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Birth weight, Breastfeeding, Maternal Smoking and Caries Trajectories

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ABSTRACT

Evidence on the effect of low birth weight, breastfeeding and maternal smoking on childhood caries is mainly cross-sectional. We examined the association of these three putative early life factors with caries increment over 4 years among young children. We used data from a 4-year longitudinal caries-risk assessment study carried out among Scottish children. Early life factors were measured when children were aged 1 year (baseline). Caries assessment was repeated annually from ages 1 to 4, and the number of decayed, missing and filled primary tooth surfaces (dmfs) used as a repeated outcome measure. The associations of low birth weight, breastfeeding and maternal smoking with dmfs at baseline and over time (trajectories) were assessed in linear mixed models. A total of 1102 children were included in this analysis. Birth weight, breastfeeding and maternal smoking were not associated with dmfs at baseline. However, low birth weight and maternal smoking were associated with the rate of change in dmfs. By wave 4, the predicted mean difference in dmfs was 1.86 between children with low and normal birth weight and 1.66 between children of smoking and non-smoking mothers. Children with low birth weight and smoking mothers had greater caries increments than those with normal weight and non-smoking mothers, respectively. There was no association between breastfeeding duration and childhood caries, either at baseline or over time.

INTRODUCTION

Dental caries is the most common health condition worldwide, affecting one-third of the global population (Kassebaum et al. 2015). The complex and multi-factorial risk factors for child caries have been extensively examined (Fisher-Owens et al. 2007; Segura et al. 2014; Selwitz et al. 2007). Proximal risk factors such as bacteria, sugars intake, oral hygiene and use of preventive dental services have been identified as important predictors of the disease (Harris et al. 2004; Reisine and Psoter 2001; Seow 2012). Recently, attention has shifted to early life factors and parental influences. Among these, the role of birth weight, breastfeeding and maternal smoking is far from settled.

Low birth weight, a marker of fetal growth, has been linked to a variety of chronic diseases in later life (Barker and Thornburg 2013; Calkins and Devaskar 2011). Impaired fetal nutrition and growth may affect the development of primary teeth, which starts in utero (Nelson et al. 2013). A review of the literature only identified 4 papers (1 longitudinal), none of which supported a relationship between low birth weight and subsequent development of caries (Burt and Pai 2001). After that review, two new longitudinal studies have reported contradicting results (Kay et al. 2010; Nirunsittirat et al. 2016). The beneficial effects of exclusive breastfeeding on child and mother's health are well known (Kramer and Kakuma 2012; Victora et al. 2016). The picture is not that clear with regards to child caries though. Four reviews, based mainly on cross-sectional studies, have yielded inconsistent findings (Avila et al. 2015; Ribeiro and Ribeiro 2004; Tham et al. 2015; Valaitis et al. 2000). Moreover, breastfeeding for longer than 12 months and nocturnal feeding may be associated with greater caries experience in primary teeth (Chaffee et al. 2014; Tham et al. 2015). Others have also recognized the role of certain parental attributes such as health behaviors and oral health status as distal risk factors for child caries (Hooley et al. 2012; Seow et al. 2009). While the relationship between parental behaviors like diet, oral hygiene and dental visits, appears to be straightforward, other behaviors such as maternal smoking, found to be associated with child caries in a review, including one cohort study (Hanioka et al. 2011), are more difficult to explain. Environmental tobacco can increase child susceptibility to dental caries by affecting tooth mineralization, plaque composition and salivary function (Tanaka et al. 2015; Zhou et al. 2014).

The few longitudinal studies of early life influences on childhood caries have been typically based on a single caries assessment. Such a design, albeit prospective, precludes evaluating early life effects on changes in caries status (caries increments or trajectories). A life course approach to caries

epidemiology would enable assessing the relationship between early life factors and the gradual accumulation of the disease overtime. The aim of this study was to examine the association between three putative early life factors (low birth weight, breastfeeding and maternal smoking) and caries increment over 4 years among Scottish young children.

METHODS

This study used data from a 4-year longitudinal caries-risk assessment study carried out with the overarching aim of identifying markers for caries in pre-school infants. The survey protocol was approved by Tayside Committee on Medical Research Ethics (Radford et al. 2000; Radford et al. 2001). The present study adheres to the Strengthening the Reporting of Observational Studies statement (Vandenbroucke et al. 2007).

Study population

The parents/guardians of all 1981 children born in Dundee, Scotland, during one calendar year (April 1993 – March 1994) were asked for permission to allow their children to be dentally examined and for other family and child information to be collected through parental questionnaires. Water supplies in Dundee were not fluoridated during the study period. From a total of 1703 consented infants, 1455 (73%) participated in at least one component of the survey in wave 1 (when children were 1-year-old). Of them, 1419 were dentally examined and 1248 completed parental questionnaires. All eligible infants were re-approached annually to participate in subsequent survey waves at ages 2, 3 and 4 years. During the follow up period, overall participation rates were 72% (n=1436) in wave 2, 65% (n=1292) in wave 3 and 71% (n=1412) in wave 4.

A total of 1419 infants participated in at least one dental examination over the 4 years, of which 317 (22%) were excluded for missing data on covariates. Caries data were available for 1085, 1006, 853 and 946 children in waves 1, 2, 3 and 4, respectively. Furthermore, 765 (69%) contributed to 4 waves of caries data, 207 (19%) to 3 waves, 79 (7%) to 2 waves and 51 (5%) to 1 wave.

Variables selection

All dental examinations were carried out by a calibrated examiner (HB) using direct vision and artificial light with the child in the supine position at age 1 year and upright position at ages 2, 3 and 4 years. Examination was carried out as close to the child's birthday as was feasible (76% of dental examinations were carried out within 3 months of each infant's birthday). Caries was diagnosed at the

d_1 threshold (caries into enamel). The examiner received a 3-day training course before data collection every year. Intra-examiner reliability from repeated examinations was good (Kappa=0.75). The number of decayed, missing and filled tooth surfaces (dmfs index) was calculated for each infant at every wave, and used as the repeated outcome measure.

Data on early life factors and covariates were extracted from questionnaires completed in wave 1, except for mother's education that was collected in wave 4. Birth weight was transcribed from children's health handbook, in which the data were recorded by medical staff at birth, to the survey questionnaire. Birth weight was classified as low (<2500g) and normal ($\geq$2500g). Parents also provided information on breast and bottle feeding and the age at which the child stopped breastfeeding and/or started bottle feeding. This information was used to classified (non-exclusive) breastfeeding duration as never, <6 months and $\geq$6 months. Maternal smoking at wave 1 was self-reported in two possible categories (smoker or non-smoker).

A number of family, maternal and child predictors were also included as covariates. Child factors were sex, age in months, birth order and toothbrushing frequency. Maternal factors were age at child birth and education. Family factors were socioeconomic position (SEP) and marital status. Family SEP was measured through parental employment (both unemployed, one employed and both employed) and the DEPCAT score, a 7-point ordinal score that ranks all postcode sectors from 1 (most affluent) to 7 (most deprived) using 4 Census variables that have been shown to best correlate with health outcomes: car ownership, male unemployment, head of household in low social class and household overcrowding (Carstairs 1995). DEPCAT scores were further grouped into three conventional groups, namely 1 and 2 (affluent); 3-5 (intermediate); and 6 and 7 (deprived).

Statistical analysis

All analyses were performed with STATA version 13 (StataCorp LP, College Station, TX). Descriptive analyses were carried out to examine early life family and child factors and their associations with children's caries experience at each wave. T-test was used to compare dmfs levels by child's sex, birth order and birth weight, maternal smoking and marital status, whereas analysis of variance was used to compare dmfs levels by maternal age at birth, maternal education, breastfeeding duration, parental employment, area deprivation and child's toothbrushing behavior.

Linear mixed effects (LME) models were used to estimate the 4-year caries increment and the associated 95% confidence interval (CI) using the four year-on-year caries assessments. LME models use all available outcome data over the follow-up period, handle unequally spaced observations over time and take into account the fact that repeated measures on the same individual are correlated (Singer and Willett 2003; Twisk 2013). We fitted both the intercept and the slope with time as random effects, allowing for individual differences in dmfs at baseline and rates of change in dmfs over the follow-up period (Bernabé et al. 2016). No constraints were imposed on the values of the covariance matrix (unstructured). Child age in months (centered at 12 months, the average age at baseline) was used as the underlying time scale in all models and fitted as a continuous time indicator.

We first estimated a model without any covariates (null model) to establish the rate of change in dmfs with age within the observed period. We then examined the association between early life factors and dmfs increment over the 4-year follow-up in sequential models. The first LME model included terms for all time-invariant covariates (child's sex, birth order, birth weight, breastfeeding duration and toothbrushing behavior, and maternal smoking, education and age at birth, marital status, parental employment and area deprivation). The main effect for each predictor in this model estimates the effect on dmfs at baseline. We proceeded to test the association of early life factors with dmfs increment over time by adding the interaction (product term) between each predictor and the time indicator to the main effects model. This interaction estimates the effect of the predictor on dmfs increment over 4 years. A formal statistical test of the contribution of the product term was obtained by contrasting nested models using the Likelihood ratio test (a smaller model including all main effects and a larger model including all main effects and the interaction). The final LME model included all main effects for early life factors plus any significant interactions. We presented significant associations with changes in dmfs using line graphs (caries trajectories) to aid interpretation.

RESULTS

A total of 1102 children (46% female), with a mean age of 12.8 months at baseline (Standard Deviation: 1.7, range: 7-20) were included in this analysis. Children excluded from the study sample because of missing data on covariates were older and non-breastfed, had low weight at birth and greater caries experience, had single and poorer parents and younger, less educated and smoking mothers. The mean dmfs was 0.05 (SD: 0.42, range: 0-8, caries-free: 1.9%), 0.70 (3.03, 0-28, 10.7%), 1.43 (4.94, 0-68, 23.2%) and 3.57 (7.51, 0-62, 45.6%) at wave 1, 2, 3 and 4, respectively.

Overall, 5.2% of children were born weighing less than 2500g and 17.6% were breastfed for at least 6 months. In addition, 33.5% of mothers were smokers. Table 1 shows the associations of low birth weight, breastfeeding and maternal smoking with covariates. Breastfeeding was more common among children born second or later, older and more educated mothers, children in families with parents in employment and living in more affluent areas. Smoking was more common among younger, single and less educated mothers, workless families and those in more deprived areas. Interestingly, child's toothbrushing frequency was negatively associated with low birth weight and maternal smoking and positively associated with breastfeeding.

Table 2 shows crude associations with children's dmfs levels at each wave. Children born with low weight had greater dmfs at wave 4 (5.58) than those born with normal weight (3.45). Children breastfed for up to 6 months and those breastfed for 6 months or longer had lower dmfs at wave 4 (2.77 and 2.95 respectively) than those who were never breastfed (4.20). Smoking mothers had children with higher dmfs at every wave than non-smoking mothers. Parental employment and area deprivation, maternal education and age at birth, and child's birth order and toothbrushing frequency were also associated with children's dmfs.

The null LME model showed that children's dmfs increased by 0.09 units (95%CI: 0.08 to 0.10) for every month increase in age. There was a strong negative covariance between intercept and slope (-0.08; 95%CI: -0.11 to -0.06), indicating that children with the lowest baseline dmfs had the steepest dmfs increment. The main effects model showed that birth weight, breastfeeding and maternal smoking were not associated with dmfs at baseline (Table 3). However, they were associated with the rate of change in dmfs over 4 years when added to the main effects model one at a time (all $p<0.05$). Birth order, maternal education, parental employment, area deprivation and child's toothbrushing behavior were also associated with the rate of dmfs increment at this stage. The final LME model included the main effects of birth weight, breastfeeding, maternal smoking and covariates along with the interactions of time with maternal education ($p<0.001$), parental employment ($p<0.001$), maternal smoking ($p=0.006$) and birth weight ($p=0.039$). All other factors did not remain significantly associated with the rate of change in dmfs and were therefore left out of the final model.

There was a greater dmfs increment in children of low birth weight, with smoking and less educated mothers, and in families with neither parent in employment (Figure 1). By wave 4, the predicted mean difference in dmfs was 1.86 (95%CI: 0.03 to 3.74) between children with low and normal birth weight

and 1.66 (95%CI: 0.57 to 2.75) between children of smoking and non-smoking mothers. The predicted mean differences in dmfs between mothers with no qualification and those with secondary, A levels and degree or higher education were 0.83 (95%CI: -0.54 to 2.20), 2.31 (95%CI: 0.73 to 3.89) and 2.70 (95%CI: 0.69 to 4.71), respectively. Finally, the predicted mean differences in dmfs between children in workless families and those in families with one parent and both parents in employment were 2.26 (95%CI: 0.45 to 3.87) and 2.80 (95%CI: 1.20 to 4.41), respectively.

DISCUSSION

This study provides evidence on the role of risk factors during the first year of life and early childhood caries. Children with low weight at birth and those with smoking mothers had steeper caries increments over 4 years than their corresponding counterparts, over and above the effect of well-known determinants of caries development at family, maternal and child level. On the other hand, our findings did not support an association between breastfeeding duration and childhood caries.

Some study limitations need to be addressed. First, we used data from a birth cohort that started in 1993/94. Although some may question whether our findings are still relevant today, the role of biological and behavioral factors in explaining health variations has not changed since those were first identified (undernutrition and sugars intake remain related to dental caries despite changes over time). That said, the present findings await corroboration from studies using contemporaneous data. Second, although the study sample was large and included 78% of those who participated in the baseline survey, it was generally healthier and wealthier than those lost to follow-up. Thus, the present results reflect valid relationships between the variables of interest, but are not generalizable to the study population. Third, although information on maternal behaviors was measured concurrently, it relied on self-reports, which may be subject to measurement bias. Although biomarkers are an alternative to self-reported smoking, they inform about exposure but do not measure behavior. Self-reports are thus a valid means of obtaining information about health behaviors and they are commonly used in epidemiological surveys. Fourth, we assessed early life factors at a single point in time (baseline). This is the simplest scenario in life course epidemiology and unlikely to represent the complex interplay of factors influencing caries development (some factors may have changed during the follow-up period). Further studies, using alternative methods to assess early life factors over multiple times, are therefore encouraged.

We found that low birth weight and maternal smoking put children in a trajectory of increasing dental caries. For each factor, there were no baseline differences in caries experience between exposed and unexposed children, but their caries trajectories tended to diverge over time. The magnitude of the effect was such that by wave 4, low birth weight children and those with smoking mothers had, respectively, 1.86 and 1.66 more tooth surfaces with caries than their corresponding counterparts. These findings support the view that the prenatal and postnatal environments are important for children's dental status (Hooley et al. 2012; Leong et al. 2013). They also underscore the advantages of focusing on accumulation of disease over time. Measuring caries at one specific age/time point may explain why previous studies were not able to identify associations.

A possible mechanism linking low birth weight and childhood caries is by affecting the development of the dentition during fetal life. There is evidence suggesting that infants with very low birth weight had an increased risk for enamel hypoplasia than those with normal weight at birth (Nelson et al. 2013), and that developmental enamel defects, hypoplasia in particular, increase the susceptibility of caries development (Vargas-Ferreira et al. 2015). Whether our findings reflect the effect of preterm birth or the infant being small for gestational age or a combination of both is unknown. Future studies would benefit from including information on gestational age or prematurity to tease out potential pathways.

As for the association between maternal smoking and child caries, it is possible that such a relationship is confounded by family SEP. However, our results were robust to adjustments for multiple SEP indicators. Exposure to cigarette smoke in fetal and post-natal life may impair post-eruptive mineralization of teeth; decrease salivary buffering capacity, IgA levels and flow rate; and increase colonization by cariogenic bacteria (Hanioka et al. 2011; Zhou et al. 2014). As we measured post-natal exposure to maternal (not family) smoking, we suggest maternal smoking may be a proxy for mothers' risk taking behaviors and child rearing practices. Mothers who adopt unhealthy behaviors are less likely to take good care of their children's oral health. It is also plausible that maternal smoking could impact on children's general health; subsequently the child may receive long-term or repeated treatments with sugary and/or steroid medications that may increase the child's risk for caries (Phillips et al. 2016).

Breastfeeding was not associated with childhood caries either at baseline or over time. Although breastfed children had lower caries trajectories than non-breastfed children, this association was fully attenuated after controlling for other factors. As we only assessed breastfeeding duration, further

studies should look into exclusive breastfeeding to confirm the present findings. That said, our findings reinforce the notion that breastfeeding does not affect dental status. Although recent studies have shown that breastfeeding beyond the first year of life may be related to higher caries prevalence, evidence is just starting to build up and therefore not a reason to discontinue breastfeeding. Our findings also emphasize the strong role played by family socioeconomic position and maternal education, factors for which clear gradients in childhood caries trajectories were identified.

The present findings have some implications for further research and practice. Acknowledging key maternal influences as potential risk factors for children's oral health and describing some of the underlying causes of these relationships is a step forward to expand our understanding of the distal risk factors for child caries on top of proximal behavioral and biological causes of caries that have been extensively studied. Furthermore, identifying some maternal attributes as possible risk factors for dental caries highlights the importance of adopting a broader approach to promoting children's oral health which should consider maternal health compromising behaviors, life events and socioeconomic circumstances, as well as focusing on the proximal causes of early childhood caries.

CONCLUSION

This prospective study shows that low birth weight and maternal smoking, but not breastfeeding duration, were associated with caries trajectories from ages 1 to 4 among Scottish children. Low birth weight children and those with smoking mothers had greater increases in dental caries than children with normal weight and non-smoking mothers.

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The authors declare no conflicts of interest in relation to this work.

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Table 1. Early life factors by family and child characteristics (n=1,102)

Baseline predictors	n	%	Low birth weight		Breastfeeding ≥6 months		Maternal smoking	
			n	%	n	%	n	%
Child's sex								
Male	592	53.7	32	5.4	104	17.6	202	34.1
Female	510	46.3	25	4.9	90	17.7	167	32.8
P value[a]			*0.707*		*0.188*		*0.629*	
Birth order								
First born	506	45.9	31	6.1	68	13.4	163	32.2
Second born or later	596	54.1	26	4.4	126	21.1	206	34.6
P value			*0.188*		*<0.001*		*0.410*	
Maternal age at birth								
16-24 years	331	30.0	18	5.4	29	8.8	158	47.7
25-34 years	691	62.7	33	4.8	135	19.5	188	27.2
35-44 years	80	7.3	6	7.5	30	37.5	23	28.8
P value for trend			*0.814*		*<0.001*		*<0.001*	
Maternal education								
No qualification	250	22.7	12	4.8	25	10.0	124	49.6
Secondary	291	26.4	20	6.9	29	10.0	99	34.1
A levels	177	16.1	10	5.7	46	26.0	39	22.0
Degree or higher	88	8.0	7	8.0	45	51.1	7	8.0
P value for trend			*0.386*		*<0.001*		*<0.001*	
Marital status								
Married	1039	94.3	56	5.4	189	18.2	325	31.3
Single	63	5.7	1	1.6	5	7.9	44	69.8
P value			*0.186*		*0.091*		*<0.001*	
Parental employment								
None employed	147	13.3	9	6.1	14	9.5	87	59.2
One employed	414	37.6	17	4.1	82	19.8	151	36.5
Both employed	541	49.1	31	5.7	98	18.1	131	24.2
P value for trend			*0.754*		*<0.001*		*<0.001*	
Area deprivation								
Affluent	281	25.5	17	6.1	79	28.1	54	19.2
Intermediate	276	25.1	15	5.4	54	19.6	81	29.4
Deprived	545	49.5	25	4.6	61	11.2	234	42.9
P value for trend			*0.356*		*<0.001*		*<0.001*	
Child's toothbrushing frequency								
No brushing	263	23.9	22	8.4	35	13.3	107	40.7
Once a day	353	32.0	14	4.0	68	19.3	107	30.3
Twice a day or more	486	44.1	21	4.3	91	18.7	155	31.9
P value for trend			*0.035*		*0.005*		*0.033*	

[a] Chi-square test was used for comparisons

Table 2. Child's caries experience (dmfs index) by family and child characteristics

Baseline predictors	Age 12 months	Age 24 months	Age 36 months	Age 48 months
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Child's sex				
Male	0.04 (0.35)	0.82 (3.46)	1.69 (5.55)	3.64 (7.63)
Female	0.05 (0.49)	0.56 (2.43)	1.14 (4.14)	3.49 (7.37)
P value[a]	*0.625*	*0.174*	*0.106*	*0.754*
Birth order				
First born	0.03 (0.25)	0.56 (2.61)	1.17 (5.42)	3.02 (6.89)
Second born or later	0.06 (0.53)	0.81 (3.35)	1.64 (4.53)	4.02 (7.95)
P value	*0.143*	*0.195*	*0.169*	*0.040*
Birth weight				
≥2500g	0.05 (0.43)	0.66 (2.94)	1.41 (4.96)	3.45 (7.28)
<2500g	0.02 (0.13)	1.31 (4.40)	1.85 (4.68)	5.58 (10.56)
P value	*0.605*	*0.136*	*0.546*	*0.044*
Maternal age at birth				
16-24 years	0.04 (0.29)	1.08 (3.75)	1.78 (6.07)	4.63 (8.32)
25-34 years	0.05 (0.49)	0.56 (2.74)	1.34 (4.59)	3.26 (7.30)
35-44 years	0.03 (0.22)	0.41 (2.08)	0.97 (2.72)	2.38 (5.53)
P value	*0.758*	*0.038*	*0.381*	*0.017*
Maternal education				
No qualifications	0.09 (0.67)	0.97 (3.67)	1.98 (4.79)	5.72 (9.37)
Secondary	0.07 (0.38)	0.59 (2.57)	1.59 (5.77)	3.76 (8.36)
A levels	0.00 (0.00)	0.33 (1.29)	0.73 (2.79)	2.13 (5.08)
Degree or higher	0.07 (0.64)	0.08 (0.65)	0.44 (1.81)	1.48 (3.21)
P value	*0.336*	*0.021*	*0.014*	*<0.001*
Breastfeeding duration				
Never	0.03 (0.28)	0.86 (3.44)	1.72 (5.62)	4.20 (7.83)
<6 months	0.04 (0.49)	0.48 (2.35)	1.15 (4.49)	2.77 (6.71)
≥6 months	0.09 (0.61)	0.48 (2.36)	1.05 (3.12)	2.95 (7.59)
P value	*0.232*	*0.089*	*0.194*	*0.020*
Marital status				
Married	0.05 (0.44)	0.69 (3.00)	1.44 (5.04)	3.53 (7.54)
Single	0.00 (0.00)	0.81 (3.51)	1.40 (3.03)	4.18 (6.79)
P value	*0.369*	*0.761*	*0.955*	*0.556*
Maternal smoking				
Non-smoker	0.03 (0.30)	0.42 (2.19)	1.14 (4.77)	2.78 (6.51)
Smoker	0.09 (0.59)	1.27 (4.24)	2.04 (5.23)	5.18 (9.00)
P value	*0.023*	*<0.001*	*0.012*	*<0.001*
Parental employment				
None employed	0.11 (0.53)	1.82 (4.96)	3.09 (7.68)	6.42 (10.13)
One employed	0.04 (0.46)	0.60 (2.75)	1.49 (5.36)	3.65 (7.51)
Both employed	0.03 (0.35)	0.49 (2.49)	1.00 (3.53)	2.88 (6.64)
P value	*0.139*	*<0.001*	*0.001*	*<0.001*
Area deprivation				
Affluent	0.02 (0.36)	0.51 (2.91)	0.83 (3.60)	2.14 (6.73)
Intermediate	0.05 (0.39)	0.60 (2.44)	1.24 (4.14)	3.32 (7.72)
Deprived	0.06 (0.47)	0.85 (3.36)	1.88 (5.87)	4.47 (7.67)
P value	*0.493*	*0.294*	*0.027*	*<0.001*
Child's toothbrushing frequency				
No brushing	0.04 (0.51)	0.96 (3.28)	1.63 (3.85)	4.65 (8.55)
Once a day	0.04 (0.41)	0.76 (3.60)	1.58 (5.19)	4.07 (8.93)
Twice a day or more	0.05 (0.38)	0.52 (2.39)	1.22 (5.28)	2.64 (5.42)
P value	*0.880*	*0.174*	*0.528*	*0.002*

[a] t-test was used when comparing two groups and analysis of variance when comparing three groups

Table 3. Linear mixed effects (LME) models for the association between early life factors and children's caries experience over 4 years (n=1,102)

Baseline predictors	Model with main effects			Model with main effects and interactions[b]		
	Coef.	[95% CI]	p value	Coef.	[95% CI]	p value
Child's age[a]	0.09	[0.08, 0.10]	<0.001	0.16	[0.12, 0.21]	<0.001
Sex (reference: Male)						
Female	-0.14	[-0.35, 0.07]	0.190	-0.14	[-0.34, 0.07]	0.192
Birth order (reference: First born)						
Second born or later	0.09	[-0.14, 0.31]	0.454	0.09	[-0.14, 0.31]	0.451
Birth weight (reference: ≥2500g)						
<2500g	0.09	[-0.37, 0.55]	0.700	-0.12	[-0.66, 0.41]	0.648
Maternal age at birth (reference: 16-24 years)						
25-34 years	-0.04	[-0.31, 0.22]	0.758	-0.04	[-0.31, 0.22]	0.756
35-44 years	-0.05	[-0.50, 0.41]	0.847	-0.05	[-0.50, 0.41]	0.846
Maternal education (reference: No qualifications)						
Secondary	-0.02	[-0.32, 0.28]	0.902	0.08	[-0.26, 0.42]	0.647
A levels	-0.06	[-0.41, 0.29]	0.750	0.23	[-0.17, 0.62]	0.270
Degree or higher	-0.08	[-0.53, 0.38]	0.748	0.25	[-0.27, 0.77]	0.340
Breastfeeding duration (reference: Never)						
<6 months	0.02	[-0.23, 0.28]	0.860	0.02	[-0.23, 0.28]	0.855
≥6 months	0.06	[-0.25, 0.37]	0.706	0.06	[-0.25, 0.37]	0.710
Marital status (reference: Married)						
Single	-0.18	[-0.65, 0.29]	0.457	-0.18	[-0.65, 0.29]	0.446
Maternal smoking (reference: Non-smoker)						
Smoker	0.15	[-0.09, 0.39]	0.231	-0.05	[-0.33, 0.23]	0.744
Parental employment (reference: none employed)						
One employed	-0.30	[-0.65, 0.05]	0.092	-0.05	[-0.45, 0.35]	0.808
Both employed	-0.32	[-0.68, 0.04]	0.085	0.00	[-0.41, 0.41]	0.992
Area deprivation (reference: affluent)						
Intermediate	-0.02	[-0.32, 0.27]	0.868	-0.02	[-0.32, 0.27]	0.876
Deprived	-0.03	[-0.31, 0.25]	0.846	-0.03	[-0.31, 0.25]	0.850
Child's toothbrushing frequency (reference: no brushing)						
Once a day	-0.03	[-0.31, 0.25]	0.836	-0.03	[-0.32, 0.25]	0.827
Twice or more a day	-0.04	[-0.30, 0.23]	0.789	-0.04	[-0.30, 0.23]	0.791
Time X birth weight (<2500g)				0.05	[-0.01, 0.10]	0.098
Time X maternal education (reference: no qualification)						
Secondary				-0.02	[-0.06, 0.01]	0.238
A levels				-0.06	[-0.10, -0.02]	0.004
Degree or higher				-0.07	[-0.12, -0.02]	0.009
Time X maternal smoking (Smoker)				0.04	[0.01, 0.07]	0.005
Time X parental employment (reference: none employed)						
One employed				-0.05	[-0.09, -0.01]	0.014
Both employed				-0.07	[-0.11, -0.02]	0.002

[a] Child's age was assessed in months and centered at 12 years (the average age at baseline). The coefficient represents the dmfs increment for every month increase in age.

[b] Only significant interactions were included in the final LME model. We report a global test for each interaction, which was derived from contrasting nested models using the likelihood ratio test.

Figure 1. Predicted mean dmfs according to birth weight, maternal smoking, maternal education and parental employment. Predicted values derived from a LME model including terms for child's sex, age (time indicator), birth order, birth weight, breastfeeding duration and toothbrushing frequency, maternal age at birth, education and smoking, marital status, parental employment and area deprivation and product terms for time with birth weight, maternal smoking, maternal education and parental employment.