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Change in periodontitis during pregnancy and the risk of pre-term birth and low birthweight

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Abstract

Aim: Determine whether periodontitis progression during pregnancy is associated with adverse birth outcomes.

Methods: We used clinical data and birth outcomes from the Obstetrics and Periodontal Therapy Study, in which randomly selected women received periodontal treatment before 21 weeks of gestation ($N = 413$) or after delivery (410). Birth outcomes were available for 812 women and follow-up periodontal data for 722, including 75 whose pregnancies ended < 37 weeks. Periodontitis progression was defined as $\geqslant 3$ mm loss of clinical attachment. Birth outcomes were compared between non-progressing and progressing groups using the log rank and *t* tests, separately in all women and in untreated controls.

Results: The distribution of gestational age at the end of pregnancy ($p > 0.1$) and mean birthweight (3295 *versus* 3184 g, $p = 0.11$) did not differ significantly between women with and without disease progression. Gestational age and birthweight were not associated with change from baseline in percentage of tooth sites with bleeding on probing or between those who did *versus* did not progress according to a published definition of disease progression ($p > 0.05$).

Conclusions: In these women with periodontitis and within this study's limitations, disease progression was not associated with an increased risk for delivering a pre-term or a low birthweight infant.

Key words: disease progression; low birthweight; periodontal disease; pregnancy; pre-term birth

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Many studies have reported an association between maternal periodontal disease and the risk for adverse pregnancy outcomes (see, e.g. Xiong et al. 2006, Vergnes & Sixou 2007). A recent meta-analysis concluded that women with periodontitis are approximately two to three times more likely than periodontally healthy women to deliver a pre-term, low birthweight or pre-term and low birthweight infant (Vettore et al. 2006). The nature and consistency of the association, however, continues to be debated (Vettore et al. 2006, Michalowicz & Durand 2007, Vettore et al. 2008). Isolating the effects of periodontitis on birth outcomes is difficult because of the multifactorial nature of these outcomes (Goffinet 2005). Pre-term birth and periodontitis also share several important risk factors such as low socioeconomic status, smoking and black race.

It is possible that the foetal–placental unit in women with progressive periodontitis is exposed to inflammatory mediators that precipitate pre-term labour and delivery. For example, aggressive periodontitis has been associated with elevated levels of interleukin-6 (Il-6) in saliva (Aurer et al. 1999). When elevated in the serum or amniotic fluid, Il-6 predicts pre-term labour and delivery (Greci et al. 1998, von Minckwitz et al. 2000).

Periodontal disease progresses sporadically and episodically, and common clinical periodontal measures and indices [e.g. probing depth, clinical attachment loss (CAL)] may not reflect current disease activity (Page & DeRouen 1992). Furthermore, the rate of clinical disease progression is relatively low, even in untreated patients (Lindhe et al. 1989).

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Thus, relatively large numbers of women are needed for the study of associations between disease progression during pregnancy and birth outcomes.

To date, only one research group has examined the association between progressive periodontitis and adverse pregnancy outcomes (Riche et al. 2002, Offenbacher et al. 2006). They reported that pre-term birth rates (<32 weeks gestation) were significantly higher in women with progressive periodontitis when compared with those with stable or non-progressing disease (6.4% *versus* 1.8%, $p<0.001$) (Offenbacher et al. 2006). Pre-term birth rates <37 weeks did not differ significantly between these groups. The same researchers reported that the association between disease progression and the risk for pre-term birth before 37 weeks was significant in pre-eclamptic but not in non-pre-eclamptic women (Riche et al. 2002).

We previously reported that non-surgical treatment in pregnant women with periodontitis did not significantly alter the rates of pre-term birth, low birthweight or foetal growth restriction (Michalowicz et al. 2006). The present paper's analyses examine the relationship between progressive periodontitis and the risk for pre-term birth and low birthweight using data from the Obstetrics and Periodontal Therapy (OPT) Study.

Methods

Details about the OPT Study and its obstetrical and clinical periodontal results have been reported elsewhere (Michalowicz et al. 2006). The OPT Study was a randomized, single-blind controlled trial designed to determine whether non-surgical periodontal treatment alters the frequency and severity of pre-term delivery in women with periodontitis. Women were recruited from obstetrics clinics in Minneapolis, MN; Lexington, KY; Jackson, MS, USA and New York, NY, USA that serve populations at an increased risk for pre-term birth. Eligible women had periodontitis, defined as four or more teeth with probing depth (PD) of at least 4 mm and a CAL of at least 2 mm, and bleeding on probing (BOP) for at least 35% of tooth sites. Women were ineligible if they had multiple foetuses, required antibiotic prophylaxis before dental treatment, had any medical condition that precluded elective dental treatment or were likely to have <20 teeth remaining after treatment of moderate to severe caries, abscesses or other non-periodontal pathoses. Following baseline assessments between 13 weeks 0 days and 16 weeks 6 days gestation, women were randomly assigned to receive scaling and root planing before 21 weeks of gestation ($N = 413$) or after delivery (410). Women were also seen for monthly visits, during which treatment women received tooth polishings and oral hygiene instructions, and control women received brief examinations.

At baseline, all women were evaluated by a dentist for essential dental treatment needs. To eliminate oral sources of infection or pain during pregnancy, teeth with urgent or emergent care needs were treated with temporary or permanent restorations, endodontic therapy or extractions before 21 weeks of gestation. Over half of the women (58.7%) were judged to have essential dental care needs and nearly three-fourths of these (72.7%) completed the recommended treatment (Michalowicz et al. 2008).

Periodontal assessment

Women received comprehensive periodontal examinations at baseline and again at 21–24 and 29–32 weeks gestation. Using a manual probe, calibrated and blinded examiners measured PD, gingival recession and BOP at six sites on all teeth excluding third molars. CAL was calculated from the PD and recession measures. BOP was scored as present or absent.

Rescue periodontal treatment

During the monthly follow-up visits, participants were monitored for oral adverse events including abscesses, exophytic soft tissue lesions and gingival hyperplasia. Periodontitis progression, defined in the study protocol as an increase in CAL from baseline of at least 3 mm, was monitored at the follow-up periodontal examination visits.

All women with oral lesions or progressive periodontitis were offered treatment, which was not delayed until post-partum unless contraindicated because of advanced gestation. Abscesses and exophytic or hyperplastic lesions could be treated with scaling, root planing, soft tissue curettage, or by surgical excision. Therapists also had the discretion to monitor rather than treat certain lesions. Women with progressive periodontitis at fewer than six tooth sites received root planing at the affected teeth only. Control women with progressive periodontitis at six or more sites were offered full-mouth scaling and root planing. Treatment group participants with progressive disease at six or more tooth sites were referred to a consulting periodontist and could receive a second course of full-mouth scaling and root planing and/or systemic antibiotics, or subgingival irrigation with antimicrobial solutions.

Pregnancy outcomes

Gestational age was determined at baseline using the woman's last menstrual period information and ultrasound data as described elsewhere (Carey et al. 2000). Birthweight was abstracted from the child's medical record by blinded and trained nurses. Gestational age at delivery was available for 812 women. Birth outcomes were not available for six treatment women (four were lost to follow-up, one withdrew consent and one electively aborted the pregnancy) and five controls (three were lost to follow-up, one withdrew consent and one electively aborted the pregnancy).

Change in periodontitis during pregnancy

We studied the relationship between change in periodontitis during pregnancy and adverse birth outcome using three definitions of change. First, we used our *a priori* definition of disease progression, which was any increase in CAL $\geqslant$ 3 mm. Women with and without $\geqslant$ 3 mm of CAL at any tooth site were termed, respectively, as having ''progressive'' or ''non-progressive'' disease. We also calculated the *change* from baseline in the percentage of sites with BOP and then grouped participants into tertiles in terms of this change. Finally, we used a definition of progression used previously to explore the relationship between periodontitis progression and birth outcomes: ''Four or more (tooth) sites with 2 mm or more of increasing probing depths at each site, with the post-partum PD being 4 mm or more'' (Offenbacher et al. 2006). Because we did not examine women post-partum, we used the last examination data available for this classification.

Statistical analyses

We included subjects who had both follow-up periodontal data and birth outcomes. Time-to-event analyses used as the event time gestational age at the end of pregnancy, where those lost to

follow-up ($n = 7$), withdrawing consent ($n = 2$) and having elective abortions ($n = 2$) were censored at the last available follow-up visit or the elective abortion. Otherwise, gestational ages were censored at 37 weeks (259 days).

We compared birth outcomes between non-progressing and progressing groups using all women and controls only. We were required by the study's data and safety monitoring board and the applicable institutional review boards to offer treatment to all women who were found to have progressive disease. In this sense, we observed the natural history of periodontitis in control women to the point of clinical disease progression, defined as an increase in CAL $\geqslant$ 3 mm.

In analysing controls only, we compared groups with non-progressive and progressive periodontitis using time-to-event analyses and the log-rank test and Kaplan–Meier plots. When all treatment and control women were included, the time-to-event analyses used Cox regression including treatment group and the interaction of treatment group with progression status. Additional analyses examined the effects of additional or rescue treatment on birth outcomes. For these, we included in the models an indicator of receipt of rescue (for controls) or additional treatment (for treatment group women) before delivery and, as needed, the interaction between initial group assignment and the receipt of rescue treatment. Time-to-event analyses based on tertiles of change included the interaction of treatment group with tertile of change.

Simple comparisons of two groups used either a two-sample *t*-test (for continuous dependant variables like birthweight) or Pearson's χ^2 test (for categorical dependant variables like tertile of baseline BOP). Other analyses of continuous dependant variables used multiple linear regressions. Analyses were conducted using JMP (v. 4 and v. 7, SAS Institute Inc.).

In defining change from baseline to follow-up for clinical periodontal measures, we used the second post-randomization examination (29–32 weeks of gestation) when it was available, and otherwise used the first post-randomization examination (21–24 weeks).

Results

Summary of sample population

Follow-up periodontal data were available for 722 women (87.7% of randomized women), including 645 who experienced a live full-term birth, 69 a live pre-term birth and six a spontaneous abortion (pregnancy loss before 20 weeks) or pre-term stillbirth (pregnancy loss between 20 weeks and 36 weeks 6 days). Two women had follow-up periodontal data but no birth outcome data. Women who experienced an event (spontaneous abortion or stillbirth or live pre-term birth) before 29–32 weeks were not recalled for a post-partum periodontal examination. For these women, changes in periodontal status were determined using baseline and 21–24-week clinical data, if available. The rate of live pre-term births, as a fraction of all live births, was lower in women who had follow-up periodontal data (69/714 or 9.7%) when compared with women who did not (13/79 or 16.5%).

Of those with follow-up periodontal data, 115 women (15.9%), including 60 controls, experienced progressive periodontitis, defined as an increase in CAL $\geqslant$ 3 mm. [Note: previously (Michalowicz et al. 2006), we reported progression based on adverse event reports made during the study, which were not always consistent with the study's periodontal measurements.] Forty-six women (6.4%), including 26 controls, lost at least 3 mm of clinical attachment *at more than one* tooth site. Overall though, only a small fraction of all tooth sites were affected (0.17% in the treatment group and 0.28% in the control group). Based on Offenbacher et al. (2006), 135 (18.7%) women had progressive disease, including 30/352 (8.5%) treatment women and 105/370 (28%) untreated controls.

Nine women (three treatment, six controls) experienced progressive disease at six or more tooth sites. Of these, one treatment group subject and two controls received full-mouth scaling and root planing, one control received full-mouth scaling and root planing plus systemic antibiotics and one treatment group subject received systemic antibiotics alone. The others were treated after delivery or declined treatment. Of the 54 controls who lost clinical attachment at fewer than six sites, 25 were treated before delivery (22 received localized scaling and root planing at the affected teeth and three had the lesion excised or the affected tooth extracted).

Gestational age at the end of pregnancy

Disease progression defined as any CAL $\geqslant$ 3 mm. Overall, pregnancies ended before 37 weeks in 64/605 (10.6%) women with stable disease and in 11/115 (9.6%) women with progressive disease. Figure 1 depicts the distribution of gestational ages of pregnancies ending before 37 weeks in all women, by disease progression status. The curve for women

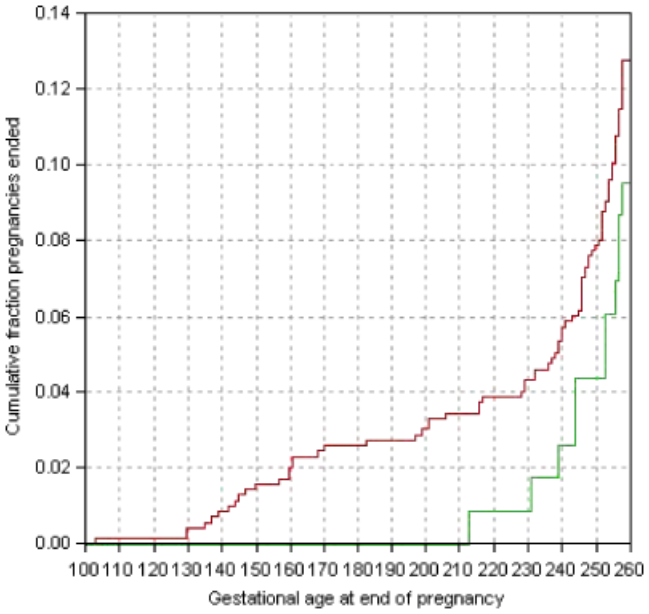

Fig. 1. Distribution of gestational age at the end of pregnancy in all the women, by disease progression defined as an increase in attachment loss $\geqslant$3 mm. The red and green lines show the cumulative fraction of pregnancies ended for each gestational age; the red line denotes the number of women who had no progressing sites after baseline, and the green line represents the number of women who had at least one progressing site ($p = 0.31$).

with non-progressive disease (red line) lies above that for women with progressive disease (green line), indicating that the latter group tended to have fewer pre-term events and longer gestation. The difference, however, was not statistically significant ($p = 0.31$. Table 1). The distributions of gestational age did not differ between progressing and non-progressing groups in control women only (Table 1). Pregnancies ended before 37 weeks for 7/60 (11.7%) controls with progressive disease, only one of which occurred before 32 weeks. When considering all subjects, the provision of additional or rescue treatment did not significantly affect gestational age at delivery ($p = 0.43$ from Cox regression, $p = 0.41$ for the interaction between rescue treatment and group assignment in the same regression). For controls only, the provision of rescue treatment did not significantly affect gestational age at delivery ($p = 0.32$).

Disease progression defined by Offenbacher et al. (2006). The distribution of gestational ages at the end of pregnancy did not differ significantly between women with and without disease progression when considering all the women ($p = 0.54$, Fig. 2) or controls alone ($p = 0.33$). Again, the provision of additional or rescue treatment did not significantly affect gestational age at delivery in all the subjects ($p = 0.47$) or in controls alone ($p = 0.67$).

Change in disease status according to change from baseline in percentage of sites BOP. Women were grouped according to change in the percentage of sites with BOP. The 33rd and 67th percentiles of the distribution of change (defining the boundaries between the first and second and between the second and third tertiles) were -20.2 and -1.8 for all the women and -7.1 and 0.7 for controls alone, where negative values indicate a reduction from baseline in BOP.

Considering all the women, tertiles of change in percentage BOP had a borderline significant association with gestational age at the end of pregnancy ($p = 0.06$). Within each of the treatment groups (treatment or control), those in the lowest (best) tertile tended to have fewer pre-term events and longer gestation than those in the highest (worst) tertile. Control women who experienced relatively large reductions in BOP had the most favourable birth outcomes whereas treatment group women who experienced the smallest improvements in BOP had the least favourable birth outcomes. These differences, however, were not statistically significant. Considering controls alone, gestational age at the end of pregnancy did not differ significantly among the tertiles of change in BOP ($p = 0.43$, Table 1).

Table 1. p values from Cox regressions (for analysis of all women) and log rank test (for controls only) comparing the distributions of gestational age at the end of pregnancy in women with and without changes from baseline in their periodontal condition

	All women	Controls only
Periodontitis progression		
CAL $\geqslant$ 3 mm (yes/no)	0.31	0.73
Offenbacher and colleagues definition (yes/no)	0.54	0.33
Change in percentage of sites with BOP		
Comparing among tertiles*	0.06	0.43

*For all women, tertiles I–III were -20.2 or less, > -20.2 but < -1.8, and -1.8 or greater, respectively, where negative values indicate an improvement from baseline. For controls only, tertiles I–III were -7.1 or less; > -7.1 but < 0.7, and 0.7 or greater.
CAL, clinical attachment loss; BOP, bleeding on probing.

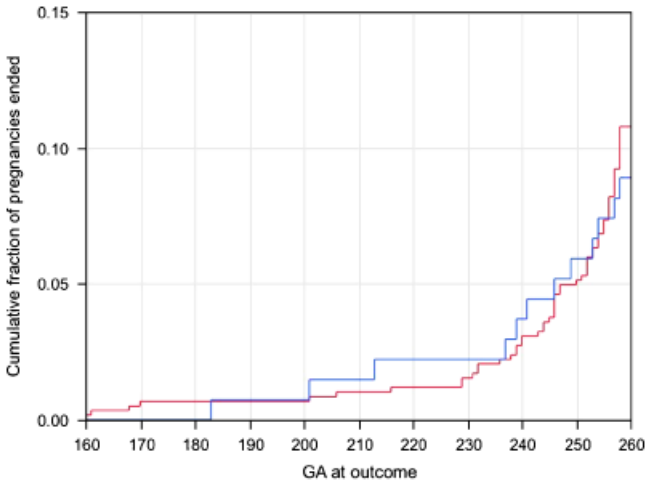

Fig. 2. Gestational age at the end of pregnancy for all women, by disease progression according to Offenbacher et al. (2006). The red and blue lines show the cumulative fraction of pregnancies ended for each gestational age; the red line shows the number of women who did not progress, and the blue line represent the number of women who did progress ($p = 0.54$).

Table 2. Mean birth weight (g, $\pm$ SEM), by change in maternal periodontal status

	All women	Controls only
Disease progression defined as CAL $\geqslant$ 3 mm		
Yes*	3295 $\pm$ 64	3319 $\pm$ 93
No	3184 $\pm$ 26	3154 $\pm$ 39
Disease progression according to Offenbacher et al. (2006)		
Yes†	3236 $\pm$ 61	3320 $\pm$ 59
No	3247 $\pm$ 25	3226 $\pm$ 37
Tertile of change in percentage of sites with BOP‡		
I	3248 $\pm$ 54	3250 $\pm$ 55
II	3271 $\pm$ 38	3237 $\pm$ 55
III	3199 $\pm$ 53	3271 $\pm$ 53

*$N = 115$ in all women, 60 in controls.
†$N = 135$ in all women, 105 in controls.
‡Table 1 footnote for details.
CAL, clinical attachment loss; BOP, bleeding on probing.

Birthweight

Table 2 lists the average birth weights according to change in maternal periodontal status. Among all women, the mean birthweight was higher, although not significantly, for women with progressive disease, defined as any CAL $\geqslant$ 3 mm, compared with those with non-progressing conditions ($p = 0.11$). The same trend was noted in the controls only ($p = 0.11$). The mean birthweight did not differ significantly between groups with and without disease progression as defined by Offenbacher et al. (2006) when considering all the women ($p = 0.87$) or controls only ($p = 0.17$). The mean birthweight also did not differ

significantly among groups according to tertiles of change in BOP, considering all the women ($p = 0.54$) or controls only ($p = 0.90$, Table 2).

Pre-eclampsia

Finally, we tested whether the relationship between these pregnancy outcomes and periodontal disease progression differed in pre-eclamptic and non-pre-eclamptic women as suggested by others (Riche et al. 2002). Pre-eclampsia was defined as pregnancy-associated hypertension occurring 4 h to 14 days after an episode of pregnancy-associated proteinuria in a woman with no previous hypertension or proteinuria; pregnancy-associated hypertension in conjunction with pulmonary oedema or thrombocytopenia ($< 100\,000$ platelets/mm^3); or the syndrome of haemolysis, elevated liver enzymes and low platelets (HELLP). For these analyses, we included all treatment and control women and carried out Cox regressions with independant variables pre-eclampsia (yes/no) and tertile of change in percentage of BOP and their interaction. Forty-six women with follow-up periodontal data were diagnosed with pre-eclampsia.

Pre-eclampsia was strongly associated with delivery before 37 weeks (relative hazard = 4.8, 95% CI 2.7–8.4) and low birthweight [adjusted average ($\pm$ SE) in non-pre-eclamptic women = 3287 ($\pm$ 26); in pre-eclamptic women, 2868 ($\pm$ 104); $p < 0.001$]. However, the interaction between pre-eclampsia and tertile of change in the percentage of sites with BOP was not statistically significant ($p > 0.1$), indicating that pre-eclampsia did not affect the relationship (or lack thereof, in this case) between change in BOP and risk for pre-term delivery or low birthweight.

Discussion

The OPT Study was a randomized clinical trial designed to determine whether non-surgical periodontal treatment of pregnant women improves pre-term birth rates. The present study – secondary data analyses of the OPT Study data – was conducted to explore the relationships between periodontal disease progression and birth outcomes. Neither maternal periodontal disease progression after 13–17 weeks of gestation nor change in the percentage of tooth sites with BOP was significantly associated with risk for pre-term delivery or low birthweight. We found similar results when testing for associations separately in all study subjects and in untreated controls alone. This suggests that the relationship between change in periodontal status and birth outcomes is largely unaffected by non-surgical periodontal treatment. Our findings are consistent with an earlier study that found no significant association between progressive periodontitis and the risk for pre-term birth at < 37 weeks (Offenbacher et al. 2006). In this earlier report, however, progressive disease was associated with very pre-term birth risk (< 32 weeks). In contrast, we found no evidence that progressive disease increases a woman's risk for very pre-term delivery. Of the 115 women in the current study who experienced progressive disease, defined as CAL $\geqslant 3$ mm, only one delivered before 32 weeks (Fig. 1). Of the 135 women who met Offenbacher et al.'s (2006) criteria for disease progression, only three (2.2%) delivered before 32 weeks (Fig. 2).

Our study has several limitations. First, we analysed data from a clinical trial and not from a prospective cohort study. The trial was not designed to address the hypothesis of the current analyses. Notably, 413 women in this trial were randomized to receive treatment during their pregnancy, and 395 received this care. Because treatment may have confounded the relationship between disease progression and pregnancy outcomes, we analysed all subjects and included in the Cox regression models treatment group assignment. We also analysed the smaller group of untreated controls, only three of whom received full-mouth root planing before delivery. The consistency of findings between these groups provides some assurances that our findings are robust.

Another limitation of the current study is the number of women who were missing follow-up periodontal data. Although follow-up periodontal data were available for 87.7% of all OPT women, a disproportionate number of women with early ''events'' were missing these data. For example, while 90% (645/711) of full-term women and 85% (69/82) of live-pre-term women had follow-up periodontal data, only 31% (6/19) of women who experienced a spontaneous abortion or stillbirth had follow-up data. As mentioned earlier, this deficiency was a result of the study protocol, which exited women from the trial once their pregnancy ended. Without post-baseline data, we could not determine periodontitis progression in these women. Thus, our findings regarding associations between disease progression and early pregnancy losses should be viewed with particular caution.

We also offered treatment to all women with progressive periodontitis. Because periodontal treatment is not contraindicated during pregnancy and because we asked participants not to seek dental care outside of the trial, we could not ethically withhold care from women with documented progressive periodontitis. Thus, any effect that progressive periodontitis may have on these pre-term birth and low birthweight would have been mitigated by rescue treatment. In a sense, these control women ''crossed over'' into the treatment group, which may have limited our ability to detect associations between progressive disease and adverse pregnancy outcomes. However, when compared with women randomized to the treatment group, these control women received treatment only after their condition worsened and at a later point in their pregnancy. Thus, any effects that periodontal disease activity had on the foetal–placental unit would have been undisturbed up to the time of rescue treatment. This may be particularly relevant because increases in levels of inflammatory mediators in the periodontal tissues – which have been suggested to lie in the causal pathway between this periodontitis and adverse pregnancy outcomes – often precede the onset of clinical disease. For example, levels of prostaglandin E2 begin to increase in gingival crevicular fluid several months before disease is detected clinically (Offenbacher et al. 1986, Preshaw et al. 1999). Despite this, however, it is still possible that longer exposures to inflammatory mediators or bacteria associated with disease progression are necessary to adversely affect birth outcomes. Finally, repeated periodontal therapy may activate immune responses, which in turn affect pregnancy outcomes. One way this might occur is through increased Toll-like receptor 4 expression on placental trophoblasts, which has been associated with pre-eclampsia, but not pre-term labour (Kim et al. 2005).

In addition, not all women with progressive disease received initial treatment or re-treatment before delivery. As mentioned, only three of six controls

with generalized progressive disease were treated before delivery. Similarly, 25 of 54 controls with localized disease received any treatment before delivery. The remaining controls with progressive disease were treated after delivery or refused treatment. Furthermore, we found no evidence that rescue treatment (in controls) or additional treatment (in treatment group subjects) had a significant effect on gestational age at delivery (all p values >0.3). Because of the relatively small number of untreated subjects with progressive disease, however, we had low statistical power to detect significant effects.

Finally, teeth that were deemed non-restorable were extracted before 21 weeks of gestation in both the treatment and the control groups. We did not enrol women if we thought they would no longer meet the periodontal disease enrolment criteria following essential dental treatment, which included extractions. Nonetheless, tooth extraction is a form of periodontal intervention that was performed following randomization and for both groups. To the extent that this treatment improved a woman's periodontal condition, it may have masked any effect of disease progression (and periodontal treatment) on pre-term delivery or low birthweight. To further explore this issue, we compared changes in clinical measures between controls who had and did not have teeth extracted as part of essential dental treatment. One hundred and eleven control women had at least one tooth extracted (63 had one and 32 had two). The change from baseline in the percentage of tooth sites with BOP, however, did not differ significantly between women who did and did not have teeth extracted (-1.7% points *versus* -1.5% points, respectively; $p = 0.94$). The percentage of controls with progressive disease, defined as CAL $\geqslant 3$ mm, also did not differ significantly between these groups (15.3% *versus* 14.4%, $p = 0.82$). Thus, tooth extractions as part of essential dental care did not significantly alter a control woman's risk for progressive disease. We cannot rule out the possibility, however, that extractions exerted some systemic effect that altered a woman's risk for adverse pregnancy outcomes.

The relatively small number of women with pre-term deliveries (75), progressive periodontitis (115 or 135, depending on the definition used) and pre-eclampsia (46) limited our power to detect slight associations among these outcomes. In general, women with progressive disease did not tend to have worse pregnancy outcomes than those without progressive disease. For example, the distribution curve of gestational ages at delivery for women with progressive disease lies below that for women without progressive disease (Fig. 1), which indicates that the latter group tended to have more and earlier pre-term deliveries than the former. In addition, the mean birthweights tended to be higher, but not significantly so, in progressing compared with non-progressing women (Table 2). Thus, there is no reason to infer that our failure to find a positive association between disease progression and adverse pregnancy outcomes was because the sample lacked statistical power.

There are also several important differences between our current study and a previous one that reported an association between disease progression and risk for very pre-term birth. Offenbacher et al. (2006) examined 1020 women early in the second trimester and again post-partum. In contrast, our follow-up examinations were conducted at 29–32 weeks of gestation. It is possible that women who experienced progressive disease after the OPT Study's final exam were at an increased risk for pre-term birth or low birthweight infants. It is unlikely that these events occurred before 32 weeks, however, because this is when we last examined women. Also, all women in our study had periodontitis at baseline. Periodontitis may be a risk factor for adverse pregnancy outcomes despite our previous finding that non-surgical treatment does not reduce this risk (Goldenberg & Culhane 2006). If true, OPT women would have been at an increased risk for these outcomes as a result of their existing disease, and our study may have lacked the statistical power to detect any small but additional increase in risk attributed to disease progression. Offenbacher et al. (2006) did not specify how many of their women with progressive disease were healthy at baseline. It is possible that very pre-term birth is associated with disease progression only in previously healthy women. Finally, as mentioned earlier, we provided periodontal treatment to roughly half of these women before 21 weeks of gestation. Offenbacher and colleagues used a prospective cohort study design that did not include treatment.

While most studies have found an association between periodontitis and risk for pre-term birth and low birthweight (Xiong et al. 2006), our findings are consistent with several other reports (Davenport et al. 2002, Noack et al. 2005, Vettore et al. 2008). For example, Vettore et al. (2008) reported that women with the most extensive periodontal pocketing (PD $\geqslant 4$ mm) were at a significantly *lower* risk for delivering a low birthweight infant. Similarly, Davenport et al. (2002) found a significant inverse or negative relationship between the mean pocket depth and the risk for pre-term birth and low birthweight. While most studies suggest that maternal periodontitis is associated with an increased risk for adverse pregnancy outcomes, large epidemiological studies and additional clinical trials are needed to further explore the nature of this association, which appears to be present in some but not all populations.

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Clinical Relevance

Scientific rationale for the study: Maternal periodontitis and disease progression during pregnancy have been associated with an increased risk for pre-term birth. We used data from a recent clinical trial to explore the possible associations between progressive periodontitis and birth outcomes.

Principal findings: The distribution of gestational age at delivery and mean birthweights did not differ significantly between women who experienced progressive periodontitis and those who did not.

Clinical implication: While it is important to treat dental diseases, including periodontitis, during pregnancy, women whose periodontal condition worsens during pregnancy are not at an increased risk for adverse pregnancy outcomes.