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Subtypes of early childhood caries predict future caries experience

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Abstract

Objectives: To test whether postulated subtypes of early childhood caries (ECC) are predictive of subsequent caries experience in a population-based cohort of Swedish children.

Methods: The study included children aged between 3 and 5 years at study entry with dental records available for at least 5 years of follow-up. Dental record data were retrieved from the Swedish Quality Registry for Caries and Periodontal disease (SKaPa) for the initial and follow-up visits. Participants who had ECC at study entry were assigned to one of five ECC subtypes (termed classes 1–5) using latent class modelling of tooth surface-level caries experience. Subsequent experience of caries was assessed using the decayed, missing and filled surfaces indices (dmfs/DMFS) at follow-up visits, and compared between ECC subtypes using logistic and negative binomial regression modelling.

Results: The study included 128 355 children who had 3 or more dental visits spanning at least 5 years post-baseline. Of these children, 31 919 had caries at the initial visit. Baseline ECC subtype was associated with differences in subsequent disease experience. As an example, 83% of children who had a severe form of ECC at age 5 went on to have caries in the permanent dentition by the end of the study, compared to 51% of children who were caries-free at age 5 (adjusted odds ratio of 4.9 for new disease at their third follow-up).

Conclusions: ECC subtypes assigned at a baseline visit are associated with differences in subsequent caries experience in both primary and permanent teeth. This suggests that the development and future validation of an ECC classification can be used in addition to current prediction tools to help identify children at high risk of developing new caries lesions throughout childhood and adolescence.

KEYWORDS
caries prediction, children, ECC, latent class analysis

1 | INTRODUCTION

Early childhood caries (ECC) is defined as the presence of one or more decayed (non-cavitated or cavitated), missing (due to caries) or filled tooth surfaces in any tooth in the primary dentition in a child 6 years and younger.[1] It is an important disease of childhood as it affects the oral and general wellbeing of the child, in addition to the economic, educational and generalized impairment to quality of life and costs this disease has on society.[2] Sequalae of dental caries can include impaired eating, and educational disadvantage as well as the need for invasive treatment, for example under sedation or general anaesthesia.[3,4] The global burden of ECC remains high despite a reduction in caries prevalence in recent decades.[5] Thus, there remains a high burden of both restored and unrestored caries lesions in children, which is a major problem in the global context of non-communicable diseases of health.[6]

In the clinical setting, it would be useful to understand which children are at highest risk of caries. Past caries experience is a recognized predictor for new caries experience,[7] and caries experience in primary teeth can predict caries experience in the permanent dentition.[8] This may be because children who develop caries at a young age have a high burden of genetic, environmental, or behavioural risk factors, and these same risk factors are important for both primary and permanent teeth. If so, clinically manifest disease is acting as a proxy measure for underlying risk factors. Viewed another way, some children may be 'disease active' where the person-level disease activity continuously and progressively affects more tooth surfaces as these emerge in the oral cavity. The overarching goal of this study is to determine whether proposed subtypes of ECC are predictive of future disease.

The use of clinical subtypes in health research has developed considerably over the last decade with the use and validation of subtypes in a variety of disease phenotypes including depression,[9] Alzheimer's disease[10] and type II diabetes,[11] which all exhibit heterogeneous clinical phenotypes. These subtypes exhibit varying differences in genetic, clinical and -omics profiles, providing one way to help understand the different processes implicated in complex diseases. One way to identify these subtypes is through latent class analyses, which differentiate individuals based on unobserved latent variables[12] derived from observed variables included in the dataset. Latent class analyses have advantages over other clustering methods; the use of a parametric model-based approach means it is possible to undertake model selection utilizing parameters such as Akaike information criterion (AIC) and Bayesian information criterion (BIC) to establish an optimal number of subtypes.[13] These approaches have previously been applied in adults to explore caries[14] and periodontitis traits,[15] but to date, there are few applications to early childhood caries. Emerging evidence suggests that heterogeneity in the clinical presentation of ECC can be resolved into subtypes with differing underlying aetiology.[16] If so, aetiological differences between these subtypes might result in different patterns of subsequent disease presentation, and different initial presentations of caries might proxy different underlying risk factors. ECC subtype classification might therefore be a useful tool in identifying children

who are especially susceptible to new or progressive disease and help improve assessment, prediction and diagnosis of caries within paediatric, but also adult, populations,[17] in comparison with traditional models of caries risk assessment and prediction, which are recognized to have limitations in their utility.[8,18]

If different presentations of disease represent different underlying processes, then characterizing the pattern of presentation should add diagnostic value[19] in a clinical setting. With better understanding of the underlying molecular, genetic, microbiological and environmental risk factors underlying different diseases, it may be possible to propose effective targeted interventions. This concept of personalized or precision dentistry has been discussed in the literature, with a goal towards delivering interventions personalized to the patient for the managed prevention and treatment of oral diseases,[12,20] but to date, there are few practical applications.

This study aimed to investigate whether ECC subtypes can predict variation in subsequent caries experience and to test the hypothesis that children with different patterns of ECC at initial presentation would have differences in subsequent disease experience. If so, this could highlight a role for assigning caries subtypes in precision risk assessment.

2 | METHODS

2.1 | Study group

The study used a longitudinal design nested in a national Swedish register of dental records. From a basic cohort of 492 350 children with data from dental examinations from the Swedish Quality Registry for Caries and Periodontal Disease (SKaPa, www.skapareg.se), children between 3 and 5 years old at their first visit were retained (n = 208 112 children) (Figure 1). SKaPa is a national register that started to compile data from dental examinations in 2008. Data are automatically extracted from electronic patient dental examination records from all public dental clinics in Sweden in addition to a growing number of private clinics. In Sweden, free dental care is offered, and provided, to all children at the public care clinics, and therefore, the data from SKaPa are considered representative of the entire population of Swedish children. While nationally representative, these data must be understood in a greater global context—rates of dental caries and untreated disease in Sweden are not representative of the global context of ECC, as there is a substantial gap in the burden of caries in the primary dentition that remains untreated between high-income countries and others.[6] From this initial baseline cohort, participants were excluded if they did not have information on at least three follow-up visits spanning over 5 years. The final study group was 128 355 children (Figure 1).

2.2 | Caries coding and analyses

Each tooth surface was charted separately and given a status code representing the condition of that tooth surface, as determined by

FIGURE 1 Flow chart of final analysis sample
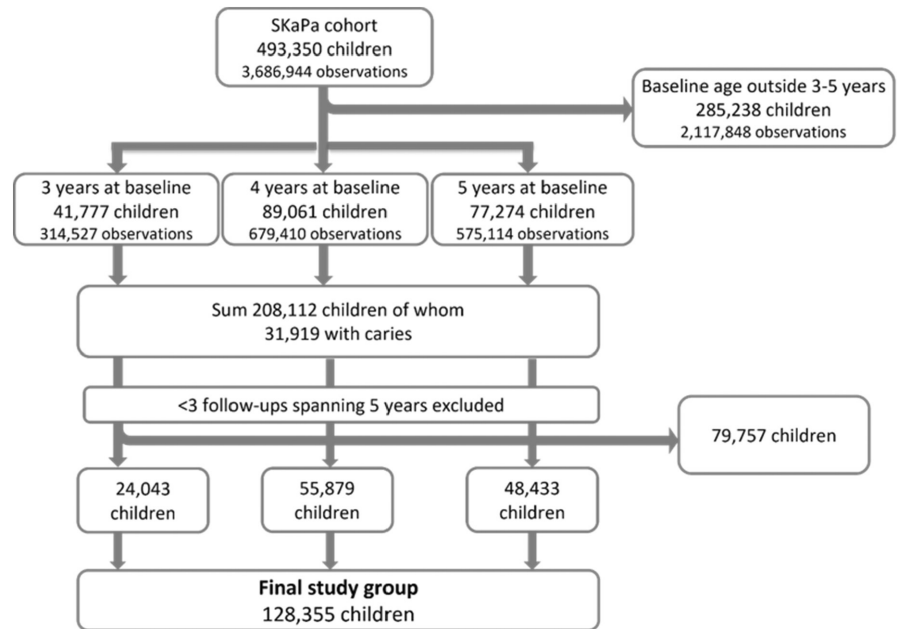
the examining dentist. Status codes for each tooth surface (buccal, lingual, mesial, distal and occlusal) were extracted from the SkaPa register and re-coded to either caries-free (no sign of demineralisation, demineralisation limited to the outer enamel or fissure sealant) or caries-affected. Surfaces coded with a demineralisation reaching the enamel-dentin junction or extending into the dentin (i.e. equating to ICDAS levels 3 and above including radiographs when the approximal surfaces could not be inspected), secondary caries, restoration, and a tooth with a crown placement or extracted due to caries or for endodontic reasons were coded as caries-affected. Tooth surfaces with ambiguous codes or which were missing for reasons other than caries (i.e. extraction for trauma, orthodontic or unknown reasons) were coded as caries-free. Age, sex, living in a socio-economic deprived area as defined by prevalent parental unemployment and high criminality, and dentist-assigned caries risk score (DARS) were extracted from the register. This study uses the terms dmfs (decayed, missing and filled surfaces in the primary dentition) and DMFS (decayed, missing and filled surfaces in the permanent dentition) for summary caries experience scores.

Children who were aged 3, 4 or 5 years at study entry and with at least 1 tooth surface coded as caries-affected were assigned to one of 5 ECC subtypes (Class 1–5) using latent class analysis (LCA). The analysis was performed using the software package poLCA in R (version 1.4.1). Children who were caries-free at baseline were treated as a reference group for comparison of subsequent caries experience. The LCA was ran for models including 1–8 classes. Model fit statistics were generated, and we used parameters for estimation including AIC and BIC and a bootstrapped likelihood ratio test. A 5-class model was selected, due to the high confidence in latent class allocation (mean posterior probabilities ranged from 0.92 to 0.96 and entropy 0.89).

For longitudinal analyses, a minimum of three follow-up visits were required. This included a follow-up visit 2–3 years post-baseline for examination of primary teeth, an examination at the age of 6 and

an examination reviewing permanent teeth at least 5 years after the 6 years examination.

Subsequent caries experience in the primary dentition was measured as the difference in dmfs scores between the baseline and subsequent visit. A dichotomous outcome was also created reflecting whether children had any caries experience (dmfs greater than at baseline) or no new caries-affected surfaces (dmfs unchanged since baseline) in the primary dentition.

Caries experience in the permanent dentition was measured using the DMFS score. A dichotomous outcome was created for any caries-affected tooth surfaces in the permanent dentition (DMFS ≥ 1) or no caries in the permanent dentition. All permanent tooth surfaces were considered as caries-free at baseline, given that these teeth were unerupted when the participants entered the study. Any new caries experience in permanent teeth was therefore considered to be manifestations of incident (i.e. 'new') disease.

For some participants, information on the caries risk score as determined by the dentist was available. Where available, the DARS was extracted from the first baseline visit, that is the same visit that latent class allocations were developed from, and a sensitivity analysis was performed to compare the performance of the DARS and baseline latent class in predicting new caries experience (i.e. incident disease). The DARS was scored as no/low, medium or high risk.

2.3 | Statistical analyses

Logistic regression was performed to estimate the association between baseline ECC subtype and odds of developing new caries experience in primary teeth, and odds of developing any caries experience in permanent teeth. Negative binomial regression was used to estimate the association between baseline ECC subtype and the counts of subsequent caries-affected tooth surfaces. Models were

fitted separately in children aged 3, 4 and 5 years at study entry. Models were adjusted for sex and follow-up age. The results are expressed as odds ratios (OR), representing the odds of any incident disease in the test group divided by the odds of any incident disease in the control group, and incidence rate ratio (IRR), representing expected count of caries-affected surfaces in the test group divided by the expected count of caries-affected surfaces in the control group.[21]

Sensitivity analysis was performed using the DARS caries risk assessment tool using the subset of participants with a DARS score available. Comparative statistics were generated including a Vuong analysis to assess the model fit between the ECC subtype and DARS models of prediction. The Vuong analysis is a test of closeness of fit and can be informative about which model is a better description of the observed data.[22]

Sensitivity analysis was performed to model whether ECC subtype is predictive of caries outcome conditional on the DARS score, where both ECC and DARS were fitted as predictors in the same model.

2.4 | Ethics statement

The study was approved by the Swedish Ethical Review Authority (Dnr 2019–05031) as well as the directors of each County Council in Sweden. The study followed the Helsinki declaration including that the person with parental responsibility consented to participation at the child's regular dental examination. This study adhered to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidance and a STROBE checklist is included in the supplementary file as S6.

3 | RESULTS

In total, 208 112 children aged 3–5 years old at baseline were potentially eligible for inclusion in the study. Latent class modelling was performed on 31 919 children (15.3%) who had evidence of caries experience at baseline. Latent class modelling was performed on all
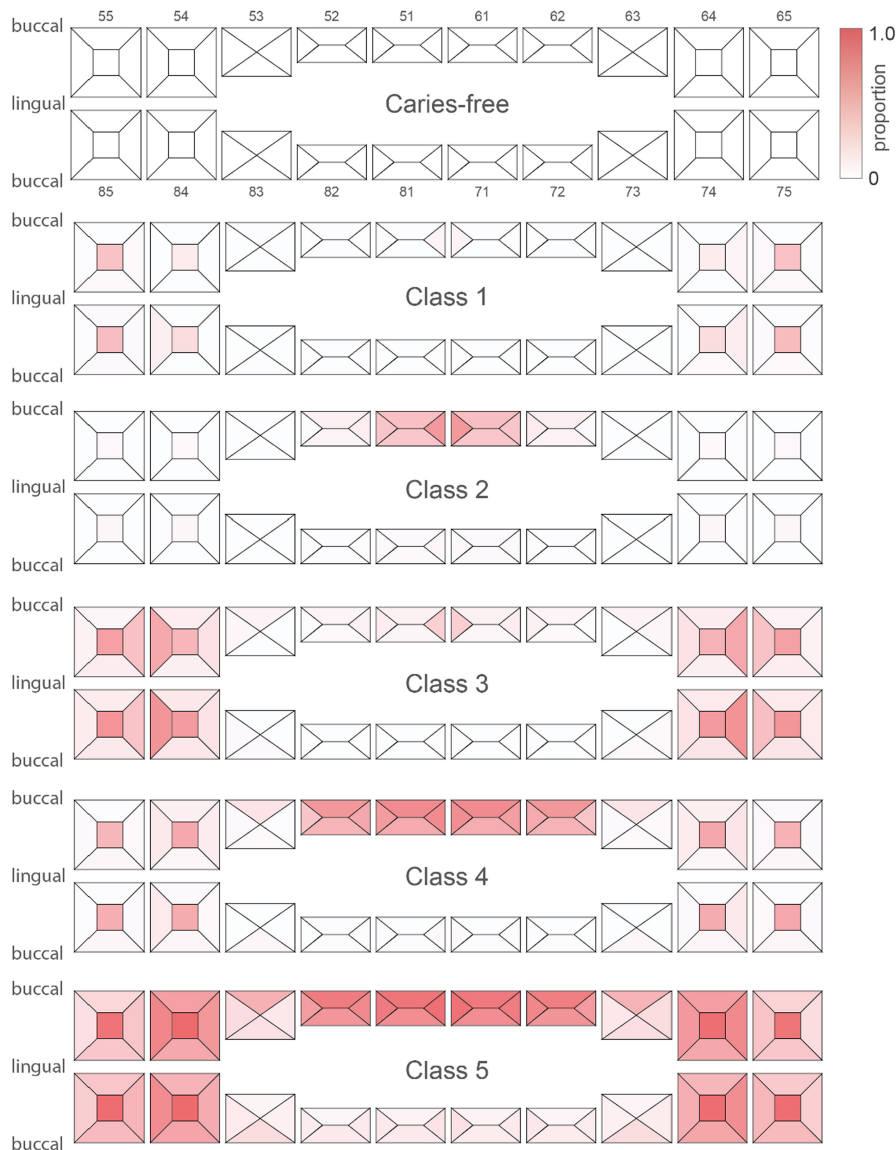

FIGURE 2 Graphical representation of the 5 ECC classes included in analysis. The scale represents the proportion of individuals in the specific class with caries experience on that surface

children who had caries at baseline (including those with no follow-up data available) as this helps improve model fit, therefore reducing the uncertainty in class allocations and reducing regression dilution bias in the subsequent longitudinal analysis.

Of the eligible children, 128 355 had follow-up data for at least 3 further visits spanning at least 5 years of follow-up and were included in the final sample. These children were classified into 5 subtypes of ECC, with differing caries severity between the 5 classes.

A child at baseline who was recorded as caries-free in the latent class calculation is referred to as Class 0. Class 1 refers to caries mainly affecting pits and fissures of molar teeth, Class 2 refers to caries affecting smooth surface anterior teeth, Class 3 has similar distribution of affected surfaces to class 1 but with greater severity, Class 4 has similar distribution of surfaces to class 2 but with greater severity and Class 5 is rampant caries affecting most tooth surfaces. The distribution of caries lesions within the mouth in these different classes is summarized as the proportion of individuals with caries at each tooth surface in each class and presented graphically (Figure 2).

The mean dmfs (sd) and key baseline demographic indicators are reported in Table 1. In longitudinal analysis, baseline latent class was associated with subsequent incident caries experience during follow-up. Children with ECC at baseline had greater odds and higher incidence rate than children who at baseline were caries free. Among children who had ECC, there were differences in subsequent caries experience in children with different classes of ECC at baseline. Many of the children who had severe ECC at baseline went on to develop caries in the permanent dentition. When looking at the burden of incident disease (i.e. count of tooth surfaces which became caries-affected during follow-up), there were similar associations, where children with ECC had greater incidence rate ratios for caries surfaces than children who were caries-free at baseline. The results are shown graphically in Figure 3 and are provided in full within the supplementary material in Table S2.

In addition to predicting future disease onset (odds) and severity (count), it is possible that baseline class predicts the spatial distribution of disease within the mouth. To explore this, the distribution of caries experience in the permanent dentition is summarized by baseline class, in the 5-year-old cohort who were between the ages of 11–13 at their third visit (n = 48 433). This group was chosen as an example as there was the largest mean (sd) interval between baseline and visit 3 in years at 7.5 (0.6) years. When examining the distribution of caries-affected surfaces at the final visit, there was a trend for people in the more severe ECC groups to have more caries lesions, and weak evidence for a difference in distribution in caries lesions (Figure 4).

For comparison, sensitivity analysis was performed in the subset of participants with available baseline DARS. This subset included 29 786 children. Logistic and negative binomial regression analyses were performed in this same subset using DARS and latent class as predictors, and the model fits were compared. In general, the models had similar performance for the age 3 cohort, but latent class provided better prediction than DARS for children aged 4 or 5 years at baseline, as illustrated by the Vuong test results in Table 2.

ECC subtype continued to perform well in predicting subsequent disease experience in sensitivity analyses adjusted for DARS (Table S5).

TABLE 1 Baseline demographics of children included in the study

	Caries-free	Class 1	Class 2	Class 3	Class 4	Class 5	Total
_N_ (%) children	103 725 (80.8)	12 921 (10.1)	4595 (3.6)	3873 (3.0)	2251(1.8)	990 (0.8)	128 355
Mean age (sd) years	4.14 (0.74)	4.43 (0.64)	4.29 (0.68)	4.63 (0.55)	4.27 (0.66)	4.43 (0.63)	4.19 (0.73)
Sex (% female)	49.8	49.0	44.5	43.5	46.2	40.4	49.2
Mean (sd) dmfs	0 (0)	2.67 (1.8)	4.39 (2.5)	11.30 (5.1)	14.20 (6.0	35.50 (14.1)	1.29 (4.5)
DARS[a] (n)							
No/low risk (score 0) (% of non-missing)	22 894 (92.5)	689 (24.9)	407 (41.7)	66 (9.0)	38 (9.2)	15 (11.2)	24 109 (80.9)
Medium risk (score 1) (% of non-missing)	1620 (6.5)	1167 (42.2)	309 (31.6)	179 (24.3)	110 (26.6)	30 (22.4)	3415 (11.5)
High risk (score 2) (% of non-missing)	248 (1.0)	907 (32.8)	261 (26.7)	491 (66.7)	266 (64.3)	89 (66.4)	2262 (7.6)
Missing scores	78 963	10 158	3618	3137	1837	856	98 569
Deprived area[b] (n)							
0 (% of non-missing)	89 478 (95.8)	11 203 (88.3)	3866 (86.9)	3172 (83.0)	1758 (79.8)	771 (79.4)	110 248 (93.8)
1 (% of non-missing)	449 (0.5)	172 (1.4)	67 (1.5)	89 (2.3)	57 (2.6)	24 (2.5)	858 (0.7)
2 (% of non-missing)	1588 (1.7)	494 (3.9)	188 (4.2)	200 (5.2)	142 (6.4)	72 (7.4)	2684 (2.3)
3 (% of non-missing)	1844 (2.0)	820 (6.5)	330 (7.4)	361 (9.4)	245 (11.1)	104 (10.7)	3704 (3.2)
Missing	10 366	232	144	51	49	971	10 861

[a]DARS = Dentist-assigned caries risk score using a 3-level scale, no/low risk, medium risk and high risk.
[b]A deprived area is a geographically defined district with low socio-economic status and high criminal impact on the local community and is scored as 0 = low deprivation area, 1 = deprived area, 2 = risk area and 3 = highly deprived area.
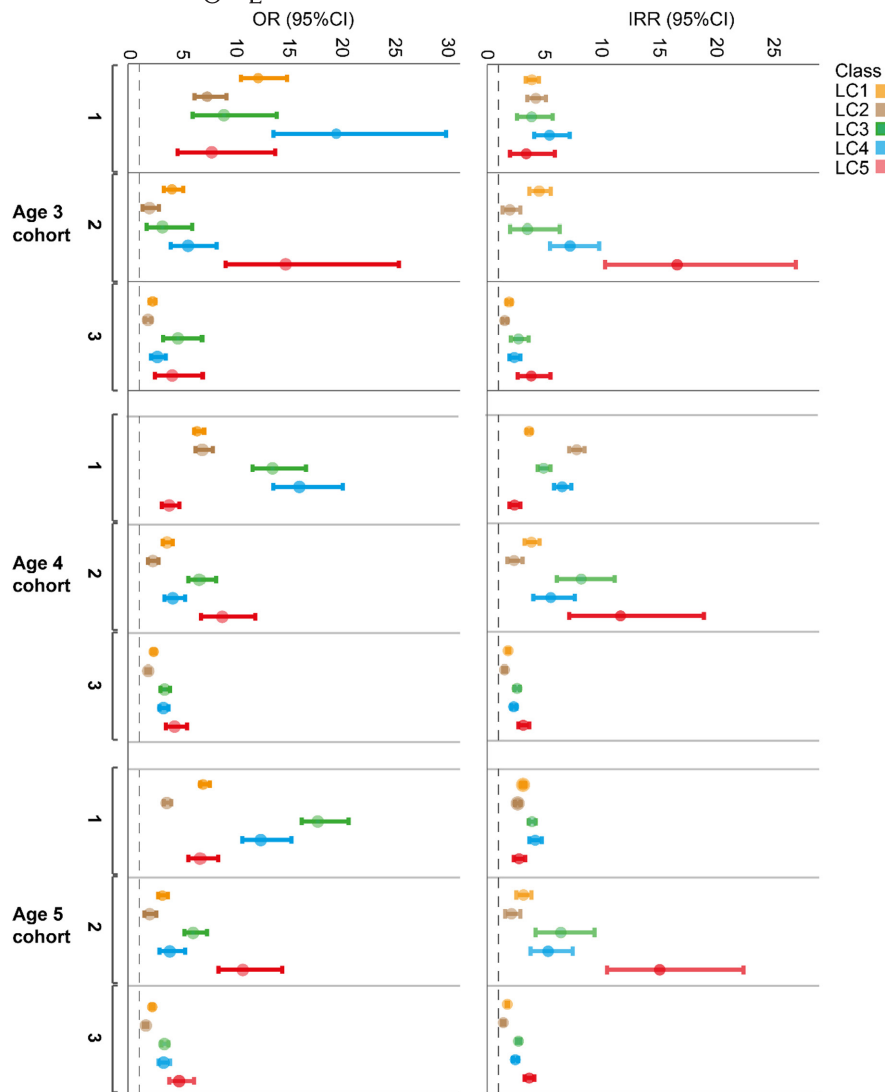
FIGURE 3 Estimates of association between baseline ECC class and subsequent caries outcomes. Outcome 1 = 2–3 years post-baseline, 2 = at age 6, 3 = at minimum 5 years post-baseline. The plot is split by the association between subtype and odds of incident disease (OR) and between subtype and count of new disease (IRR)

4 | DISCUSSION

This study tested the hypothesis that children with different patterns of ECC at initial presentation would have differences in subsequent disease experience. The study found that children with all subtypes of ECC at baseline had greater risk for developing caries in permanent teeth than children who were caries-free at baseline, in keeping with existing literature,[8] but demonstrated that this risk differs between groups with different initial presentation. The greatest risk was seen in the ECC subtypes with most severe initial caries presentation. These relationships were stable when comparing children aged 3, 4 and 5 years at entry into the study. This may be because children who have severe ECC at presentation have oral health behaviours,[23] microbial profiles[24] or genetic predisposition,[25] which place them at high risk for progressive or new disease. Given that the study was nested in a primary care register, the results cannot be explained as a result of inability to access care,[26] but there may be differences in the patterns of health service use or actual care delivered between groups. The results are novel (in that no previous results using the same approach are available for comparison), but

are in keeping with cross-sectional comparison of children in different ECC subtypes, who are reported to have different biological and environmental risk factors.[16] Compared to baseline dentist-assigned risk score, ECC subtype performed well in estimating caries risk. This suggests that determining children's ECC subtypes could be complementary to existing risk assessments that are known to not perform well.[8,18] The success of using this approach to estimate caries risk or predict incident disease, in the absence of the traditional risk factors for ECC, suggests that subtypes are acting as an indirect proxy measure of biological and lifestyle risk factors.

Analysis in the primary dentition is difficult to interpret, and this may be due to bias from measurement phenomena. Children with all subtypes of ECC were at high risk of developing further disease in primary teeth; however, there was no clear dose–response relationship between ECC subtype and further caries in primary teeth, and there was variation between different age groups, where children who were older at baseline developed fewer new carious surfaces in comparison with younger children. This may relate to saturation of the dmfs index. As there are a finite number of surfaces (i.e. 88 in the primary dentition) that can become carious, children who entered
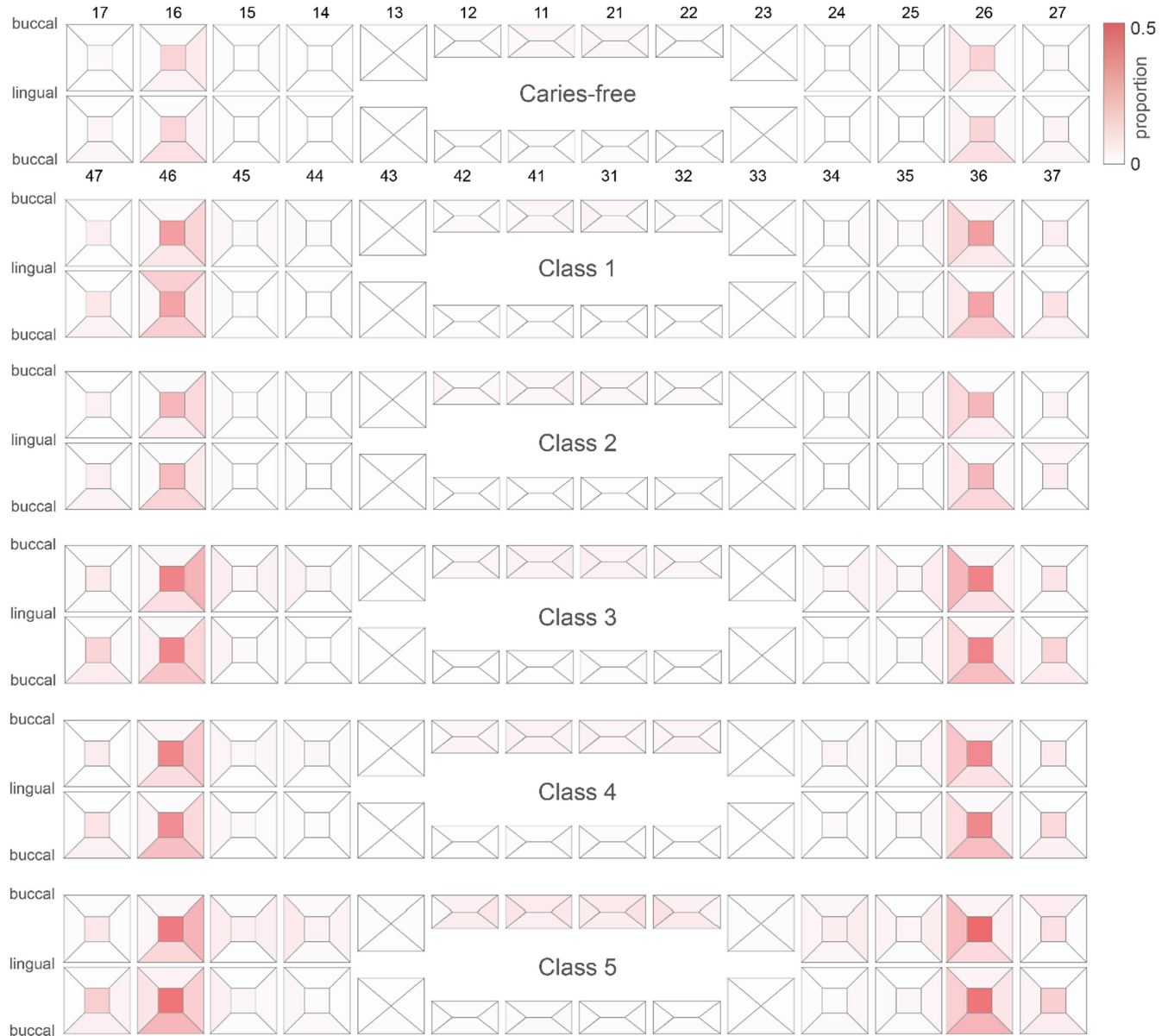
FIGURE 4 Graphical representation of the 5 ECC classes included in analysis for the children aged 5 years at baseline at their third visit (ages 11–13). The scale represents the proportion of individuals in the specific class with caries experience on that surface

the study with a higher number of affected surfaces (e.g. children in class 5 had almost half of their dentition already affected by caries at baseline) had less potential to develop new disease, creating a bias towards the null which is stronger in children with high caries experience at baseline, that is older children and those in the more severe ECC classes. It is also possible that saturation occurs when high-risk surfaces (for example approximal surfaces) develop caries more readily than low-risk surfaces.

In this study, 19.2% of children included in the final sample had ECC, versus 15.3% in baseline group. This may indicate a sampling bias, where the final study group is enriched for children at higher risk as these children attend a dentist more regularly for screening or treatment so are more likely to have enough follow-up visits to meet the inclusion criteria. We note that the prevalence of ECC

in this study is slightly higher than previously reported (11.4%).[27] Despite this, the prevalence of ECC in the study remains low in a global context, reflecting that Sweden has one of the lowest prevalences of ECC globally.[28] Caution is needed when considering other populations where the risk factors and patterns of disease presentation may differ. Regardless of local differences in profile, however, it seems likely that a similar approach may yield improvement in caries assessment, but this is not tested in the present study.

The main strengths of the study include the large sample size, nationally representative sampling frame and use of data from clinical examinations. Data from SKaPa have recently been validated in 6- and 12-year-olds, demonstrating satisfactory reliability and validity for the assessment of dental caries.[29]

TABLE 2 Summary of Vuong test results comparing the fit of the latent class model against the dentist-assigned caries risk (DARS) model

		3-year-old cohort			4-year-old cohort			5-year-old cohort		
		Z statistic	p value	Preferred model	Z statistic	p value	Preferred model	Z statistic	p value	Preferred model
Odds ratio at	Raw	0.44	.33	Latent Class	0.13	.45	Latent Class	3.11	<.01	Latent Class
follow-up 1	AIC[a]	0.30	.38	Latent Class	0.04	.45	Latent Class	3.02	<.01	Latent Class
	BIC[b]	−0.17	.43	DARS	−0.30	.38	DARS	2.67	<.01	Latent Class
Incident rate	Raw	−2.18	.01	DARS	2.77	<.01	Latent Class	−0.51	.31	DARS
ratio at follow-up 1	AIC[a]	−2.43	<.01	DARS	2.70	<.01	Latent Class	−0.68	.25	DARS
	BIC[b]	−3.27	<.01	DARS	2.45	<.01	Latent Class	−1.30	.10	DARS
Odds ratio at	Raw	1.42	.08	Latent Class	2.85	<.01	Latent Class	0.58	.28	Latent Class
follow-up 2	AIC[a]	0.93	.18	Latent Class	2.54	<.01	Latent Class	0.25	.40	Latent Class
	BIC[b]	−0.74	.23	DARS	1.37	.08	Latent Class	−0.97	.17	DARS
Incident rate	Raw	1.25	.11	Latent Class	3.11	<.01	Latent Class	0.85	.20	Latent Class
ratio at follow-up 2	AIC[a]	0.57	.29	Latent Class	2.78	<.01	Latent Class	0.36	.36	Latent Class
	BIC[b]	−1.76	.04	DARS	1.53	.06	Latent Class	−1.43	.07	DARS
Odds ratio at	Raw	0.62	.27	Latent Class	1.87	.03	Latent Class	3.30	<.01	Latent Class
follow-up 3	AIC[a]	0.26	.40	Latent Class	1.67	.05	Latent Class	3.07	<.01	Latent Class
	BIC[b]	−0.98	.16	DARS	0.92	.18	Latent Class	2.24	.01	Latent Class
Incident rate	Raw	0.47	.32	Latent Class	1.87	.03	Latent Class	4.07	<.01	Latent Class
ratio at follow-up 3	AIC[a]	0.13	.45	Latent Class	1.67	.05	Latent Class	3.90	<.01	Latent Class
	BIC[b]	−1.02	.15	Latent Class	0.92	.18	Latent Class	3.27	<.01	Latent Class

[a]AIC (Akaike information criterion).
[b]BIC (Bayesian information criterion).

The main limitation is that data on biological and environmental, such as exposure to fluoride and diet, as causes of caries, as these data were not available due to being derived from a national registry. We are therefore unable to comment on the underlying mechanisms driving high caries rates in some classes and suggest this as a topic for future research. For the purposes of prediction, however, we note that it is not necessary to understand the underlying mechanism, as we do not aim to identify causal mechanisms in this study.

The definition of ECC used in this study differed from the conventional definition which includes non-cavitated caries lesions.[1] In the present study, ECC only included children with carious lesions at the level of ICDAS 3 and above. This threshold was chosen as it can be difficult to diagnose initial caries lesions, for example a white spot lesion.[30] The data derived from SKaPa is obtained through national registry data, and therefore, we believed there would be greater concordance between examiners detecting and recording established caries lesions, in contrast to caries lesions defined as ICDAS levels 1 and 2, and therefore, these initial lesions were excluded from the study sample group.

In summary, the study shows that assignment of ECC subtype at baseline visit can help caries risk assessment and prediction, and highlights a potentially new avenue for precision dentistry.[8] The results from this study further bolster the existing knowledge that past caries experience is a strong predictor for future experience. Finally, we note that ECC remains a prevalent disease even in this cohort in a country with low caries experience and access to comprehensive dental care.

CONFLICT OF INTEREST

There are no conflicts of interest.

DATA AVAILABILITY STATEMENT

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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