years of age and older. For all participants, the questionnaire included an item regarding their mother's country of origin. If this item was not filled in, it was decided to identify the mother's background-origin by the family name of the participant (in Norway it is fairly common for the family name of a child to include both the father's and mother's name). Other variables obtained from the questionnaire were educational level of caregivers, number of caregivers in the household, frequency of toothbrushing, frequency of tooth flossing during the last 3 months, gingival bleeding during toothbrushing, and pain or discomfort during toothbrushing. Additional questions given to participants under the age of 12 years were age of starting toothbrushing, whether they get assistance if tooth flossing is performed, whether they had cordial/milk from a bottle after the age of 1 year, and whether drinks or food were offered or available in bed in the evening/during the night. The coding is presented

in Additional file 3, Table S1A and Table S1B. Lower and upper jaws were categorized as (0) mandible and (1) maxilla. The oral cavity was dichotomized into (0) right side (first and fourth quadrant) and (1) left side (second and third quadrant). The dentition was dichotomized into (0) primary second molars and (1) permanent first molars. Tooth surfaces were categorized as (0) buccal surface, (1) distal surface, (2) lingual surface, (3) mesial surface and (4) occlusal surface.

The JIA-specific clinical variables included were JIA category, medication, age of disease onset in years, disease duration in years, activity/remission status, physician's global assessment of disease activity visual analogue scale (MDgloVAS), patient/parent-reported global assessment of overall well-being visual analogue scale (PRgloVAS), Childhood Health Assessment Questionnaire (CHAQ) hygiene item tooth brushing. The coding is presented in Additional file 3, Table S1C.

Examinations

Experienced pediatric rheumatologists at each of the three university hospitals were responsible for the examinations of the participants with JIA. Elaboration of the JIA-specific clinical background variables, collected by the pediatric rheumatologists, are presented in Additional file 4. Both children and adolescents with JIA and the controls underwent caries assessment based on bitewing radiographs (BW) combined with visual inspection as part of a thorough oral examination. Five dentists underwent calibration courses and exercises. The caries calibration sessions are described in Additional file 5. Decayed, missing, and filled surfaces were registered according to a detailed 5-graded diagnostic tool [18]. Grades 1–2 denoted enamel lesions and grades 3–5 dentin lesions. Missing teeth were defined as teeth extracted due to caries or indicated for extraction. From the age of 5 years BW were taken when there was intermolar contact, but not if fixed orthodontic appliances were present. If fixed orthodontic appliances were present, only occlusal surfaces were examined by visual inspection. To achieve maximum comparability of dentition in children at various shedding/eruption stages, only molars were assessed (at younger than 10 years, primary second molars, and at 10 years and older, permanent first molars). Norwegian studies have found primary second molars to be the teeth most susceptible to caries in 5-year-olds [19], and the first permanent molars the teeth mostly affected at 12–18 years of age [20].

Statistical methods

Data were analyzed using SPSS version 25.0 (IBM Corp. Released 2013, IBM SPSS Statistics for Windows, Armonk NY: IBM Corp) and STATA version 16 (Stata Corp LP, College Station, TX). For reliability statistics, linear weighted Cohen's kappa and percent agreement values were used. Mean and SD were used to describe continuous clinical and demographic variables. Chi-squared tests were used to assess differences in categorical variables between individuals with JIA and the control group. Because the data for presence of caries (0 = no, 1 = yes) had a clustered 3-level hierarchical structure with surfaces (level 1) clustered within teeth (level 2), and teeth clustered within individuals (level 3), random intercept logistic models (RIM) were fitted using multilevel mixed-effects logistic regressions. Illustration of the levels in the multilevel models, according to the dichotomous caries outcome variable and background variables are presented in Additional file 6, Table S1. The formulas estimated (using restricted maximum likelihood REML) using mixed effects (random intercept) logistic regression were:

$$logit\left(P\left(Y_{ijk}=1\right)\right)=\beta_0+\beta_1^T X_{ijk}+\beta_{0i}+\beta_{0ij}+e_{ijk}$$

$$Y_{ijk}\sim Binomial(n_i,p_i)$$

$$\beta_{0i}\sim N\left(0,\sigma_v^2\right)$$

$$\beta_{0ij}\sim N\left(0,\sigma_u^2\right)$$

$$icc_v=\frac{\sigma_v^2+\sigma_u^2}{\sigma_v^2+\sigma_u^2+\pi^2/3}$$

$$icc_u=\frac{\sigma_u^2}{\sigma_v^2+\sigma_u^2+\pi^2/3}$$

The multilevel models account for clustering of caries data for sites (k-level) within teeth (j-level) and within individuals (i-level). Intra-class correlation coefficients (ICC) for the matching pairs were tested using separate mixed effects logistic models. Sociodemographic and behavioral characteristics that were statistically significantly associated with JIA status and presence of caries ($d_{1\text{-}5}fs/D_{1\text{-}5}FS>0$) were included as potential confounders in the mixed-effects logistic regression analysis. Additionally, clinical features statistically associated with presence of caries ($d_{1\text{-}5}fs/D_{1\text{-}5}FS>0$) in unadjusted analysis and the main exposure variable (JIA/control group) were adjusted for in the mixed-effect logistic regression analysis. The effect of dependency of caries data at individual level and tooth level was assessed by calculating ICCs, applying the described formulas. The ICC will also express variations between teeth

Table 1 Sociodemographic and behavioral characteristics of 224 individuals with juvenile idiopathic arthritis and 224 controls, aged 4–16 years

Variable	Individuals with JIA (n = 224)	Control group (n = 224)	*p* value
Educational level of caregivers, n (%)			
Mother			
High school/vocational school	75 (35.4)	54 (26.1)	0.04
University/college	137 (64.6)	153 (73.9)	
Father			
High school/vocational school	121 (57.9)	87 (42.6)	< 0.01
University/college	88 (42.1)	117 (57.4)	
Share household with, n (%)			
Two caregivers in the household*	172 (79.6)	187 (84.2)	0.21
Only one caregiver in the household	44 (20.4)	35 (15.8)	
Frequency of toothbrushing, n (%)			
Once a day or less/do not know	51 (23.6)	49 (22.2)	0.72
Twice a day, or more	165 (76.4)	172 (77.8)	
Frequency of tooth flossing during the last 3 months, n (%)			
Daily or more	19 (8.8)	19 (8.6)	0.94
Several times weekly or less/do not know	196 (91.2)	201 (91.4)	
Toothpaste, n (%)			
Fluoride toothpaste	204 (94.4)	212 (96.4)	0.34
Fluoride-free toothpaste /do not know	12 (5.6)	8 (3.6)	
During toothbrushing, gingival bleeding occurs, n (%)			
Sometimes or more/do not know	122 (57.3)	103 (46.6)	0.03
Never	91 (42.7)	118 (53.4)	
During toothbrushing, pain or discomfort occurs, n (%)			
Yes/do not know	25 (11.7)	22 (10.0)	0.55
No	188 (88.3)	199 (90.0)	

* Also includes living across two households, given two caregivers in both households. Some participants did not respond to the questionnaires. Chi-squared test level of significance $p < 0.05$

and individuals as a proportion of the total variance. ICC varies between 0 (implying caries is independent within individuals) and 1 (indicating no variation of caries within an individual). Post-hoc test was applied by Scheffe's method to adjust significance levels in multiple comparisons in the multilevel mixed-effects logistics regressions. p values less than 0.05 were considered statistically significant.

Ethical approval

The study was approved by the regional ethics committee (2012/542/REC). Approval was also received by leaders of different County Dental Health Authorities, at different Oral Health Centre of Expertise, and at the three pediatric departments at university hospitals. Written informed consent was signed before participation. This sub-study as part of the NorJIA study was registered at ClinicalTrials.gov (No: NCT03904459).

Results

Sample characteristics

Of the 360 eligible children and adolescents with JIA, 228 underwent the medical assessment, yielding a response rate of 63.3% (Fig. 1). The corresponding response rate for controls was 224/294 (76.2%). Mean age of participants with JIA and controls was 12.0 years (SD 3.2) ($p = 0.98$). In comparison, the mean age of the 132 eligible JIA patients who declined to participate was 10.5 (SD 3.5) years ($p < 0.01$). The proportion of girls was slightly higher for the participants with JIA, compared to the group of JIA patients who declined participation (59.2% vs 58.3%, $p = 0.03$).

After the medical examination, a further 4 declined participation, resulting in a total of 224 participants with JIA who underwent the oral health assessment (Fig. 1). For this sub-study, mean age of both participants with JIA and controls was 12.0 years (SD 3.2) ($p = 0.97$). The

Table 2 Behavioral characteristics of 98 individuals with juvenile idiopathic arthritis and 98 controls < 12 years

Variable	Individuals with JIA (n = 98)	Control group (n = 98)	*p* value
Age at start of toothbrushing, n (%)			
1 year and older/do not know	81 (83.5)	81 (82.7)	0.87
Under the age of 1 year	16 (16.5)	17 (17.3)	
Does the child get assistance if tooth flossing is performed? n (%)			
Yes	35 (47.3)	39 (51.3)	
No/do not know	39 (52.7)	37 (48.7)	0.62
Cordial/milk on bottle after the age of 1 year, n (%)			
Yes/do not know	45 (46.4)	41 (41.8)	0.52
No	52 (53.6)	57 (58.2)	
Drinks or food offered/available in bed during evening/nights, n (%)			
Yes/do not know	11 (11.5)	9 (9.2)	0.60
No	85 (88.5)	89 (90.8)	

Some participants did not respond to the questionnaires. Chi-squared test level of significance $p < 0.05$

number of girls among participants with JIA and controls was 133 (59.4%) and 134 (59.8%), respectively. A total of 94.2% (211/224) of all pairs were matched according to mother's background of origin (an assumption based on family name was made for 10 participants).

Two significant differences between the JIA group and controls were observed (Table 1). First, 137 (64.6%) of mothers in the JIA group versus 153 (73.9%) of mothers in the control group had higher education ($p = 0.04$), while numbers for fathers were 88 (42.1%) and 117 (57.4%) ($p < 0.01$). Second, individuals with JIA reported more frequent gingival bleeding during toothbrushing (57.3% vs. 46.6%, $p = 0.03$). No other significant differences were found between the two groups in sociodemographic or behavioral characteristics (Tables 1, 2). Five participants did not have an initial caries examination (due to temporary misinterpretation of study instructions at the very beginning of data collection), so the subsequent analyses include 219 individuals with JIA and 224 controls. The remaining oral health variables will be presented in an upcoming article.

Concomitant diagnoses and medication use

Concomitant diagnoses and use of medication that were a potential oral health threat to individuals with JIA and the controls, are presented in Additional file 2, Table S1.

Calibration

Four caries calibration exercises are described in Additional file 5, and the weighted Cohen's kappa values of these exercises were 0.61, 0.61, 0.91 and 0.65, respectively.

Caries prevalence at individual level

No significant differences in caries prevalence could be found between the JIA group and the control group regarding primary and permanent molars, whether enamel caries was included or not. In the JIA group, 23.0% (14/61) experienced caries at $d_{1\text{-}5}$f-level (decayed and/or filled teeth in the primary dentition, enamel caries included) and 6.6% (4/61) at $d_{3\text{-}5}$f-level (enamel caries not included) in one or more primary second molars, while the corresponding proportions in the control group were 27.4% (17/62) and 11.3% (7/62). Individuals in the JIA group and the control group experienced caries in permanent first molars at $D_{1\text{-}5}$F-level (decayed and/or filled teeth in the permanent dentition, enamel caries included), 51.9% (82/158) and 50.0% (81/162) respectively. At $D_{3\text{-}5}$F-level (enamel caries not included) the corresponding numbers were 36.1% (57/158) and 28.4% (46/162). No permanent molars were extracted or indicated for extraction due to caries, but 2 individuals with JIA and 1 of the control had one or two primary molars extracted (teeth n = 5). In both groups, and for both primary and permanent molars, the occlusal surface was the one most prone to caries, and the proportion of enamel lesions exceeded dentin lesions (Fig. 2).

Multilevel analyses

Due to the weak correlation between the matching pairs (ICC = 0.08), the original matching in the data was not accounted for in the final multilevel models. Multilevel analysis regressing caries prevalence on JIA status while adjusting for socio-behavioral characteristics and clinical features (intra-oral characteristics) revealed no statistically significant association between JIA status and presence of caries in primary and permanent teeth ($d_{1\text{-}5}$ fs/$D_{1\text{-}5}$FS > 0, Table 3). Participants with mothers that had high school (or equivalent) education had statistically significantly higher odds of caries (OR = 2.07, 95% CI: 1.24–3.46) than participants with mothers with university-level education. Compared to buccal surface, the occlusal and mesial surfaces of the molars had statistically significantly higher odds of caries, primary and permanent teeth combined. The corresponding odds ratios were 5.06 (95% CI: 3.76–6.83) and 1.66 (95% CI: 1.21–2.29). Compared to the buccal surface, the distal and lingual surfaces had statistically significant lower odds of caries (OR = 0.40, 95% CI: 0.27–0.61 and OR = 0.63, 95% CI: 0.43–0.91, respectively). For a multilevel model with no covariates, the ICC was 0.52, indicating that 52% of the variance in the caries outcome variable was between rather than within individuals. In the adjusted analysis, the ICC was 0.56. The ICCs were found to be statistically significant ($p < 0.01$).

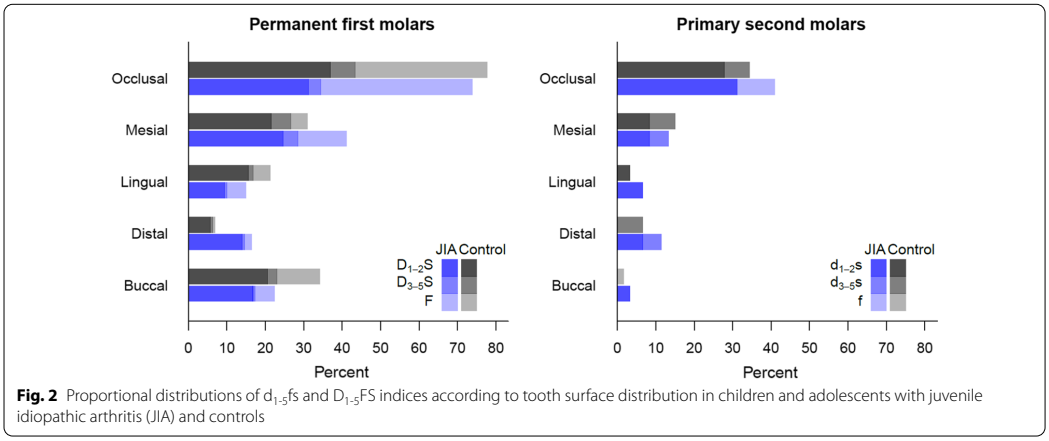

Fig. 2 Proportional distributions of $d_{1-5}fs$ and $D_{1-5}FS$ indices according to tooth surface distribution in children and adolescents with juvenile idiopathic arthritis (JIA) and controls

Surface-specific caries according to JIA group and dentition (permanent/primary molars)

Participants in both the JIA group and the control group were more likely to have caries on the occlusal surfaces than on the buccal surfaces in both primary and permanent teeth (Table 4). Participants in the JIA group were more likely to have caries on the mesial surfaces than on the buccal surfaces of their permanent teeth, whereas controls were more likely to have caries on the mesial surface than on the buccal surfaces of their primary teeth. All ICCs were statistically significant (all $p < 0.01$). There was a statistically significant interaction between surface in the permanent dentition and group affiliation (JIA/control group) ($p < 0.01$) on presence of caries, whereas in the primary dentition the corresponding interaction was nonsignificant ($p = 0.66$).

Disease-specific variables associated with caries

No statistically significant associations were found between JIA-specific features and caries in the primary and permanent teeth combined (Table 5). However, analyzing the dentitions separately, the category Oligoarthritis extended (OR = 20.82, 95% CI: 1.57–275.42) and the category Polyarthritis Rheumatoid Factor (RF) negative (OR = 2.48, 95% CI: 1.13–5.45) had statistically significant higher odds for caries, with reference to Oligoarthritis persistent in the primary and permanent dentition, respectively (results not shown in Table 5). In the primary dentition, individuals with MDgloVAS score > 0 had statistically significant higher odds for caries (OR = 5.78, 95% CI: 1.04–32.28), compared to individuals with MDgloVAS score = 0. At surface level (primary and permanent dentition combined), compared to the buccal surface, the occlusal surface (OR = 6.30, 95% CI: 4.11–9.66) and the mesial surface (OR = 2.44, 95% CI: 1.56–3.82) were statistically significantly associated with caries. In the unadjusted analysis the ICC was 0.47 ($p < 0.01$).

Discussion

This matched comparative cross-sectional study did not reveal any overall significant difference in caries prevalence between individuals with JIA and controls, both when enamel caries was included or not. Few individuals experienced extractions and only primary molars were extracted. In both primary and permanent dentitions, the occlusal surface was most prone to caries. A lower educational level of participants' mothers was associated with presence of caries, independent of group affiliation. There was a stronger trend for increased risk of mesial approximal caries (mesial surfaces compared to buccal surface) in the permanent molars of the JIA group, than in the control group. Few JIA disease-specific variables were associated with presence of caries, but no strong conclusions can be drawn because of low number of participants in some of the categories.

A strength of this study is the application of multilevel analyses of surface-specific measures, facilitating exploration and accounting for the clustered structure of the outcome data. As far as we know, multilevel analysis has previously not been applied in studies examining dental caries among young individuals with JIA. Furthermore, improved statistical management accounting for clustering effects of the data is in demand in dental research [21]. In caries epidemiology, the clustered structure of the data (surfaces clustered within teeth, and teeth clustered within individuals) is often ignored and each surface or tooth is treated as an independent observation. This approach is adequate if the within-cluster

Table 3 Multilevel mixed-effects logistic regression analyzing the relationships among health status, sociodemographic and behavioral characteristics, and oral variables with the dichotomized outcome variable presence of caries ($d_{1\text{-}5}$ fs/$D_{1\text{-}5}$FS > 0 or = 0)

	Unadjusted analysis		Adjusted analysis	
	OR (95% CI)	***p* value**	**OR (95% CI)**	***p* value**
Health status				
Control group	1	Ref	1	Ref
JIA group	1.07 (0.70–1.65)	0.77	1.02 (0.62–1.66)	0.95
Educational level of mother				
University/college	1	Ref	1	Ref
High school/vocational school	1.93 (1.20–3.09)	0.01	2.07 (1.24–3.46)	0.01
Educational level of father				
University/college	1	Ref		
High school/vocational school	1.38 (0.87–2.19)	0.17		
Household structure				
Two caregivers*	1	Ref		
One caregiver	1.36 (0.78–2.37)	0.29		
Toothpaste				
Fluoride toothpaste	1	Ref		
Fluoride-free toothpaste**	1.11 (0.40–3.08)	0.84		
Frequency of toothbrushing				
Twice a day or more	1	Ref		
Once a day or less **	1.35 (0.81–2.25)	0.26		
Frequency of tooth flossing during the last 3 months				
Daily or more	1	Ref		
Several times weekly or less**	0.98 (0.44–2.18)	0.96		
During toothbrushing, gingival bleeding occurs				
Never	1	Ref	1	Ref
Sometimes or more **	1.69 (1.09–2.64)	0.02	1.52 (0.94–2.48)	0.09
During toothbrushing, pain or discomfort occurs				
No	1	Ref		
Yes**	3.11 (1.62–5.98)	< 0.01		
Jaw				
Mandible	1	Ref		
Maxilla	1.01 (0.84–1.20)	0.96		
Side				
Right side	1	Ref		
Left side	1.01 (0.84–1.21)	0.91		
Surface				
A: Buccal	1^{BDE}	< 0.01*	1^{BDE}	< 0.01***
B: Distal	0.45 (0.31–0.65)^{ADE}	< 0.01	0.40 (0.27–0.61)^{ADE}	< 0.01
C: Lingual	0.66 (0.46–0.93)^{DE}	0.02	0.63 (0.43–0.91)^{DE}	0.01
D: Mesial	1.67 (1.23–2.26)^{ABCE}	< 0.01	1.66 (1.21–2.29)^{ABCE}	< 0.01
E: Occlusal	4.86 (3.65–6.45)^{ABCD}	< 0.01	5.06 (3.76–6.83)^{ABCD}	< 0.01
ICC	0.52		0.56	

JIA, juvenile idiopathic arthritis; ICC, intra-class correlation coefficient

* Also includes living across two households with two caregivers in each household. **The answer option "Do not know" is assigned to the variable associated with negative impact on oral health. *Overall *p* value. Surfaces statistically significant in post-hoc analyses are marked with superscript letters. Scheffe adjusted *p* values in post-hoc analyses $p < 0.05$

Table 4 Multilevel mixed-effects logistic regression for surfaces associated with presence of caries ($d_{1\text{-}5}fs/D_{1\text{-}5}FS > 0$ or $= 0$)

	Individuals with JIA				Control group			
	Permanent dentition		Primary dentition		Permanent dentition		Primary dentition	
	OR (95% CI), Unadjusted	*p* value	OR (95% CI), Unadjusted	*p* value	OR (95% CI), Unadjusted	*p* value	OR (95% CI), Unadjusted	*p* value
A:Buccal	1^{DE}	< 0.01*	1^{E}	0.01*	1^{BE}	< 0.01*	1^{E}	0.01*
B:Distal	0.66 (0.38–1.15)^{DE}	0.14	4.36 (0.81–23.34)^{E}	0.09	0.15 (0.08–0.30)^{ACDE}	< 0.01	4.34 (0.46–40.94)^{E}	0.20
C:Lingual	0.67 (0.38–1.16)^{DE}	0.15	2.18 (0.36–13.14)^{E}	0.39	0.56 (0.34–0.91)^{BE}	0.02	2.06 (0.18–23.88)^{E}	0.56
D:Mesial	2.28 (1.43–3.65)^{ABCE}	< 0.01	5.21 (0.99–27.40)^{E}	0.05	0.92 (0.59–1.45)^{BE}	0.73	14.26 (1.73–117.18)	0.01
E:Occlusal	5.01 (3.20–7.85)^{ABCD}	< 0.01	34.25 (6.88–170.54)^{ABCD}	< 0.01	3.25 (2.17–4.86)^{ABCD}	< 0.01	34.66 (4.34–276.53)	< 0.01
ICC	0.49		0.78		0.54		0.57	

JIA, juvenile idiopathic arthritis; ICC, intra-class correlation coefficient

* Overall *p* value. Surfaces statistically significant in post-hoc analyses are marked with the superscript letters of the pertinent surfaces. Scheffe adjusted *p* values in post-hoc analysis $p < 0.05$

correlation or intra-class correlation coefficient (ICC) (i.e. correlation between teeth and surfaces for the same individual) is very small, because then the impact of clustering on the analysis can be disregarded [22]. Contrary, in case of increased ICC, suitable statistical analysis for clustered data must be implemented if the unique measure of teeth and surfaces are to be used. The calculated ICCs in this study were statistically significant, demonstrating presence of caries within the individual to be dependent, hence the application of mixed-effect logistic regressions was crucial. Another strength of this study is the large number of participants compared to other studies focusing on caries among young individuals with JIA. In addition, all disease categories were represented in the JIA cohort. The applied multicenter design, including three out of four existing regional pediatric rheumatology centers in Norway, ensured representativeness of the Norwegian population for this group with JIA.

This study also has some weaknesses. For instance, even with the relatively large sampling, possible non-response bias for participants with JIA should not be ignored [23]. The non-responders were slightly but significantly younger, and there was a slightly lower proportion of girls, these factors might have influenced the data and analyses. A weakness might be that potential confounders such as dietary habits were not analyzed. Also, a weak correlation between the matching pairs, indicating that the background variables sex, age, center site, and background origin (western/non-western) were not sufficient matching variables for the present outcome ($d_{1\text{-}5}fs/D_{1\text{-}5}FS > 0$). This resulted in convergence problems if matching was added to the mixed effects models, hence adjustment for the correlation between the matching pairs were omitted.

In 1985 and 1987, Storhaug et al. [24, 25] reported increased caries experience among pre-school and school-aged children with JIA in Norway. This finding is in accordance with international studies of less recent data reporting a high burden of caries among young individuals with JIA [26, 27]. The data in the articles by Storhaug et al. were collected as part of a cohort of disabled individuals, however, including no control group for comparison. There have been no other Norwegian studies more recent than Storhaug et al. that have considered caries epidemiology among young individuals with JIA. It is worth noting that in the intervening years, there has been a substantial caries decline in the western world [28], which should be kept in mind when comparisons with older studies are performed. The modest number of individuals experiencing extractions in the present study emphasizes this trend of caries decline. If we restrict comparisons to studies from the last decade, our finding of no difference in caries burden between individuals with JIA and controls, is mostly in accordance with the literature on this topic [12, 13, 29, 30]. One study even reported of higher caries experience in primary teeth among the participants without JIA compared to participants with JIA, but these findings were based on a small sample size [31]. A recent study has found high levels of caries experience among adolescents with JIA, but the reference of comparison was epidemiological data from different German populations, not a matched control group [32]. There are other contributing factors that probably explain why caries prevalence in young individuals with JIA has in recent years become comparable with the general population. Difficulties with tooth brushing and flossing (due to limited mouth opening and upper limb dysfunction) have repeatedly been highlighted as risk factors for caries in individuals with JIA. Better overall treatment of JIA and especially more effective drugs [9, 10] have presumably increased temporomandibular and upper limb function, thus enabling some individuals to manage more efficient

Table 5 Unadjusted multilevel mixed-effects logistic regression analyzing the relationship between disease-specific features and oral variables, with the dichotomized outcome variable presence of caries ($d_{1\text{-}5}fs/D_{1\text{-}5}FS > 0$ or $= 0$) in children and adolescents with juvenile idiopathic arthritis (JIA)

	Respondents, n	OR (95% CI)	*p* value
JIA category			
Oligoarthritis persistent	77	1	0.29*
Systemic arthritis	7	0.93 (0.17–5.17)	0.94
Oligoarthritis extended	20	1.88 (0.65–5.43)	0.24
Polyarthritis, RF positive	4	3.07 (0.38–24.83)	0.29
Polyarthritis, RF negative	49	2.19 (0.99–4.85)	0.05
Psoriatic arthritis	8	2.99 (0.67–13.34)	0.15
Enthesitis-related arthritis	23	0.64 (0.21–1.96)	0.44
Undifferentiated arthritis	31	0.84 (0.31–2.26)	0.74
Steroids, ongoing			
No steroids ongoing	215	1	Ref
Steroids ongoing	4	2.31 (0.26–20.58)	0.45
Steroids, ever used			
No steroids ever used	172	1	Ref
Steroids ever used	47	1.30 (0.63–2.71)	0.48
DMARDs, ongoing			
No sDMARDs nor bDMARDs ongoing	73	1	0.78*
sDMARDs, but no bDMARDs ongoing	60	0.82 (0.37–1.79)	0.61
bDMARDs ongoing (with or without sDMARDs)	86	1.06 (0.52–2.16)	0.88
DMARDs, ever used**			
No sDMARDs nor bDMARDs ever used	51	1	0.61*
sDMARDs, but no bDMARDs ever used	79	1.32 (0.58–3.01)	0.50
bDMARDs ever used (with or without sDMARDs)	89	1.48 (0.66–3.31)	0.34
Age at JIA onset			
$\leq$ 6 years	110	1	Ref
> 6 years	109	1.66 (0.90–3.07)	0.11
Disease duration			
$\leq$ 5 years	117	1	Ref
> 5 years	102	1.35 (0.73–2.48)	0.34
Remission status***			
Inactive disease/remission on/off medication	130	1	ref
Continued activity/flare	89	1.16 (0.63–2.16)	0.63
MDgloVAS			
VAS = 0	140	1	Ref
VAS > 0	79	1.26 (0.67–2.37)	0.48
PRgloVAS****			
VAS = 0	106	1	Ref
VAS > 0	108	1.24 (0.67–2.29)	0.49
CHAQ hygiene item tooth brushing****			
Without any difficulty	203	1	Ref
With some/much difficulty/unable to do/not applicable	11	1.03 (0.26–4.09)	0.96
Jaw			
Mandible		1	Ref
Maxilla		1.02 (0.79–1.32)	0.86
Side			
Right side		1	Ref
Left side		1.14 (0.88–1.46)	0.33

Table 5 (continued)

	Respondents, n	OR (95% CI)	*p* value
Surface			
A: Buccal		1[DE]	< 0.01*
B: Distal		0.82 (0.49–1.38)[DE]	0.46
C: Lingual		0.74 (0.44–1.26)[DE]	0.27
D: Mesial		2.44 (1.56–3.82)[ABCE]	< 0.01
E: Occlusal		6.30 (4.11–9.66)[ABCD]	< 0.01
ICC		0.47	

RF, Rheumatoid Factor; sDMARDs, synthetic disease-modifying antirheumatic drugs; bDMARDs, biologic disease-modifying antirheumatic drugs; MDgloVAS, Physician's global assessment of disease activity; PRgloVAS, Patient's global assessment of overall wellbeing; CHAQ, Childhood Health Assessment Questionnaire; ICC, intra-class correlation coefficient

* Overall *p* value. Surfaces statistically significant in post-hoc analyses are marked with the superscript letters of the pertinent surfaces. Scheffe adjusted *p* values in post-hoc analyses $p < 0.05$. For 'JIA category', 'other medication ongoing and ever used', and post- hoc analysis showed no differences (all *p* values > 0.05). **Include both previously used and ongoing medication. ***Disease activity according to Wallace and the American College of Rheumatology (ACR) provisional criteria [43, 44]. ****Responses (n = 5) are missing

oral hygiene routines than before. It is also well known that orofacial dysfunction or pain may be associated with disadvantageous diet, such as softer, more refined carbohydrates combined with frequent intake. Furthermore, as mentioned in the introduction, alternative sweeteners and sugar alternatives in pediatric drugs in general [11] may have reduced the risk for future caries development.

Low socio-economic status is a known risk factor for caries development, despite the availability of free public dental services for children and adolescents in the Nordic countries [33, 34]. There is also a strong association between social disadvantage and poor child health [35]. In studies of caries epidemiology published in the last decade, social risk factors in individuals with JIA have gained limited attention. The finding in the present study, that parental educational level was lower for the JIA group than the control group, is in line with a recent study by Grevich et al. [30]. One possible explanation for this difference could be that more university-educated parents were willing to have their child participate as controls, and thus our control matching might be a bit skewed despite a high response rate. A difference between our results and Grevich et al. [35] is that the latter did not find parental educational level to be associated with caries outcome, in contrast to the present study which found an association between presence of caries and educational level achieved by the mother, independent of group affiliation.

Surface-specific caries in the permanent dentition differed significantly according to group affiliation. A trend observed in the permanent molars of the JIA group was an increased risk for mesial approximal caries (mesial surface, compared to buccal surface), in contrast to the control group. Effective prophylactic strategies targeting occlusal or buccal/lingual surfaces (e.g., fissure sealants) are not applicable to approximal lesions, so preventing these lesions demands greater effort from the patient themselves (e.g., by flossing). The importance of preventing interproximal invasive procedures are highlighted in the literature as studies suggest approximal composite restorations to be associated with increased caries in the adjacent surface [36] and future periodontal attachment loss as observed in adults [37]. Special attention should be given to young individuals with JIA aimed at preventing and managing approximal lesions.

To various extent, previous researchers have investigated whether disease-specific variables in rheumatological conditions are associated with dental caries [12, 13, 29, 30, 32, 38, 39]. A recent study by Grevich et al. [30] found no associations between categories of JIA and caries status, and no association between JIA duration and caries. Other studies have found no associations between caries and restricted mouth opening [12, 13, 32], involvement of upper limbs [12, 13, 32], temporomandibular pain [32], or medication used [13]. However, a positive correlation between disease activity and functional disability and DMFT index has been reported [29]. In addition, an older study (2004) reported of higher caries experience among participants with polyarthritis (RF negative) than the control group (n = 13), and that caries was associated with TMJ dysfunction [38]. The discrepancies among studies could be explained by improved health care in JIA in general and more effective drugs in particular [9, 10]. In the present study, participants with oligoarthritis extended JIA had statistically significantly higher odds for caries in the primary dentition, and participants with polyarthritis RF negative JIA had statistically significantly higher odds for caries in the permanent dentition, compared to children with oligoarthritis persistent arthritis. When the pediatric rheumatologist

reported disease activity (MDgloVAS score > 0), children had statistically significant higher odds for caries in the primary dentition compared to individuals with no activity reported by the physician (MDgloVAS score = 0). The low number of participants in some of the categories means that no general conclusions can be drawn, but it is reasonable to think that disease-specific outcomes consistent with increased disease activity may be associated with caries.

Individuals who are treated with potent immunosuppressives are at increased risk of systemic complications from dental infections [40], and children with JIA should not have untreated decayed teeth, especially in light of the general risk for dental sepsis in severely caries-affected children [41]. This present study shows that, in both individuals with JIA and without, the proportion of enamel lesions exceeded the proportion of dentine lesions in both dentitions, which has been a common recent trend of caries distribution [42]. Surface-specific caries in the permanent dentition differed significantly according to group affiliation (JIA/control group), with a trend towards increased risk of mesial approximal caries (mesial surface compared to buccal surface) in the permanent molars of the JIA group. Clearly, the potential benefit of promotive and preventive dental strategies should be emphasized for this group.

Even though young individuals with JIA have less caries now than they have had historically, clinical practitioners must not ignore that many children and adolescents with JIA use immunosuppressive treatment, which needs special considerations. These children and adolescents must be spared the additional burden of dental caries, implying optimal maintenance and prophylactic oral care.

Conclusions

No overall difference in caries prevalence between children and adolescents with JIA and controls was found. For both groups, maternal educational level of high school (as opposed to university) and tooth surface were associated with presence of caries. Surface-specific caries in the permanent dentition differed significantly according to group affiliation (JIA/control group). Associations between JIA disease-specific variables and presence of caries cannot be excluded. Due to predominance of enamel lesions, the potential for preventative dental strategies is considerable. To be able to make an appropriate caries risk assessment for children and adolescents with JIA, and to assess whether disease-specific factors are associated with caries, prospective clinical studies with sufficient sample sizes are needed.

Abbreviations

ACR: American College of Rheumatology; bDMARDs: Biologic disease-modifying antirheumatic drugs; BW: Bitewing radiographs; CHAQ: Childhood Health Assessment Questionnaire; CI: Confidence interval; CRP: C-reactive protein; dfs/DFS: Decayed and filled surfaces; dmft/DMFT: Decayed, missing and filled teeth; ESR: Erythrocyte sedimentation rate; ICC: Intra-class correlation coefficient; ILAR: International League of Associations for Rheumatology; JIA: Juvenile idiopathic arthritis; MDgloVAS: Clinics physician's global assessment of disease activity visual analogue scale; NorJIA: The Norwegian JIA Study (Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis (JIA)); OR: Odds ratios; PDS: Public Dental Service; PRgloVAS: Patient/parent-reported global assessment of overall wellbeing visual analogue scale; RF: Rheumatoid Factor; RIM: Random intercept logistic models; SD: Standard deviations; sDMARDs: Synthetic disease-modifying antirheumatic drugs; TMJ: Temporomandibular joint; VAS: Visual analogue scale.

Supplementary Information

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Additional file 1. Sample size calculation

Additional file 2. Table S1. Concomitant diagnoses and medication use among individuals with JIA and the controls that are a potential oral health threat.

Additional file 3: Table S1A. Categories for sociodemographic and behavioral characteristics (4–16 years), as originally coded and as re-coded for analyses. **Table S1B.** Categories for behavioral characteristics (< 12 years), as originally coded and re-coded for analyses. **Table S1C.** Categories for disease-specific features, as originally coded (if obtained) and re-coded for analyses.

Additional file 4. Elaboration of the JIA-specific clinical background variables, collected by the pediatric rheumatologists

Additional file 5. Calibration

Additional file 6: Table S1. Illustration of the levels in the multilevel models, according to the dichotomous caries outcome variable and background variables.

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Authors' contributions
EGG: Contributed to the design and data collection of this sub-study, wrote the manuscript in consultation with MSS, ANÅ and SAL. MSS: Conceived and designed this sub-study. ANÅ: Conceived the idea of performing multilevel analysis. SAL: Performed biostatistics. MR: Aided in interpretation and writing of the manuscript and to the design and data collection of the NorJIA study. JF, JH, PF, KT, KR: Contributed to data collection and provided valuable comments. AR, AB, KL, XS, LC: Provided valuable comments. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Regional Committees for Medical and Health Research Ethics (2012/542/REC), Rogaland, Vestland (West). Written informed consents were obtained from the caregivers and the adolescents as appropriate. The study was registered at ClinicalTrials.gov (No: NCT03904459). All procedures were performed in accordance with relevant guidelines.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Clinical Dentistry, The Faculty of Medicine, University of Bergen, Årstadveien 19, 5009 Bergen, Norway. [2]Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology (NTNU), Trondheim, Norway. [3]Department of Pediatrics, St. Olav's Hospital, Trondheim, Norway. [4]Department of Oral and Maxillofacial Surgery, Haukeland University Hospital, Bergen, Norway. [5]Oral Health Centre of Expertise in Western Norway-Vestland, Bergen, Norway. [6]Department of Oral Maxillofacial Radiology, Faculty of Odontology, Malmö University, Malmö, Sweden. [7]Public Dental Health Competence Centre of Northern Norway (TkNN), Tromsø, Norway. [8]Department of Clinical Dentistry, The Arctic University of Norway, Tromsø, Norway. [9]Department of Otorhinolaryngology, Division of Oral and Maxillofacial Surgery, University Hospital of North Norway, Tromsø, Norway. [10]Center for Oral Health Services and Research (TKMidt), Trondheim, Norway. [11]Department of Pediatrics, Haukeland University Hospital, Bergen, Norway. [12]Department of Radiology, University Hospital of North Norway, Tromsø, Norway.

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ORIGINAL ARTICLE

Dental plaque and gingival bleeding in adolescents with juvenile idiopathic arthritis and controls: a multilevel analysis

Elisabeth Grut Gil[a], Anne Nordrehaug Åstrøm[a], Stein Atle Lie[a], Marite Rygg[b,c], Johannes Fischer[a], Annika Rosén[a,d], Athanasia Bletsa[a,e], Keijo Luukko[a], Xie-Qi Shi[a,f], Josefine Halbig[g,h], Paula Frid[g,h,i], Lena Cetrelli[b,j], Karin Tylleskär[k], Karen Rosendahl[h,l] and Marit Slåttelid Skeie[a,j]

[a]Department of Clinical Dentistry, University of Bergen, Bergen, Norway; [b]Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology (NTNU), Trondheim, Norway; [c]Department of Pediatrics, St. Olavs Hospital, Trondheim, Norway; [d]Department of Oral and Maxillofacial Surgery, Haukeland University Hospital, Bergen, Norway; [e]Oral Health Centre of Expertise in Western Norway, Vestland, Norway; [f]Department of Oral Maxillofacial Radiology, Faculty of Odontology, Malmö University, Malmö, Sweden; [g]Public Dental Health Competence Centre of Northern Norway (TkNN), Tromsø, Norway; [h]Department of Clinical Dentistry, The Arctic University of Norway, Tromsø, Norway; [i]Department of Otorhinolaryngology, Division of Oral and Maxillofacial Surgery, University Hospital of North Norway, Tromsø, Norway; [j]Center for Oral Health Services and Research, Mid-Norway (TkMidt), Trondheim, Norway; [k]Department of Pediatrics, Haukeland University Hospital, Bergen, Norway; [l]Department of Radiology, University Hospital of North Norway, Tromsø, Norway

ABSTRACT

Objective: To explore whether plaque and gingival bleeding are more frequently experienced by adolescents with juvenile idiopathic arthritis (JIA) compared to matched controls without JIA; explore whether surface- and site-specific periodontal outcomes vary between the two groups; and for participants with JIA, investigate associations between disease-specific features and periodontal outcomes.

Material and methods: In this comparative cross-sectional study, selected surfaces, and sites of index teeth in 10–16-year-olds with JIA and matched controls were examined by modified versions of Simplified Oral Hygiene Index (OHI-S) and Gingival Bleeding Index (GBI). Mixed-effects logistic regressions, reporting odds ratios (OR) with 95% confidence interval (CI), were applied. Intra-class correlation coefficients (ICCs) were calculated to quantify the degree of dependency of measures within the same individual.

Results: 144 and 159 adolescents with JIA were evaluated according to OHI-S and GBI; corresponding numbers of controls were 154 and 161. Plaque and gingival bleeding were more frequent in individuals with JIA than controls. Adjusted analyses showed association between JIA status and OHI-$S > 0$ (OR $= 2.33$, 95% CI: $1.47 - 3.67$, ICC $= 0.45$) and GBI > 0 (OR $= 1.54$, 95% CI: $1.10 - 2.16$, ICC $= 0.41$ and 0.30). Surface-specific distribution of plaque varied among the two groups.

Conclusions: Our results highlight the importance of increased awareness of oral health care in patients with JIA and that surface- and site-specific differences in periodontal outcomes exist between individuals with JIA and controls. Few JIA disease-specific variables associated with plaque or gingival bleeding.

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Adolescent; dental plaque; gingival diseases; oral health; juvenile idiopathic arthritis

Introduction

Juvenile idiopathic arthritis (JIA) is the most prevalent chronic arthritis condition in childhood and adolescence [1]. The likelihood of dental clinicians to meet young individuals with JIA in their practice is high, especially in the Nordic countries where relatively high incidence rates of JIA have been reported [2] and regular free oral health care to children and adolescents is often provided by the Public Dental Service (PDS) [3]. In Norway, an incidence rate of JIA in 23/100,000 children per year has been demonstrated [2,4].

Historically, a high burden of dental caries has been reported in children and adolescents with JIA [5–8]. More recently, however, the reported prevalence has decreased and is now on a level with that of the general population [9,10]. Nevertheless, a recent systematic review, suggested that plaque, gingivitis, and periodontitis were more common amongst children and adolescents with JIA as compared to individuals without JIA [9]. However, the included studies varied, being different in size, design, and statistical approach, thus, the results should be interpreted with caution.

As the dentition involves multiple teeth, clustering of measurements is common in dental research [11], with teeth clustered within the patient. Units within a cluster may be

CONTACT Elisabeth Grut Gil elisabeth.gil@uib.no Department of Clinical Dentistry, Faculty of Medicine, University of Bergen, Årstadveien 19, Bergen, 5009, Norway

For the NorJIA (Norwegian JIA Study – Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis).

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exposed to identical external factors or share related characteristics [12]. Hence, as periodontium is the supporting structure of the dentition, it is likely that oral hygiene and gingival bleeding are more comparable around teeth within the same patient (cluster), than between different patients. The dependency between teeth within the same patient requires adjustment, since ignoring this may lead to underestimated standard errors, too small *p*-values, and enhanced chance of incorrectly rejecting the null hypothesis (Type I error) [13]. The epidemiologic nomenclature of clustering often refers to individuals nested within groups such as families and schools, while dental research often presents a special type of natural clustering [14] with surfaces clustered within teeth and teeth clustered within individuals. Statistical t-tests are frequently used in publications in dental journals [11] and are a commonly used approach on measures aggregated to patient level (e.g. GBI (Gingival Bleeding Index) or OHI (Oral Hygiene Index)), even if the measures originally were on tooth level. Hence, using simple statistical tests and aggregated data (at patient level), additional information on correlation (non-independency) within the patient is lost. We sought to overcome this problem by using multilevel modelling, an approach which, to the best of our knowledge, has not yet been applied in studies addressing periodontal health among young individuals with JIA.

The aims of this study were to explore whether plaque and gingival bleeding are more frequently experienced by adolescents with JIA as compared to matched controls without JIA. Additionally, we explored whether surface- and site-specific periodontal outcomes vary between the two groups. Finally, and specifically for participants with JIA, we investigated possible associations between disease-specific features and the periodontal outcome variables. We hypothesise that participants with JIA have more plaque and gingival bleeding, as well as more variance in surface- and site-specific distribution of the periodontal outcome variables than participants without JIA (controls). We also hypothesise that plaque and gingival bleeding vary according to the value on JIA specific features within the group of JIA patients.

Material and methods

Study design

Baseline data from a prospective longitudinal multicenter study, NorJIA[1], are used in this comparative cross-sectional sub-study evaluating periodontal health of adolescents from 10–16 years. The multicenter study included children and adolescents (4–16 years old) diagnosed with JIA by a paediatric rheumatologist according to the criteria defined by the International League of Associations for Rheumatology (ILAR) [15] and presented a written informed consent. There were no participants with major medical comorbidities such as congenital facial anomalies, skeletal dysplasia, or malignancies in the cohort. Data for the present sub-study were collected between April 2015 and August 2018. Baseline data on dental caries has recently been published with a similar methodological approach (sample size calculation included) [10].

Participants

Three university hospitals, located in western, central, or northern Norway, were involved in the recruitment. Participant flow diagram are presented in Figure 1. A total of 228 individuals were included in the medical examination, while four participants declined a further oral health assessment. Participants having an oral examination ($n = 224$) were matched 1:1 with controls corresponding to sex, age, centre site, and mothers' country of origin (western or non-western). The controls were enrolled from seven Public Dental Service (PDS) clinics and did not have JIA or substantially no other chronic diseases (Additional file 1, Supplementary Table 1). Both rural and urban areas were represented. For the controls, data collection was combined with a planned regular dental examination and as an incentive for participation two cinema tickets were offered. For this sub-study only adolescents (10–16 years) were evaluated, hence 162 adolescents with JIA and 162 controls were enrolled.

Questionnaires and construction of variables

A questionnaire including socio-behavioral and subjective clinical information was given all participants (and/or caregivers, as appropriate) [10]. Variables included in this sub-study were educational level of caregivers, number of caregivers in the household, mothers' country of origin, frequency of toothbrushing, frequency of tooth flossing during the last 3 months, gingival bleeding during toothbrushing, pain or discomfort during toothbrushing, frequency of intraoral ulceration(s) and perception of dry mouth. Family name of the participant was evaluated if the item regarding mothers' country of origin was missing (in Norway quite often the family name of a child includes both father's and mother's name). Finally, participants with JIA, were asked if they had received information about the importance of good oral health in relation to the JIA diagnosis, and if so, they were asked to specify the health profession of the communicator. The coding of these self-reported variables is presented in Additional file 2, Supplementary Table 1A. Specifically for participants with JIA, exploratory data analysis was facilitated by including the variables; JIA category, various blood tests, medication, age of disease onset, disease duration, activity/remission status, physician's global assessment of disease activity visual analogue scale (MDgloVAS), patient/parent-reported global assessment of overall well-being visual analogue scale (PRgloVAS), Childhood Health Assessment Questionnaire (CHAQ) hygiene item tooth brushing. The coding is presented in Additional file 2, Supplementary Table 1B.

Examinations

The participants with JIA were examined by experienced paediatric rheumatologists at one of the three university hospitals. The disease-specific clinical background variables and blood tests are described in detail in Additional file 3 [10] and Additional file 4, respectively. The oral assessments of selected index teeth, surfaces, and sites, carried out by one

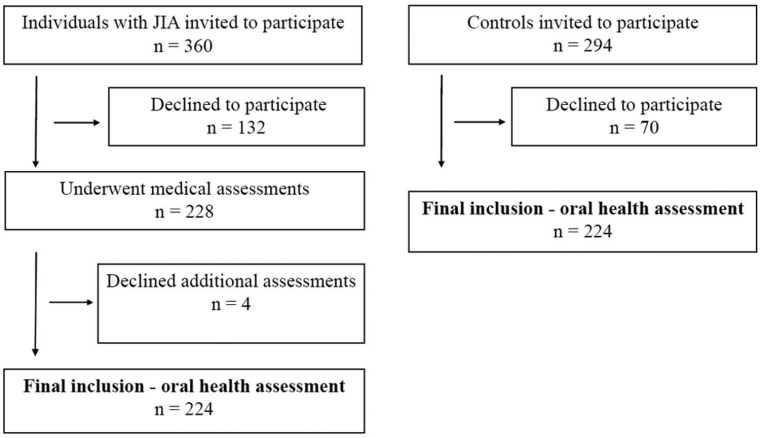

Figure 1. Participant flow diagram of children and adolescents with juvenile idiopathic arthritis (JIA) and controls.

out of five dentists, are shown in Additional file 5, Supplementary Table 1. As the present study is part of a comprehensive oral health examination in the NorJIA project, involving multiple clinical variables, a full mouth protocol was not possible. Instead Simplified Oral Hygiene Index (OHI-S) by Greene and Vermillion [16] was decided on, accordingly selected index teeth were first permanent molars and one incisor in the upper- and lower jaw. OHI-S consists of two components, the simplified Debris Index (DI-S) and the simplified Calculus Index (CI-S). However, registration of oral hygiene was modified as subgingival calculus was not recorded (supragingival calculus was recorded). Only fully erupted teeth were scored, and in case of fixed orthodontic appliances, the assessment was not done. Gingival bleeding was evaluated on the same index teeth represented in S-OHI, by using a modified Gingival Bleeding Index (GBI) introduced by Ainamo and Bay [17]. This index was modified as no horizontal movement of the probe on the surface was performed, instead a vertical movement at three sites on the respective surface (mesial, medial, and distal) was implemented. Probing of the orifice of the gingival crevice was done with a World Health Organisation (WHO) periodontal measuring probe with a 0.5 mm ball tip. Additionally, fissure of lip and/or corner of lip, gingival ulcers with discontinuation of the epithelia of at least 3 mm, buccal ridging, tongue indentation, buccal gingival hyperplasia (buccal side of the lower and upper anterior teeth), and potential mouth dryness (by evaluating if dental mirror sticks to buccal mucosa) were recorded. The coding of these variables is presented in Additional file 2, Supplementary Table 1C. The coding of the clinical oral variables is presented in Additional file 2, Supplementary Table 1D.

Training process

Prior to the study, the dentists underwent theoretical courses in how to use the modified version of the OHI-S and the modified version of the GBI. Uncertainties about the procedures were discussed until clarity. The dentists were given a plastic-coated instruction sheet of the written descriptions to accompany the oral examinations as a guide. To illustrate the force to be applied on probing of gingival sulcus to determine gingival bleeding, the dentists practiced with a dental probe on a digital letter weight (Wedo Package Scale Paket 50 Plus). At two different sessions, three intervals with seven attempts were performed.

Statistical methods

Data were analysed using SPSS version 25.0 (IBM Corp. Released 2013, IBM SPSS Statistics for Windows, Armonk NY: IBM Corp) and STATA version 16 (Stata Corp LP, College Station, TX). To describe continuous demographic and clinical variables mean and standard deviations (SD) were applied. To evaluate differences in categorical variables between children with and without JIA chi-squared tests were applied. Linear regression models, with robust variance estimates correcting for matching, were used to explore differences in the aggregated indexes OHI-S and GBI, between the matching pairs. The data of the modified version of the OHI-S (OHI-$S > 0$) had a clustered 2-level hierarchical structure with surfaces/tooth (level 1) clustered within individuals (level 2) and GBI (GBI $>$ 0) had a clustered 3-level hierarchical structure with sites/surfaces (level 1) clustered within teeth (level 2), and teeth clustered within individuals (level 3). Consequently, random intercept logistic models (RIM) were applied. The levels in the multilevel models with regard to the dichotomous periodontal outcome variables and background variables are illustrated in Additional file 6, Supplementary Tables 1A and 1B. The formulas estimated (using restricted maximum likelihood REML), for the 3-level data, using mixed-effects (random intercept) logistic regression were:

$$logit(P(Y_{ijk} = 1)) = \beta_0 + \beta_1^T X_{ijk} + \beta_{0i} + \beta_{0ij} + e_{ijk}$$
$$Y_{ijk} \sim Binomial(n_i, p_i)$$
$$\beta_{0i} \sim N(0, \sigma_v^2)$$

$$\beta_{0ij} \sim N(0, \sigma_u^2)$$

$$icc_v = \frac{\sigma_v^2 + \sigma_u^2}{\sigma_v^2 + \sigma_u^2 + \pi^2/3}$$

$$icc_u = \frac{\sigma_u^2}{\sigma_v^2 + \sigma_u^2 + \pi^2/3}$$

icc_u is the intra class correlation for the measurements clustered within teeth, while icc_v is the intra class correlation for the measurements of the teeth clustered within individual. For the 2-level data, the mixed-effects logistic regression models were:

$$logit(P(Y_{ij} = 1)) = \beta_0 + \beta_1^T X_{ij} + \beta_{0i} + e_{ij}$$

$$Y_{ij} \sim Binomial(n_i, p_i)$$

$$\beta_{0i} \sim N(0, \sigma_v^2)$$

$$icc_v = \frac{\sigma_v^2}{\sigma_v^2 + \pi^2/3}$$

icc_v is the intra class correlation for the measurements of the teeth clustered within individual.

The multilevel models account for clustering of periodontal data for sites (k) within teeth (j) and within individuals (i). By applying separate mixed-effects logistic models, intra-class correlation coefficients (ICC) for the matching pairs were tested. Outcome measure was periodontal data as represented by OHI-$S > 0$ and GBI > 0 and the main exposure variable was JIA group status (JIA/control group). Possible confounders in the mixed-effects logistic regression analysis were identified consequent to socio-behavioral, and subjective clinical variables that were statistically significantly associated with JIA status and the respective periodontal outcome variables (OHI-$S > 0$ or GBI > 0). These possible confounding variables together with oral variables statistically associated with the periodontal outcome variables in unadjusted analysis and the main exposure variable (JIA/control group) were adjusted for in the mixed-effects logistic regression analysis. Specifically, for participants with JIA, age and gender were adjusted for in the mixed-effects logistic regression analysis. By calculating the ICCs the effect of dependency was evaluated at individual level (oral hygiene and gingival bleeding data), and at tooth level (gingival bleeding data). The ICC demonstrate variations between teeth and individuals as a proportion of the total variance. ICC varies between 0 (implying the respective periodontal health variable is independent within individuals/teeth) and 1 (implying no variation of the respective periodontal health variable within an individual, *i.e.* no variation between clusters). Scheffe post-hoc test was used to adjust significance levels in multiple comparisons in the mixed-effects logistics regressions. P-values below 0.05 were regarded as statistically significant.

Ethical approval

Approval was given regional ethics committee (2012/542/REC). Leaders of different County Dental Health Authorities, at different Oral Health Centre of Expertise, and at the three paediatric departments at the university hospitals also approved the study. Before participation written informed consent was signed. The NorJIA study is registered at ClinicalTrials.gov (No: NCT03904459).

Results

Sample characteristics

As previously described [10], the response rates for the individuals with JIA and controls were 63.3% (228/360) and 76.2% (224/294), respectively (Figure 1). The proportion of girls was less among the eligible individuals with JIA who declined participation, compared to the participants with JIA (58.3% vs 59.2%, p=.027) [10]. Also, mean age among the individuals with JIA who declined participation was smaller compared to the cohort as a whole (10.5 (SD 3.5) years, p<.001) [10].

The 224 participants with JIA who recieved an oral health examination were matched to a control [10]. Mean age of both individuals with JIA and controls was 12.0 years (SD 3.2) (p=.974). Also 133 (59.4%) of the participants with JIA were girls, corresponding number in the control group were 134 (59.8%). Among the 224 pairs, 211 (94.2%) of the pairs were matched in relation to mother's background of origin (for 10 individuals the family name was evaluated).

Oral hygiene and gingival bleeding were exclusively assessed on participants 10 years and older resulting in 162 individuals with JIA and 162 controls. For this sub-study, a total of 144 and 159 individuals with JIA were evaluated according to OHI-S and GBI, corresponding numbers for the control group were 154 and 161 (Additional file 5, Supplementary Table 1). The age group in this sub-study correspond to adolescence according to the World Health Organisation [18].

Ninety-four mothers in the JIA group (62.3%) *vs.* 111 (76.6%) in the control group had higher education (p=.008) (Table 1). Corresponding figures for fathers were 62 (41.9%) and 86 (60.6%) (p=.001). A larger proportion of individuals with than without JIA, confirmed dry mouth on a regular basis (7.9% *vs.* 2.5%, p=.030). Forty-three responders with JIA (43/149, 28.9%) reported that they had received information about the importance of good oral health in relation to the JIA diagnosis. The information was mainly communicated by physicians and dentists (results not shown). Potential oral health risk factors (concomitant diagnoses and use of medication among the participants) are presented in Additional file 1, Supplementary Table 1.

Experience of plaque and gingival bleeding in individuals with and without JIA

The two components of the modified OHI-S; DI-S and CI-S showed a mean score of 0.66 (SD 0.38) and 0.03 (SD 0.09) in individuals with JIA, and 0.54 (SD 0.40) and 0.03 (SD 0.09) in controls, respectively. Sixteen individuals with JIA and 16 controls had calculus (CI-$S > 0$). Mean OHI-S score altogether was 0.69 (SD 0.39) amongst individuals with JIA and 0.57 (SD 0.42) amongst the controls. All scores, except for the CI-S, showed statistically significant differences between the two

Table 1. Socio-behavioral, and subjective clinical characteristics of 162 individuals with juvenile idiopathic arthritis and 162 controls, aged 10–16 years.

Variable	JIA ($n = 162$)	Controls ($n = 162$)	p-value
Educational level of caregivers, n (%)			
Mother			**.008**
High school/vocational school	57 (37.8)	34 (23.5)	
University/college	94 (62.3)	111 (76.6)	
Father			**.001**
High school/vocational school	86 (58.1)	56 (39.4)	
University/college	62 (41.9)	86 (60.6)	
Share household with, n (%)			
Two caregivers in the household*	119 (76.8)	130 (81.3)	.329
Only one caregiver in the household	36 (23.2)	30 (18.8)	
Frequency of toothbrushing, n (%)			
Once a day or less/do not know	33 (21.3)	38 (23.9)	.581
Twice a day, or more	122 (78.7)	121 (76.1)	
Frequency of tooth flossing during the last 3 months, n (%)			
Daily or more	16 (10.4)	16 (10.1)	.924
Several times weekly or less/do not know	138 (89.6)	143 (89.9)	
During toothbrushing, gingival bleeding occurs, n (%)			
Sometimes or more/do not know	96 (62.3)	85 (53.5)	.112
Never	58 (37.7)	74 (46.5)	
During toothbrushing, pain or discomfort occurs, n (%)			
Yes/do not know	20 (13.2)	21 (13.2)	.990
No	132 (86.8)	138 (86.8)	
Frequency of intraoral ulceration(s) (≥3 mm), n (%)			
Once a month or more	11 (7.5)	17 (10.6)	.348
Several times yearly (but less seldom than once a month) or less/do not know	136 (92.5)	144 (89.4)	
Perception of dry mouth on a regular basis, n (%)			
Yes	12 (7.9)	4 (2.5)	**.030**
No/do not know	140 (92.1)	157 (97.5)	

*The variable includes living across two households, given two caregivers in both households. Not all participants responded to the questionnaires. Chi-squared test level of significance $p<.05$.
Significant values are marked in bold.

groups ($p<.012$). The OHI-S score had a beta (mean difference between individuals with JIA and controls) of 0.12 (95% CI: 0.03 – 0.21) ($p=.010$) when correcting for matching pairs. Figure 2 demonstrates mean score with error bars of the modified DI-S, CI-S and OHI-S, separately for individuals with and without JIA. Mean percentage score of the modified GBI showed a statistically higher value in individuals with JIA than in controls (17.72 (SD 16.83) *vs.* 12.56 (SD 14.32), $p=.004$). The GBI score had a beta (mean difference between individuals with JIA and controls) of 5.16 (95% CI: 1.67 – 8.66) ($p=.004$) when correcting for matching pairs. Figure 3 demonstrates mean percentage score with error bars of the modified GBI, separately for individuals with and without JIA.

Multilevel analyses

The correlation between the matching pairs for the dichotomised outcome variables OHI-$S>0$ and GBI $>$ 0 were weak (ICC = 0.01 and ICC $<$ 0.001, respectively), consequently the original matching in the data was not accounted for in the final multilevel models. Regressing OHI-S (presence of plaque (DI-$S>0$) and/or calculus (CI-$S>0$) on JIA status while adjusting for socio-behavioral, and clinical characteristics showed a statistically significant association between JIA status and OHI-$S>0$ (Odds Ratio (OR) = 2.33, 95% Confidence Interval (CI): 1.47 – 3.67) (Table 2). Corresponding finding for gingival bleeding (GBI $>$ 0) was OR = 1.54, 95% CI: 1.10 – 2.16 ($p=.013$) (Table 2). Independent of JIA status, molars were more likely to present with OHI-$S>0$ compared to incisors (OR = 5.43, 95% CI: 3.73 – 7.91, $p<.001$), and lingual surfaces (36, 46) were more likely to present with OHI-$S>0$ compared to buccal surfaces (11, 31, 16, 26) (OR = 2.81, 95% CI: 1.67 – 4.73, $p<.001$). Corresponding ORs for GBI $>$ 0 were 1.78 (95% CI: 1.31 – 2.42, $p<.001$) and 1.24 (95% CI: 0.83 – 1.83, $p=.291$). In the multilevel model with oral hygiene (OHI-$S>0$) as outcome variable, the ICC at individual level with no covariates was 0.32, demonstrating that 32% of the variance in the oral hygiene variable was between rather than within individuals. In the adjusted analysis, the ICC was 0.45. Corresponding ICC with gingival bleeding (GBI $>$ 0) as outcome variable were 0.29 and 0.30, respectively. The ICC at tooth level with gingival bleeding (GBI $>$ 0) as outcome variable was 0.43 with no covariates, demonstrating that 43% of the variance in the gingival bleeding variable was between rather than within teeth. In the adjusted analysis, the corresponding ICC was 0.41. All ICCs were statistically significant ($p<.001$).

Surface- and site-specific periodontal health by group affiliation

Table 3 depicts the results from mixed-effects modelling regressing side-, jaw-, and surface-specific traits on OHI-$S>0$ and side-, jaw-, surface- and site-specific traits on GBI $>$ 0, separately for individuals with and without JIA. Figure 4 and Figure 5 demonstrate prevalence with error bars of OHI-$S>0$ at surface level and GBI $>$ 0 at site level, separately for individuals with and without JIA. There was a statistically significant interaction between surface and group affiliation ($p<.001$) on OHI-$S>0$. Whereas the interaction between surface and group affiliation ($p=.351$), and site and group affiliation ($p=.27$) were nonsignificant on presence of gingival bleeding (GBI $>$ 0). Among both individuals with JIA and

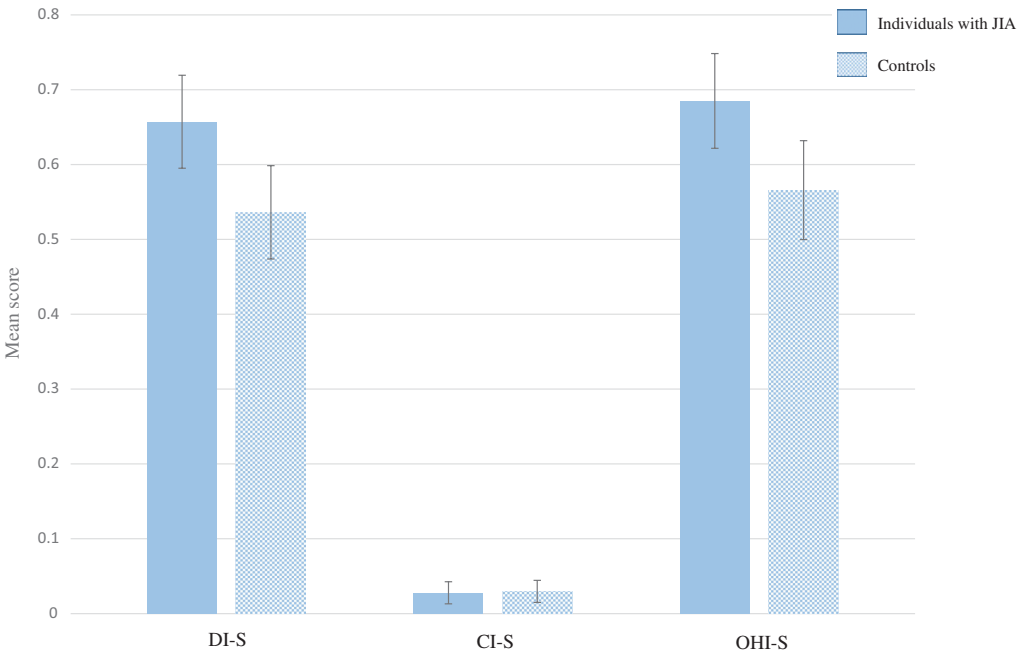

Figure 2. Mean score of simplified Debris Index (DI-S), simplified Calculus Index (CI-S) and simplified Oral Hygiene Index (OHI-S) among individuals with juvenile idiopathic arthritis (JIA) and controls.

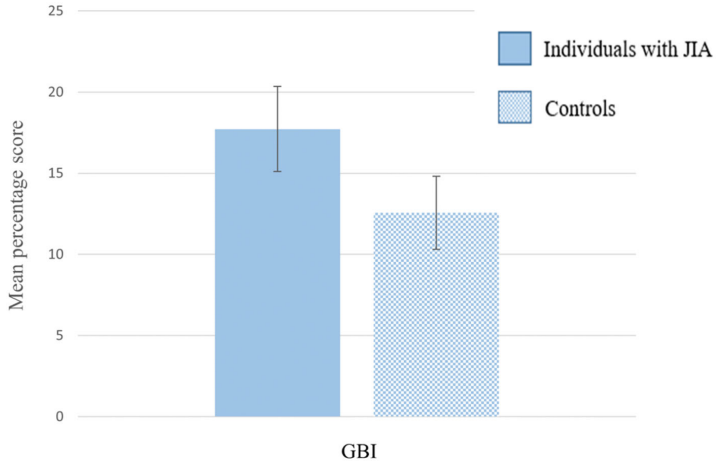

Figure 3. Mean percentage score of Gingival Bleeding Index (GBI) among individuals with juvenile idiopathic arthritis (JIA) and controls.

controls, the likelihood of OHI-$S > 0$ was statistically significantly less on buccal surface of maxillary central (OR = 0.20, 95% CI: 0.12 – 0.34 and OR = 0.14, 95% CI: 0.08 – 0.26) and on buccal surface of mandibular central (OR = 0.17, 95% CI: 0.10 – 0.28 and OR = 0.18, 95% CI: 0.10 – 0.31) compared to buccal surface of maxillary 1. molars. Among the controls only, the ORs of OHI-$S > 0$ was statistically significantly less in maxilla compared to mandibula (OR = 0.39, 95% CI: 0.28 – 0.53) and statistically significantly larger on lingual surface of mandibular 1. molars than on the buccal surfaces of maxillary 1. molars (OR = 5.63, 95% CI: 3.57 – 8.88).

Disease-specific variables associated with the periodontal health variables

Adjusted mixed-effects logistic regressions showed a statistically significantly higher risk of OHI-$S > 0$ in individuals with systemic arthritis, compared to individuals with oligoarthritis

Table 2. Group affiliation, socio-behavioral, and clinical characteristics in relation to oral hygiene (OHI-$S > 0$), and gingival bleeding (GBI > 0). Unadjusted and adjusted mixed-effects logistic regression.

	OHI-$S > 0$[a]				GBI > 0[b]			
	Unadjusted analyses		Adjusted analyses[c]		Unadjusted analyses		Adjusted analyses[d]	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Health status								
Control group	1	ref	1	ref	1	ref	1	ref
JIA	1.92 (1.35 – 2.73)	**<.001**	2.33 (1.47 – 3.67)	**<.001**	1.62 (1.19 – 2.20)	**.002**	1.54 (1.10 – 2.16)	**.013**
Educational level of mother								
University/college	1	ref			1	ref	1	ref
High school/vocational school	1.04 (0.70 – 1.56)	.844			1.47 (1.04 – 2.07)	**.030**	1.38 (0.96 – 1.98)	.081
Educational level of father								
University/college	1	ref			1	ref		
High school/vocational school	0.74 (0.50 – 1.07)	.109			1.04 (0.74 – 1.46)	.815		
Household structure								
Two caregivers[e]	1	ref			1	ref		
One caregiver	1.01 (0.65 – 1.58)	.950			1.24 (0.84 – 1.81)	.277		
Frequency of toothbrushing								
Twice a day or more	1	ref			1	ref		
Once a day or less[f]	1.70 (1.11 – 2.61)	**.015**			1.27 (0.88 – 1.83)	.209		
Frequency of tooth flossing during the last 3 months								
Daily or more	1	ref			1	ref		
Several times weekly or less[f]	1.23 (0.66 – 2.28)	.513			1.40 (0.82 – 2.38)	.220		
During toothbrushing, gingival bleeding occurs								
Never	1	ref			1	ref		
Sometimes or more[f]	1.21 (0.83 – 1.75)	.320			1.57 (1.14 – 2.17)	**.006**		
During toothbrushing, pain or discomfort occurs								
No	1	ref			1	ref		
Yes[f]	1.06 (0.61 – 1.83)	.842			0.94 (0.59 – 1.51)	.796		
Frequency of intraoral ulceration(s) (>3mm)								
Several times yearly (but less seldom than once a month) or less/do not know	1	ref			1	ref		
Once a month or more	0.53 (0.28 – 0.98)	**.043**			1.01 (0.58 – 1.75)	.971		
Perception of dry mouth on a regular basis								
No/do not know	1	ref			1	ref		
Yes	1.59 (0.72 – 3.50)	.249			1.70 (0.86 – 3.37)	.125		
Jaw								
Mandible	1	ref	1	ref	1	ref	1	ref
Maxilla	0.59 (0.47 – 0.73)	**<.001**	1.02 (0.67 – 1.56)	.914	0.46 (0.39 – 0.54)	**<.001**	0.51 (0.37 – 0.72)	**<.001**
Side								
Right side	1	ref			1	ref		
Left side	0.95 (0.77 – 1.18)	.665			1.10 (0.94 – 1.29)	.230		
Anterior/posterior								
Incisors	1	ref	1	ref	1	ref	1	ref
Molars	8.48 (6.36 – 11.32)	**<.001**	5.43 (3.73 – 7.91)	**<.001**	2.13 (1.77 – 2.56)	**<.001**	1.78 (1.31 – 2.42)	**<.001**
Surface (tooth)								
Buccal (11, 31, 16, 26)	1	ref	1	ref	1	ref	1	ref
Lingual (36, 46)	5.60 (4.27 – 7.35)	**<.001**	2.81 (1.67 – 4.73)	**<.001**	2.63 (2.24–3.10)	**<.001**	1.24 (0.83 – 1.83)	.291
Site (surface)								
A: Mesial (buccal, lingual)					1[BC]	**<.001**[g]	1[BC]	**<.001**[g]
B: Medial (buccal, lingual)					1.45 (1.19 – 1.77)[A]	**.001**	1.55 (1.26-1.92)[A]	**<.001**
C: Distal (buccal, lingual)					1.47 (1.21 – 1.80)[A]	**.001**	1.49 (1.20–1.84)[A]	**.001**

(*continued*)

Table 2. Continued.

	OHI-S > 0[a]				GBI > 0[b]			
	Unadjusted analyses		Adjusted analyses[c]		Unadjusted analyses		Adjusted analyses[d]	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
ICC individual level	0.32		0.45		0.29		0.30	
ICC tooth level					0.43		0.41	
AIC	2311.34		1987.75		4466.88		3911.16	

[a]Dichotomised outcome variable (present or absent) of the modified version of the simplified oral hygiene index (OHI-S). OHI-S consists of two components, the simplified Debris Index (DI-S) and the simplified Calculus Index (CI-S) [16]. 144 individuals with JIA and 154 controls were evaluated according to the modified OHI-S.
[b]Dichotomised outcome variable (present or absent) of the modified version of Gingival Bleeding Index (GBI) [17]. 159 individuals with JIA and 161 controls were evaluated according to the modified GBI.
[c]Adjusted for: Health status (main exposure variable), jaw, anterior/posterior, surface (tooth).
[d]Adjusted for: Health status (main exposure variable), educational level of mother, jaw, anterior/posterior, surface (tooth), site (surface).
[e]Also includes living across two households, given two caregivers in both households.
[f]The answer option "Do not know" are included in the variable associated with negative impact on oral health.
[g]Overall *p*-value. Surfaces and sites statistically significant in Post hoc analyses are marked using superscript uppercase letters. Scheffe adjusted *p*-values in Post hoc analysis $p<.05$.
Significant values are marked in bold.
Abbreviations: JIA: Juvenile idiopathic arthritis; ICC: intraclass correlation coefficient; AIC: Akaike Information Criteria.

persistent (OR = 5.20, 95% CI: 1.07 − 25.32) (Table 4). However, due to small number of participants in some of the categories no conclusions can be made. Individuals aged >6 years at JIA onset had a statistically significantly higher risk of plaque OHI-$S > 0$ in the adjusted analysis, compared to individuals aged ≤6 years at JIA onset (OR = 1.80, 95% CI: 1.08 − 3.00) (Table 4). The seven participants reporting difficulties with tooth brushing, according to CHAQ hygiene item Tooth brushing, had statistically significantly higher risk of gingival bleeding (GBI > 0), compared to participants reporting no difficulties (OR = 2.92, 95% CI: 1.14 − 7.45). For the multilevel model with covariates analysing disease-specific features in relation to oral hygiene (OHI-$S > 0$) the ICC at individual level was 0.29 ($p<.001$). In relation to gingival bleeding (GBI > 0), the respective ICC was 0.27 ($p<.001$), whilst the ICC at tooth level was 0.41 ($p<.001$).

Other clinical characteristics of oral cavity independent of plaque and gingival bleeding

No statistically significant differences of other clinical characteristics were found between individuals with JIA and controls (Table 5).

Discussion

Plaque and gingival bleeding were more frequently experienced in individuals with JIA as compared to controls without JIA. Surface-specific distribution of plaque varied between the two groups. Individuals older than 6 years at JIA onset had higher risk of plaque, compared to individuals 6 years or younger at disease onset.

An important strength of the present study is the multilevel modelling, considering the clustered structure of the data and facilitating optimal utilisation of outcome data. In view of the statistically significant ICCs calculated in this study, the application of mixed-effects logistic regressions was essential. This also shows that periodontal outcome variables within the individuals (plaque and gingival bleeding) and within teeth (gingival bleeding) are highly dependent. A weak correlation between the matching pairs was observed, demonstrating that the background variables (sex, age, centre site, and background-origin) were weak matching variables for the periodontal outcome variables. Consequently, convergence problems occurred if matching was added to the mixed-effects models and the original matching in the data was not accounted for in the multilevel models. Anyhow, linear regression analyses correcting for matching were performed, demonstrating statistically significant mean difference in the aggregated indexes OHI-S and GBI between the matching pairs. Hormonal changes in puberty are known to exacerbate gingival inflammation (puberty gingivitis) and occurs at different ages for girls and boys [21]. Although the individual's pubertal stage varies with age and adolescents with chronic rheumatic conditions might experience delayed puberty [22], the comparative design strengthened the results. Regarding representativeness of the Norwegian adolescent population of JIA, three out of four existing

Table 3. Oral variables including side, jaw, and surfaces in relation to oral hygiene (OHI-$S > 0$), and side, jaw, surfaces, and sites in relation to gingival bleeding (GBI > 0) by group affiliation. Unadjusted mixed-effects logistic regression.

	OHI-$S > 0$[a]				GBI > 0[b]			
	JIA		Controls		JIA		Controls	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Side								
Right side	1	ref	1	ref	1	ref	1	ref
Left side	0.93 (0.68 – 1.26)	.673	0.98 (0.73 – 1.31)	.881	1.11 (0.90 – 1.37)	.331	1.09 (0.86 – 1.38)	.480
Jaw								
Mandible	1	ref	1	ref	1	ref	1	ref
Maxilla	0.91 (0.67 – 1.23)	.530	0.39 (0.28 – 0.53)	**<.001**	0.50 (0.40 – 0.62)	**<.001**	0.41 (0.32 – 0.52)	**<.001**
Surface (tooth)								
A: Buccal surface of maxillary 1. molars (16, 26)	1^{CD}	**<.001**[c]	1^{BCD}	**<.001**[c]	1^{BC}	**<.001**[c]	1^{B}	**<.001**[c]
B: Lingual surface of mandibular 1. molars (36, 46)	1.35 (0.89 – 2.06)^{CD}	.164	5.63 (3.57 – 8.88)^{ACD}	**<.001**	1.98 (1.54 – 2.54)^{ACD}	**<.001**	2.77 (2.06 – 3.73)^{ACD}	**<.001**
C: Buccal surface of maxillary central (11)	0.20 (0.12 – 0.34)^{AB}	**<.001**	0.14 (0.08 – 0.26)^{AB}	**<.001**	0.43 (0.29 – 0.64)^{ABD}	**<.001**	0.62 (0.39 – 0.97)^{B}	**.036**
D: Buccal surface of mandibular central (31)	0.17 (0.10 – 0.28)^{AB}	**<.001**	0.18 (0.10 – 0.31)^{AB}	**<.001**	0.95 (0.68 – 1.32)^{BC}	.750	1.11 (0.75 – 1.65)^{B}	.611
Site (tooth)								
A: Mesiobuccal site of maxillary 1. molars (16, 26)					1^{E}	**<.001**[c]	1^{EF}	**<.001**[c]
B: Mediobuccal site of maxillary 1. molars (16, 26)					1.27 (0.78 – 2.09)^{E}	.338	1.00 (0.51 – 1.96)^{EF}	1.000
C: Distobuccal site of maxillary 1. molars (16, 26)					2.18 (1.36 – 3.48)	**.001**	2.97 (1.66 – 5.33)	**<.001**
D: Mesiolingual site of mandibular 1. molars (36, 46)					2.13 (1.33 – 3.40)	**.002**	3.07 (1.72 – 5.49)	**<.001**
E: Mediolingual site of mandibular 1. molars (36, 46)					4.60 (2.93 – 7.21)^{ABGHIKL}	**<.001**	6.75 (3.87 – 11.77)^{ABGH}	**<.001**
F: Distolingual site of mandibular 1. molars (36, 46)					2.26 (1.42 – 3.60)	**.001**	3.78 (2.13 – 6.71)^{AB}	**<.001**
G: Mesiobuccal site of maxillary central (11)					0.44 (0.20 – 0.94)^{E}	**.034**	0.51 (0.19 – 1.35)^{E}	.172
H: Mediobuccal site of maxillary central (11)					0.60 (0.30 – 1.20)^{E}	.147	0.81 (0.35 – 1.92)^{E}	.636
I: Distobuccal site of maxillary central (11)					0.84 (0.44 – 1.61)^{E}	.596	1.67 (0.80 – 3.48)	.172
J: Mesiobuccal site of mandibular central (31)					1.83 (1.04 – 3.23)	**.036**	1.69 (0.81 – 3.52)	.162
K: Mediobuccal site of mandibular central (31)					0.99 (0.53 – 1.86)^{E}	.971	1.69 (0.81 – 3.52)	.162
L: Distobuccal site of mandibular central (31)					1.34 (0.74 – 2.42)^{E}	.338	1.84 (0.89 – 3.81)	.099
ICC individual level	0.30		0.31		0.28		0.29	
ICC tooth level					0.48		0.44	
AIC	1095.35		1206.67		2459.39		2002.14	

[a]Dichotomised outcome variable (present or absent) of the modified version of the simplified oral hygiene index (OHI-S) [16]. 144 individuals with JIA and 154 controls were evaluated according to the modified OHI-S.
[b]Dichotomised outcome variable (present or absent) of the modified version of Gingival Bleeding Index (GBI) [17]. 159 individuals with JIA and 161 controls were evaluated according to the modified GBI.
[c]Overall *p*-value. Surfaces and sites statistically significant in Post hoc analyses are marked using superscript uppercase letters. Scheffe adjusted *p*-values in Post hoc analysis $p<.05$.
Significant values are marked in bold.
Abbreviations: JIA: Juvenile idiopathic arthritis; ICC: intraclass correlation coefficient; AIC: Aikake Information Criteria.

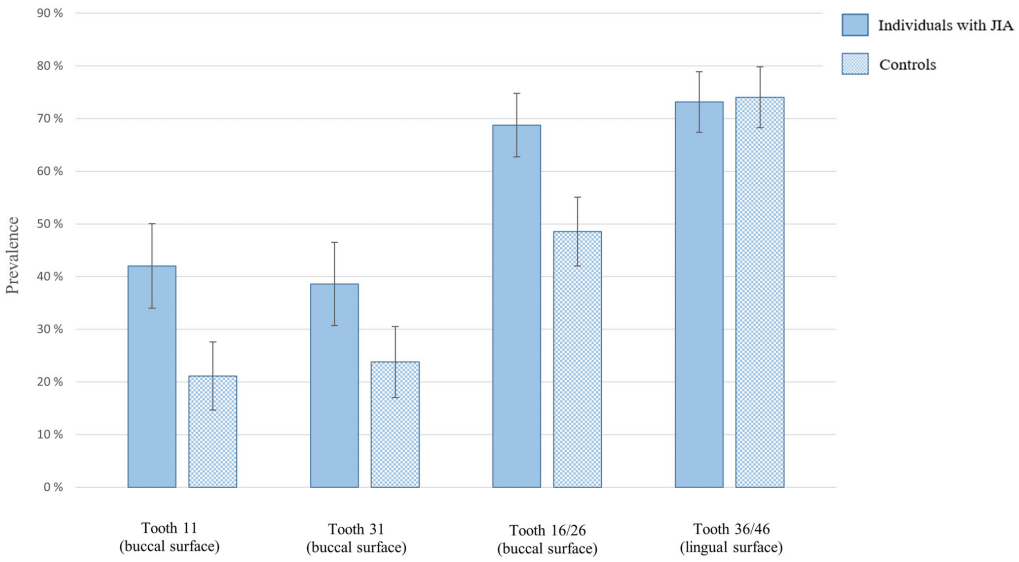

Figure 4. Percentage (95% confidence interval represented as error bars) of plaque or calculus (OHI-$S > 0$) at surface level among individuals with juvenile idiopathic arthritis (JIA) and controls.

Norwegian regional paediatric rheumatology centres were involved in the recruitment, all JIA categories were included, and the sample size was relatively large in this field of research. However, potential non-response bias for individuals with JIA should not be disregarded [23]. Other limitations in the present study were the use of index teeth, as a full mouth registration could potentially be more informative, also a full mouth protocol would have statistical advantage, however results demonstrate appropriate power. The present study did not consider that some participants had erupting premolars adjacent to index-teeth examined. Mixed dentition may have an impact on the oral environment, however the mesial surfaces being closest to erupting premolars were not scored. Also, the impact of non-steroidal anti-inflammatory drugs (NSAIDs) frequently used by individuals with JIA and folic acid supplementation, administered to prevent side effects of methotrexate [24], might have been evaluated. NSAIDs and folic acid constitute potential confounders to gingival bleeding as NSAIDs are suggested to decrease inflammatory signs of gingivitis [25], and it has been suggested that supplementation of folic acid improves gingiva's resistance to local irritants, hence reduces gingival inflammation [26]. Another limitation was the modification of the diagnostics tools, complicating comparisons with other epidemiological studies.

In our study we found that individuals with JIA were more likely to have plaque and gingival bleeding compared to their peers. This compares well with the study of Welbury et al. [8], presenting the highest sample size in the previously mentioned systematic review [9]. A recently published article from 2019 [27], thus not included in the systematic review, with a relatively large sample size (85 individuals with JIA) found gingival inflammation as measured by bleeding on probing (BOP) to be increased in adolescents with JIA. In our study one might speculate that the higher level of education amongst caregivers in the control group as compared to the JIA group might have biased the results, as more frequent toothbrushing and lower plaque score are reported in adolescents with caregivers having higher educational level [28]. However, we found no association between caregivers' educational level and plaque or gingival bleeding in the adjusted analysis in the present study. Only two studies [27,29] focussing on gingival health among individuals with JIA have described socioeconomic background characteristics of the participants, and only Grevich et al. [27] adjusted for socioeconomic covariates known to influence oral health [30]. This could perhaps be a component in explaining the divergent findings in this field.

Accumulation of dental plaque, denoted as biofilm, is affected by the ability and motivation of oral hygiene procedures. Function ability, *e.g.* disability in upper limbs or temporomandibular joints (TMJs) has been highlighted as a risk factor for reduced oral hygiene among individuals with JIA [8,31,32]. In the present study, there was no difference in the reported oral behaviours between individuals with and without JIA, but individuals with JIA reporting difficulties with tooth brushing, according to CHAQ hygiene item Tooth brushing, had higher risk of gingival bleeding, compared to individuals with JIA reporting no difficulties. This finding is most likely consistent with plaque-induced gingivitis. Nevertheless, other host factors, such as salivary composition and amount, diet, gingival inflammation, chewing effects and movements of the soft tissues, status of tooth surface, and the microbial composition of the biofilm itself

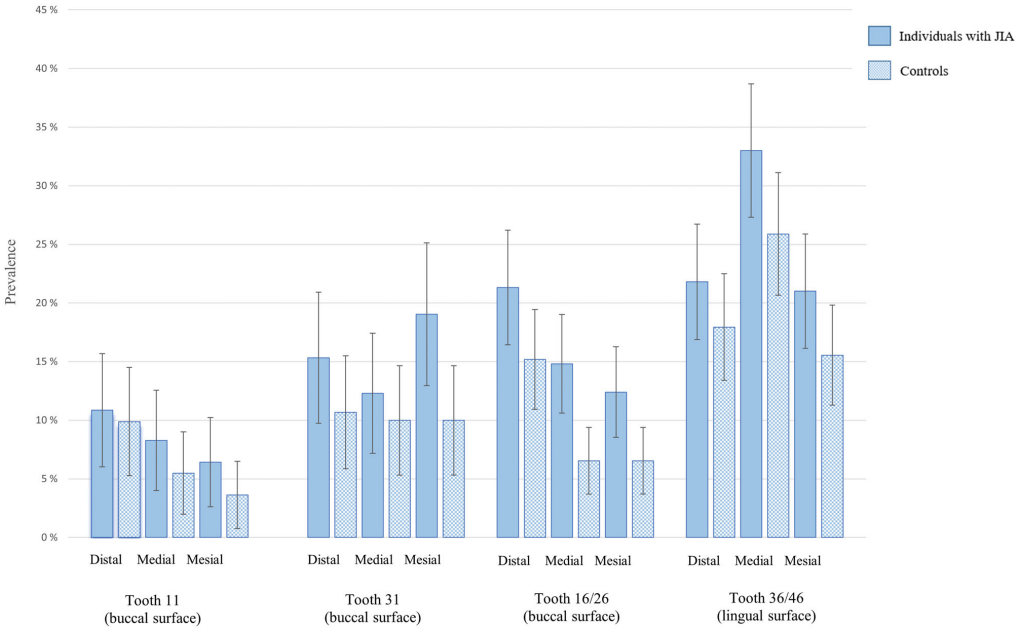

Figure 5. Percentage (95% confidence interval represented as error bars) of gingival bleeding (GBI > 0) at site level among individuals with juvenile idiopathic arthritis (JIA) and controls.

may play a role in the amount of plaque accumulation [33,34]. In total absence of oral hygiene [35] and if oral hygiene were performed, but without special instructions [36], more plaque accumulation in molars compared to anterior teeth and in mandibular dentition compared to maxillary dentition, have been demonstrated [35,36]. In the present study, molars presented a higher risk of plaque as compared to anterior teeth, but only the control group had a significant increased risk of plaque in the mandible, compared to the maxilla. Microbial species have also shown to differ significantly across tooth types and location, with the highest mean total count at the lower molars [34]. Significant difference between the two groups in the present study were notable for buccal surface of first permanent molars in the maxilla, presenting increased risk of plaque, and possibly an increased risk of gingival bleeding of mediobuccal site in the individuals with JIA as compared to the controls. Altered salivary composition and flow rate among individuals with JIA are reported [7,37–42], as saliva significantly influences dental biofilm [43] the proximity of buccal surface of first molars to the exit of the parotid ducts may postulate a relation between increased risks of plaque on this surface among individuals with JIA. Considering the statistically significant interaction between surface and group affiliation on presence of plaque in the present study, biological host variations point towards a role in the variation in distribution and amount of plaque between individuals with JIA and controls, however the nature of plaque are fluctuating, and only longitudinal studies can detect such relations.

Grevich et al. [27] suggested microbiota as a potential contributing factor to the disease pathogenesis of JIA and gingivitis. A recent NorJIA-based study by Frid et al. [44] evaluated salivary oral microbiome, plaque, and gingival bleeding score of some of the individuals with JIA ($n = 59$) and controls ($n = 34$), also included in the present study. Among the individuals with JIA, a higher abundance of microbiota associated with chronic inflammation was found, and dysbiosis of the salivary microbiome in individuals with JIA was suggested to trigger local immune response, including gingival bleeding. Different systemic factors may modify the immune-inflammatory response, such as medication [45] and nutrition [46,47], and perhaps some individuals with JIA are more prone to gingival bleeding due to susceptibility of disrupted symbiosis between the biofilm and host immune-inflammatory response, known to cause gingivitis [48]. To our knowledge, only one other study [27] has explored the association between disease-specific features and periodontal health outcomes in young individuals with JIA by use of regression analyses. In the present study no JIA disease-specific feature were found to be associated with gingival bleeding, except the CHAQ hygiene item Tooth brushing. Age at JIA onset was found to be associated with increased risk of plaque in the present study. Some researchers suggest mechanisms of JIA disease vary with age at onset [49], but it is difficult to make any presumptions regarding this finding.

This study clearly demonstrates the need for improved oral hygiene among individuals with JIA. A meta-analysis from 2011 [50] "showed that plaque accumulation and gingival inflammation scores significantly increased the

Table 4. Disease-specific features and oral variables in relation to oral hygiene (OHI-$S > 0$) and gingival bleeding (GBI > 0) among participants with juvenile idiopathic arthritis (JIA). Unadjusted and adjusted mixed-effects logistic regression.

	OHI-$S > 0$[a]					GB$I > 0$[b]				
		Unadjusted analyses		Adjusted analyses[c]			Unadjusted analyses		Adjusted analyses[c]	
	n	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	n	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
JIA category										
Oligoarthritis persistent	50	1	**.039**[d]	1	.089[d]	55	1	.735[d]	1	.774[d]
Systemic arthritis	5	6.24 (1.30 – 30.07)	**.022**	5.20 (1.07 – 25.32)	**.041**	5	1.02 (0.30 – 3.42)	.979	1.18 (0.34 – 4.05)	.791
Oligoarthritis extended	11	0.93 (0.36 – 2.38)	.876	1.09 (0.42 – 2.83)	.858	14	1.48 (0.68 – 3.22)	.320	1.43 (0.65 – 3.14)	.377
Polyarthritis, RF positive	3	0.54 (0.10 – 2.82)	.464	0.62 (0.12 – 3.26)	.573	4	3.38 (0.95 – 12.02)	.060	3.42 (0.95 – 12.30)	.060
Polyarthritis, RF negative	29	1.75 (0.89 – 3.45)	.104	1.77 (0.90 – 3.47)	.099	33	1.30 (0.73 – 2.32)	.365	1.36 (0.77 – 2.42)	.293
Psoriatic arthritis	5	2.00 (0.50 – 8.02)	.328	2.41 (0.59 – 9.80)	.218	5	2.03 (0.64 – 6.51)	.232	1.89 (0.59 – 6.10)	.286
Enthesitis-related arthritis	21	1.31 (0.62 – 2.77)	.475	1.18 (0.56 – 2.50)	.669	21	1.21 (0.62 – 2.37)	.571	1.22 (0.62 – 2.40)	.570
Undifferentiated arthritis	20	0.89 (0.42 – 1.88)	.752	0.86 (0.40 – 1.81)	.683	22	1.12 (0.58 – 2.17)	.737	1.17 (0.60 – 2.26)	.648
Human leukocyte antigen B27 (HLA-B27)										
Negative	105	1	ref	1	ref	116	1	ref	1	ref
Positive	39	1.05 (0.60 – 1.83)	.874	1.03 (0.59 – 1.79)	.916	43	1.18 (0.74 – 1.88)	.495	1.21 (0.76 – 1.93)	.421
Antinuclear antibodies (ANA)[e]										
Negative	77	1	ref	1	ref	85	1	ref	1	ref
Positive	26	0.96 (0.52 – 1.79)	.893	1.11 (0.58 – 2.12)	.749	32	0.84 (0.48 – 1.45)	.526	0.75 (0.42 – 1.34)	.338
Rheumatoid factor (RF)[f]										
Negative	135	1	ref	1	ref	150	1	ref	1	ref
Positive	5	0.55 (0.15 – 2.08)	.376	0.55 (0.15 – 2.05)	.372	5	1.33 (0.41 – 4.38)	.635	1.34 (0.41 – 4.39)	.625
Anti-cyclic citrullinated peptide (anti-CCP)[g]										
Negative	122	1	ref	1	ref	136	1	ref	1	ref
Positive	7	1.12 (0.35 – 3.57)	.842	1.18 (0.38 – 3.72)	.774	8	1.21 (0.47 – 3.10)	.698	1.11 (0.44 – 2.82)	.825
Serum C-reactive protein (CRP)[h]										
<5 mg/L	133	1	ref	1	ref	147	1	ref	1	ref
≥5 mg/L	8	0.85 (0.29 – 2.46)	.757	0.76 (0.26 – 2.21)	.613	9	0.90 (0.35 – 2.30)	.827	0.89 (0.35 – 2.26)	.802
Erythrocyte sedimentation rate (ESR)										
<20 mm/h	139	1	ref	1	ref	153	1	ref	1	ref
≥20 mm/h	5	0.91 (0.24 – 3.42)	.886	0.84 (0.23 – 3.14)	.798	6	0.74 (0.24 – 2.27)	.597	0.75 (0.24 – 2.29)	.609
Age at JIA onset										
≤6 years	50	1	ref	1	ref	59	1		1	
>6 years	94	1.84 (1.10 – 3.07)	**.020**	1.80 (1.08 – 3.00)	**.025**	100	1.26 (0.81 – 1.94)	.307	1.23 (0.79 – 1.91)	.354
Disease duration										
≤5 years	74	1	ref	1	ref	80	1		1	
>5 years	70	0.61 (0.37 – 1.00)	.050	0.64 (0.39 – 1.04)	.071	79	1.04 (0.69 – 1.59)	.847	1.04 (0.69 – 1.58)	.850
Steroids, ongoing										
No steroids ongoing	141	1	ref	1	ref	155	1	ref	1	ref
Steroids ongoing	3	3.96 (0.57 – 27.31)	.162	2.85 (0.40 – 20.10)	.294	4	0.47 (0.11 – 1.96)	.302	0.52 (0.13 – 2.17)	.371
Steroids, ever used										
No steroids ever used	112	1	ref	1	ref	124	1	ref	1	ref
Steroids ever used	32	1.41 (0.77 – 2.59)	.265	1.37 (0.75 – 2.50)	.306	35	0.93 (0.56 – 1.54)	.773	0.95 (0.58 – 1.58)	.851
DMARDs, ongoing										
No sDMARDs nor bDMARDs ongoing	55	1	.768[d]	1	.784[d]	60	1	.252[d]	1	.250[d]
sDMARDs, but no bDMARDs ongoing	37	1.07 (0.57 – 2.03)	.827	1.12 (0.59 – 2.13)	.731	40	0.64 (0.37 – 1.11)	.113	0.64 (0.36 – 1.11)	.113
bDMARDs ongoing[i]	52	1.24 (0.69 – 2.20)	.473	1.23 (0.69 – 2.17)	.487	59	0.76 (0.47 – 1.22)	.254	0.76 (0.47 – 1.22)	.251
DMARDs, ever used										
No sDMARDs nor bDMARDs ever used	42	1	.644[d]	1	.660[d]	45	1	.698[d]	1	.718[d]
sDMARDs, but no bDMARDs ever used	49	1.16 (0.62 – 2.17)	.648	1.19 (0.64 – 2.22)	.591	53	0.82 (0.48 – 1.40)	.468	0.82 (0.48 – 1.41)	.481
bDMARDs ever used[i]	53	1.34 (0.73 – 2.48)	.350	1.33 (0.72 – 2.44)	.362	61	0.81 (0.49 – 1.36)	.429	0.82 (0.49 – 1.37)	.451

(*continued*)

Table 4. Continued.

	OHI-S > 0[a]					GBI > 0[b]				
		Unadjusted analyses		Adjusted analyses[c]			Unadjusted analyses		Adjusted analyses[c]	
	n	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	n	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Remission status[j]										
Inactive disease/remission on/off medication	86	1	ref	1	ref	95	1	ref	1	ref
Continued activity/flare	58	0.94 (0.56 – 1.56)	.798	1.02 (0.61 – 1.70)	.951	64	0.94 (0.62 – 1.45)	.793	0.93 (0.61 – 1.43)	.748
MDgloVAS										
VAS = 0	92	1	ref	1	ref	101	1	ref	1	ref
VAS > 0	52	0.93 (0.56 – 1.57)	.796	1.03 (0.61 – 1.73)	.920	58	1.06 (0.68 – 1.63)	.811	1.04 (0.67 – 1.61)	.853
PRgloVAS										
VAS = 0	72	1	ref	1	ref	79	1	ref	1	ref
VAS > 0	68	0.86 (0.52 – 1.42)	.552	0.86 (0.52 – 1.40)	.534	76	0.97 (0.63 – 1.48)	.879	0.98 (0.64 – 1.50)	.924
CHAQ hygiene item Tooth brushing[k]										
Without any difficulty	134	1	ref	1	ref	148	1	ref	1	ref
With some/much difficulty/unable to do/not applicable	6	1.50 (0.44 – 5.17)	.518	1.53 (0.45 – 5.20)	.497	7	2.70 (1.05 – 6.94)	**.040**	2.92 (1.14 – 7.45)	**.025**
Jaw										
Mandible	–	1	ref	1	ref	–	1	ref	1	ref
Maxilla	–	0.91 (0.67 – 1.23)	.530	0.91 (0.67 – 1.23)	.530	–	0.50 (0.40 – 0.62)	**<.001**	0.50 (0.40 – 0.62)	**<.001**
Side										
Right side	–	1	ref	1	ref	–	1	ref	1	ref
Left side	–	0.93 (0.68 – 1.26)	.637	0.93 (0.68 – 1.26)	.637	–	1.11 (0.90 – 1.37)	.331	1.11 (0.90 – 1.37)	.332
Anterior/posterior										
Incisors	–	1	ref	1	ref	–	1	ref	1	ref
Molars	–	6.26 (4.26 – 9.19)	**<.001**	6.27 (4.27 – 9.21)	**<.001**	–	2.15 (1.68 – 2.74)	**<.001**	2.15 (1.68 – 2.74)	**<.001**
Surface (teeth)										
Buccal (11, 31, 16, 26)	–	1	ref	1	ref	–	1	ref	1	ref
Lingual (36, 46)	–	2.99 (2.09 – 4.29)	**<.001**	2.99 (2.09 – 4.29)	**<.001**	–	2.38 (1.92 – 2.96)	**<.001**	2.38 (1.92 – 2.96)	**<.001**
Site (surface)										
A: Mesial (buccal, lingual)	–	–	–	–	–	–	1[B]	**.025**[d]	1[B]	**.025**[d]
B: Medial (buccal, lingual)	–	–	–	–	–	–	1.39 (1.07 – 1.80)[A]	**.013**	1.39 (1.07 – 1.80)[A]	**.013**
C: Distal (buccal, lingual)	–	–	–	–	–	–	1.33 (1.02 – 1.72)	**.034**	1.33 (1.02 – 1.72)	**.034**
ICC individual level	–	0.30	–	0.29	–	–	0.28	–	0.27	–
ICC tooth level	–	–	–	–	–	–	0.42	–	0.41	–
AIC	–	1095.35	–	1095.69	–	–	2459.39	–	2461.42	–

[a]Dichotomised outcome variable (present or absent) of the modified version of the simplified oral hygiene index (OHI-S) [16]. 144 individuals with JIA were evaluated according to the modified OHI-S.
[b]Dichotomised outcome variable (present or absent) of the modified version of Gingival Bleeding Index (GBI) [17]. 159 individuals with JIA were evaluated according to the modified GBI.
[c]Adjusted for: Gender and age.
[d]Overall *p*-value.
[e]Responses ($n = 42$) are missing.
[f]Responses ($n = 4$) are missing.
[g]Responses ($n = 15$) are missing.
[h]Responses ($n = 3$) are missing.
[i]With or without sDMARDs.
[j]Disease activity according to Wallace and the American College of Rheumatology (ACR) provisional criteria [19, 20].
[k]Responses ($n = 4$) are missing.
Surfaces statistically significant in Post hoc analysis is marked using superscript uppercase letters.
Scheffe adjusted *p*-values in Post hoc analysis $p<.05$. Regarding JIA category and other medication ongoing and ever used Post hoc analysis showed no difference (all *p*-values $>.05$).
Significant values are marked in bold.
Abbreviations: RF: Rheumatoid Factor; sDMARDs: synthetic disease-modifying antirheumatic drugs; bDMARDs: biologic disease-modifying antirheumatic drugs; MDgloVAS: Physician's global assessment of disease activity; PRgloVAS: Patient's global assessment of overall wellbeing; CHAQ: Childhood Health Assessment Questionnaire; ICC: intraclass correlation coefficient; AIC: Aikake Information Criteria.

Table 5. Other clinical characteristics of oral cavity among individuals with juvenile idiopathic arthritis (JIA) and controls ≥10 years.

Variable	JIA ($n = 162$)	Controls ($n = 162$)	*p*-value
Fissure of lip and/or corner of lip, n (%)			
No clear findings	154 (98.1)	155 (95.7)	.217
Yes	3 (1.9)	7 (4.3)	
Gingival ulcers with discontinuation of epithelia of at least 3 mm, n (%)			
No	154 (98.7)	156 (96.3)	.168
Yes	2 (1.3)	6 (3.7)	
Buccal mucosa ridging, n (%)			
No	133 (84.7)	133 (82.1)	.531
Yes	24 (15.3)	29 (17.9)	
Tongue indentation, n (%)			
No	145 (93.0)	140 (86.4)	.056
Yes	11 (7.1)	22 (13.6)	
Gingival hyperplasia (buccal side of the lower and upper anterior teeth), n (%)			
No clear findings	156 (97.5)	152 (93.8)	.106
Yes	4 (2.5)	10 (6.2)	
Dental mirror sticks to buccal mucosa, n (%)[a]			
No	158 (98.1)	162 (100.0)	.081
Yes	3 (1.9)	0 (0.0)	

[a]Potential mouth dryness was recorded by evaluating if dental mirror sticks to buccal mucosa. Some registrations are missing.
Significant values are marked in bold.

prevalence of bacteraemia following toothbrushing". Considering the immunosuppressant therapy used by many of the young individuals with JIA, optimal oral health and professional maintenance in this group is emphasised.

JIA encompasses a heterogenous group disease categories requiring individualised and optimised treat-to target strategies. While remission on medication is an accessible goal for many, more focus will switch to treatment tolerance, adverse events and risk of infections. Future research should address longitudinal studies with adequate sample sizes in more homogeneous JIA groups with special focus on disease activity, drug exposure, and its relation to oral health status. Furthermore, to increase knowledge of plausible susceptibility to periodontal disease among individuals with JIA, studies specifically targeting host variation with regard to immune response, microbial diversity, salivary gland involvement, and nutrition are needed.

Conclusions

Plaque and gingival bleeding were more frequently experienced in individuals with JIA as compared to controls without JIA. Multilevel analyses showed an interaction between surface and group affiliation on the presence of plaque. Few JIA disease-specific variables were associated with plaque or gingival bleeding, however, results suggest that certain features may increase individual's susceptibility. Our results underscore the importance of increased awareness of oral health care in patients with JIA amongst health care providers.

Note

1. The Norwegian JIA Study – Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis (JIA).

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Ethics approval and consent to participate

The study was approved by the Regional Committees for Medical and Health Research Ethics (2012/542/REC), Rogaland, Vestland (West). Written informed consents were obtained from the caregivers and the adolescents as appropriate. The study was registered at ClinicalTrials.gov (No: NCT03904459). All procedures were performed in accordance with relevant guidelines.

Author contributions

EGG: Contributed to the design and data collection of this sub-study, performed statistical analysis, and wrote the manuscript in consultation with **MSS**, **ANÅ** and **SAL**. **MSS:** Conceived and designed this sub-study. **ANÅ:** Conceived the idea of performing multilevel analysis. **SAL:** Performed statistical analysis. **MR:** Aided in interpretation and writing of

the manuscript and to the design and data collection of the NorJIA study. **JF, JH, PF, KT, KR:** Contributed to data collection and provided valuable comments. **AR, AB, KL, XS, LC:** Provided valuable comments. All authors have read and approved the manuscript.

Disclosure statement

The authors declare that they have no competing interests.

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Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Paper III

Oral health-related quality of life in 4-16-year-olds with and without juvenile idiopathic arthritis.

Gil EG, Skeie MS, Halbig J, Jönsson B, Lie SA, Rygg M, Fischer J, Rosén A, Bletsa A, Luukko K, Shi XQ, Frid P, Cetrelli L, Tylleskär K, Rosendahl K, Åstrøm AN.

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RESEARCH

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Oral health-related quality of life in 4–16-year-olds with and without juvenile idiopathic arthritis

Elisabeth G. Gil[1*], Marit S. Skeie[1,2], Josefine Halbig[3,4], Birgitta Jönsson[5,3], Stein Atle Lie[1], Marite Rygg[6,7], Johannes Fischer[1], Annika Rosén[1,8], Athanasia Bletsa[1,9], Keijo Luukko[1], Xie-Qi Shi[1,10], Paula Frid[3,4,11], Lena Cetrelli[2,6], Karin Tylleskär[12], Karen Rosendahl[4,13] and Anne N. Åstrøm[1]

Abstract

Background: Few studies have investigated oral health-related quality of life (OHRQoL) in young individuals with juvenile idiopathic arthritis (JIA). Aims were to investigate whether OHRQoL differs between children and adolescents with JIA compared to controls without JIA, while adjusting for socio-demographic-, behavioral- and oral health-related covariates. Furthermore, to explore whether socio-behavioral and oral health-related covariates of OHRQoL vary according to group affiliation and finally, specifically for individuals with JIA, to investigate whether disease-specific features associate with OHRQoL. We hypothesized that participants with JIA have poorer OHRQoL compared to participants without JIA.

Methods: In this comparative cross-sectional study participants with JIA (n = 224) were matched to controls without JIA (n = 224). OHRQoL was assessed according to Early Childhood Oral Health Impact Scale (ECOHIS) (4–11-years-olds) and the child version of Oral Impacts on Daily Performances (Child-OIDP) (12–16-years-olds). JIA-specific characteristics were assessed by pediatric rheumatologists and socio-demographic, behavioral and self-reported oral health information collected by questionnaires. Index teeth were examined for caries by calibrated dentists. Multiple variable analyses were performed using logistic regression, reporting odds ratio (OR) and 95% confidence interval (CI). Two-way interactions were tested between group affiliation and the socio-behavioral- and oral health-related variables on the respective outcome variables.

Results: In total, 96 participants with JIA and 98 controls were evaluated according to ECOHIS, corresponding numbers for Child-OIDP was 125 and 124. Group affiliation was not associated with impaired ECOHIS or Child-OIDP in adjusted analyses (OR = 1.95, 95% CI 0.94–4.04 and OR = 0.99, 95% CI 0.46–2.17, respectively). Female adolescents with JIA were more likely than males to report oral impacts according to Child-OIDP. Continued activity or flare was found to adversely affect Child-OIDP, also self-reported outcome measures in JIA associated with Child-OIDP.

Conclusions: This study did not provide consistent evidence to confirm the hypothesis that children and adolescents with JIA are more likely to have impaired OHRQoL compared to their peers without JIA. However, female adolescents with JIA were more likely than males to report impacts on OHRQoL. Furthermore, within the JIA group,

*Correspondence: elisabeth.gil@uib.no

[1] Department of Clinical Dentistry, University of Bergen, Bergen, Norway
Full list of author information is available at the end of the article

adolescents with continued disease activity, flare or reporting pain, physical disability, had higher risk than their counterparts of impaired OHRQoL.

Keywords: Adolescent, Child, Quality of life, Dental caries, Oral health, Juvenile idiopathic arthritis

Background

As the most common chronic rheumatic disease in children, juvenile idiopathic arthritis (JIA) represents a complex heterogeneous group of arthritis and might constitute an important cause of disability and reduced quality of life [1, 2]. Pooled estimates of incidence and prevalence rates for Caucasians are 8.3/100,000 and 32.6/100,000, respectively, but estimates vary greatly across countries [3]. For most children JIA is a chronic, often life-long, disease. Objectives of disease management is remission, minimizing comorbidities and harmful side-effects of medication, and achieving best possible function, growth and development, quality of life, and social involvement [4].

Several manifestations of rheumatic diseases are observed in the oral cavity such as mucosal lesions, reduced salivary flow and inflammation in periodontal tissues [5]. Previous reviews have demonstrated poor oral health indicators in children with JIA [6, 7]. A recent systematic review and meta-analysis by our research team focusing on oral disease and problems among children and adolescents with JIA, revealed, however, that dental caries in young individuals with JIA was comparable to that of the general population, whereas periodontal diseases and temporomandibular disorder (TMD) were estimated to be more prevalent, compared to individuals without JIA [8].

According to the definition of the World Dental Federation [9, 10], reflecting the biopsychosocial view of health addressed by the World Health Organization [11], oral health encompasses "the ability to speak, smile, taste, touch, chew, swallow, and convey a range of emotions through facial expressions with confidence and without pain, discomfort, and disease of the craniofacial complex". To capture the different dimensions of oral health, oral health-related quality of life (OHRQoL) measurements are conducive, as conventional clinical oral indices alone are insufficient to assess the multifaceted nature of oral health. Generic OHRQoL instruments have been developed to measure physical- and psycho-social consequences of various oral diseases and problems, whereas condition specific OHRQoL measures capture subtle variance in specific oral conditions [12]. Measuring OHRQoL in children are challenging due to continuous dental, facial and cognitive development [13]. Thus, age-dependent generic child OHRQoL indices have been developed for self- or proxy-reporting of children's OHRQoL [12], such as the Child Oral Health-related Quality of Life measure (COHQoL) [14–16], the child version of Oral Impacts on Daily Performances (Child-OIDP) [17], and the Early Childhood Oral Health Impact Scale (ECOHIS) [18]. The latter specifically developed for younger children. Only ECOHIS and Child-OIDP have been validated in the context of a Norwegian child and adolescent population [19]. Although these indices have been used to evaluate OHRQoL in children and adolescents with chronic diseases [20, 21], studies investigating OHRQoL in children and adolescents with JIA are scarce [22–26].

Isola et al. [23] reported that individuals with temporomandibular joint (TMJ) arthritis had poorer OHRQoL compared to individuals with JIA without TMJ arthritis and controls, using the Child Perception Questionnaire ($CPQ_{11\text{-}14}$), a component of the inventory COHQoL. Using $CPQ_{11\text{-}14}$, Polizzi et al. [25] found JIA patients with periodontitis to have poorer OHRQoL, compared to JIA patients without periodontitis and controls. Santos et al. [22] observed no difference in impaired OHRQoL in individuals with JIA compared to controls using the Parental-Caregiver Perceptions Questionnaire, another component of the COHQoL inventory. The Psychosocial Impact of Dental Aesthetics Questionnaire has also been used among adolescents with JIA and controls of same age, indicating that adolescents with JIA were less concerned by dental aesthetics than controls [24]. Furthermore, Rahimi et al. [26] documented self-reported orofacial symptoms and dysfunction to be frequent in adolescents with JIA and by using $CPQ_{11\text{-}14}$ they found orofacial symptoms to have a negative impact on OHRQoL.

Evidently, demographic- and socio-economic characteristics in addition to clinical indicators of oral health, play a prominent role as independent determinants of OHRQoL [27–29]. However, none of the previous studies assessing OHRQoL in children and adolescents with JIA [22–26] have included socio-economic characteristic of the participants as important covariates of OHRQoL. Thus, knowledge of the impact of social-economic characteristics on OHRQoL among young individuals with JIA and whether the impact of those characteristics differs between individuals with and without JIA is quite limited. Hence, high-quality research focusing on OHRQoL in children and adolescents with JIA is in demand [8]. Such studies are important as they facilitate

comprehension of the relationship between oral health and general health [13].

The aims of this study were to investigate whether OHRQoL, assessed by the ECOHIS and Child-OIDP scale, differs between children and adolescents with JIA compared to controls without JIA, while adjusting for socio-demographic-, behavioral- and oral health-related covariates. Furthermore, to explore whether socio-behavioral and oral health-related covariates of OHRQoL vary according to group affiliation and finally, specifically for individuals with JIA, to investigate whether disease-specific features associate with OHRQoL. We hypothesized that participants with JIA have poorer OHRQoL compared to participants without JIA.

Methods

Study design and participants

NorJIA[1] is a prospective longitudinal multicenter study that contributes baseline data to the present comparative cross-sectional study. Baseline data on dental caries have recently been published [30], whereby sample size calculation and calibration are presented. A detailed description of sample size calculation (according to caries estimates) and calibration are presented in Additional files 1 and 2, respectively. Young individuals (4–16 years old) with JIA, diagnosed according to the criteria specified by the International League of Associations for Rheumatology (ILAR) [31] were invited to participate. The only exclusion criterion was the lack of written informed consent. Baseline data were collected between April 2015 and August 2018.

Specialists in pediatrics at three out of total four university hospitals, widely distributed across Norway (western, central, and northern Norway), were responsible for the enrollment of children and adolescents with JIA. After a thorough medical examination the participants were referred for an oral examination at the corresponding Oral Health Centre of Expertise and matched 1:1 with controls based on sex, age, center site, and mothers' country of origin (western or non-western). The controls were without JIA and underwent an oral examination at one of seven different Public Dental Service clinics, representing both rural and urban communities [30]. The controls' appointment was coordinated with a planned regular oral health check, and as incentive for participation, two cinema tickets were provided. The term group affiliation in this article reflects participants with JIA or controls.

[1] The Norwegian JIA Study – Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis (JIA).

Oral health questionnaires

Self-administered questionnaires provided socio-demographic, behavioral and self-reported oral health information [30]. Socio-demographic variables included educational level of caregivers, number of caregivers in the household and mother's country of origin. Behavioral variables consisted of toothbrushing and tooth flossing frequency, while self-reported oral health indicators were gingival bleeding during toothbrushing and pain or discomfort during toothbrushing. Moreover, evaluation of self-reported oral health and satisfaction with appearance of teeth (global measures) were collected (for the participants ≥ 12 years the global oral health measures were assessed by an interview). The coding of these self-reported variables is shown in Additional file 3: Table S1.

ECOHIS

A validated Norwegian version of ECOHIS [19], originally developed by Pahel et al. [18], was used to evaluate caregivers' perception of the OHRQoL of their 4–11 years-old children and their families with reference to the child's entire lifetime experience of oral diseases and dental treatment. ECOHIS consists of thirteen items, composing the child impact section (first nine items) and the family impact section (last four items). Each item, originally assessed in terms of never = 0 to very often = 5, was dichotomized (0 = not affected, including the original category 0 and 1 = affected, including the original categories 1–5) and dummy variables were summarized into the Child impact- and Family impact scores. The ECOHIS total score was calculated by adding the Child impact and Family impact scores. Participants having two or more items of the ECOHIS unanswered were excluded from the analysis. The response category "I don't know" were coded as missing and not considered in the analyses. Variables and response categories as originally coded and as re-coded for analyses are shown in Additional file 4: Table S1.

Child-OIDP

Among participants 12–16 years, OHRQoL was measured by interview, using the 8-item Child-OIDP frequency inventory. The OIDP inventory was initially constructed for adults [32] and later modified for children [17]. This index considers difficulty in performing eight daily activities (eating, speaking, cleaning teeth, smiling-laughing-and showing teeth without embarrassment, sleeping and relaxing, emotional balance, social contact, schoolwork) due to problems with mouth or teeth, during the past 3 months. Each of the eight items, originally assessed in terms of never = 0 to every day/almost every day = 3, was dichotomized (0 = not affected, including the original category 0 and

1 = affected, including the original categories 1–3) and the dummy variables were summarized, forming the Child-OIDP simple count (SC) score. The Child OIDP SC score was dichotomized into 0 = no impacts and 1 = 1–8 impacts. Participants with two or more items of the Child-OIDP unanswered were excluded from the analysis. Variables and response categories as originally coded and as re-coded for analyses are shown in Additional file 5: Table S1.

Medical examinations of the participants with JIA

The participants with JIA were examined by experienced pediatric rheumatologists and the included background variables in this sub-study were JIA category according to the ILAR classification criteria [31], age at JIA onset, disease duration, medication, activity/remission status, physician's global assessment of disease activity visual analogue scale (MDgloVAS) [33], patient/parent-reported pain intensity visual analogue scale (VAS pain) [33], patient/parent-reported global assessment of overall well-being visual analogue scale (PRgloVAS) [33]. All visual analogue scales were measured on a 21-numbered circle VAS (0 = minimal impact, 10 = maximal impact), and reported by the parent if the child were below 9 years, otherwise by the patient. Disability was reported with the Childhood Health Assessment Questionnaire (CHAQ) (0 = no disability, 3 = maximal disability) [34]. The disease-specific clinical background variables are described in detail in Additional file 6 [30] and the coding of these variables is shown in Additional file 7: Table S1.

Oral examination of all participants

The oral assessment was performed by calibrated dentists (n = 5) [30]. For this sub-study, the examination was restricted to caries in the primary second molars in the youngest age group [4–9-year-olds] and in permanent first molars in the oldest age group [10–16-year-olds]. A detailed 5-graded diagnostic tool was applied for decayed lesions, in which grades 1–2 represented enamel lesions and grades 3–5 dentin lesions [35]. Filled surfaces were also reported. Missing teeth were not included in this sub-study as very few teeth (primary teeth: n = 5) were extracted or indicated for extraction due to caries [30]. The caries examination consisted of both visual inspection and bitewing (BW) radiographs. BW was not taken if intermolar contact was lacking, the participants were younger than 5 years or in case of fixed orthodontic appliances when only occlusal surfaces were examined. As a background variable, caries was dichotomized as presence ($d_{1\text{-}5}f/D_{1\text{-}5}F > 0$) or absence ($d_{1\text{-}5}f/D_{1\text{-}5}F = 0$) of caries.

Statistical methods

SPSS version 25.0 (IBM Corp. Released 2013, IBM SPSS Statistics for Windows, Armonk NY: IBM Corp) and STATA version 16 (Stata Corp LP, College Station, TX) were used for data analysis. Linear weighted Cohen's kappa was used to evaluate inter- and intra-rater reliability for the caries measurements. Mean and standard deviations (SD) were used to describe continuous demographic variables. Categorical variables were compared between individuals with JIA and controls by Cross tabulation and Chi-squared tests. Logistic regression analyses were applied with ECOHIS total score and Child-OIDP SC score as binary outcome measures reporting odds ratio (OR) and 95% confidence interval (CI). Negative binomial regression was implemented as a supplementary analysis with ECOHIS total score and Child-OIDP SC score as count variables reporting incidence rate ratios (IRR) with 95% CI. The multiple variable regression analyses included the main exposure variable, group affiliation, adjusted for covariates in terms of socio-behavioral- and clinical oral health-related variables that were statistically significantly associated with group affiliation and/or the respective OHRQoL outcomes in the unadjusted analysis. The adjusted regression analyses specifically for participants with JIA, included the covariates age, gender and parental educational level, and the JIA-specific variables were adjusted separately. McFadden's R^2 was applied as a measure for the goodness of fit of the logistic regression models. The JIA categories, systemic arthritis (n = 7) and undifferentiated arthritis (n = 31) were not included in the statistical analysis. Internal consistency reliability of the OHRQoL inventories was assessed using Cronbach's alpha. Discriminant validity was assessed by comparing the OHRQoL inventories with global measures of oral health. Two-way interactions were tested between group affiliation and the socio-behavioral- and oral health-related variables on ECOHIS and Child-OIDP. *P*-values less than 0.05 were considered statistically significant.

Ethical approval

The regional ethics committee (2012/542/REC) approved the study. Approval was also obtained by leaders of different County Dental Health Authorities, at different Oral Health Centre of Expertise, and at the three pediatric departments at the university hospitals. Written informed consent was signed prior to

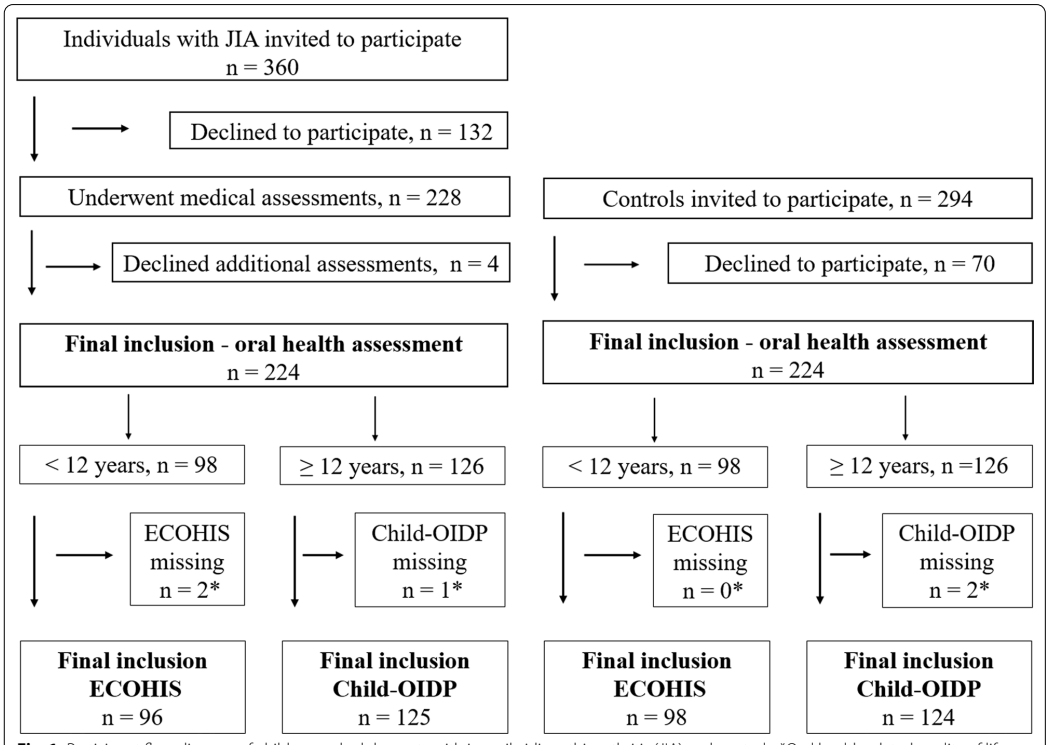

Fig. 1 Participant flow diagram of children and adolescents with juvenile idiopathic arthritis (JIA) and controls. *Oral health related quality of life (OHRQoL) inventories having two or more unanswered items were excluded from the analysis. ECOHIS = Early Childhood Oral Health Impact Scale, Child-OIDP = Child Oral Impacts on Daily Performance

participation. The NorJIA study is registered at ClinicalTrials.gov (No: NCT03904459, 05.04.2019).

Results

Sample characteristics

As depicted in Fig. 1, 228 individuals with JIA were submitted to the medical examination, resulting in a response rate of 63.3% (228/360) [30]. Concerning potential non-response bias, the mean age of the 132 eligible individuals with JIA who declined participation was 10.5 (SD = 3.5) years ($p < 0.001$). The proportion of females was slightly lower amongst the individuals with JIA who declined participation, compared to the participants with JIA (58.3% vs 59.2%, $p = 0.027$) [30].

Four participants with JIA did not undergo the oral examination, hence 224 participants were matched to controls (Fig. 1). The controls' response rate was 76.2% (224/294) [30]. The matching resulted in 133 (59.4%) females in the JIA group and 134 (59.8%) females in the control group. The mean age for both groups was 12.0 years (both SD = 3.2) ($p = 0.974$) [30]. According to mother's background of origin, 94.2% (211/224) of the pairs were matched [30]. As depicted in Fig. 1, 96 individuals with JIA and 98 controls were evaluated according to ECOHIS and 125 individuals with JIA and 124 controls were evaluated according to Child-OIDP.

Table 1 depicts the distribution of socio-demographic-, behavioral and oral health-related characteristics according to group affiliation for all participants aged 4–16 years. Higher proportions of mothers in the control group had high educational level compared to mothers of participants with JIA (73.8% versus 64.3%, $p = 0.036$). Corresponding figures among fathers were 57.1% *vs.* 42.5% ($p = 0.003$). Higher proportions of individuals with than without JIA reported gingival bleeding during toothbrushing (56.9% *vs.* 46.6%, $p = 0.033$). Concomitant diagnoses and medication use among the participants that may constitute an oral health threat are presented in a recently published article on dental caries in this study population [30].

Table 1 Distribution of socio-behavioral-, subjective clinical- and oral characteristics among individuals with juvenile idiopathic arthritis (JIA) and controls

Variable	JIA (n = 221)	Controls (n = 222)	*p*-value
Educational level of caregivers, n (%)			
Mother			
High school/vocational school	75 (35.7)	54 (26.2)	0.036[a]
University/college	135 (64.3)	152 (73.8)	
Father			
High school/vocational school	119 (57.5)	87 (42.9)	0.003[a]
University/college	88 (42.5)	116 (57.1)	
Share household with, n (%)			
Two caregivers in the household[b]	170 (79.4)	185 (84.1)	0.209
Only one caregiver in the household	44 (20.6)	35 (15.9)	
Frequency of toothbrushing, n (%)			
Twice a day, or more	163 (76.2)	170 (77.6)	0.719
Once a day or less/do not know	51 (23.8)	49 (22.4)	
Frequency of tooth flossing during the last 3 months, n (%)			
Daily or more	19 (8.9)	18 (8.3)	0.806
Several times weekly or less/do not know	194 (91.1)	200 (91.7)	
During toothbrushing, gingival bleeding occurs, n (%)			
Sometimes or more/do not know	120 (56.9)	102 (46.6)	0.033[a]
No	91 (43.1)	117 (53.4)	
During toothbrushing, pain or discomfort occurs, n (%)			
Yes/do not know	25 (11.9)	21 (9.6)	0.449
No	186 (88.2)	198 (90.4)	
Dental caries			
$d_{1\text{-}5}ft/D_{1\text{-}5}FT^c = 0$	118 (54.9)	124 (55.9)	0.838
$d_{1\text{-}5}ft/D_{1\text{-}5}FT^c > 0$	97 (45.1)	98 (44.1)	

[a] $p < 0.05$; χ^2 test. [b]Also includes living across two households, given two caregivers in both households. [c]Decayed and/or filled teeth in the primary or permanent dentition, enamel caries included. Some variables had missing information

Calibration

Four caries calibration exercises (described in Additional file 2) resulted in weighted Cohen's kappa values of 0.61, 0.61, 0.91, and 0.65, respectively.

Distribution of OHRQoL according to group affiliation

Table 2 depicts the distribution of the single items of ECOHIS and the total ECOHIS scores among the 4–11-year-olds according to group affiliation. Some single items (n = 6) differed significantly between the JIA group and controls with higher proportions of individuals being affected in the JIA group compared to the controls. The family impact score > 0 was also more frequently reported among participants with JIA (45.8% *vs.* 25.5%, $p < 0.05$). Internal consistency reliability of the ECOHIS total score in terms of Cronbach's alpha was 0.87 in participants with JIA and 0.79 in the control group (Table 2).

As shown in Table 3, neither the Child-OIDP SC nor the single item scores differed significantly between adolescents 12–16-years old with and without JIA, although a pattern towards more frequent impacts was observed in the JIA group compared to the controls. Cronbach's alpha values of the Child-OIDP SC score were 0.83 in the participants with JIA and 0.79 in the control group (Table 3).

Discriminant validity of the OHRQoL measures

Additional file 8: Table S1 shows the frequency distribution of the ECOHIS- and Child-OIDP SC scores according to global measures of oral health, separately in children and adolescents with and without JIA. Among participants with JIA and controls, the ECOHIS scores were higher in parents who rated their child's oral health as bad/reported dissatisfaction with appearance of teeth, compared to those who perceived their child's oral health as good/ reported satisfaction with the appearance. The Child-OIDP SC scores were higher among participants reporting dissatisfaction with appearance of teeth, compared to participants reporting satisfaction with appearance of teeth.

Table 2 Distribution of the dichotomized items of the Early Childhood Oral Health Impact Scale (ECOHIS) and ECOHIS scores among individuals with juvenile idiopathic arthritis (JIA) (n = 96) and the controls (n = 98)

Item > 0*	JIA n (%)	Controls n (%)
Child impact section		
Pain in the teeth, mouth, or jaws?	59 (62.8)	49 (50.0)
Because of dental problems or the need for dental treatment		
Difficulty drinking hot or cold beverages?	26 (27.1)	18 (18.4)
Difficulty eating some foods?	32 (33.3)[a]	17 (17.4)
Difficulty pronouncing any words?	14 (14.6)[a]	5 (5.1)
Missed daycare, pre-school, or school?	25 (26.0)	17 (17.4)
Trouble sleeping?	18 (18.8)	17 (17.4)
Irritable or frustrated?	30 (31.6)	25 (25.5)
Avoided smiling or laughing when around other children?	13 (13.7)[a]	5 (5.1)
Avoided talking to other children?	8 (8.3)[a]	2 (2.0)
Family impact section		
Have you or another family member, due to dental problems or dental treatment of your child		
Been upset?	21 (21.9)	12 (12.2)
Felt guilty?	17 (17.7)	9 (9.2)
Taken time-off from work?	38 (39.6)[a]	19 (19.4)
Had financial impact on your family?	8 (8.33)[a]	1 (1.0)
Child impact score > 0	74 (77.1)	64 (65.3)
Cronbach's alpha Child impact score	0.81	0.73
Family impact score > 0	44 (45.8)[a]	25 (25.5)
Cronbach's alpha Family impact score	0.71	0.65
ECOHIS total score > 0	77 (80.2)	67 (68.4)
Cronbach's alpha ECOHIS total score	0.87	0.79

[a] $p < 0.05$; χ^2 test (no results were statistically significant). *The items are dichotomized as 0 not affected and 1 affected. Four participants had missing or replied "I don't know" to one item in total

Table 3 Distribution of the dichotomized items of Child Oral Impacts on Daily Performance (Child-OIDP) and the simple count Child-OIDP score among individuals with juvenile idiopathic arthritis (n = 125) and the controls (n = 124)

Item > 0*	JIA n (%)	Controls n (%)
Eating	24 (19.2)	13 (10.5)
Speaking	7 (5.6)	5 (4.0)
Toothbrushing	14 (11.2)	11 (8.9)
Smiling and laughing	9 (7.2)	8 (6.5)
Sleeping and relaxing	11 (8.8)	4 (3.2)
Emotional balance	13 (10.4)	5 (4.0)
Socialization and contact with people	3 (2.4)	2 (1.6)
Study	6 (4.8)	2 (1.6)
Child-OIDP simple count (SC) score > 0	33 (26.4)	27 (21.8)
Cronbach's alpha Child-OIDP SC score > 0	0.83	0.79

[a] $p < 0.05$; χ^2 test. *The items are dichotomized as 0 not affected and 1 affected at least once or twice a month. None of the included participants had any items missing

OHRQoL by group affiliation adjusted for socio-behavioral and clinical variables

Table 4 shows the results from unadjusted and adjusted ordinary logistic regression analyses of ECOHIS and Child-OIDP according to group affiliation. Increased odds ratios of having ECOHIS > 0 or OIDP > 0 were not statistically significant among participants with JIA in adjusted logistic regression analyses. Adjusted ordinary logistic regression analyses revealed a statistically significant association between $d_{1\text{-}5}ft/D_{1\text{-}5}FT > 0$ and ECOHIS total score > 0 (OR = 3.39, 95% CI 1.40–8.22). Reporting pain or discomfort occurring during toothbrushing increased the likelihood of having Child-OIDP SC score > 0 (OR = 7.76, 95% CI 3.09–19.50). Adolescents with mothers reporting low educational level had significantly lower odds ratio for oral impacts according to Child-OIDP SC score (OR = 0.32, 95% CI 0.13–0.82). Corresponding to Table 4, negative binomial regression revealed almost similar results (Additional file 9:

Table 4 Group affiliation, socio-behavioral, and clinical characteristics in relation to the outcome variable Early Childhood Oral Health Impact Scale (ECOHIS) total score > 0 and Child Oral Impacts on Daily Performance (Child-OIDP) simple count (SC) score > 0

	Unadjusted regression						Adjusted regression					
	ECOHIS total score > 0			Child-OIDP SC score > 0			ECOHIS total score > 0[a]			Child-OIDP SC score > 0[b]		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Group affiliation												
Control group	Ref			Ref			Ref			Ref		
JIA	1.88	(0.97–3.64)	0.064	1.29	(0.72–2.32)	0.396	1.95	(0.94–4.04)	0.072	0.99	(0.46–2.17)	0.987
Educational level of mother												
University/college	Ref			Ref			Ref			Ref		
High school/vocational school	1.29	(0.64–2.63)	0.477	0.63	(0.30–1.30)	0.209	0.87	(0.39–1.92)	0.729	0.32	(0.13–0.82)	**0.018**
Educational level of father												
University/college	Ref			Ref			Ref			Ref		
High school/vocational school	1.70	(0.89–3.27)	0.111	1.20	(0.63–2.26)	0.582	1.44	(0.64–3.25)	0.377	1.71	(0.76–3.83)	0.194
Household structure[c]												
Two caregivers[c]	Ref			Ref								
One caregiver	1.75	(0.55–5.59)	0.347	0.98	(0.45–2.14)	0.963						
Frequency of toothbrushing, n (%)												
Twice a day, or more	Ref			Ref			Ref					
Once a day or less/do not know	2.45	(1.07–5.61)	**0.035**	1.10	(0.55–2.23)	0.785	2.54	(0.99–6.54)	0.054			
Frequency of tooth flossing during the last 3 months, n (%)												
Daily or more	Ref			Ref								
Several times weekly or less/do not know	0.81	(0.17–3.90)	0.792	0.82	(0.34–1.97)	0.654						
During toothbrushing, gingival bleeding occurs												
Never	Ref			Ref			Ref			Ref		
Sometimes or more/do not know	1.38	(0.69–2.75)	0.363	1.66	(0.83–3.31)	0.149	1.10	(0.52–2.34)	0.810	1.38	(0.61–3.12)	0.447
During toothbrushing, pain or discomfort occurs												
No	Ref			Ref						Ref		
Yes/do not know	1.24	(0.24–6.38)	0.801	9.69	(4.25–22.10)	**< 0.001**				7.76	(3.09–19.50)	**< 0.001**
Dental caries												
$d_{1\text{-}5}ft/D_{1\text{-}5}FT^d = 0$	Ref			Ref			Ref			Ref		
$d_{1\text{-}5}ft/D_{1\text{-}5}FT^d > 0$	3.43	(1.44–8.19)	**0.006**	1.96	(1.05–3.67)	**0.036**	3.39	(1.40–8.22)	**0.007**	1.70	(0.81–3.56)	0.163

Unadjusted and adjusted ordinary logistic regressions

[a] ECOHIS > 0 regressed on group affiliation and adjusted for socio-behavioral factors (parental educational level, frequency of toothbrushing and bleeding during toothbrushing) and dental caries. McFadden's $R^2 = 8.9\%$.
[b] OIDP > 0 regressed on group affiliation and adjusted for socio-behavioral factors (parental educational level, bleeding during toothbrushing and pain or discomfort during toothbrushing) and dental caries. McFadden's $R^2 = 14.1\%$. [c] Also includes living across two households, given two caregivers in both households. [d] Decayed and/or filled teeth in the primary or permanent dentition, enamel caries included. OR = odds ratios. CI = confidence interval. JIA = juvenile idiopathic arthritis. P-values < 0.05 are marked in bold

Table S1). However, adjusted negative binomial regressions showed a statistically significant increased incidence rate ratio of negatively impacted ECOHIS among participants with JIA compared to controls (IRR = 1.61, 95% CI 1.16–2.23) (Additional file 9).

A significant two-way interaction between group affiliation and gender on Child-OIDP SC score was revealed by logistic regression ($p = 0.015$). Stratified analyses revealed that females had higher odds ratio for having Child-OIPD SC score > 0 compared to males, among participants with JIA (OR = 6.12, 95% CI 2.29–16.30, $p < 0.001$) (not presented in any table). Amongst the controls, females had higher odds ratio for having Child-OIPD SC > 0 compared to males (OR = 1.23, 95% CI 0.52–2.90), although not statistically significant (not presented in any table).

Disease-specific features in relation to OHRQoL

Table 5 shows the results from adjusted ordinary logistic regression analyses of disease-specific features in relation to ECOHIS and Child-OIDP among children and adolescents with JIA. Covariates were age, gender and parental educational level, and the JIA-specific variables were adjusted separately. Children with ongoing or ever used biologic DMARDs (disease-modifying antirheumatic drugs) were more likely than their counterparts without ongoing or ever used biologic DMARDs to have ECOHIS > 0 (OR = 7.59, 95% CI 1.77–32.67, $p = 0.006$ and OR = 9.20, 95% CI 1.93–43.97, $p = 0.005$). Adolescents categorized 'not oligoarthritis persistent' (comprising oligoarthritis extended, polyarthritis RF positive and RF negative, psoriatic arthritis, and enthesitis-related arthritis) had statistically significantly increased odd ratio of having Child-OIDP SC > 0, compared to participants in the JIA category oligoarthrits persistent (OR = 6.29, 95% CI 1.83–21.63). Adolescents with continued activity or flare revealed statistically significantly increased odds ratio of having Child-OIDP SC > 0, compared to participants with inactive disease or remission (OR = 3.01, 95% CI 1.15–7.89). This also applied to the self-reported pain (VAS pain > 0), compared to no pain (VAS pain = 0), and self-reported physical disability (CHAQ > 0), compared to no disability (CHAQ = 0) (OR = 4.39, 95% CI 1.20–16.14, OR = 4.21, 95% CI 1.40–12.68, respectively). Corresponding to Table 5, negative binomial regression revealed almost similar results (Additional file 10: Table S1).

Discussion

To our knowledge, this is one of the first studies to estimate the proportion and socio-, behavioral and clinical covariates of OHRQoL in young people with and without JIA. Present findings based on multiple variable logistic regression analysis did not confirm the hypothesis that children and adolescents with JIA have poorer OHRQoL than their counterparts without JIA. According to the ECOHIS scores this conclusion is unsure, since the adjusted binominal regression analyses showed an increased risk of impaired ECOHIS scores amongst the 4–11-year-olds with JIA compared to controls. Although the proportions who confirmed impacts according to ECOHIS and Child- OIDP scores were substantial across both groups, and always tended to be higher among children and adolescents with than without JIA, neither scale scores varied by group affiliation in the adjusted logistic regression analyses. Independent of JIA status, the likelihood of impaired OHRQoL increased by caries experience among the younger participants. Among the older participants, Child OIDP associated negatively and positively with maternal education and having pain/discomfort during toothbrushing, respectively. Although the socio-behavioral and clinical distribution of OHRQoL scores were less variant across the two groups of participants, female adolescents with JIA were more likely than males to report oral impacts according to Child OIDP. The corresponding association in the control group was not significant. Specifically, for adolescents with JIA, continued activity or flare was found to adversely affect Child-OIDP, indicating that sub-groups of JIA may have reduced OHRQoL, Also, self-reported outcome measures of the disease (VAS pain and CHAQ) associated with Child-OIDP.

Important strengths of the study were that the study group of individuals with JIA was relatively large and might be representative of the Norwegian population of children and adolescents with JIA. Also, a well-matched control group and the adjustment of various socio-demographic, behavioral, and clinical covariates strengthened the results [27, 36]. The present study revealed that both ECOHIS and Child-OIDP discriminated significantly according to global measures of oral health indicating satisfactory psychometrical properties of both instruments across the investigated groups. Other strengths were the meticulous calibration of caries examiners before and during the study and the use of the previous validated OHRQoL instruments in the context of Norwegian children and adolescents, which also showed a satisfactory internal consistency reliability [19]. Among limitations to be considered were a potential non-response bias among the participants with JIA [37] and the small subgroups of JIA disease categories that might have prevented valid interpretation of the relation between various disease categories and OHRQoL. Furthermore, considering the multilevel influences of oral health, other potential confounding variables of OHRQoL have not been adjusted for in the present study [38]. As a sub-study, the sample size calculation in the present article was based in caries figures and not on OHRQoL. This questions the study's

Table 5 JIA disease-specific features and dental caries in relation to Early Childhood Oral Health Impact Scale (ECOHIS) total score > 0 and Child Oral Impacts on Daily Performance (Child-OIDP) simple count (SC) score > 0

	ECOHIS total score > 0							Child-OIDP SC score > 0						
	Unadjusted regressions				Adjusted regressions[a]			Unadjusted regressions				Adjusted regressions[a]		
	n	OR	95% CI	*p*-value	OR	95% CI	*p*-value	n	OR	95% CI	*p*-value	OR	95% CI	*p*-value
JIA category														
Oligoarthritis persistent	32	Ref			Ref			44	Ref			Ref		
Not oligoarthritis persistent[b]	45*	3.64	(1.09–12.08)	**0.035**	3.32	(0.82–13.40)	0.092	62**	6.32	(1.99–20.01)	**0.002**	6.29	(1.83–21.63)	**0.004**
Age at JIA onset														
≤ 6 years	64	Ref			Ref			46	Ref			Ref		
> 6 years	32	0.82	(0.29–2.36)	0.719	0.61	(0.17–2.11)	0.430	79	1.03	(0.45–2.35)	0.952	1.52	(0.56–4.14)	0.414
Disease duration														
≤ 5 years	57	Ref			Ref			60	Ref			Ref		
> 5 years	39	3.13	(0.94–10.34)	0.062	2.81	(0.77–10.27)	0.117	65	0.97	(0.44–2.17)	0.948	0.87	(0.34–2.19)	0.762
Steroids, ever used														
No steroids ever used	74	Ref			Ref			99	Ref			Ref		
Steroids ever used	22	0.79	(0.25–2.53)	0.696	0.57	(0.15–2.14)	0.409	26	1.32	(0.51–3.41)	0.572	2.32	(0.79–6.88)	0.128
DMARDs, ongoing														
No sDMARDs nor bDMARDs ongoing	26	Ref			Ref			49	Ref			Ref		
sDMARDs, but no bDMARDs ongoing	34	2.04	(0.64–6.55)	0.230	2.00	(0.57–7.02)	0.280	27	2.68	(0.95–7.58)	0.063	1.38	(0.41–4.65)	0.601
bDMARDs ongoing[c]	36	5.82	(1.38–24.56)	**0.016**	7.59	(1.77–32.67)	**0.006**	49	1.27	(0.49–3.29)	0.630	1.20	(0.40–3.62)	0.743
DMARDs, ever used														
No sDMARDs nor bDMARDs ever used	15	Ref			Ref			37	Ref			Ref		
sDMARDs, but no bDMARDs ever used	43	2.52	(0.70–9.01)	0.155	3.41	(0.91–12.79)	0.069	38	2.50	(0.87–7.21)	0.090	1.20	(0.37–3.82)	0.764
bDMARDs ever used[c]	38	5.67	(1.30–24.66)	**0.021**	9.20	(1.93–43.97)	**0.005**	50	1.35	(0.47–3.88)	0.573	1.15	(0.35–3.72)	0.822
Disease status[d]														
Inactive disease/remission on/off medication	59	Ref			Ref			74	Ref			Ref		
Continued activity/flare	37	2.81	(0.85–9.32)	0.091	2.65	(0.81–8.65)	0.106	51	3.62	(1.57–8.34)	**0.003**	3.01	(1.15–7.89)	**0.025**
MDgloVAS														
VAS = 0	63	Ref			Ref			79	Ref			Ref		
VAS > 0	33	2.27	(0.68–7.54)	0.182	2.29	(0.71–7.44)	0.168	46	2.74	(1.21–6.23)	**0.016**	1.98	(0.77–5.08)	0.156
VAS pain														
VAS = 0	36	Ref			Ref			45	Ref			Ref		
VAS > 0	60	1.27	(0.46–3.56)	0.646	1.13	(0.38–3.42)	0.825	76	4.16	(1.46–11.86)	**0.008**	4.39	(1.20–16.14)	**0.026**
PRgloVAS														
VAS = 0	25	Ref			Ref			34	Ref			Ref		
VAS > 0	71	1.91	(0.65–5.61)	0.238	1.69	(0.52–5.50)	0.386	87	3.38	(1.08–10.58)	**0.037**	2.54	(0.65–9.97)	0.182

Table 5 (continued)

	ECOHIS total score > 0							Child-OIDP SC score > 0						
	Unadjusted regressions				Adjusted regressions[a]			Unadjusted regressions				Adjusted regressions[a]		
	n	OR	95% CI	*p*-value	OR	95% CI	*p*-value	n	OR	95% CI	*p*-value	OR	95% CI	*p*-value
CHAQ[e]														
CHAQ = 0	37	Ref			Ref			54	Ref			Ref		
CHAQ > 0	59	1.58	(0.57–4.36)	0.382	1.76	(0.58–5.37)	0.322	71	6.38	(2.26–18.06)	**< 0.001**	4.21	(1.40–12.68)	**0.011**
Dental caries														
$d_{1\text{-}5}ft/D_{1\text{-}5}FT^f = 0$	65	Ref			Ref			54	Ref			Ref		
$d_{1\text{-}5}ft/D_{1\text{-}5}FT^f > 0$	29	2.60	(0.69–9.87)	0.160	1.97	(0.49–7.97)	0.342	68	2.04	(0.84–4.96)	0.117	1.63	(0.57–4.65)	0.362

Unadjusted and adjusted ordinary logistic regressions

[a] Adjusted for: gender, age and educational level of mother and educational level of father. For the adjusted models McFadden's R^2 varied between 7.0%-15.4% (ECOHIS total score > 0) and 10.6%-19.3% (Child-OIDP SC score > 0). [b]Includes oligoarthritis extended, polyarthritis RF positive and RF negative, psoriatic arthritis, and enthesitis-related arthritis. [c]With or without sDMARDs. [d]Disease activity according to Wallace [66] and the American College of Rheumatology provisional criteria [67]. [e]Self-reported physical disability measured with the disease-specific and validated Childhood Health Assessment Questionnaire (CHAQ) (0 = no difficulty and 3 = unable to do) [34]. [f]Decayed and/or filled teeth in the primary or permanent dentition, enamel caries included. Some registrations are missing. *Oligoarthritis extended (n = 11), polyarthritis, RF positive (n = 1) and RF negative (n = 24), psoriatic arthritis (n = 3), and enthesitis-related arthritis (n = 6). **Oligoarthritis extended (n = 11), polyarthritis, RF positive (n = 1) and RF negative (n = 26), psoriatic arthritis (n = 5), and enthesitis-related arthritis (n = 17). RF = rheumatoid factor. sDMARDs = synthetic disease-modifying antirheumatic drugs. bDMARDs = biologic disease-modifying antirheumatic drugs. MDgloVAS = physician's global assessment of disease activity visual analogue scale (VAS). VAS pain = patient/parent-reported pain intensity. PRgloVAS = patient's global assessment of overall wellbeing. All visual analogue scales were measured on a 21-numbered circle VAS (0–10). CHAQ = Childhood Health Assessment Questionnaire (0 = no disability, 3 = maximum disability). OR = odds ratios. CI = confidence interval. JIA = juvenile idiopathic arthritis. P-values < 0.05 are marked in bold

statistical power and needs to be kept in mind while interpreting the results. Finally, evaluation of OHRQoL among the youngest study participants were only conducted by parental proxy-reporting and may reduce the quality of data collected. Thus, evidence suggests that parents tend to underestimate the impact of children's oral problems as their perspective is different and they might have limited knowledge of their children's social and emotional well-being [39].

Some descriptive studies have been conducted in European countries evaluating OHRQoL by the application of ECOHIS [19, 40–43]. Except for one study conducted in Norway by Skeie et al. [19], all of these studies evaluated OHRQoL in preschool children below the age of 6 years, hence complicating direct comparisons with the present study. Whereas the proportion of ECOHIS child impacts in this study amounted to 77.1% in the JIA group and 65.3% among controls, the corresponding figure among children in the study by Skeie et al. [19] was 71.0%. In contrast, the proportions of adolescents with and without JIA having impacts according to the Child-OIDP in the present study were 26.4% and 21.8%, a higher rate of 42.7% was found among adolescents in the study by Skeie et al. [19]. These differences in children's and adolescents' impact proportions might be attributed to minor age differences in the study groups investigated (also 17- and 18-year-olds were included in the study by Skeie et al.). The subjective and dynamic aspects of OHRQoL is based on individual experiences values and perceptions [44]. Thus, OHRQoL varies across groups within and across countries, as well as over time [44]. Nevertheless, many studies using Child-OIDP have been published [45–47]. A recent systematic review on OHRQoL in adolescents measured by use of Child-OIDP worldwide, reported prevalence rates of impacts within a wide range among adolescents 12 years and older, 15.8%-87% respectively [47].

Few studies have compared sub-scale OHRQoL scores with healthy controls. As shown in Table 2 physical- and psychosocial aspects of the Child impact scores and 'taken time off from work' from the family impact subscale were the most frequently reported impacts in both groups of younger children investigated. However, the prevalence of child impacts were consistently higher in the JIA group than among the controls, particularly regarding impacts related to physical and psycho-social functioning. Also, according to Table 3, the number of adolescents reporting impacts on the single OIDP items tended to be higher among participants with JIA, compared to controls. Physical aspects in terms of difficulty eating was most frequent among the 8 single OIDP scores. Impact of the function "eating" has also been demonstrated to be related to TMJ arthritis [23]. Although neither scale scores varied by group affiliation in the adjusted logistic regression analyses, children and adolescents with JIA seems to carry a particular burden regarding physical and psycho-social functioning. This is consistent with previous evidence that rheumatic diseases may result in important functional and psychosocial impairments, though examined among adult populations [48].

The present results showed that neither the ECOHIS-nor the Child OIDP scores varied by group affiliation in adjusted logistic regression analyses. This supports the findings of Santos et al. [22], who observed no significant difference in OHRQoL scores between individuals with JIA and controls, as perceived by their caregivers. However, comparisons with other studies are problematic as various OHRQoL instruments have been utilized, adjustment for covariates is seldom implemented and participants in the relevant studies are categorized specifically according to oral health status (e.g., JIA + TMJ arthritis, JIA + periodontitis) [22–25]. A plausible contributing factor of comparable OHRQoL between participants with JIA and controls is improved therapeutic effect, especially increased efficacy of pharmaceutical drugs, in the management of JIA [49, 50].

Independent of group affiliation, caries experience associated significantly with impaired OHRQOL amongst 4–11-year-olds in the present study. This corresponds with previous studies conducted across cultural contexts [51, 52]. The ECOHIS scale was originally developed to assess the impact of dental caries but have been widely used as generic OHRQoL instrument [45]. A systematic review by Kumar et al. [36] found that higher parental education associated with better OHRQoL in children. Contrary, we found that adolescents having lower educated mothers were less likely than their counterparts with higher educated mothers to report oral impacts according to Child OIDP. However, research findings in this area are conflicting and some studies have documented insignificant associations between parental socio-economic status and children's OHRQoL [36, 51].

Female adolescents with JIA were significantly more likely than male adolescents to report oral impacts according to Child-OIDP; the corresponding association in the control group was nonsignificant. Other studies reporting poorer OHRQoL among female participants compared to males, by the employment of Child-OIDP, consider females more sensitive to problems and appearance than males [53, 54]. Even in the biological era, pain and depressive symptoms, known to impact the quality of life, are common in JIA patients [55–57]. Comparable to findings in the general pediatric population, research

focusing on young individuals with JIA indicates, although inconsistently, a gender difference; females report such complaints more frequently than males, and the complaints become apparent in their adolescent years [58–63]. This may provide an explanation for female adolescents with JIA reporting poorer OHRQoL in this study.

Several JIA-specific covariates related to disease activity and patient/parent-reported pain, and functional disability were associated with Child-OIDP in the present study. OHRQoL is recognized to be part of health-related quality of life [64, 65], hence the association between patient/parent-reported covariates and OHRQoL was anticipated. In the present study biologic DMARDs, ongoing or ever used, were shown to be associated with impaired ECOHIS scores amongst the younger population with JIA. Thus, a more severe disease course as indicated by biologic DMARDs ongoing or ever used, is suggested to be associated with OHRQoL. No disease-specific inventory exists to evaluate OHRQoL in individuals with JIA. Accordingly, various impacts of JIA-specific features on OHRQoL are not necessarily identified by the generic instruments utilized in this study.

Conclusions

This study did not provide consistent evidence to confirm the hypothesis that children and adolescents with JIA are more likely to have impaired OHRQoL compared to their peers without JIA. However, female adolescents with JIA were more likely than males to report impacts on OHRQoL. Furthermore, within the JIA group, adolescents with continued disease activity, flare or reporting pain, or physical disability, had higher risk than their counterparts of impaired OHRQoL.

Abbreviations

bDMARDs: Biologic disease-modifying antirheumatic drugs; CHAQ: Childhood Health Assessment Questionnaire; Child-OIDP: Child Oral Impacts on Daily Performances; COHQoL: Child Oral Health-related Quality of Life measure; CPQ_{11-14}: Child Perception Questionnaire; DMARDs: Disease-modifying antirheumatic drugs; BW: Bitewing radiographs; CHAQ: Childhood Health Assessment Questionnaire; CI: Confidence interval; dfs/DFS: Decayed and filled surfaces; ECOHIS: Early Childhood Oral Health Impact Scale; ILAR: International League of Associations for Rheumatology; IRR: Incidence rate ratios; JIA: Juvenile idiopathic arthritis; MDgloVAS: Physician's global assessment of disease activity visual analogue scale; NorJIA: The Norwegian JIA Study (Temporo-mandibular Involvement, Oral Health, Uveitis, Bone Health and Quality of Life in Children with Juvenile Idiopathic Arthritis); OHRQoL: Oral health-related quality of life; OR: Odds ratios; PRgloVAS: Patient/parent-reported global assessment of overall wellbeing visual analogue scale; RF: Rheumatoid Factor; SC: Simple count; SD: Standard deviations; sDMARDs: Synthetic disease-modifying antirheumatic drugs; TMD: Temporomandibular disorder; TMJ: Temporomandibular joint; VAS: Visual analogue scale; VAS pain: Patient/parent-reported pain intensity visual analogue scale.

Supplementary Information

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Additional file 1. Sample size calculation.

Additional file 2. Calibration.

Additional file 3. Table S1. Categories for socio-behavioral characteristics, as originally coded and as re-coded for analyses.

Additional file 4. Table S1. Categories for Early Childhood Oral Health Impact Scale (ECOHIS) (4–11 years) and questions regarding satisfaction with oral health (global measures), as originally coded and as re-coded for analyses.

Additional file 5. Table S1. Categories for Child Oral Impacts on Daily Performances (Child-OIDP) (12–16 years) and questions regarding satisfaction with oral health (global measures), as originally coded and as re-coded for analyses.

Additional file 6. Description of JIA-specific background variables.

Additional file 7. Table S1. Categories for JIA-specific background variables, as originally coded and re-coded for analyses.

Additional file 8. Table S1. Discriminant validity of the Early Childhood Oral Health Impact Scale (ECOHIS) and Child Oral Impacts on Daily Performances (Child-OIDP) according to the global measures and group affiliation.

Additional file 9. Table S1. Group affiliation, socio-behavioral, and clinical characteristics in relation to the outcome variable Early Childhood Oral Health Impact Scale (ECOHIS) total score and Child Oral Impacts on Daily Performance (Child-OIDP) simple count (SC) score. Unadjusted and adjusted negative binominal regressions.

Additional file 10. Table S1. Disease-specific features and dental caries in relation to the outcome variable Early Childhood Oral Health Impact Scale (ECOHIS) total score and Child Oral Impacts on Daily Performance (Child-OIDP) simple count (SC) score. Unadjusted and adjusted negative binominal regressions.

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Author contributions

EGG: Contributed to the design and data collection of this sub-study, performed statistical analysis, and wrote the manuscript in consultation with ANÅ, MSS and SAL. ANÅ and MSS: Conceived and designed this sub-study. SAL: Performed statistical analysis. MR: Aided in interpretation and writing of the

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Regional Committees for Medical and Health Research Ethics (2012/542/REC), Rogaland, Vestland (West). Written informed consents were obtained from the caregivers and the adolescents as appropriate. The study was registered at ClinicalTrials.gov (No: NCT03904459, 05.04.2019). All procedures were performed in accordance with relevant guidelines.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Clinical Dentistry, University of Bergen, Bergen, Norway. [2]Center for Oral Health Services and Research, TkMidt, Trondheim, Norway. [3]Public Dental Health Competence Centre of Northern Norway (TkNN), Tromsø, Norway. [4]Department of Clinical Medicine, The Arctic University of Norway, Tromsø, Norway. [5]Department of Periodontology, Institute of Odontology, University of Gothenburg, Gothenburg, Sweden. [6]Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology (NTNU), Trondheim, Norway. [7]Department of Pediatrics, St. Olavs Hospital, Trondheim, Norway. [8]Department of Oral and Maxillofacial Surgery, Haukeland University Hospital, Bergen, Norway. [9]Oral Health Centre of Expertise in Western Norway-Vestland, Bergen, Norway. [10]Department of Oral Maxillofacial Radiology, Faculty of Odontology, Malmö University, Malmö, Sweden. [11]Department of Otorhinolaryngology, Division of Oral and Maxillofacial Surgery, University Hospital of North Norway, Tromsø, Norway. [12]Department of Pediatrics, Haukeland University Hospital, Bergen, Norway. [13]Department of Radiology, University Hospital of North Norway, Tromsø, Norway.

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Publisher's Note

APPENDIX I

Appendix I includes the search strategy for the six databases (Medline, Embase, CINAHL, SweMed+, Cochrane Library, and Web of Science). Research articles in English were an inclusion criterion. After the removal of duplicates, a total of 97 studies were found. Further elimination of reviews, case reports, conference abstracts, and studies focusing on older age groups, general health, or other oral health indicators (e.g., TMD, malocclusion, periodontitis, saliva) resulted in the final fulfillment of 29 studies. Three of these 29 studies (80, 110, 111) belonged to our research group and were not presented in the introduction.

Ovid MEDLINE 25.06.2022

Nr.	Search strategy	hits
1	exp Dental Plaque /	17218
2	exp Oral Hygiene /	20490
3	exp Gingivitis/	11855
4	exp Oral Health /	19232
5	exp Dental Caries /	49166
6	exp Child /	2084533
7	exp Adolescent /	2180166
8	(child or children or adolescent*).ab,kw,ti.	1544437
8	periodontal.ab,kw,ti.	65018
10	gingivitis.ab,kw,ti.	8677
11	teeth.ab,kw,ti	122127
12	dental.ab,kw,ti.	242867
13	caries.ab,kw,ti.	46896
14	oral health related quality of life.ab,kw,ti.	3160
15	oral health-related quality of life.ab,kw,ti.	3160
16	ohrqol.ab,kw,ti.	1847
17	juvenile idiopathic arthritis.ab,kw,ti.	6420
18	juvenile rheumatoid arthritis.ab,kw,ti.	3158
19	(JIA or JRA).ab,kw,ti.	5895
20	1 or 2 or 3 or 4 or 5 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	408931
21	6 or 7 or 8	3682766
22	17 or 18 or 19	10452
23	20 and 21 and 22	81
24	limit 23 to (english language and yr="1985 -Current")	73
25	24 and "Journal Article" [Publication Type]	71

EMBASE 02.07.2022

Nr.	Search strategy	hits
1	exp tooth plaque/	20170
2	exp mouth hygiene/	29440
3	exp gingivitis/	17904
4	exp gingiva bleeding/	7012
5	exp dental caries/	52286
6	exp child/	2897097
7	exp adolescent/	1676853

8	(child or children or adolescent*).ab,kw,ti.	1930774
9	periodontal.ab,kw,ti.	64402
10	gingivitis.ab,kw,ti.	8863
11	teeth.ab,kw,ti.	117239
12	dental.ab,kw,ti.	235280
13	caries.ab,kw,ti.	44062
14	oral health related quality of life.ab,kw,ti.	3180
15	oral health-related quality of life.ab,kw,ti.	3180
16	ohrqol.ab,kw,ti.	1828
17	juvenile idiopathic arthritis.ab,kw,ti.	13205
18	juvenile rheumatoid arthritis.ab,kw,ti.	3701
19	juvenile chronic arthritis.ab,kw,ti.	1369
20	(JIA or JRA or JCR).ab,kw,ti.	12974
21	1 or 2 or 3 or 4 or 5 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	394998
22	6 or 7 or 8	4107560
23	17 or 18 or 19 or 20	21017
24	21 and 22 and 23	138
25	limit 24 to (english language and yr="1985 -Current" and article)	79

CINAHL 25.06.2022

Nr.	Search strategy	hits
1	(MH "Dental Hygiene")	5,343
2	(MH "Gingivitis+")	2,245
3	(MH "Dental Plaque")	3,480
4	(MH "Dental Caries")	13,509
5	(MH "Child+")	733,458
6	(MH "Adolescence+")	579,206
7	child or children or adolescent*	877,358
8	periodontal	19,689
9	gingivitis	2,977
10	teeth	48,812
11	dental	131,634
12	caries or decay or cavities or cavity	41,375
13	oral health related quality of life	1,712
14	ohrqol	859
15	juvenile idiopathic arthritis	3,451

16	juvenile rheumatoid arthritis	179,080
17	S1 OR S2 OR S3 OR S4 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14	179,080
18	S15 OR S16	4,119
19	S5 OR S6 OR S7	1,252,228
20	S17 AND S18 AND S19	34
21	S17 AND S18 AND S19 **Limiters** - Published Date: 18850101-20221231; English Language; Research Article	24

SveMed+ 25.06.2022

Nr.	Search strategy	hits
1	exp:"Dental Plaque"	104
2	exp:"Oral Hygiene"	352
3	exp:"Gingivitis"	80
4	exp:"Oral Health"	670
5	exp:"Dental Caries"	520
6	exp:"Child"	11791
7	exp:"Adolescent"	9922
8	children	12338
9	adolescent*	9995
10	periodontal	582
11	gingivitis	122
12	teeth	346
13	dental	3004
14	caries	522
15	oral health related quality of life	82
16	ohrqol	0
17	juvenile idiopathic arthritis	62
18	juvenile rheumatoid arthritis	62
19	JIA	7
20	JRA	6
21	#1 OR #2 OR #3 OR #4 OR #5 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16	3526
22	#6 OR #7 OR #8 OR #9	17334
23	#17 OR #18 OR #19 OR #20	73
24	#22 AND #23 AND #24	3

Cochrane 25.6

NR.	Search strategy	hits
1	MeSH descriptor: [Dental Plaque] explode all trees	2645
2	MeSH descriptor: [Gingivitis] explode all trees	1501
3	MeSH descriptor: [Dental Caries] explode all trees	2871
4	MeSH descriptor: [Child] explode all trees	61335
5	MeSH descriptor: [Adolescent] explode all trees	110231
6	MeSH descriptor: [Oral Hygiene] explode all trees	3825
7	MeSH descriptor: [Oral Health] explode all trees	266

8	(oral health related quality of life):ti,ab,kw	255937
9	(ohrqol):ti,ab,kw	676
10	(child or children or adolescent*):ti,ab,kw	576
11	(juvenile idiopathic arthritis):ti,ab,kw	741
12	((juvenile rheumatoid arthritis):ti,ab,kw	48794
13	(JIA or JRA):ti,ab,kw	52160
14	(periodontal or gingivitis or teeth or dental or caries):ti,ab,kw	255937
15	#1 or #2 or #3 or #6 or #7 or #8 or #9 or #14	
16	#11 or #12 or #13	1039
17	#15 and #16 and #17	6

Web of Science, 25.06.2022

Nr.	Search strategy	Hits
1	(TI=(dental plaque or oral hygiene or gingivitis or periodontal or oral health or dental caries or teeth or oral health related quality of life or oral related quality of life) AND TI=(juvenile idiopathic arthritis or juvenile rheumatoid arthritis)) Index Date : 1985-01-01 to 2022-01-31. Document type: Articles. Language: English	14

APPENDIX II

Appendix II includes the self-administered questionnaires providing socio-demographic, behavioral, and self-reported oral health information. The two versions are the questionnaire for the participants 4-11 years completed by the caregivers and the questionnaire for the participants 12 years and older. The items used as variables in the papers of this thesis are highlighted in yellow.

Tannhelserelatert spørreskjema til foresatte

(For barn under 12 år)

OM BARNET OG FAMILIEN

Barnet bor sammen med:

- ❑ Mor og far
- ❑ Bare mor
- ❑ Bare far
- ❑ Andre, spesifiser: _____

Mors utdanning

- ❑ Grunnskole
- ❑ Videregående/yrkesskole
- ❑ Universitet/høyskole kort (inntil 4 år)
- ❑ Universitet/høyskole lang (5 år eller mer)
- ❑ Ukjent

Fars utdanning

- ❑ Grunnskole
- ❑ Videregående/yrkesskole
- ❑ Universitet/høyskole kort (inntil 4 år)
- ❑ Universitet/høyskole lang (5 år eller mer)
- ❑ Ukjent

Om mors fødeland:

- ❑ Født i Norge
- ❑ Ikke født i Norge
- ❑ Vet ikke

Dersom mor ikke er født i Norge, oppgi mor sitt fødeland:

- ❑ Fødeland: _____
- ❑ Vet ikke

Dersom mor ikke er født i Norge, oppgi hvor mange år mor har bodd i Norge:

- ❑ År: _____
- ❑ Vet ikke

Om fars fødeland:

- ❑ Født i Norge
- ❑ Ikke født i Norge
- ❑ Vet ikke

Dersom far ikke er født i Norge, oppgi far sitt fødeland:

- ❑ Fødeland: _____
- ❑ Vet ikke

Dersom far ikke er født i Norge, oppgi hvor mange år far har bodd i Norge:

- ❑ År: _____
- ❑ Vet ikke

OM TANNHELSEVANER

Hvilken type tannkrem bruker barnet?

- ❑ Voksentannkrem med fluor
- ❑ Barnetannkrem med fluor
- ❑ Tannkrem uten fluor
- ❑ Bruker ikke tannkrem
- ❑ Vet ikke

Hvor ofte blir barnets tenner pusset?

- ❑ Aldri
- ❑ De fleste dager
- ❑ En gang daglig
- ❑ To ganger, eller flere, daglig
- ❑ Vet ikke

Ved barnets tannpuss, hvor stor mengde tannkrem tas på tannkosten? (Oppgi omtrentlig)

- ❑ Ertestor
- ❑ Litt mer en ertestor
- ❑ 1 cm
- ❑ Vet ikke

Hvor ofte har barnet brukt tanntråd de siste 3 månedene?

- ❑ Mange ganger daglig
- ❑ To ganger daglig
- ❑ Daglig
- ❑ Mange ganger ukentlig
- ❑ Mange ganger per måned, men ikke hver uke
- ❑ Sjeldent
- ❑ Aldri
- ❑ Vet ikke

I tilfelle barnet bruker tanntråd, får barnet hjelp til det?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Bruker barnet fluortabletter?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Dersom barnet bruker fluortabletter, følges dosering etter aktuell alder?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Bruker barnet fluorskyll?

- ❑ Ja

- ❑ Nei
- ❑ Vet ikke

Dersom barnet bruker fluorskyll, følges dosering etter aktuell alder?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Hvor gammelt var barnet ved oppstart av tannpuss?

- ❑ Ikke begynt
- ❑ Under 1 år
- ❑ 1-2 år
- ❑ Over 2 år
- ❑ Vet ikke

Fikk barnet saft/melk på flaske etter 1-årsalder?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Får barnet drikke eller mat i sengen om kvelden eller natten?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Hvis barnet får drikke i sengen om kvelden eller natten, hvilken drikke får hun/han da? (Flere svar er mulig)

- ❑ Vann
- ❑ Melk
- ❑ Saft
- ❑ Juice
- ❑ Sjokolademelk (eks. O'boy/Nesquick)
- ❑ Annet; spesifiser: _____
- ❑ Vet ikke

OM BARNETS TANNHELSE

Hvilket inntrykk har du/dere av barnets opplevelse av tannpuss?

- ❑ Smertefullt
- ❑ Ubehagelig
- ❑ Helt greit
- ❑ Vet ikke

Hvis barnet har smerte/ubehag ved tannpuss, hvor tror du/dere det kommer fra? (Flere svar er mulig)

- ❑ Kjeveledd
- ❑ Ellers, beskriv _____
- ❑ Vet ikke

Opplever du/dere at barnet blør fra tannkjøttet ved tannpuss?

- ❑ Hver dag
- ❑ De fleste dager
- ❑ En dag i uken
- ❑ Av og til
- ❑ Aldri
- ❑ Vet ikke

Opplever du/dere at barnet vanligvis er tørr i munnen?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Opplever du/dere at barnet er plaget av munntørrhet om natten (f.eks. ved at barnet ber om drikke om natten)?

- ❑ Nei, aldri
- ❑ Nei, sjelden
- ❑ Ja, av og til
- ❑ Ja, ofte

- ❑ Vet ikke

Opplever du/dere at barnet er plaget av munntørrhet om dagen?

- ❑ Nei, aldri
- ❑ Nei, sjelden
- ❑ Ja, av og til
- ❑ Ja, ofte
- ❑ Vet ikke

Opplever du/dere at barnet er engstelig for tannbehandling?

- ❑ Nei
- ❑ Ja
- ❑ Ja, og har tidligere fått narkose eller beroligende medikamenter ved behandling
- ❑ Vet ikke

OM UBEHAG I MUNNEN

Opplever du/dere at barnet gir uttrykk for å ha sår i munnen?

- ❑ Én eller flere ganger per måned
- ❑ Flere ganger årlig, men sjeldnere enn en gang per måned
- ❑ Sjeldnere enn en gang per år
- ❑ Aldri
- ❑ Vet ikke

Dersom barnet uttrykker å ha sår i munnen, unngår hun/han å spise noen typer mat i slike perioder?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Dersom barnet uttrykker å ha ubehag i kjeve/kjeveledd, unngår hun/han å spise noen typer mat i slike perioder?

- ❑ Ja
- ❑ Nei

❑ Vet ikke

Har barnet barneleddgikt?

❑ Ja

❑ Nei

DE RESTERENDE SPØRSMÅLENE GJELDER BARE DERSOM BARNET HAR LEDDGIKTSYKDOM

Dersom barnet får faste medisiner i form av tabletter eller mikstur, gis medisinen sammen med drikke? Velg det alternativet som passer best (bare ett svar er mulig)

❑ Ja, som oftest sammen med vann

❑ Ja, som oftest sammen med melk eller melkebaserte drikker (Litago, O'boy, Biola, drikkeyoghurt e.l.)

❑ Ja, som oftest sammen juice

❑ Ja, som oftest sammen med saft/brus med sukker

❑ Ja, som oftest sammen med saft/brus uten sukker (Fun light el.l.)

❑ Vet ikke

Hvordan vil du beskrive barnets inntak av væske i en periode med økt sykdomsaktivitet pga. leddgiktsykdommen?

❑ Drikker mer enn ellers

❑ Drikker mindre enn ellers

❑ Drikker som det vanligvis gjør

❑ Vet ikke

I perioder med økt sykdomsaktivitet pga. leddgiktsykdomen, opplever du at barnet drikker mer av noen type drikker enn ellers? (Flere svar er mulig)

❑ Ja, mer vann

❑ Ja, mer melk eller melkebaserte drikker (Litago, O'boy, Biola, drikkeyoghurt e.l.)

❑ Ja, mer juice

❑ Ja, mer saft/brus med sukker

❑ Ja, mer saft/brus uten sukker (Fun light el.l.)

❑ Nei, drikker like mye av alle typer drikke som ellers

❑ Vet ikke

Hvordan vil du beskrive tannpussingen hos barnet i en periode med økt sykdomsaktivitet pga. leddgiktsykdommen?

❑ Tennene pusses mer grundig enn ellers

- ❑ Tennene pusses på samme måte som ellers
- ❑ Tennene pusses mindre grundig enn ellers
- ❑ Vet ikke

Hvis barnet pusser tennene selv, hender det av ulike årsaker (knyttet til leddgiktsykdommen) at hun/han ikke klarer å pusse tennene så godt som du/dere hadde villet? (Flere svar er mulig)

- ❑ Nei
- ❑ Ja, pga. ubehag i arm
- ❑ Ja, pga. ubehag i kjeve/kjeveledd
- ❑ Ja, annet, beskriv: _____
- ❑ Vet ikke
- ❑ Barnet pusser ikke tennene selv

Har du/dere som foresatt blitt informert om viktigheten av god tannhelse for barn med leddgikt?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Hvis ja på forrige spørsmål, hvem ble du/dere informert av? (Flere svar er mulig)

- ❑ Helsesøster
- ❑ Lege
- ❑ Tannpleier
- ❑ Tannlege
- ❑ Annet; spesifiser: _____
- ❑ Vet ikke
- ❑ Har ikke blitt informert

Takk for din besvarelse!

Tannhelserelatert spørreskjema til deg som er 12 år og eldre

OM DEG OG FAMILIEN DIN

Bor du sammen med:

- ❑ Mor og far

- ❑ Bare mor
- ❑ Bare far
- ❑ Andre, spesifiser: _____

Mors utdanning

- ❑ Grunnskole
- ❑ Videregående/yrkesskole
- ❑ Universitet/høyskole kort (inntil 4 år)
- ❑ Universitet/høyskole lang (5 år eller mer)
- ❑ Ukjent

Fars utdanning

- ❑ Grunnskole
- ❑ Videregående/yrkesskole
- ❑ Universitet/høyskole kort (inntil 4 år)
- ❑ Universitet/høyskole lang (5 år eller mer)
- ❑ Ukjent

Om mors fødeland:

- ❑ Født i Norge
- ❑ Ikke født i Norge
- ❑ Vet ikke

Dersom mor ikke er født i Norge, oppgi mor sitt fødeland:

- ❑ Fødeland: _____
- ❑ Vet ikke

Dersom mor ikke er født i Norge, oppgi hvor mange år mor har bodd i Norge:

- ❑ År: _____
- ❑ Vet ikke

Om fars fødeland:

- ❑ Født i Norge

- ❑ Ikke født i Norge
- ❑ Vet ikke

Dersom far ikke er født i Norge, oppgi far sitt fødeland:

- ❑ Fødeland: _____
- ❑ Vet ikke

Dersom far ikke er født i Norge, oppgi hvor mange år far har bodd i Norge:

- ❑ År: _____
- ❑ Vet ikke

OM TANNHELSEVANER

Hvilken type tannkrem bruker du?

- ❑ Voksentannkrem med fluor
- ❑ Barnetannkrem med fluor
- ❑ Tannkrem uten fluor
- ❑ Bruker ikke tannkrem
- ❑ Vet ikke

Bruker du andre fluorpreparater?

- ❑ Fluortabletter
- ❑ Fluor skyllevæske
- ❑ Fluor tyggegummi
- ❑ Annet
- ❑ Vet ikke

Hvor ofte pusser du tennene?

- ❑ Aldri
- ❑ De fleste dager
- ❑ En gang daglig
- ❑ To ganger daglig, eller flere
- ❑ Vet ikke

Når du pusser tennene, hvor stor mengde tannkrem tar du på tannkosten? (Oppgi omtrentlig)

- ❑ Ertestor
- ❑ Litt mer enn ertestor
- ❑ 1 cm
- ❑ 2 cm
- ❑ Mer enn 2 cm
- ❑ Vet ikke

Hvor ofte har du brukt tanntråd de siste 3 månedene?

- ❑ Mange ganger daglig
- ❑ To ganger daglig
- ❑ Daglig
- ❑ Mange ganger ukentlig
- ❑ Mange ganger per måned, men ikke hver uke
- ❑ Sjeldent
- ❑ Aldri
- ❑ Vet ikke

OM TANNHELSE

Føler du deg vanligvis tørr i munnen?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Føler du deg tørr i munnen om natten?

- ❑ Nei, aldri
- ❑ Ja, sjelden
- ❑ Ja, av og til
- ❑ Ja, ofte
- ❑ Vet ikke

Føler du deg tørr i munnen om dagen?

- ❑ Nei, aldri
- ❑ Ja, sjelden
- ❑ Ja, av og til
- ❑ Ja, ofte
- ❑ Vet ikke

Opplever du at det av og til er smertefullt eller ubehagelig å pusse tenner?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Hvis du av og til har smerte eller ubehag ved tannpuss, hvor opplever du det kommer fra? (Flere svar er mulig)

- ❑ Kjeveledd
- ❑ Ellers, beskriv: _____
- ❑ Vet ikke

Blør du fra tannkjøttet ved tannpuss?

- ❑ Hver dag
- ❑ De fleste dager
- ❑ En dag i uken
- ❑ Av og til
- ❑ Aldri
- ❑ Vet ikke

Er du engstelig for tannbehandling?

- ❑ Nei
- ❑ Ja
- ❑ Ja, og tidligere har jeg fått narkose eller beroligende medikamenter ved behandling
- ❑ Vet ikke

OM UBEHAG I MUNNEN

Har du sår i munnen?

- ❑ Én eller flere ganger per måned
- ❑ Flere ganger årlig, men sjeldnere enn en gang per måned
- ❑ Sjeldnere enn en gang per år
- ❑ Aldri
- ❑ Vet ikke

Dersom du har sår i munnen, unngår du da å spise noen typer mat?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Dersom du har ubehag i kjeve/kjeveledd, unngår du da å spise noen typer mat?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Har du barneleddgikt?

- ❑ Ja
- ❑ Nei

RESTEN AV SPØRSMÅLENE I SPØRRESKJEMAET GJELDER BARE DERSOM DU HAR LEDDGIKTSYKDOM

Dersom du tar faste medisiner i form av tabletter eller mikstur, tar du medisinen sammen med drikke? Velg det alternativet som passer best (bare ett svar er mulig)

- ❑ Ja, som oftest sammen med vann
- ❑ Ja, som oftest sammen med melk eller melkebaserte drikker (Litago, O'boy, Biola, drikkeyoghurt e.l.)
- ❑ Ja, som oftest sammen juice

- ❑ Ja, som oftest sammen med saft/brus med sukker
- ❑ Ja, som oftest sammen med saft/brus uten sukker (Fun light el.l.)
- ❑ Vet ikke

Dersom du i en periode er mye syk på grunn av leddgiktsykdommen, hvordan vil du beskrive hvordan du drikker i løpet av dagen/natten?

- ❑ Drikker mer enn ellers
- ❑ Drikker mindre enn ellers
- ❑ Drikker slik jeg vanligvis gjør
- ❑ Vet ikke

Dersom du i en periode er mye syk på grunn av leddgiktsykdommen, drikker du mer av noen type drikker enn ellers? (Flere svar er mulig)

- ❑ Ja, mer vann
- ❑ Ja, mer melk eller melkebaserte drikker (Litago, O'boy, Biola, drikkeyoghurt e.l.)
- ❑ Ja, mer juice
- ❑ Ja, mer saft/brus med sukker
- ❑ Ja, mer saft/brus uten sukker (Fun light el.l.)
- ❑ Nei, drikker like mye av alle typer drikke som ellers
- ❑ Vet ikke

Hvordan vil du beskrive tannpussingen din i en periode når du er mye syk pga. leddgiktsykdommen?

- ❑ Jeg pusser tennene mer grundig enn ellers
- ❑ Jeg pusser tennene på samme måte som ellers
- ❑ Jeg pusser tennene mindre grundig enn ellers
- ❑ Vet ikke

Hender det at du av ulike årsaker (knyttet til leddgiktsykdommen) ikke klarer å pusse tennene dine så godt som du selv hadde villet? (Flere svar er mulig)

- ❑ Nei
- ❑ Ja, på grunn av ubehag i arm

- ❑ Ja, på grunn av ubehag i kjeve/kjeveledd
- ❑ Ja, annet, beskriv: _____
- ❑ Vet ikke

Har du fått informasjon om viktigheten av god tannhelse etter at du fikk diagnosen barneleddgikt?

- ❑ Ja
- ❑ Nei
- ❑ Vet ikke

Hvis ja, på forrige spørsmål, hvem ble du informert av? (Flere svar er mulig)

- ❑ Helsesøster
- ❑ Lege
- ❑ Tannpleier
- ❑ Tannlege
- ❑ Annet; spesifiser: _____
- ❑ Vet ikke

Takk for din besvarelse!

APPENDIX III

Appendix III includes the examination protocol for participants ≥10 years and presents this study's clinical oral health variables of relevance (highlighted in yellow).

Case-nr. er sensitiv forskningsopplysning, dersom prosedyre skal legges til tannlegejournal skal case-nr. påføres etter at det er utført Case-nr:_____

Diverse vedlegg tilhørende undersøkelsesprosedyre:

1.) «Veiledning CHILD-OIDP-INDEX»
2.) «IOTN, AC»
3.) «Modifisert versjon Simplified Oral Hygiene Index (OHI-S)»
4.) «Modifisert versjon Gingival Bleeding Index»
5.) «Kariesgradering etter diagnosekriterier for karies basert på Espelid og Tveit»
6.) «The basic version of the Enamel Defects Index»
7.) «Gradering av erosjon»
8.) «Vurdering av bittavvik, horisontalt overbitt (HO) »
9.) «Ekstraorale og intraorale foto»
10.) «Felles protokoll for kjeveledd, vekst og TMD», egne skjema inngår i undersøkelsesprosedyre

Pasient tilhører	☐ Testgruppen ☐ Kontrollgruppen
Kjønn	☐ Jente ☐ Gutt
Alder ved undersøkelse HUS (testgruppen): Det er alder ved undersøkelse HUS som avgjør hvilken undersøkelsesprosedyre som skal følges	
Alder ved undersøkelse (kontrollgruppen): Kontrollgruppen skal justeres etter alder ved undersøkelse HUS	

Dato for undersøkelse	
Undersøker (for- og etternavn)	

Testgruppen

Har det gått lengre enn 4 uker mellom undersøkelse ved HUS til undersøkelse utført ved TkVest?	☐ Nei	☐ Ja, beskriv:

Samtykkeskjema (gjelder bare kontrollgruppen)

Skjema signert (må arkiveres)	☐ Ja

Helseopplysninger (helseskjema i Opus journal skal oppdateres)

Sykdommer	
Medisinbruk (noter også dose, tidspunkt og varighet) Faste medisiner og medisiner ved behov (spesifiser). For behovsmedisiner er det også ønskelig å vite omtrentlig hvor ofte pasienten bruker dette medikamentet.	
Allergier	☐ Ingen kjente ☐ Ja, beskriv:

NB!
CHILD-OIDP-INDEX (f.o.m. 12 år) og IOTN,AC (f.o.m. 8 år) anses som forskningsdata og skal ikke inngå i epikrise. Men dersom funn ved CHILD-OIDP-INDEX og IOTN,AC som tyder på at pasientens livskvalitet påvirkes negativt skal det informeres om i epikriseskjema til lokal tannklinikk. Forbehold er at pasienten (dersom pasienten er 12 år eller eldre) eller foresatt (dersom pasienten er under 12 år) samtykker til at aktuell informasjon oversendes til lokal tannklinikk.

Dersom aktuelt å informere lokal tannklinikk om funn Child-OIDP-INDEX eller IOTN,AC, samtykker pasient/foresatt til det ☐ Ja ☐ Nei, beskriv: _____

Pasient/foresatt skal informeres om CHILD-OIDP-INDEX og IOTN, AC.

CHILD-OIDP-INDEX (S. Gherunpong, G. Tsakos and A. Sheiham, 2004)
Utføres fra og med 12 år som intervju (intervjuet skal utføres før den kliniske undersøkelsen).
Ett svaralternativ krysses av.

Vennligst se laminert vedlegg.

«I løpet av de tre siste månedene, hvor ofte har problemer med tenner og munnhule gjort det vanskelig for deg …….»:

1a.) Spising	☐	Aldri	☐	En eller to ganger månedlig	☐	En eller to ganger i uken	☐	Hver dag/nesten hver dag
1b.) Snakking	☐	Aldri	☐	En eller to ganger månedlig	☐	En eller to ganger i uken	☐	Hver dag/nesten hver dag
1c.) Tannbørsting	☐	Aldri	☐	En eller to ganger månedlig	☐	En eller to ganger i uken	☐	Hver dag/nesten hver dag
1d.) Smiling, le og vise tenner uten å bli flau	☐	Aldri	☐	En eller to ganger månedlig	☐	En eller to ganger i uken	☐	Hver dag/nesten hver dag
1e.) Søvn, avslapping	☐	Aldri	☐	En eller to ganger månedlig	☐	En eller to ganger i uken	☐	Hver dag/nesten hver dag
1f.) Følelsesmessig balanse	☐	Aldri	☐	En eller to ganger månedlig	☐	En eller to ganger i uken	☐	Hver dag/nesten hver dag
1g.) Sosial kontakt	☐	Aldri	☐	En eller to ganger månedlig	☐	En eller to ganger i uken	☐	Hver dag/nesten hver dag
1h.) Utførelse av skolearbeidet	☐	Aldri	☐	En eller to ganger månedlig	☐	En eller to ganger i uken	☐	Hver dag/nesten hver dag
Tilleggsspørsmål:								
2a.) Hvordan anser du din tannhelse å være?								
☐	Svært god	☐	God	☐	Verken god eller dårlig	☐	Dårlig	☐ Svært dårlig
2b.) Hvor fornøyd eller misfornøyd er du med utseende på tennene dine?								
☐	Svært fornøyd	☐	Fornøyd	☐	Verken fornøyd eller misfornøyd	☐	Misfornøyd	☐ Svært misfornøyd

Index Of Treatment Need (IOTN), Aesthetic Component (AC) (Brook and Shaw, 1989)
Skal ikke utføres for pasienter med fast kjeveortopedisk apparatur.

Pasient og foresatte (uavhengig av hverandre) blir bedt om å rangere utseende på sine/sitt barns tenner, ut i fra AC i IOTN-index (gradering 1-10). Vennligst se laminert vedlegg. «Vennligst pek ut det bildet du/dere synes ligner mest på dine/ditt barns tenner.»		
Gradering valgt av pasient (1-10)	Noter nummer:	
Foresatt tilstede	☐ Ja	☐ Nei
Gradering valgt av foresatt (1-10)	Noter nummer:	

Høyde og vekt (gjelder bare kontrollgruppen)

Instruksjon for måling:

-Høyde: Veggholdt eller sammenleggbar høydemåler. Uten sko. Føttene samlet og inntil vegg. Be pasienten stå så rak og stram som mulig og be dem ta et dypt innpust rett før målingen.

-Vekt: Lett bekledning (bukse, t-skjorte og sokker).

Høyde (cm) (én decimal)	cm		Vekt (kg) (én decimal)	kg
Er måling av høyde/vekt utført iht. undersøkelsesprosedyre	☐ Ja ☐ Nei, beskriv:			

Spørreskjema

Gjelder bare kontrollgruppen, testgruppen har utfylt skjemaene på sykehuset

Pasient har fylt ut skjema	☐ Tannhelserelatert spørreskjema til deg over 12 år (dersom pasienten er over 12 år) ☐ Kosthold og fysisk aktivitet (12 år er veiledende grense for utfylling, kan gjerne fylles ut i samarbeid barn/foresatt) «Fravær» i slutten av spørreskjema skal ikke fylles ut av kontrollgruppen
Foresatt har fylt ut skjema	☐ CHQ-PF50 «Hjelpebehov» i slutten av spørreskjema skal ikke fylles ut av kontrollgruppen ☐ Tannhelserelatert spørreskjema til foresatte (dersom pasienten er under 12 år) ☐ Kosthold og fysisk aktivitet (12 år er veiledende grense for utfylling, kan gjerne fylles ut i samarbeid foresatt/barn) «Fravær» i slutten av spørreskjema skal ikke fylles ut av kontrollgruppen ☐ ECOHIS- foresatte (pasient < 12 år)

Røntgen

CBCT, OPG og CEPH utføres ved Institutt for klinisk odontologi (IKO)

Testgruppen	☐ BW (fra 5-år) (skal ikke utføres om manglende intermolar kontakt eller pasienten har fast kjeveortopedisk apparatur)	☐ Ikke tatt BW	☐ Manglende intermolar kontakt ☐ Fast kjeveortopedisk apparatur ☐ Annet, beskriv:
	☐ CBCT	☐ Ikke tatt CBCT, beskriv:	
	☐ CEPH (skal ikke utføres dersom pasienten har fast kjeveortopedisk apparatur)	☐ Ikke tatt CEPH	☐ Fast kjeveortopedisk apparatur ☐ Annet, beskriv:
	☐ OPG	☐ Ikke tatt OPG, beskriv:	
Kontrollgruppen	☐ BW (fra 5-år) (skal ikke utføres om manglende intermolar kontakt eller pasienten har fast kjeveortopedisk apparatur)	☐ Ikke tatt BW	☐ Manglende intermolar kontakt ☐ Fast kjeveortopedisk apparatur ☐ Annet, beskriv:
OPG og CEPH opptak utført ved IKO er lagt til pasientens tannlegejournal TkVest (gjelder bare testgruppen)	☐ Ja	☐ Nei, beskriv:	

Kommentar/funn til utført røntgen
CBCT (testgruppen) beskrives av radiolog ved TkVest og epikrise sendes til henvisende lege
CEPH (testgruppen) er et analyseverktøy for senere kjeveortopedisk vurdering
BW:

- For pasienter uten barneleddgikt: Kun kariesundersøkelse på indekstenner utføres(under punkt «Kariesundersøkelse»). Samtidig med undersøkelsen tilknyttet JIA-prosjekt, utføres en rutineundersøkelse ved lokal tannklinikk. Funn i forbindelse med rutineundersøkelse registreres i Opus journal.
- For pasienter med barneleddgikt: Kun kariesundersøkelse på indekstenner utføres (under punkt «Kariesundersøkelse»).
  I epikriseskjema ber vi ansvarlig tannlege gjennomgå BW for eventuelle andre funn.

OPG (gjelder ikke kontrollgruppen), beskriv:	☐ Screening OPG utført	☐ Ingen spesielle anmerkninger

Modifisert måling av salivasekresjon (gjelder bare testgruppen)

Referanse for utførelse av måling salivasekresjon: Jonsson et al. (2011) Diagnostikk av munntørrhet og bruk av saliva som diagnostisk verktøy
Referanseverdier salivasekresjon: Birkeland og Løkken (2005) Munntørrhet – forekomst, diagnostikk og kliniske problemer

Måling er utført av sykepleier ved Haukeland Universitetssykehus (HUS).
Det er utarbeidet prosedyre ved måling av salivasekresjon som bør følges.
Målingen er bare en screening, ikke grunnlag for diagnose.

Dato målingen er utført ved HUS:			
Klokkeslett målingen er utført:			
Er måling av salivasekresjon utført iht. prosedyre?	☐ Ja	☐ Nei, spesifiser:	☐ Ukjent
Har deltager fulgt forhåndsregler før målinger av salivasekresjon?	☐ Ja	☐ Nei, spesifiser:	☐ Ukjent
Er vekt (Scout™ Pro) benyttet ved måling salivasekresjon?	☐ Ja	☐ Nei, spesifiser:	☐ Ukjent

N.B. Klassifiseringen «meget lav», «lav» og «normal» salivasekresjon under, er referanseverdier beregnet for voksne og er ikke tilpasset for barn.

Salivasekresjon, ustimulert (ml/min):	(ml/min)	☐ Meget lav (<0,1ml/min)	☐ Lav (0,10-0,25 ml/min)	☐ Normal (>0,25 ml/min)
Salivasekresjon, stimulert (ml/min):	(ml/min)	☐ Meget lav (<0,7ml/min)	☐ Lav (0,7-1,0 ml/min)	☐ Normal (>1,0 ml/min)

I tillegg til opplysninger om aktuelle sykdommer og medikamenter som pasienten bruker (oppdatert under «helseopplysninger»), er det også ønskelig med en detaljert oversikt over faste medisiner og eventuelt behovsmedisin tatt dagen før og samme dag målingen utføres (noter også dose og tidspunkt).
-Dagen før:

-Samme dag:

Spørsmål i forbindelse med måling av salivasekresjon (spørsmålene skal stilles til både test- og kontrollgruppen)

«Føler du deg tørr i munnen?»	☐ Ja	☐ Nei	
Dersom ja: «Hvor ofte føler du deg tørr i munnen?»	Beskriv:		
Dersom ja: Når på døgnet føler du deg tørr i munnen?	Beskriv:		
«Har du brukt andre medisiner over en lengre periode tidligere, som du nå har sluttet med?» (Dersom ja, vurder behov for å notere ev tidligere medikament i pasientens helseskjema Opusjournal)	☐ Nei	☐ Ja, beskriv:	
«Dersom du bruker astmamedisin i form av inhalator, skyller du munnen med vann etterpå?»	☐ Ja	☐ Nei	☐ Bruker ikke inhalator

Modifisert versjon av Simplified Oral Hygiene Index (OHI-S) (Greene and Vermillion, 1964)
Skal ikke utføres for pasienter med fast kjeveortopedisk apparatur.
Subgingival status skal ikke vurderes.

Vennligst se laminert vedlegg.

Når det er tvil om grad, velg den laveste

Indekstenner:	16, 26, 36, 46, 11, 31
Score:	0 – 3 (Dersom indekstann ikke tilstede eller tann/flate ekskluderes; bruk kode X)

	Score (0-3)	
	Plakk	**Tannstein**
Bukkal:		
16		
11		
26		
31		
Total:		

Lingual:		
36		
46		
Total:		

Gradering av plakk/tannstein utføres ved bruk av «nr. 23 ende på WHO periodontal measuring probe»

Se vedlagt laminat for informasjon om utførelse, score, eksklusjonskriterier etc.

Minst seks flater må være undersøkt for at plakk- index eller tannstein-index kan regnes ut

Plakk-index = $\frac{\text{(The buccal-scores) + (The lingual-scores)}}{\text{(Total number of examined buccal and lingual surfaces)}}$ = [ ]

Tannstein-index = $\frac{\text{(The buccal-scores) + (The lingual-scores)}}{\text{(Total number of examined buccal and lingual surfaces)}}$ = [ ]

Oral Hygiene Index (individual oral hygiene index) = Plakk index + Tannstein index = [ ] (én decimal)

Modifisert versjon av Gingival Bleeding Index (Ainamo and Bay, 1975)

Ved anmerkning helse (helseskjema i tannlegejournal skal oppdateres) som indikerer forhåndsregler ved subgingival sondering, ekskluderes denne undersøkelsen

«A blunt pocket probe is used for gentle probing of the orifice of the gingival crevice. No pain should be caused by the probing. If bleeding occurs within about 10 seconds after testing, a positive finding is recorded"

Index er modifisert ved at sonden forsiktig føres ned i øvre del av gingival sulcus, for så å fjernes igjen, uten en horisontal bevegelse langs tannflaten

Vennligst se laminert vedlegg for mer detaljert beskrivelse av utførelse.

Instrument: "WHO periodontal measuring probe with 0,5 mm ball tip"

Indekstenner:	16, 26, 36, 46, 11, 31
Koder:	0 = ingen blødning 1 = blødning X = tann ikke tilstede

Bleeding Index	Bukkalt				Lingualt	
	16	11	26	31	36	46
Mesio-						
Mid-						
Disto-						

Gingival blødningsindex (uttrykt i prosent, %) = $\frac{\text{antall punkt med blødning}}{\text{antall punkt undersøkt}} \cdot 100\% =$ ____ (én decimal)

Noter undersøkte flater med eventuell kjeveortopedisk bracket (noter tann og flate):

Nå skal indekstenner, ved behov, rengjøres (profesjonell rengjøring vha. gummikopp og profylaksepasta).

Kariesundersøkelse; flatenivå

For pasienter med fast kjeveortopedisk apparatur, skal kun karies kun registreres på okklusalflaten.

Når det er tvil om kariesgrad velg den laveste
Standardisert oppsett ved røntgenregistrering
Fissurforsegling regnes som en sunn flate

Vennligst se laminert vedlegg.

Indekstenner: 16, 26, 36, 46

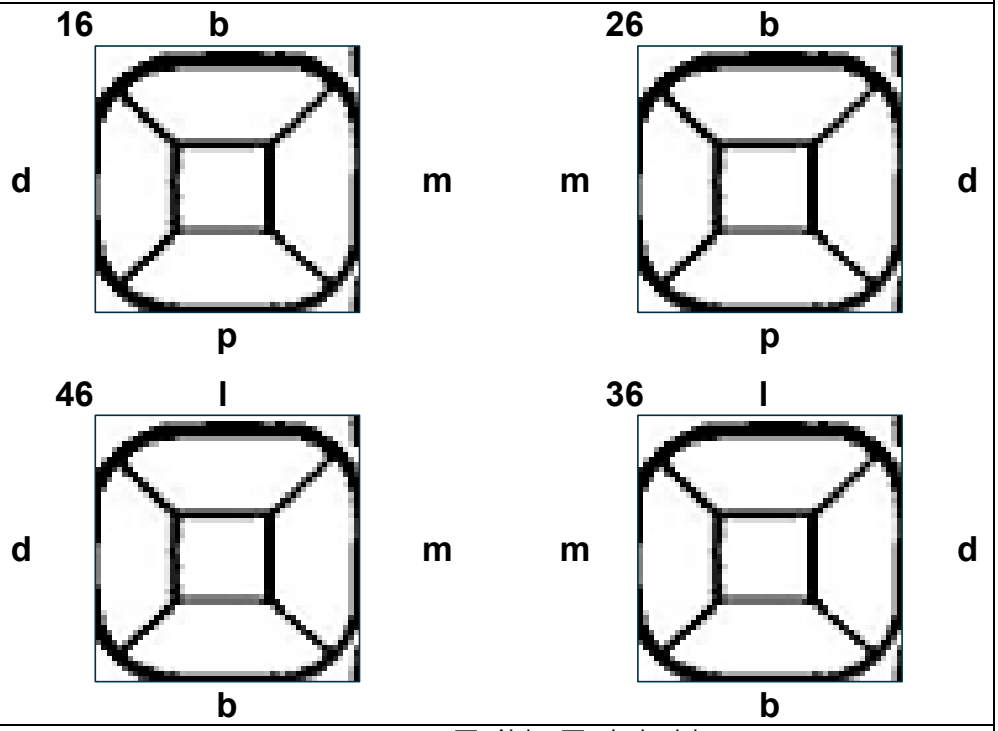
Koder, på flatenivå:

(Kariesgradering etter diagnosekriterier for karies basert på Espelid og Tveit)

Det skal noteres i alle flater. Dersom det foreligger flere diagnoser på en flate, registrer alle aktuelle diagnoser på flaten

0 = sunn flate
1 = karies grad 1
2 = karies grad 2
3 = karies grad 3
4 = kariesgrad 4
5 = karies grad 5
6 = sekundærkaries grad 1-2. 6 (grad 1) = 6(1), 6 (grad 2) = 6(2)
7 = sekundærkaries grad 3-5. 7 (grad 3) = 7(3), 7 (grad 4) = 7(4), 7 (grad 5) = 7(5)
8 = fylt flate uten karies
10 = tann mangler av andre grunner enn karies (sett tallet «10» over hele tannen)
11 = tann har stålkrone/helkrone (sett tallet «11» over hele tannen). NB! Dersom funn sekundærkaries skal det også noteres
20 = tann ekstrahert pga karies/tann indikert for ekstraksjon pga karies (sett tallet «20» over hele tannen)
NB! Det skal ikke innhentes opplysninger fra Opus/tannlegejournal, pas./foresatte må spørres vedrørende ev ekstraksjon pga. karies
Dersom tann indikert for ekstraksjon må det informeres om i epikriseskjema til lokal tannklinikk

Q = dersom overlapping BW (eller lignende) som fører til at kontur ikke kan følges, ekskluderes flaten (sett «Q» i aktuelle flateområder)



Andre funn i forbindelse med kariesundersøkelse ☐ Nei ☐ Ja, beskriv:

The basic version of the Enamel Defects Index (Brook et al. (2001) The development of a new index to measure enamel defects, Elcock et al. (2006) The new Enamel Defects Index: testing and expansion)

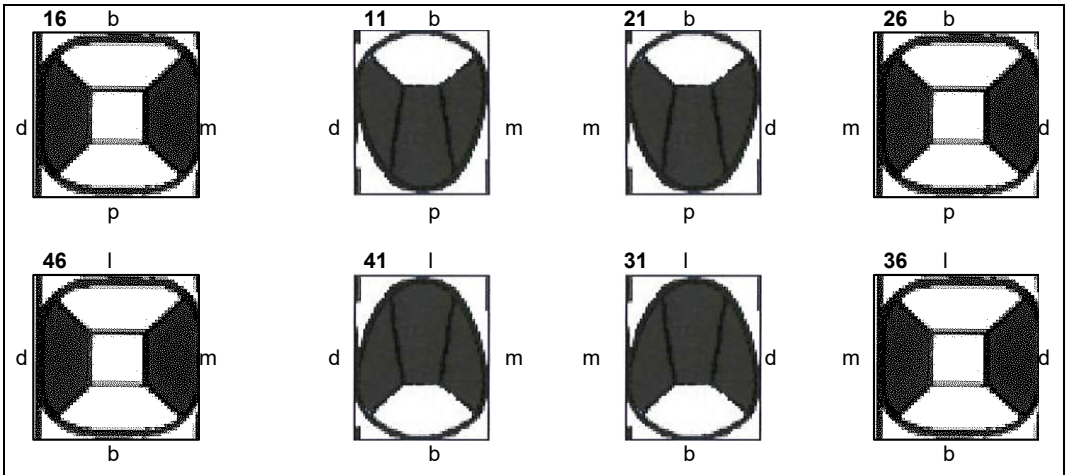
Vennligst se laminert vedlegg.

Ved minimal forstyrrelse der en er i tvil, noteres ingen kode

Eksklusjonskriterier: Karies eller restaurering i så utstrakt omfang at sikker bedømming av flate umuliggjøres, eventuelt brackets (dersom pasienten har fast kjeveortopedisk apparatur). Noter kode «X». Dersom tann ikke tilstede noteres også kode «X»

Det skal noteres i alle flater. Dersom det foreligger flere diagnoser på en flate, registrer alle aktuelle diagnoser på flaten

Indekstenner:	11, 21, 31, 41, 16, 26, 36, 46 (gjeldende flater; bukkalt i front og okklusalt/palatinalt/lingualt/bukkalt molarer)
Koder: Diagnosekriterier basert på "The basic version of the Enamel Defects Index"	0 = Sunn flate 1 = Hypoplasi 2 = Opasitet 3 = Posteruptiv fraktur av emalje X = Tann ikke tilstede, ev tann/flate ekskluderes fra undersøkelse (se eksklusjonskriterier)



Utviklingsforstyrrelser med eksponert dentin	☐ Nei	☐ Ja, beskriv:		
Er det primære tannsettet generelt affisert?	☐ Nei	☐ Ja	☐ Kan ikke bedømmes	
Er det permanente tannsettet generelt affisert?	☐ Nei	☐ Ja	☐ Kan ikke bedømmes	
Er både det permanente og primære tannsettet generelt affisert?	☐ Nei	☐ Ja	☐ Kan ikke bedømmes	
Tatt foto av defekt? (Foto skal lagres i røntgenprogram/Opus)	☐ Nei	☐ Ja, beskriv:		

Foto skal også tas ved usikker diagnose (forut endelig vurdering)

Simplified erosion partial recording system (SEPRS) (A. Hasselkvist, A. Johansson, AK. Johansson, 2010)

Vennligst se laminert vedlegg.

Eksklusjonskriterier: Karies eller restaurering i så utstrakt omfang at sikker bedømming av flate umuliggjøres, eventuelt retainer/brackets palatinalt overkjeve. Noter kode «X». Dersom tann ikke tilstede noteres også kode «X»

Dersom usikkerhet ved gradering, vennligst vurder også modeller

Når det er tvil om grad, velg den laveste

Indekstenner:	11, 21, 36, 46
Score: (Erosjonsgradering etter Johansen et al 1996)	0 – 4 (Dersom indekstann ikke tilstede, eller flate ekskluderes; noter kode «X») Beskrivelse av cupping grade 1, Rounded cusp tip: «Changed morphology compared to the assumed original anatomy at the time of eruption» (Ved vurdering av skala for cupping; bruk gjerne en lommedybdemåler)

SEPRS	11 palatinalt	21 palatinalt
Erosjon 0-4 skala		

	36 okklusalt	46 okklusalt
Cupping 0-4 skala		

Approximalflater involvert?	☐ Nei	☐ Ja, beskriv tann/flater:
Forekomst av skulder?	☐ Nei	☐ Ja, beskriv tann/flater:

Undersøkelse av slimhinner

Fissurer (≥ 3mm)	☐ Ingen tydelige funn	☐ Leppe	☐ Leppevinkel
Ulcerasjoner (≥ 3mm)	☐ Nei	☐ Ja, beskriv:	
Buccal mucosa ridging	☐ Nei	☐ Ja, beskriv:	
Impresjoner tunge	☐ Nei	☐ Ja, beskriv:	
Bukkal gingival hyperplasi (front; 3-3 okj. og 3-3 ukj.)	☐ Ingen tydelige tegn	☐ Ja, beskriv region:	
Andre funn	☐ Nei	☐ Ja, beskriv:	
Tatt foto av funn ifm. undersøkelse av slimhinner (Foto skal lagres i røntgenprogram/tannlegejournal)	☐ Nei	☐ Ja, beskriv:	

Saliva

Oppleves normal vha speiltest (bukkale kinnslimhinne)	☐ Ja	☐ Nei, beskriv:

Kontrollgruppen

Pasienten tilhører kontrollgruppen og har, eller har hatt, fast kjeveortopedisk apparatur?	☐ Ja	☐ Nei
Dersom, ja, skal pasienten utelukkes videre fra «Vurdering av bittavvik», «Uvaner (nåværende eller tidligere)», «IOTN-index, AC» og «Intraorale foto» (det er ønskelig med ekstraorale foto).		

Vurdering av bittavvik

Vennligst se laminert vedlegg (vedrørende horisontalt overbitt). Dette er ikke en fullverdig vurdering av kjeveortopedisk behandlingsbehov.

Ansiktsform	Asymmetri	☐ Ingen tydelige tegn	☐ Asymmetrisk, deviasjon mot høyre	☐ Asymmetrisk, deviasjon mot venstre		
	Profil	☐ Konveks	☐ Rett	☐ Konkav		
Midtlinjeavvik i forhold til ansiktets midtlinje (for at midtlinjeavvik skal registreres må avviket være ≥ 1mm)		☐ Ingen avvik	☐ Mot venstre overkjeve ☐ Mot venstre underkjeve	☐ Mot høyre overkjeve ☐ Mot høyre underkjeve		
		☐ Ikke registrerbar, beskriv:				
«Mandibular deviation at maximal mouth opening (≥3mm)», ref. EUROtmJOINT protokoll; "TMJ Clinical Examination Form", pt.11		☐ Mandibular deviation to the right	☐ Mandibular deviation to the left	☐ No deviation – straight position as in closed mouth		
Tvangsføring Få pasienten til å slappe av, ta tak i haken og før mandibula opp til første tannkontakt og registrer videre bevegelse derfra (til maks interkuspidasjon). Gjenta flere ganger til sikker diagnose.	☐ Ingen tvangsføring	☐ Mesialt / Anteriort	☐ Lateralt venstre	☐ Lateralt høyre		
	☐ Ikke registrerbar, beskriv:					
Respirasjon (ved hjelp av speiltest)		☐ Munn	☐ Både nese og munn			
Kontakt mellom tannrekkene ved svelging		☐ Ja	☐ Nei			
Mentaliskontraksjon (ved svelging)		☐ Ja	☐ Nei			
Taleavvik (s-lyd)		☐ Ja	☐ Ikke tydelig tegn			
Tungepress	☐ Ikke tydelig tegn	☐ Svelging	☐ Tale	☐ Avslapping		
Tonsiller	☐ Normal	☐ Forstørret	☐ Inflammerte	☐ Tidligere utført tonsillektomi		
Pasienten får behandling ved kjeveortoped		☐ Nei	☐ Ja, hvilken kjeveortoped:			
Pasienten har tidligere hatt kjeveortopedisk behandling		☐ Nei				
		☐ Ja, beskriv behandling, når den ble avsluttet og behandlende kjeveortoped:				

Dersom pasienten får behandling ved kjeveortoped; er behandlingen avtagbar?	☐ Nei	☐ Ja, avtagbar apparatur / plate(r)	
Kommentar til eventuell avtagbar kjeveortopedisk behandling:			
Pasienten har fast kjeveortopedisk apparatur	☐ Nei	☐ Ja	
NB! For pasienter (tilhørende testgruppen) med fast kjeveortopedisk apparatur skal behandlende kjeveortoped kontaktes for å få digital kopi av CEPH og OPG, samt kopi av modeller ved behandlingsstart.			
Pasient/foresatt godkjenner at denne informasjon innhentes ved kjeveortoped	☐ Nei	☐ Ja	

Neste 3 punkt gjelder kun for pasienter uten fast kjeveortopedisk apparatur:			
Sagittal relasjon, 6-års molarer. (Bruk speil bukkalt for 16/26, slik at en oppnår 90° synsvinkel)	☐ Angle klasse I (nøytralposisjon)	☐ Angle klasse II (distalokklusjon) (Gjeldende dersom avvik ≥2mm fra Angle klasse I)	
	☐ Angle klasse III (mesialokklusjon) (Gjeldende dersom avvik ≥2mm fra Angle klasse I)	☐ Ikke registrerbar, beskriv:	
Horisontalt overbitt (mm)			mm
Tatt modeller og bittregistrering	☐ Ja	☐ Nei, spesifiser:	

Andre kommentarer/funn i forbindelse med vurdering av bittavvik som ikke er inkludert i undersøkelsen «vurdering av bittavvik»

Beskriv:

Er det uvaner (nåværende eller tidligere) som kan påvirke, eller har påvirket, tannstillingen?

Fingersuging	☐ Nei	☐ Ja, nåværende	☐ Ja, tidligere. Spesifiser når uvanen ble avsluttet:
Neglebiting	☐ Nei	☐ Ja, nåværende	☐ Ja, tidligere. Spesifiser når uvanen ble avsluttet:
Blyanttygging	☐ Nei	☐ Ja, nåværende	☐ Ja, tidligere. Spesifiser når uvanen ble avsluttet:
Smokkbruk	☐ Nei		☐ Ja, tidligere. Spesifiser når uvanen ble avsluttet:

Foto (standardisert opptak, se laminert vedlegg) (Disse foto anses som forskningsdata og skal ikke lagres i røntgenprogram/tannlegejournal)

I prosjektet skal rå-foto (originalt opptak) i tillegg til redigert versjon lagres. Redigering skal gjøres ved hjelp av standardisert mal i Adobe Photoshop Cs6. Husk sikkerhetskopi av både originalt opptak og redigerte foto.

Ekstraorale foto (totalt 7 stk) Viktig at pasientens øyne følger en horisontal linje, at bakgrunn er hvit og at pasienten sitter i en vanlig stol.			
Foto 1	Portrettbilde. Pasienten ser rett frem uten å smile. Be pasienten lukke munnen.		
Foto 2	Portrettbilde. Pasienten ser rett frem og smiler.		
Foto 3	Profil av hele pasientens ansikt.		
Foto 4 og 5	Nærbildeprofil; underprofil av øyne og inklusiv hake (venstre og høyre side tas foto av).		
Foto 6	Portrettbilde. Pasienten ser rett fram og gaper maksimalt.		
Foto 7	Portrettbilde. Pasienten ser rett frem og biter på tvers av ispinne, linjal eller lignende.		
Tatt ekstraorale foto	☐ Ja	☐ Nei, beskriv:	
Intraorale foto (totalt 5 stk)			
Foto 1	Foto tas midt forfra, i full okklusjon.		
Foto 2 og 3	Full okklusjon og underkjeve i retrudert leie (venstre og høyre side tas foto av). Viktig at 6-års-molarer fremkommer i foto.		
Foto 4 og 5	Okklusale foto av over- og underkjeve.		
Tatt intraorale foto	☐ Ja	☐ Nei, beskriv:	

Felles protokoll for kjeveledd, vekst og TMD (egne skjema inngår i undersøkelsesprosedyre)

Gjeldende protokoller utfylt	☐ Ja	☐ Nei
Gjeldende spørreskjema utfylt	☐ Ja	☐ Nei

Andre kommentarer/funn i forbindelse med TMD undersøkelse

Beskriv:

Bruxism. Spørsmål til pasient/foresatt (uavhengig av dag/natt gnissing)

Gnisser pasienten tenner?	☐ Ja	☐ Nei	☐ Vet ikke
Har foresatt lagt merke til at barnet gnisser tenner?	☐ Ja	☐ Nei	☐ Vet ikke
Dersom ja, be pasient/foresatt utdype:			

Traumeerfaring

Spørsmål til pasient/foresatte: «Har du/barnet hatt tannskade (traume pga. slag eller fall) som førte til behov for å oppsøke tannhelsetenesta?»	☐ Ja	☐ Nei	☐ Vet ikke

Spesialisttannhelsetjenesten (gjelder bare testgruppen)

Har pasienten vært fulgt opp av spesialisttannhelsetjenesten ifm JIA-diagnose (spørsmål til pasient/foresatte)	☐ Ja, siden (oppgi årstall):	☐ Nei	☐ Vet ikke

Henvisning fra HUS i forbindelse med JIA storkontroll (gjelder bare testgruppen)

Henvisning fra HUS må scannes i pasientens tannlegejournal

Fremkommer det opplysninger eller ønsker i henvisningen fra HUS som krever mer omfattende undersøkelse enn denne standardundersøkelsen?	☐ Ja, beskriv:	☐ Nei
Dersom ja, er alle opplysninger/ønsker fra henvisning ivaretatt? Beskriv:		

Injeksjoner kjeveledd (gjelder bare testgruppen)

	☐ Nei	☐ Vet ikke	☐ Ja, beskriv:
Har pasienten fått injeksjon(er) kjeveledd? (Dersom «ja» skal disse opplysningene registreres i helseskjema Opus/tannlegejournal)			

Annet

Beskriv:

Funn avdekket ved undersøkelse som anses av slik alvorlighetsgrad at oppfølging/behandling bør skje om ikke for lang tid

Pasientens faste tannlege informert per telefon (må journalføres)

Beskriv:

☐ Pasientens faste tannlege foretar videre vurdering, oppfølging/behandling eller henvisning

☐ Direkte henvisning til TkVest (ev annen kompetanse) ved prosjektgruppen utført (etter enighet med ansvarlig tannlege). Beskriv:

Unntak for testgruppen ved TMD. Her er det lege som er den henvisende instans og som skal henvise når aktuelt.

Generelt

Alle foto som er tatt er lagret i røntgenprogram/tannlegejournal (unntatt bilder tatt under avsnitt «standardisert fotooptak») For foto tatt med speil, skal speilvending vurderes ifm. import røntgenprogram/Opus for å unngå at foto feiltolkes. Eventuell redigering skal opplyses om i tannlegejournal/epikriseskjema.	☐	Ja	☐	Har ikke tatt aktuelle foto	☐ Nei, beskriv:
Rene og tørre flater på indekstenner ved undersøkelse	☐	Ja	☐	Nei	
Godt samarbeid med pasient ved undersøkelse	☐	Ja	☐	Delvis, beskriv:	☐ Nei, beskriv:
Er alle planlagte undersøkelser utført iht. prosedyre?	☐ ☐	Ja Nei, spesifiser og beskriv hvorfor:			
Andre kommentarer:					

Informasjon til pasient/foresatte

Viktighet av god oral helse og oppfølging ved tannhelseteam pga. sykdom (testgruppen)	☐ Ja
Utført undersøkelse i forbindelse med dette prosjektet erstatter ikke en vanlig tannhelseundersøkelse (testgruppen)	☐ Ja
Pasient/foresatt informert om avdekkede funn i forbindelse med undersøkelsen	☐ Ja
Dersom funn av betydning OPG er pasient/foresatt informert	☐ Ja

Opus

Utført journalføring og oppdatert helseskjema i Opus	☐ Ja
Scannet epikriseskjema i pasientens Opus journal	☐ Ja

Epikriseskjema

Punktene under skal journalføres i Opus

Sendt standardisert skriv til lokal tannklinikk vedrørende scannet epikrise i Opus	☐ Ja
Gjelder testgruppen: Scannet (Opus journal) og sendt epikriseskjema til henvisende lege HUS	☐ Ja

APPENDIX IV

Appendix IV includes the written informed consents for the participants with JIA, and the participants in the control group 4-11 years and 12-16 years, respectively.

Forespørsel om deltakelse i forskningsprosjektet:
«Barn og unge med Barneleddgikt
(Juvenil Idiopatisk Arthritt (JIA)» (REK-nr 2012/542).

Bakgrunn og hensikt
Dette er et spørsmål til deg om å delta i en forskningsstudie ved Haukeland Universitetssykehus i samarbeid med Tannhelsetjenestens Kompetansesenter Vest – avdeling Hordaland (TkVest-H) og Universitetet i Bergen, der vi ønsker å kartlegge tidlige tegn til leddgikt i kjeveleddene; hvordan vi best kan påvise dette og i hvilken grad leddgikt påvirker munnhelsen, beinhelsen og livskvaliteten.

Hva innebærer studien?
Det er spesielt viktig at sykdom i kjeveleddene oppdages tidlig fordi behandling til en viss grad kan hindre videre ødeleggelse av leddet. En del studier viser også at dersom du har leddgikt, er du mer utsatt enn andre til å utvikle sykdommer i munnhulen. Også i munnen er det viktig at sykdom, som f.eks karies (tannråte) oppdages tidlig, for da kan vi i dag stanse videre sykdomsutvikling og opprettholde en god tannhelse. Dårlig tannhelse innebærer en risiko for at bakterier går i blodbanen, noe som hos denne pasientgruppen bør unngås. Tilbudet ved Haukeland Universitetssykehus går ut på at du får en noe grundigere undersøkelse enn vanlig og en ny kontroll etter to år. Både blodprøver, spyttprøve, høyde/vekt, pubertetsvurdering og leddundersøkelse, samt røntgen inkludert bentetthetsmåling (såkalt DEXA scan), MR og ultralyd-undersøkelser vil bli utført. DEXA scan og MR/ultralyd av kjeveledd er i dag ikke vanlige standardundersøkelser. I tillegg vil vi be deg (og foresatte) å fylle ut noen spørreskjema.

Tenner, munnhule og ansikt vil klinisk og bildemessig bli undersøkt ved TkVest – H som ligger like ved sykehuset. Her vil munnhule, tyggemuskulatur, bitt-forhold og kjeveledd bli undersøkt av tannleger som har interesse for pasienter med leddgikt og vet hvilke tegn de skal se etter. Kjeverøntgen samt «cone-beam computertomografi» (CBCT) av kjeveledd (som ikke er vanlige standardundersøkelser) blir tatt her, samt enkle, vanlige tannrøntgen. Har du- eller har du hatt-tannregulering, vil relevante data for det innhentes hos behandlende kjeveortoped. Også her vil du (og foresatte) bli bedt om å svare på noen spørreskjemaer. Tannlegen på din lokale tannklinikk vil bli informert om eventuelle funn som trenger oppfølging.

Mulige fordeler og ulemper
Fordelen med deltakelse er at vi i større grad enn ellers kan påvise tidlige tegn på sykdom, enten det har å gjøre med kjeveledd, tyggemuskulatur, ansiktsvekstforstyrrelse eller sykdom i munnhulen. Ulempen er at du må regne med at undersøkelsen samlet sett vil ta litt lengre tid enn ellers.

Frivillig deltakelse
Det er frivillig å delta i studien. Om du nå sier ja til å delta, kan du senere når som helst og uten å oppgi noen grunn, trekke tilbake ditt samtykke uten at det vil få betydning for videre behandling eller behandlingstilbud. Ønsker du å trekke deg, gir du beskjed til en av undertegnende, også om du bare har spørsmål om studien.

Hva skjer med prøvene og informasjonen om deg?
Prosjektet er vurdert og godkjent av Den regionale komité for medisinsk forskningsetikk i Helseregion Vest (REK III). Alle opplysninger om deg, informasjon fra blodprøver, samt lagrete blod- og spyttprøver, vil bli oppbevart på vanlig måte, ihht. gjeldende regelverk for lagring av helsedata, samt i en egen forskningsdatabase ved Haukeland Universitetssykehus / IKO/ UiB. Disse prøvene vil seinere analyseres for å undersøke mulige sykdomsframkallende faktorer, arveanleggenes betydning for leddgiktens forløp og alvorlighetsgrad og betydningen av markører for revmatisk sykdom og benhelse som kan finnes i blodet ved barneleddgikt. Kun spesielt autoriserte personer vil ha tilgang til opplysningene vedrørende deg. Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres. Ved prosjektets slutt, vil navnet ditt bli slettet fra forskningsdatabasen og de kliniske opplysningene om deg bli lagret i lege- og/ eller tannlegejournal for senere bruk.

Ved ytterligere spørsmål, kontakt

overlege/prof. Karen Rosendahl, Radiologisk avdeling, seksjon for barn (tlf.: 55975221), overlege Karin Tylleskär, Barneklinikken (tlf.: 55975246) Haukeland universitetssykehus eller 1.amanuensis/spesialist pedodonti Marit Slåttelid Skeie, Universitetet i Bergen (tlf. 55586576).

Vedr. Biobank
Blod- og spyttprøvene som blir tatt og informasjonen utledet av dette materialet vil bli lagret i en forskningsbiobank ved Haukeland Universitetssykehus. Hvis du sier ja til å delta i studien, gir du også samtykke til at det biologiske materialet og analyseresultater inngår i biobanken. Helse Bergen HF, Haukeland Universitetssykehus er ansvarshavende for forskningsbiobanken. Biobanken planlegges å vare til 2025. Etter dette vil materiale og opplysninger bli ødelagt etter interne retningslinjer.

Utlevering av materiale og opplysninger til andre - Samtykkets omfang og dine rettigheter
Ved å signere samtykkeerklæringen aksepterer du at opplysninger og eventuelt prøvemateriale kan benyttes til forskning innen barneleddgikt. I tillegg kan du bli spurt om å besvare spørreskjemaer og delta på oppfølgingstiltak for å samle inn ytterligere opplysninger. Vi vil også innhente relevante opplysninger om deg fra andre offentlige helseregistre ved behov. Hvis du sier ja til å delta i studien, gir du også ditt samtykke til at prøver og avidentifiserte opplysninger utleveres til samarbeidende forskere ved foretakene i Helse Vest og Universitetet i Bergen, samt forskere ved St. Olavs/NTNU, Universitetssykehuset NordNorge /UiT, Oslo Universitetssykehus og forskere ved samarbeidende institusjoner i Europa. Enhver utlevering av opplysninger til samarbeidende forskere vil bli lagt frem for REK.

Informasjon om utfallet av studien
Årsrapporter som presenterer resultater fra foretakets forskningsprosjekter er offentlig tilgjengelige på http://forskningsprosjekter.ihelse.net/. Vi viser også til våre forskningsnettsider på: http://www.helse-bergen.no/fagfolk/forskning/.

Karen Rosendahl	Marit Slåttelid Skeie	Karin Tylleskär
Prof./overlege	Førsteamanuensis/	Avdelingsoverlege
Barnerøntgen	Spesialist pedodonti	Barneklinikken

HELSE BERGEN
Haukeland universitetssjukehus

Skjema for samtykke til deltakelse i forskningsprosjekt
- Voksne over 16 år

Prosjekttittel	Prosjektnummer
Barn og unge med Juvenil Idiopatisk Arthritt(JIA)	*REK-nr 2012/542*

Prosjektleders navn	Klinikk/avdeling
Professor/overlege Karen Rosendahl	Radiologisk avdeling, seksjon for barn

Det er frivillig å delta i studien. Dersom du ønsker å delta, undertegner du denne samtykkeerklæringen. Om du nå sier ja til å delta, kan du senere når som helst og uten å oppgi noen grunn, trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling. Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte prosjektleder.

Jeg er villig til å delta i forskningsprosjektet:

Navn med blokkbokstaver	Fødselsnummer (11 siffer)

Dato	Underskrift

Fylles ut av representant for forskningsprosjektet

Jeg bekrefter å ha gitt informasjon om forskningsprosjektet:

Dato	Underskrift	Brukerkode (4-tegnskode)

Eventuelle kommentarer:

Skjema for samtykke til deltakelse i forskningsprosjekt
- Ungdom mellom 12 og 16 år

Prosjekttittel	Prosjektnummer
Barn og unge med Juvenil Idiopatisk Arthritt (JIA)	*REK-nr 2012/542*

Prosjektleders navn	Klinikk/avdeling
Professor/overlege Karen Rosendahl	Radiologisk avdeling, seksjon for barn

Det er frivillig å delta i studien. Dersom du ønsker å delta, undertegner du denne samtykkeerklæringen. Om du nå sier ja til å delta, kan du senere når som helst og uten å oppgi noen grunn, trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling. Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte prosjektleder.

Jeg er villig til å delta i forskningsprosjektet:

Navn med blokkbokstaver	Fødselsnummer (11 siffer)

Dato	Underskrift

”Foresatte skal være informert og samtykke til deltakelse i forskningsprosjekter for ungdom over 12 år, med mindre pasienten av forhold som bør respekteres ønsker noe annet.”

Dato	Foresattes underskrift	Rolle (mor/far/verge)

Fylles ut av representant for forskningsprosjektet

Jeg bekrefter å ha gitt informasjon om forskningsprosjektet:

Dato	Underskrift	Brukerkode (4-tegnskode)

Eventuelle kommentarer:

HELSE BERGEN
Haukeland universitetssjukehus

Skjema for samtykke til deltakelse i forskningsprosjekt
- Barn under 12 år

OBS: Det må innhentes nytt samtykke når barnet er over 16 (18) år

Prosjekttittel	Prosjektnummer
Barn og unge med Juvenil Idiopatisk Arthritis (JIA)	*REK-nr 2012/542*

Prosjektleders navn	Klinikk/avdeling
Professor/overlege Karen Rosendahl	Radiologisk avdeling, seksjon for barn

Det er frivillig å delta i studien. Dersom du på vegne av barnet sier ja til å delta, undertegner du denne samtykkeerklæringen. Om du nå sier ja til at barnet deltar, kan du senere når som helst og uten å oppgi noen grunn, trekke tilbake ditt samtykke uten at det påvirker barnets øvrige behandling. Dersom du eller barnet senere ønsker å trekke tilbake samtykket eller har spørsmål til studien, kan du kontakte prosjektleder.

Jeg sier på vegne av barnet ja til å delta i forskningsprosjektet:

Barnets navn med blokkbokstaver	Barnets fødselsnummer (11 siffer)

Dato	Foresattes underskrift	Rolle (mor/far/verge)

Fylles ut av representant for forskningsprosjektet

Jeg bekrefter å ha gitt informasjon om forskningsprosjektet:

Dato	Underskrift	Brukerkode (4-tegnskode)

Eventuelle kommentarer:

UNIVERSITETET I BERGEN
Det medisinsk-odontologiske fakultet

Forespørsel om deltakelse i forskningsprosjektet

«Barn og unge med leddgikt (Juvenil Idiopatisk Artritt)» (REK-nr 2012/542).
Foreldre

Bakgrunn og hensikt
Dette prosjektet er et tverrfaglig forskningsprosjekt hvor Tannhelsetjenesten i Hordaland er en av samarbeidspartene. Der deltar også forskere fra Haukeland Universitetssykehus (legespesialister) og Institutt for klinisk odontologi (tannlegespesialister). Hovedmålet med forskningen er å kartlegge tidlige tegn på leddgikt i kjeveledd og undersøke i hvilken grad leddgikt påvirker munnhelsen og livskvaliteten.
Du lurer sikkert hvorfor du blir bedt om å la barnet ditt delta i et forskningsprosjekt som dette, for barnet ditt har jo ikke leddgikt. Grunnen er at man i forskning ofte har behov for å sammenligne syke og friske, slik at vi kan påvise forskjeller mellom gruppene, og derved få ny kunnskap om sykdommen. I denne sammenhengen betyr det barn og unge med og uten leddgikt. Siden ditt barn er friskt, spør vi deg derfor om å la barnet ditt delta i prosjektet vårt som del av den "friske" gruppen. Som takk for hjelpen vil vi tilby dere to kinobilletter.

Hva innebærer det å delta?
Hvis du vil delta, betyr dette at barnet ditt- i tillegg til den vanlige tannhelsesjekken (som han/hun nå er innkalt til)- vil få undersøkt tyggemuskulatur, kjeveledd og bitt-forhold. Vi vil også måle barnets høyde og vekt, samt ta fotografier. Undersøkelsen vil bli utført av en tannlege som er vant med barn, og som møter opp på din lokale tannklinikk. Du og barnet ditt vil også bli bedt om å besvare noen spørreskjema. Grunnen til at vi må spørre deg om tillatelse til dette er at tannhelsedataene til barnet ditt vil bli benyttet i forskningssammenheng. Vi er derfor avhengig av ditt skriftlige samtykke (se vedlagt samtykkeskjema).

Mulige fordeler og ulemper
Fordelen med deltakelse er at barnet ditt vil få en noe grundigere undersøkelse enn ellers. Ulempen er at undersøkelsen samlet sett vil ta litt lengre tid.

Hva skjer med informasjonen om barnet?
Prosjektet er vurdert og godkjent av Den regionale komité for medisinsk forskningsetikk i Helseregion Vest (REK III), og ingen opplysninger om barnet ditt vil bli lest av utenforstående. Alle opplysninger vil bli oppbevart på vanlig måte, ihht. gjeldende regelverk for lagring av helsedata, samt i en egen forskningsdatabase ved Universitetet i Bergen. Ved prosjektets slutt, vil navnet til barnet ditt bli slettet fra forskningsdatabasen og de kliniske opplysningene bli lagret i tannlegejournalen for senere bruk. Hvis du sier ja til å la barnet ditt delta i studien, gir du også ditt samtykke til at avidentifiserte opplysninger utleveres til samarbeidende forskere ved foretakene i Helse Vest og Universitetet i Bergen, samt forskere i Trondheim og i Tromsø. Enhver utlevering av opplysninger til samarbeidende forskere vil bli lagt frem for REK.

Frivillig deltakelse
Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn, trekke ditt samtykke om å delta i studien. Dette vil ikke få konsekvenser for din videre behandling eller for behandlingstilbudene i Den offentlige tannhelsetjenesten. Ønsker du å trekke deg, gir du beskjed til en av undertegnende, også om du bare har spørsmål om studien.

Ved ytterligere spørsmål, kontakt
1.amanuensis/spesialist pedodonti Marit Slåttelid Skeie, Universitetet i Bergen (tlf. 55 586576).

Marit Slåttelid Skeie	*Karen Rosendahl*	*Karin Tylleskär*
Førsteamanuensis/ Spesialist pedodonti	Prof./ Overlege/Barnerøntgen	Overlege/ Barneklinikken

Samtykke til deltakelse i studien

Jeg er villig til å la mitt barn …….delta i studien
(barnets navn og fødselsdato)

Jeg bekrefter å ha gitt informasjon om studien

(Signert, rolle i studien, dato)

Forespørsel om deltakelse i forskningsprosjektet

«Barn og unge med leddgikt (Juvenil Idiopatisk Artritt)»
(REK-nr 2012/542) 12-16 år

Bakgrunn og hensikt
Du lurer sikkert på hvorfor du blir bedt om å delta i et forskningsprosjekt som dette, for du har jo ikke leddgikt. Grunnen er at man i forskning ofte har behov for å sammenligne syke og friske; i vårt prosjekt betyr det at vi vil sammenligne barn med – og uten leddgikt. Siden du er frisk spør vi deg om hjelp. Vi ønsker å kartlegge tidlige tegn på leddgikt i kjeveleddene, og undersøke i hvilken grad leddgikt påvirker munnhelsen og livskvaliteten. Ved å delta i studien, hjelper du oss med å nå målene våre; som takk for hjelpen får du to kinobilletter.

Hva innebærer det å delta?
Hvis du vil delta, betyr dette at du i tillegg til den vanlige tannhelsesjekken (som du nå er innkalt til), vil få undersøkt tyggemuskulatur, kjeveledd og bitt-forhold. Vi vil også måle høyden og vekten din, samt ta fotografier. Undersøkelsen vil bli gjort av en tannlege som er vant med barn og ungdom, og som møter opp på din lokale tannklinikk. Du (og foresatte) vil også bli bedt om å svare på noen spørreskjema. Grunnen til at vi må informere deg om dette er at tannhelsedataene dine vil bli benyttet i forskningssammenheng. Vi er derfor avhengige av at du og en av dine foresatte skriver under på det vedlagte skjemaet.

Mulige fordeler og ulemper
Fordelen med deltakelse er at du vil få en noe grundigere undersøkelse enn ellers. Ulempen er at du må regne med at undersøkelsen samlet sett vil ta litt lengre tid.

Hva skjer med informasjonen vi samler inn om deg?
Prosjektet er vurdert og godkjent av Den regionale komité for medisinsk forskningsetikk i Helseregion Vest (REK III), og ingen opplysninger om deg vil bli lest av utenforstående. Alle opplysninger om deg vil bli oppbevart på vanlig måte, ihht. gjeldende regelverk for lagring av helsedata, samt i en egen forskningsdatabase ved Universitetet i Bergen. Ved prosjektets slutt vil navnet ditt bli slettet fra forskningsdatabasen og de kliniske opplysningene om deg vil bli lagret i tannlegejournalen for senere bruk. Hvis du sier ja til å delta i studien, gir du også ditt samtykke til at avidentifiserte opplysninger utleveres til samarbeidende forskere ved foretakene i Helse Vest og Universitetet i Bergen, samt forskere i Trondheim og Tromsø. Enhver utlevering av opplysninger til samarbeidende forskere vil bli lagt frem for REK.

Frivillig deltakelse
Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn, trekke ditt samtykke om å delta i studien. Dette vil ikke få konsekvenser for din videre behandling eller for behandlingstilbudene i Den offentlige tannhelsetjenesten. Ønsker du å trekke deg, gir du beskjed til en av undertegnende, også om du bare har spørsmål om studien.

Ved ytterligere spørsmål, kontakt
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Marit Slåttelid Skeie	*Karen Rosendahl*	*Karin Tylleskär*
Førsteamanuensis/ Spesialist pedodonti	Prof./ Overlege/Barnerøntgen	Overlege/ Barneklinikken

Det medisinsk-odontologiske fakultet / Haukeland Universitetssykehus

Samtykke til deltakelse i studien

Jeg er villig til å delta i studien

(Navn og signatur (barn/ungdom), dato)

”Foresatte skal være informert og samtykke til deltakelse i forskningsprosjekter for ungdom over 12 år, med mindre pasienten av forhold som bør respekteres ønsker noe annet.”

(Navn og signatur (foresatte), dato)

Jeg bekrefter å ha gitt informasjon om studien

(Signert, rolle i studien, dato)

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