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Maternal and early life factors of tooth emergence patterns and number of teeth at one and two years of age

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Short title: Influences on tooth emergence patterns

Abstract

Various environmental factors have been associated with the timing of eruption of primary dentition, but the evidence to date comes from small studies with limited information on potential risk factors. We aimed to investigate associations between tooth emergence patterns and pre-conception, pregnancy and post-natal influences. Dentition patterns were recorded at ages one and two years in 2,915 children born to women in the Southampton Women's Survey from whom information had been collected on maternal factors before conception and during pregnancy. In mutually adjusted regression models we found that: children were more dentally advanced at ages one and two years if their mothers had smoked during pregnancy or they were longer at birth; mothers of children whose dental development was advanced at age two years tended to have poorer socioeconomic circumstances, and to have reported a slower walking speed pre-pregnancy; and children of mothers of Asian ethnicity had later tooth development than those of white mothers. The findings add to the evidence of environmental impacts on the timing of the eruption of primary dentition in indicating that maternal smoking during pregnancy, socio-economic status and physical activity (assessed by reported walking speed) may influence the child's primary dentition. Early life factors, including size at birth are also associated with dentition patterns, as is maternal ethnicity.

Keywords: early dentition; early life factors; maternal physical activity; maternal smoking; tooth emergence patterns

Introduction

Development of human primary dentition commences at the end of the fifth week of gestation.¹ Primary teeth erupt on average between 6 and 30 months after birth depending on the type of primary tooth. Before eruption, the tooth has completed crown formation and mineralisation while the root continues to form for a further 18 months following eruption.² On eruption, the ameloblasts responsible for enamel formation are lost and no further enamel remodelling is possible; thus the enamel acts as a permanent record of the interplay between environmental and genetic factors during its development. Obviously with time the enamel will undergo physiological wear and on occasion pathological destruction. Thus, it is likely that earlier tooth eruption has a negative impact on enamel quality.

The timing of primary incisor eruption has been studied in monozygous and dizygous twins showing a strong heritability of over 70%.³ Furthermore genome-wide association studies have identified a number of candidate genes⁴ which control tooth eruption.

Beyond genetic factors, various processes can occur during critical periods of fetal development that can result in lifelong effects on health.^{5,6} Thus variations in age of emergence of the primary dentition are likely to be influenced by pre-conception factors that act on the fetus and have an effect throughout pregnancy and infancy.

Several studies have focused on environmental influences and identified factors associated with the eruption of the primary dentition. These include weight and length at the time of birth,⁷ and in early fetal life, maternal smoking^{8,9} and malnutrition.¹⁰ Additionally, different eruption patterns have been observed in children from different ethnic origins.^{11,12} However, evidence from these studies is based on small populations and no study so far has had access

to comprehensive data collected from pre-conception through to early infancy where the strength of the association between pre-pregnancy exposures and primary tooth eruption, and their interactions with other early life exposures can be robustly examined.

This study therefore aims to examine the interrelationship of timing of the first primary tooth emergence and number of teeth at ages one and two years with pre-conception, pregnancy and postnatal factors, using data from a large mother-offspring cohort study, the Southampton Women's Survey (SWS). This is an exploratory study that aims to identify modifiable risk factors that influence primary dentition, while accounting for biological factors that contribute to tooth development.

Materials and Methods

Maternal measurements

Between 1998 and 2002, 12,583 women aged 20-34 years, who were not pregnant at the time, were recruited to the SWS from the general population in Southampton, UK.¹³ At enrolment, information about diet, lifestyle and socioeconomic conditions was collected. Maternal height was measured with a stadiometer (Seca, Birmingham, UK), weight with calibrated digital scales (Seca, Birmingham, UK) and skin folds (biceps, triceps, subscapular and supra-iliac) with Harpenden callipers (Baty International, Sussex, UK). Women were asked to categorise their walking speed into one of five categories (very slow, stroll at an easy pace, normal speed, fairly brisk, or fast), which was used as a proxy marker of overall physical activity.¹⁴ Dietary patterns were assessed using a 100-item validated food frequency questionnaire.¹⁵ Use of principal components analysis enabled the derivation of a dietary score for which higher values indicated closer adherence to dietary recommendations and thus better quality dietary patterns.¹⁶

Some 3,159 of these women were followed throughout a subsequent pregnancy, and delivered a live-born infant. Gestational age of the children was calculated by combining last menstrual period and early ultrasound data.

Child measurements

New-borns were weighed and measured at birth. Children were followed-up at age one and two years. Anthropometry was performed at birth, and at ages one and two years. At the one-year visit, the mothers were asked the age or the date at which the child's first tooth emerged. At the one- and two-year visits, children's teeth were inspected by trained nurses and the erupted teeth were recorded on a dental chart. A tooth was considered erupted if any part of the tooth had pierced the gum.

Statistical methods

Three analyses were conducted using three dentition outcomes. The first focused on age at first tooth eruption as reported by the mother at the one-year visit. The second outcome considered was the number of teeth as assessed by the nurse at the one-year visit, providing the visit occurred when the child was aged between 11.5 and 12.7 months. The final outcome was similar but using the assessment at two years providing that the visit had occurred between the age of 23.5 and 24.7 months. The restriction on ages was required because children's teeth eruption is highly dependent on child's age.¹⁷ Those age intervals were chosen as they followed the original recruitment objectives for one and two years of follow-up. All analyses were adjusted for sex, while the analyses of the number of teeth at ages one and two years were additionally adjusted for age at measurement to improve the precision of these outcome measures. Finally, an additional analysis considered post-conceptual age of

first-tooth instead of age since birth, to examine the total developmental time before tooth eruption.

Timing of first tooth eruption was analysed as a time-to-event outcome and its associations with potential risk factors were explored using Cox proportional hazards models. In these models, the effects were summarised by hazard ratios (HRs) that compare survival time “without teeth”. A $HR > 1$ indicates that the risk factor is associated with earlier eruption of the first tooth. The assumption for proportionality of hazards in the Cox models was assessed both graphically and using the test on the basis of Schoenfeld residuals. When assumptions were not met, an alternative approach for estimating survival based on Royston-Parmar parametric functions¹⁸ was used to test for validity of conclusions from the Cox model.

Number of teeth at one year of age was considered as a count variable and was regressed on the same risk factors using Poisson regression modelling. Under this model, the effects were summarised by incidence rate ratios (IRRs). An $IRR > 1$ indicates more teeth at the specific age. At two years of age, more than half the children had 16 primary teeth (55%), so the number of teeth at two years was dichotomised, with children having > 16 teeth characterised as having advanced dental development. Associations with this outcome were explored through binomial regression models, and thus effects were summarised by relative risks (RRs) with an $RR > 1$ indicating higher likelihood of having advanced dental development.

Initially unadjusted associations between the potential risk factors and the dentition outcomes were examined in univariate regression models, followed by mutually adjusted analyses in which all risk factors were included in the regression models. To avoid multi co-linearity problems, when potential risk factors were highly correlated, some risk factors were not included in the final multivariable regression models. All measures of effect (HRs, IRRs, and RRs) were termed as RRs for convenience as they are all interpreted in similar ways. Data were analysed using Stata version 13.1.¹⁹

Potential risk factors

The risk factors considered were determined by reference to the literature, and consideration of factors that influence childhood development, and specifically bone measures. Maternal social factors considered as potential predictors of all three dental outcomes were: education, receipt of benefits and Index of Multiple Deprivation, all reported at recruitment before conception of the child. Maternal demographic and lifestyle characteristics were: age at birth of child, height, weight, body mass index (BMI), skinfold thickness, smoking status during pregnancy, ethnicity, dietary score, and reported walking speed. Factors specific to the child were: sex, gestational and post-conceptual age (the latter defined as the time from conception to eruption of the first deciduous tooth), crown-heel length, weight and head circumference at birth, and duration of breast feeding.

Results

Of the 3,159 live born infants delivered to women in the SWS, 2,875 were seen at the one-year visit. Of these, the mothers of 2,629 children provided information about age of first tooth eruption, while 2,243 children had complete data on number of teeth at first year of age (nurse assessment of the number of teeth and visited between 11.5 and 12.7 months). At age two years, 2,649 children were seen in total, and 1,976 children were eligible for inclusion in our analysis. In total 2,915 children were included in at least one of the analyses of the three dentition outcomes.

Maternal and childhood characteristics are described in Table 1. The mothers averaged 30.7 years of age (Standard Deviation (SD) =3.8) at delivery of their child; half were nulliparous; 96% were white in ethnic origin; 14% were in receipt of benefits at recruitment; and 16%

smoked during pregnancy. On average, infants weighed 3.4 kilograms at birth (SD=0.5).

Almost 23% of the children were breastfed for 7 complete months or more.

Table 2 summarises the dental patterns of the children in the study. The average age of first primary tooth eruption was 30.4 weeks (SD=9.4). The first tooth for boys tended to erupt about a week earlier than for girls ($P=0.03$). At age one year, the average number of primary teeth was 6.1 (SD=2.7) and it was slightly higher for boys than for girls ($P=0.01$). At two years of age, 33% of the children had advanced dental development, with a slightly higher prevalence for boys than girls ($P=0.16$).

Later eruption of the first tooth was associated with fewer teeth at one (Spearman $r_s=-0.66$) and two years (Spearman $r_s=-0.33$) (both $P<0.001$). Children with more primary teeth at one year were more likely to have advanced dental development at two years of age ($P<0.001$) (data not shown).

Table 3 gives the unadjusted associations between maternal characteristics and the three dentition outcomes. Maternal social background was associated with the dentition patterns of their children at two years of age, with children of mothers in receipt of benefits and living in more deprived areas being more likely to have advanced dental development. Children of non-white mothers had later first tooth eruption, fewer teeth at age one year and were less likely to have advanced dental development. Children of taller and heavier mothers, of mothers who smoked during pregnancy and those who had a poorer quality diet had an earlier first tooth eruption, more teeth at the age of one year and were more likely to have >16 teeth at age two years.

Table 4 shows the relationships with perinatal factors. Babies of longer gestation and with larger size at birth had their first tooth earlier, had more teeth at age one year, and were more likely to have >16 teeth at age two years. Also, children who were breast fed for 7 complete months or more had delayed tooth eruption and fewer teeth at ages one and two years.

Due to high correlation between the sum of skinfold thickness, BMI, and weight, BMI was chosen as a summary measure of maternal adiposity to enter the final regression model. Also, due to strong correlation between gestational age, weight, crown-heel length, and head circumference at birth, crown-heel length at birth was chosen to enter the final mutually adjusted model, as this variable is a skeletal measure and might be more likely to be associated with tooth development. The significant associations from the mutually adjusted relationships of mothers' and children's early life factors with dentition outcomes are presented in Table 5. The most robust and consistent relationships were for those of maternal smoking and ethnic origin. Children of mothers who smoked during pregnancy and were of white ethnic origin had an earlier eruption of their first primary tooth, had more teeth at one year and were more likely to have advanced dental development at two years of age. Additionally, babies who were longer at birth had an earlier tooth eruption, and more teeth at ages one and two years.

When post-conceptual age was used as an outcome instead of age of first tooth eruption in the final mutually adjusted model, the effect of the risk factors in the model remained unchanged.

Several relationships of maternal adiposity, socioeconomic and lifestyle factors with early dentition, apparent in univariate analyses (Table 3), were no longer significant in the

mutually-adjusted models. However, pre-pregnancy self-reported walking speed and Index of Multiple Deprivation of residence remained significantly associated with dentition at age two years (Table 5). Children of mothers living in socially-deprived areas were more likely to have advanced dental development at two years, while children of mothers who reported a faster walking speed had fewer primary teeth at the age of two.

The findings remained similar when either gestational age, birth weight, or head circumference at birth were entered in the final model instead of crown-heel length at birth (data not shown). However, the association between smoking and age of first deciduous tooth was slightly attenuated when gestational age was used instead of crown-heel length in the final model ($P=0.07$). Also attenuated were the associations between smoking and dental advancement when gestational age, birth weight, or head circumference were included in the model (instead of crown-heel length), but they remained significant at the 10% level. When pre-pregnancy BMI was replaced by sum of skinfold thickness, results remained very similar (data not shown).

The effect of ethnicity was explored further. The “Asian” category included Indian, Pakistani, Bangladeshi and Chinese ethnic origin, and “Black” included Black Caribbean and Black African. Compared with children of white mothers, children of Asian mothers tended to have their first primary tooth erupting later (RR (95%CI):0.73 (0.57, 0.92), had fewer teeth at age one year (RR (95%CI): 0.84 (0.75, 0.94)) and were less likely to have advanced dental development at age two years (RR (95%CI): 0.54 (0.30, 0.96)). No significant differences were found between children of white and black ethnicity mothers.

Further analysis was conducted to assess differences between children included in the study and those that were not. In the current study we analysed data from 2,915 children who had information on any of the three dentition outcomes under investigation, from the original sample of 3,159 live born children. Comparison of maternal characteristics between those 2,915 and the rest of the children (N=241 after excluding three children with no obstetric data) showed that mothers of children included in the analysis were more likely to be highly educated (59% v 49%, $P=0.003$) and less likely to smoke during pregnancy (16% v 26%, $P<0.001$), as compared with mothers of children not included in this analysis. No significant differences were found in maternal body composition between the two groups of children. Comparison of neonatal characteristics showed that children included in this analysis were born after a longer gestation ($P<0.001$), were heavier ($P=0.0002$), and longer ($P=0.035$) at birth than those not included. Also, some children were lost from the final multivariable model due to missing exposure data; the maximum number was 414 (14%). Children with missing exposure data had a later eruption time ($P=0.02$) and subsequently an average of 0.6 teeth fewer teeth ($P=0.001$) compared with children who had complete exposure data.

Discussion

Main findings

We have found that children born to mothers who smoked during pregnancy had their first tooth erupting earlier in life and subsequently had more teeth at the age of one and two years. Children of mothers who lived in less advantaged areas, or reported walking more slowly had a faster rate of dental emergence, most apparent at two years of age. Additionally, children of mothers of Asian ethnicity had later onset and lower rates of eruption of primary teeth. Size at birth was also associated with the emergence of the primary dentition, with larger babies showing earlier eruption patterns.

Strengths and limitations

This study is the first to explore potential effects on early dentition from pre-conception through to early infancy based on a general population mother-offspring cohort. It is the largest study to date that has examined maternal and early life effects on childhood dentition. Early dentition patterns were ascertained robustly as trained nurses inspected children's teeth at one- and two-year visits. Nonetheless, several limitations should be considered in the interpretation of these results. Firstly, age at first tooth eruption was reported by the mother, and is thus subject to error. However, age of eruption was highly correlated with number of teeth at one year of age, with children having an earlier eruption also having more teeth at age one year ($r=-0.66$, $P<0.001$). Moreover, smoking during pregnancy was self-reported; no data on cotinine levels were available in this study to investigate accuracy of this information. However, under reporting of smoking habits might result in underestimation of any smoking effect. Maternal physical activity was assessed using self-reported walking speed, which is a subjective measure. This question was chosen as it had been used in various previous studies. It has recently been validated as a measure of walking speed in older people,¹⁴ but has not formally been validated in our age group. However, self-reported walking speed does tend to differentiate between people who are undertaking exercise and those who do not.²⁰ Although another limitation is that the study used information from a cohort based in only one city, the timing of eruption and dentition patterns observed are consistent with the literature for singleton births from London,²¹ Sweden,²² Finland⁹ and Australia.²³

Furthermore, findings from comparison between children included in this study and those that did not indicated that the group of children in this analysis is a selective group of children that were larger at birth and their mothers had higher educational attainment and had

healthier behaviours during pregnancy. However, as the analysis is based on internal comparisons the differences are unlikely to cause spurious associations between maternal and early life risk factors and dentition patterns.

Comparison with other studies

The association between self-reported smoking during pregnancy and eruption timing has been investigated by Rantakallio et al.⁸ They showed that the first tooth of children whose mothers smoked in pregnancy erupted earlier than those children whose mothers did not smoke, by an average of one week. A subsequent study found that children of mothers who smoked in pregnancy had on average 0.3 teeth more than children of non-smokers.⁹ Our findings were similar; first primary tooth of children of mothers who smoked in pregnancy erupted earlier than for children of non-smoking mothers, while at one year of age they had more teeth. The mechanisms linking maternal smoking with offspring dental development are unknown, but parallel effects of smoking on fetal bone accretion have been found²⁴ possibly indicating effects operating through maternal micronutrient status²⁵ or on placental calcium transport.²⁶

Differences in eruption timing and dental patterns of primary teeth between children of different ethnic groups have been reported previously. A study of dental patterns among Saudi Arabian children showed that they experienced delayed first primary tooth eruption when compared to Caucasian children (including children from Iceland and US).¹¹ Townsend and Hammel also noted that children of African descent acquire their teeth earlier than European children, while Asian children show a delayed eruption of first teeth.¹² An older study also showed a delayed progress in tooth eruption among Chinese (Hong Kong) children as compared with children of other ethnicities.²⁷ Our study supports this, with children of

Asian mothers having their first tooth erupting later than those of white mothers and subsequently having fewer teeth at one and two years of age. Differences in eruption timing and dental patterns between White and Asian children could be a reflection of size differences at birth. However, in the current study, Asian ethnicity had an effect on timing of eruption after adjustment for size at birth (Table 5).

Birth weight has widely been used as a marker of intrauterine nutritional environment, with low weight at birth indicating poor fetal nutrition. Additionally, children who experienced nutritional deficiencies displayed delayed primary teeth emergence.²⁸ Furthermore, other studies have shown a negative correlation between birth weight and tooth eruption timing.²⁹³⁰ Data from the current study support these findings, with babies who were heavier at birth having earlier tooth emergence.

Several studies have explored the association between being born preterm and abnormal timing of primary tooth eruption.³¹⁻³³ Viscardi et al focused only on low birth weight and preterm babies and showed a significant increased risk of delayed first tooth eruption among children of gestational age <30 weeks.³⁴ Our study showed similar results with a shorter length of gestation being associated with older age at first tooth emergence, and subsequent fewer teeth at ages one and two years. Results remained unchanged when post-conceptional age was considered instead of age since birth.

A number of different studies have tried to investigate the link between infant's maturation and dental development by exploring the number of primary teeth at specific ages. Delgado et al showed that for given ages, heavier children had more erupted teeth compared with lighter ones.³⁵ Other studies have also reported a positive association between BMI and faster

eruption rates.^{36,37} Additionally, height has been shown to be a strong predictor of child's dental patterns in early life.^{38,39} An additional effect of height at birth was also reported by Ounsted et al and later by Bastos et al.^{7,40} In agreement with these studies, our study found significant associations between number of primary teeth at one year of age and length at birth. The direction of the association was as expected, with longer babies on a faster growth trajectory having a greater number of primary teeth.

Previous studies have found no strong evidence of an association between socio-economic status and timing and patterns of tooth emergence.^{41,42} In contrast to this literature, we found that children of socially-deprived mothers were more likely to have >16 primary teeth at age two years. Additionally, children of mothers who took less physical activity (proxied by walking speed) were more likely to have advanced dental development.

Some previous studies have examined the association between breastfeeding and timing of eruption of primary teeth. Holman and Yamaguchi showed that children who were not breastfed had a delayed emergence of upper incisors but accelerated emergence of the upper second molar.²⁸ The effect of breastfeeding was also examined in the current analysis. We found that children who were breastfed for longer than seven months had delayed primary tooth eruption and fewer teeth at one and two years, but we have not examined the types of teeth that emerged. However, the association was only of borderline significance and became weaker after adjusting for maternal smoking in pregnancy.

The clinical significance of advanced dental development is uncertain. Many of the factors associated with advanced dental development are also associated with primary dental caries, for example deprivation and maternal smoking. The timing of dental eruption and the

development of subsequent dental caries has received little attention in the literature. If premature eruption does lie on the causal pathway for dental caries it may act by influencing the quality of enamel mineralisation making it more prone to dental caries. For example, in children with advanced dental development, teeth may erupt before they are fully mineralised. Mineralisation deficiencies have been associated with many pregnancy and early life exposures and are strongly related to the subsequent development of dental caries.⁴³ Alternatively a behavioural mechanism is possible; if teeth erupt earlier they require parental involvement in toothbrushing from an earlier age and for a longer duration in childhood. The importance of advanced dental development from both clinical and public health perspectives is unknown and requires further research ideally embedded within longitudinal birth cohorts to explore fully any association between advanced dental development and dental caries. Established risk factors for primary dental caries are able to explain some (often less than half) of the variation in caries levels.^{44,45} Therefore identifying other exposures that result in poor oral health is important and will ultimately influence future preventive strategies even where some risk factors are not in themselves modifiable. For example knowledge about non-modifiable exposures may help to identify children at high risk of dental caries and thus to enable targeting of preventive oral health interventions such as increased frequency of fluoride varnish application, higher concentration of fluoride in home use toothpastes, intense toothbrushing advice and or supporting parents to minimise frequency of sugary intakes in the diet.

Conclusion

The results of this study have shown a number of developmental correlates of both age at eruption of the first tooth and primary dentition at one and two years. Maternal smoking was associated with earlier eruption of the initial dentition, and a greater progression of eruption

over the first two years of post-natal life. Maternal lower socio-economic status, and slower maternal self-reported walking speed were independently associated with earlier childhood dentition patterns, most clearly linked to the number of teeth at two years of age.

These results identify children at greater risk of advanced dental development and concur with findings from earlier smaller studies. There is an apparent impact of health behaviours of women before and during pregnancy, and particularly maternal smoking, on the eruption of the primary dentition.

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Conflicts of interest

KMG has received reimbursement for speaking at conferences sponsored by companies selling nutritional products, and is part of an academic consortium that has received research funding from Abbott Nutrition, Nestec and Danone.

Ethical standards

Written consent was obtained from all women in the study and from a parent or guardian of each child. All phases of the Southampton Women's Survey were approved by the Southampton and South West Hampshire Local Research Ethics Committee.

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Table 1. Maternal and childhood demographic characteristics

	Mean/Median (SD/IQR) or N (%)
<u>N=2,915740</u>	
<u>MATERNAL CHARACTERISTICS</u>	
Age at birth of the child (yrs)	30.7 (3.8)
Height (cm)	163.2 (6.5)
BMI	24.1 (21.9-27.3)
Sum of skinfold thickness (mm)	71.9 (30.2)
Nulliparous (n/N (%))	1,510/2,912 (51.9%)
Smoking during pregnancy (n/N (%))	430/2,778 (15.5%)
Higher educational level (A levels - Degree)	1,725/2,906 (59.4%)
Receipt of benefits (before pregnancy) (n/N (%))	419/2,914 (14.4%)
Ethnic origin: White (n/N (%))	2,797/2,914 (96.0%)
<u>CHILDREN CHARACTERISTICS</u>	
Gestational age (weeks)	39.8 (1.8)
Birth weight (kg)	3.4 (0.5)
Crown-heel length (cm)	49.8 (2.1)
Head circumference (cm)	35.0 (1.4)
Duration of breast feeding (completed months)	
Never tried (n/N (%))	506/2,784 (18.2%)
Up to 6 months (n/N (%))	1,646/2,784 (59.1%)
7 or more (n/N (%))	632/2,784 (22.7%)

Table 2. Descriptive characteristics of dentition data

	All	Boys		Girls		Difference ¹
		N	Mean (SD) or %	N	Mean (SD) or %	
Age (in weeks) of first tooth (reported at one year follow-up)	30.4 (9.4)	1,374	30.1 (9.4)	1,255	30.9 (9.4)	0.03
Number of teeth (assessed at one year follow-up)	6.1 (2.7)	1,169	6.2 (2.6)	1,074	6.0 (2.7)	0.01
Number (%) of advanced dentally developed (assessed at two years follow-up)						
No (16 teeth or fewer)	1,320 (66.8%)	660	65.3%	660	68.3%	
Yes (More than 16 teeth)	656 (33.2%)	350	34.7%	306	31.7%	0.16

¹Differences in age of first tooth eruption and number of teeth at one year of age between boys and girls were explored using t-tests and differences in advanced dentally development between boys and girls were explored by chi-2 test.

Table 3. Maternal factors as predictors of age of tooth eruption and number of teeth at 1 and 2 years of FU (adjusted for child's sex and age in the second and third regression model)

Social factors	Age of first tooth eruption (weeks)		Number of teeth at one year		Advanced dentally developed (>16 teeth) at two years	
	RR ² (95% CI)	P	RR ² (95% CI)	P	RR ² (95% CI)	P
Education						
None – O levels	Reference		Reference		Reference	
A levels - Degree	0.983 (0.91,1.06)	0.661	0.979 (0.95,1.01)	0.212	0.846 (0.75,0.96)	0.009
Receipt of benefits (before pregnancy)						
No	Reference		Reference		Reference	
Yes	1.045 (0.94,1.16)	0.426	1.022 (0.97,1.07)	0.368	1.322 (1.13,1.55)	<0.001
Index of Multiple Deprivation	1.001 (1.00,1.00)	0.541	1.001 (1.00,1.00)	0.214	1.009 (1.00,1.01)	0.001
Demographic and lifestyle characteristics						
Ethnic origin						
White	Reference		Reference		Reference	
Other	0.729 (0.60,0.89)	0.001	0.826 (0.75,0.91)	<0.001	0.625 (0.41,0.96)	0.031
Height (cm)	1.008 (1.00,1.01)	0.007	1.004 (1.00,1.01)	0.003	1.008 (1.00,1.02)	0.100
Weight (kg)	1.003 (1.00,1.01)	0.014	1.002 (1.00,1.00)	0.002	1.007 (1.00,1.01)	0.001
BMI (kg/m²)	1.007 (1.00,1.01)	0.095	1.004 (1.00,1.01)	0.024	1.018 (1.01,1.03)	0.003
Pre-pregnancy: Sum of skinfold thickness	1.000 (1.00,1.00)	0.481	1.001 (1.00,1.00)	0.026	1.004 (1.00,1.01)	<0.001
In pregnancy smoking status						
No	Reference		Reference		Reference	
Yes	1.122 (1.01,1.25)	0.035	1.113 (1.06,1.17)	<0.001	1.283 (1.10,1.50)	0.002
Pre-pregnancy walking speed¹						
Very slow	Reference		Reference		Reference	
Stroll at an easy pace	0.947 (0.51,1.74)		0.927 (0.71,1.22)		0.681 (0.34,1.36)	
Normal speed	0.905 (0.50,1.64)	0.897	0.889 (0.68,1.16)	0.354	0.622 (0.32,1.21)	<0.001
Fairly brisk	0.923 (0.51,1.67)		0.870 (0.67,1.14)		0.529 (0.27,1.03)	
Fast	0.937 (0.51,1.73)		0.946 (0.72,1.24)		0.433 (0.20,0.91)	
Dietary score (z-score)	0.976 (0.94,1.02)	0.233	0.976 (0.96,0.99)	0.007	0.926 (0.87,0.99)	0.020

¹ P-values are for trend across the five categories ²RR: Relative Risk

Table 4. Early life factors as predictors of age of tooth eruption and number of teeth at 1 and 2 years of FU (adjusted for child's sex and age in the second and third regression model)

	Age of first tooth eruption (weeks)		Number of teeth at one year		Advanced dentally developed (>16 teeth) at two years	
	RR ² (95% CI)	P	RR ² (95% CI)	P	RR ² (95% CI)	P
Gestational age (days)	1.075 (1.05,1.10)	<0.001	1.035 (1.03,1.05)	<0.001	1.054 (1.02,1.09)	0.006
Birth weight (kg)	1.329 (1.24,1.43)	<0.001	1.136 (1.10,1.17)	<0.001	1.173 (1.05,1.32)	0.006
Crown-heel length at birth (cm)	1.070 (1.05,1.09)	<0.001	1.031 (1.02,1.04)	<0.001	1.050 (1.02,1.08)	0.003
Head circumference at birth (cm)	1.098 (1.07,1.13)	<0.001	1.043 (1.03,1.06)	<0.001	1.075 (1.03,1.13)	0.003
Duration of breast feeding (completed months)¹						
Never tried	Reference		Reference		Reference	
Up to 6 months	1.008 (0.91,1.12)		0.996 (0.95,1.04)		0.914 (0.78,1.07)	
7 or more	0.926 (0.82,1.05)	0.296	0.922 (0.87,0.97)	0.001	0.738 (0.60,0.90)	0.001

¹P-values are for trend across the three categories ²RR: Relative Risk

Table 5. Multivariable model of maternal and early life factors as predictors of age of tooth eruption and number of teeth at one and two years of FU (adjusted for child's sex and age in the second and third regression model)

	Age of first tooth eruption (weeks)		Number of teeth at one year		Advanced dentally developed (>16 teeth) at two years	
	RR ² (95% CI)	P	RR ² (95% CI)	P	RR ² (95% CI)	P
<u>MATERNAL FACTORS</u>						
In pregnancy smoking status						
No	Reference		Reference		Reference	
Yes	1.183 (1.04, 1.34)	0.009	1.132 (1.07, 1.19)	<0.001	1.197 (1.01, 1.42)	0.042
Maternal ethnic origin						
White	Reference		Reference		Reference	
Other	0.761 (0.62, 0.94)	0.012	0.867 (0.783, 0.962)	0.007	0.584 (0.36, 0.95)	0.029
Pre-pregnancy walking speed¹						
Very slow					Reference	
Stroll at an easy pace					0.822 (0.34, 2.00)	
Normal speed					0.788 (0.33, 1.88)	
Fairly brisk					0.673 (0.28, 1.62)	0.008
Fast					0.575 (0.22, 1.48)	
Index of Multiple Deprivation						
					1.007 (1.00, 1.01)	0.009
<u>EARLY LIFE FACTORS</u>						
Crown-heel length at birth (cm)	1.072 (1.05, 1.10)	<0.001	1.034 (1.02, 1.04)	<0.001	1.049 (1.01, 1.09)	0.006

¹ P-values are for trend across the three categories 2 RR: Relative Risk