# An umbrella review of systematic reviews of the evidence of a causal relationship between periodontal disease and adverse pregnancy outcomes: A position paper from the Canadian Dental Hygienists Association

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## ABSTRACT

Previous position papers have confirmed associations between periodontal disease and adverse pregnancy outcomes. Causal associations have not been confirmed and have been the source of much confusion for the profession and public. **Aim:** To investigate whether sufficient evidence exists for a causal relationship between periodontal disease and adverse pregnancy outcomes. **Methods:** The PICO question was "For adults in good general health who are diagnosed with periodontal disease, will receiving non-surgical periodontal therapy (NSPT), as compared to not receiving non-surgical periodontal therapy, lower their risk for adverse pregnancy outcomes?" Only systematic reviews (SRs) with or without meta-analyses (MAs) of randomized controlled trials published in the English language between 2007 and 2019 were included. Databases searched included PubMed, MEDLINE, EbscoHost, CINAHL, Scopus, Cochrane Registry of Systematic Reviews, and Clinical Trials Registry. Quality assessments were conducted by both authors using the PRISMA checklist. The Bradford Hill criteria were used to determine evidence for causality. **Results:** Of 37 records retrieved for adverse pregnancy outcomes, 9 met the criteria for inclusion and were analysed. None showed that NSPT lowers the risk for adverse pregnancy outcomes. **Conclusions:** Bradford Hill criteria analysis failed to support a causal relationship between periodontal disease and adverse pregnancy outcomes based on the most current evidence available.

## RÉSUMÉ

Les énoncés de position précédents ont confirmé des associations entre la maladie parodontale et les effets indésirables de grossesse. Des associations causales n'ont pas été confirmées et ont été la source de beaucoup de confusion pour la profession et la population. **Objectif :** Étudier s'il y a suffisamment de preuves qu'un lien de causalité existe entre la maladie parodontale et les effets indésirables de grossesse. **Méthodologie :** La question de PICO était : «Les adultes en bonne santé générale, qui ont reçu un diagnostic de maladie parodontale, auront-ils une réduction de leur risque d'effets indésirables de grossesse s'ils reçoivent une thérapie parodontale non chirurgicale (TPNC), par rapport à ne pas recevoir de thérapie parodontale non chirurgicale?» Seules les revues systématiques (RS) avec ou sans méta-analyse (MA) d'essais comparatifs randomisés publiés en anglais entre 2007 et 2019 ont été incluses. Les recherches de bases de données ont été effectuées, entre autres, dans PubMed, MEDLINE, EbscoHost, CINAHL, Scopus, le registre de revues systématiques Cochrane et le registre des essais cliniques. Des évaluations de la qualité ont été menées par les deux auteurs à l'aide de la liste de vérification PRISMA. Les critères de Bradford Hill ont été utilisés pour déterminer la preuve de causalité. **Résultats :** Dans les 37 dossiers repérés sur les effets indésirables de grossesse. **Conclusions :** Les critères d'analyse de Bradford Hill n'ont pas réussi à appuyer un lien de causalité entre la maladie parodontale et des effets indésirables de grossesse selon les preuves les plus récentes offertes.

Keywords: adverse pregnancy outcomes, low birth weight, meta-analysis, oral health AND systematic reviews, periodontal disease, periodontal treatment, preeclampsia, preterm birth

CDHA Research Agenda categories: risk assessment and management; capacity building of the profession

## CANADIAN DENTAL HYGIENISTS ASSOCIATION POSITION STATEMENT

The Canadian Dental Hygienists Association acknowledges that, although associations between periodontal disease and adverse pregnancy outcomes have previously been established, there is insufficient evidence that periodontal disease causes adverse pregnancy outcomes.

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## INTRODUCTION

Relationships between periodontal disease and a number of systemic diseases have been proposed since the late 1800s when physicians speculated that bacteria from the mouth caused everything from brain abscesses to arthritis.<sup>1,2</sup> With the onset of "periodontal medicine" in the early 1990s, studies investigating the relationships between numerous oral and systemic conditions have increased, with inflammation now recognized as a common factor. Despite the amount of research published over the last 30 years, questions remain about the exact nature of these relationships. While relationships may be in the form of associations or correlations, they should not be assumed as causal.

Unfortunately, the differences between associations and causality are not well understood and the terms are often used interchangeably. A relationship merely describes how 2 variables *might* somehow be related or connected to each other. For instance, lung cancer rates are higher for people without a postsecondary education (who tend to smoke more), but that does not mean that someone can reduce his or her cancer risk just by getting a college or university education.<sup>3</sup> An "association" refers to "a relationship between an exposure (or a characteristic) and a disease that is statistically dependent; that is, the presence of one alters the probability of observing the presence of the other. An association is a necessary condition of a causal relationship, but not all associations are causal. If there is no association, the variables are said to be independent."<sup>4</sup>

A correlation is a relationship in which there is a "Linear association between two continuous or ordinal variables. The measure of the correlation is the correlation coefficient, which ranges from 1 (perfect positive association, e.g., as one variable increases the second one also increases at the same rate) through 0 (no association) to a -1 (perfect negative association, e.g., as one variable increases, the second one decreases at the same rate)."<sup>4</sup>

In order for a relationship to be coined as "causal," actual "cause and effect" must be determined through a very rigorous set of criteria. One must be able to state with certainty that "A" causes "B" (a specific exposure has been shown to cause a specific outcome).<sup>4</sup> Randomized clinical trials (RCTs) provide the strongest evidence of cause and effect, rather than the outcome happening by chance. These experimental studies are the most methodologically challenging and ones in which the researcher controls or manipulates the variables (i.e., the intervention, its timing and dose) under investigation, such as in testing the effectiveness of a treatment, as compared to another treatment or a placebo.<sup>5</sup>

Often, when clinicians read a research article that is reporting a correlation or an association between an oral disease and a particular outcome of interest, they automatically, and incorrectly, jump to the conclusion that the relationship is causal. Prime examples of such misinterpretations are frequently found with proposed oral–systemic linkages, such as the assumption that periodontitis is one cause of heart disease or of adverse pregnancy outcomes, or that stress causes periodontitis. It is important for clinicians to understand that correlations and associations do not imply or equal causality. In fact, incorrect assumptions of causality are a major public health concern. From a public health perspective, no evidence should be considered causal unless it has gone through very rigorous scrutiny using standard public health guidelines such as the Bradford Hill criteria for causality<sup>6</sup> (Table 1).

In 2004, Lux and Lavigne<sup>7,8</sup> published a position paper for the Canadian Dental Hygienists Association (CDHA) in 2 parts, outlining the nature of the proposed linkages between periodontal disease and 4 systemic conditions: cardiovascular diseases, preterm low birth weight babies, respiratory diseases, and diabetes. Updates to those first position papers were published in the *Canadian Journal of Dental Hygiene* in November/December 2006<sup>9</sup> and January/February 2007,<sup>10</sup> in which the author reported associations between periodontal disease and cardiovascular diseases, diabetes, adverse pregnancy outcomes, and respiratory diseases (in particular, pneumonia in health-compromised seniors).

A recent systematic mapping of trial registers of clinical research trials conducted on periodontal medicine revealed 57 conditions that are currently hypothesized to be linked with periodontal diseases.<sup>11</sup> While it is beyond the scope of this current position paper to explore all of these proposed linkages, the status of 10 of these hypotheses will be evaluated in a series of position papers written by the same authors and released in the coming months by CDHA. The first paper, evaluating the evidence of a causal relationship between periodontal disease and cardiovascular diseases was published in February 2020 in this journal.<sup>12</sup> Forthcoming position papers will assess the nature of the relationships between periodontal disease and respiratory diseases, diabetes, obesity, rheumatoid arthritis, Alzheimer disease, end-stage renal disease, inflammatory cancers, and influenza.

The purpose of these updated position papers is to review the research undertaken since the publication of the last CDHA position papers in 2006 and early 2007 on these proposed relationships. Unlike the methodology used for the previous position papers and updates, this investigation is more specific in looking at whether the state of the evidence has evolved from one of associations to one of actual causality. Determining a causal relationship requires studies that have examined an intervention, thus only the highest levels of evidence will be sought for this update. This position paper is the second in the series, and investigates whether a causal relationship exists between periodontal disease and adverse pregnancy outcomes.

Table 1. The Bradford Hill criteria for causality <sup>6</sup>	Table 1.	. The	Bradford	Hill	criteria	for	causality <sup>€</sup>
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Criteria	Meaning
Strength of association	A strong association is more likely to have a causal component than is a modest association. Strength of the association is determined by the types of existing studies. The highest-level studies from the evidence pyramid would represent the strongest associations (i.e., RCTs and systematic reviews with meta-analyses). Results from these studies must demonstrate an odds ratio or relative risk of at least 2.0 or above in order to be meaningful. Anything between 1 and 2 is weak while >2 is moderate and >4 is considered strong.
Consistency	A relationship is repeatedly observed in all available studies.
Specificity	A factor influences specifically a particular outcome or population. The more specific an association between a factor and an effect, the greater the probability that it is causal.
Temporality	The cause must precede the outcome it is assumed to affect (e.g., smoking before the appearance of lung cancer). Outcome measured over time (longitudinal study).
Biological gradient (dose-response)	The outcome increases monotonically with increasing dose of exposure or according to a function predicted by a substantive theory (e.g., the more cigarettes one smokes, the greater the chance of the cancer occurring).
Plausibility	The observed association can be plausibly explained by substantive matter (i.e., biologically possible).
Coherence	A causal conclusion should not fundamentally contradict present substantive knowledge. (Studies must not contradict each other.)
Experiment	Causation is more likely if evidence is based on randomized experiments or a systematic review of randomized experiments. However, these RCTs may not be ethically possible and thus prospective rather than experimental studies, such as cohort studies, may be the highest level of evidence available.
Analogy	For analogous exposures & outcomes an effect has already been shown (e.g., effects first demonstrated on animals or an effect previously occurring on humans such as the effects of thalidomide on a fetus during pregnancy.)

Source: Lavigne SE. From Evidence to Causality: How Do We Determine Causality? [Online course]. 2018. Available from: www.dentalcare.com/en-us/professionaleducation/ce-courses/ce530

# **METHODOLOGY**

An overarching PICO question was developed for the first 5 oral-systemic connections to be explored in this series of position papers. For adverse preganancy outcomes, the PICO question was customized as follows: "For adults in good general health who are diagnosed with periodontal disease (Population), will receiving non-surgical periodontal therapy (NSPT) (Intervention), as compared to not receiving NSPT (Comparison group), lower their risk for adverse pregnancy outcomes? (Outcome)"

# **Eligibility criteria**

Both authors independently searched the literature, limiting the search to systematic reviews (SRs) with or without meta-analyses (MAs) of intervention studies using the following inclusion and exclusion criteria. SRs and MAs of observational studies were excluded.

## Search strategy

Databases searched included PubMed, MEDLINE, EbscoHost, CINAHL, Scopus, Cochrane Registry of Systematic Reviews, and Clinical Trials Registry (clinicaltrials.gov). Additionally, bibliographies of retrieved articles were searched for further relevant systematic reviews and meta-analyses and added when appropriate. The keywords used for each search were as follows: adverse pregnancy outcomes; preterm birth; low birth weight; preeclampsia; periodontal disease; periodontal treatment; oral health AND systematic reviews; meta-analysis. Search strategies (limited to publications after 2007 and in the English language) were as follows:

- adverse pregnancy outcomes and periodontal disease and systematic reviews
- adverse pregnancy outcomes and periodontal treatment and systematic reviews
- adverse pregnancy outcomes and oral health and systematic reviews

## Study selection

Both authors independently screened the titles and abstracts of all articles retrieved by the search using the inclusion criteria and then discussed their choices to reach consensus regarding their suitability for fulltext reading. Both authors independently reviewed the selected full-text articles and reached consensus on their inclusion or exclusion.

## Quality assessment

The methodological quality of the selected systematic reviews and meta-analyses was assessed blindly by both authors using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist tool.<sup>13</sup> Scores were then compared and discussed where inconsistencies occurred to reach consensus.

## Data extracted

The following information was extracted from each selected SR or MA and compiled in table format: year

#### Table 2. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Published between 2007 and 2019	Published before 2007
English language	Languages other than English
Systematic Reviews (SRs) with or without meta-analyses (MAs) of RCTs	Abstracts, posters, conference proceedings, editorials or commentaries, duplicate studies, narrative reviews, RCTs, observational studies/both cohort and case-control and systematic reviews of observational studies and/or case- control studies.
Studies involving humans	Animal studies (in vivo, ex vivo) and in vitro studies

#### Table 3. Adverse pregnancy outcomes screened articles included and deleted

	Included	Deleted	Reason for deletion
1.	lheozor-Ejiofor et al. 2017¹⁴ (15 RCTs) (Cochrane Review)	Spivakovsky 2018 <sup>25</sup> (critical summary of Iheozor-Ejiofor, Cochrane)	Duplicate (critical summary)
2.	Polyzos et al. 2010 <sup>15</sup> (1 RCT) (Greece)	Baccaglini 2011 <sup>26</sup> (critical summary of Polyzos)	Duplicate (critical summary)
3.	Kim et al. 2012 <sup>16</sup> (12 RCTs6 post-2008) (US)	Dasanyake 2013 <sup>27</sup> (critical summary of Kim)	Duplicate (critical summary)
4.	Chambrone et al. 2011 <sup>17</sup> (13 RCTs) (Brazil)	Leader <b>2011</b> <sup>28</sup> (critical summary of Chambrone)	Duplicate (critical summary)
5.	Rangel-Rincón et al. 2018 <sup>18</sup> 2-4 above included in this umbrella review (18 SRs, 19 intervention studies) (Columbia)	Vivares-Builes et al. 2018 <sup>29</sup> (Columbia)	99 SRs but all observational studies. Purpose was to establish association.
6.	Shah et al. 2013 <sup>19</sup> (SR of 13 RCTs) (India)	Corbella et al. 2016 <sup>30</sup> (Italy)	All case-control or cohort studies
7.	da Silva et al. 2017 <sup>20</sup> (4 RCTs) (Brazil)	Daalderop et al. <b>2018</b> <sup>31</sup> (The Netherlands)	23 SRs but all studies were cohort, case-control or CS
8.	Schwendicke et al. 2015 <sup>21</sup> (13 RCTs) (Germany, US, Denmark)	lde et al. 2013 <sup>32</sup>	No intervention studies
9.	Lopez et al. 2015 <sup>22</sup> (SR of 6 meta-analyses)		
10.		Abati et al. 2013 <sup>33</sup>	Only case-control studies
11.		Teshome et al. 2016 <sup>34</sup>	Only case-control studies
12.		Macones et al. 2010 <sup>35</sup>	Editorial of Polyzos
13.		Otomo-Corgel et al. 2012 <sup>36</sup>	Literature review

published, number of RCTs included, country of origin, methods used for assessing risk of bias, heterogeneity, outcomes measured, and conclusions of the findings.

## RESULTS

Thirty-seven records were retrieved in total from both the database searches and articles identified within these reviews. After eliminating duplicates and articles that were deemed ineligible based on the inclusion criteria, 9 studies<sup>14-22</sup> remained eligible for review. A flow diagram (Figure 1) illustrates the details of the selection process; Table 3 reports the reasons for elimination of the full-text articles.

Results of the quality appraisal of the 9 included SRs and MAs are shown in Table 4. Based on the 27 PRISMA checklist items, scores ranged from 11 to 27. Agreement between the 2 independent evaluators was close to 100% with scores being off by only 1 to 3 points. The quality of the studies was generally moderate to high with the exception of one study<sup>19</sup> that was deemed by both reviewers to be of very poor quality because of multiple inaccuracies in references as well as grammatical errors throughout. This study was removed from further discussion in this review.

None of the outcomes of the 9 systematic reviews and meta-analyses showed a positive result for NSPT lowering

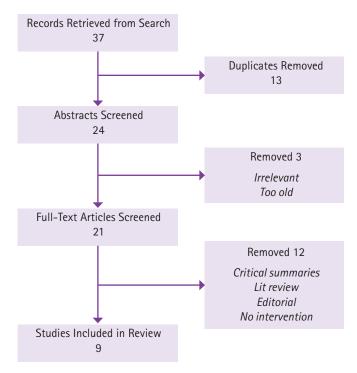


Figure 1. Adverse pregnancy outcomes search flow diagram

the risk for adverse pregnancy outcomes. Six of the studies showed no relationship between adverse pregnancy outcomes and scaling and root planing as an intervention, while 3 studies reported a "possible relationship" and one study reported a possible relationship but only with low birth weight. These results are illustrated in Table 5.

#### DISCUSSION

The purpose of this review was to explore the possible association between non-surgical periodontal therapy (NSPT) and the risk of preterm birth (PTB) and/or low birth weight (LBW) and/or pre-eclampsia. Nine systematic reviews, of which 7 contained a MA, were included in this review. Of the 2 studies without meta-analyses, one was an umbrella review<sup>18</sup> of 18 systematic reviews and the other, a systematic review of 6 meta-analyses.<sup>22</sup> There were numerous inconsistencies among the RCTs included in the 9 SRs with some reporting positive associations in their descriptive findings, but not supported in 4 of the 7 meta-analyses.

Conclusions reached in all 9 reviews were consistent in reporting no positive relationships between NSPT provided during the second trimester of pregnancy and the occurrence of preterm birth and/or low birth weight. The only systematic review that included studies on the effects of NSPT on pre-eclampsia was conducted by Kunnen and colleagues<sup>23</sup> and was included in the umbrella reviews by Rangel-Rincón.<sup>18</sup> No effect of periodontal treatment on the risk of pre-eclampsia was found in their metaanalysis. Two MAs<sup>16,21</sup> conducted subgroup analyses and found significant effects for preterm birth but only for studies conducted in low income countries where a high prevalence of low birth weight and preterm birth exists.

In the review by Chambrone et al.<sup>17</sup>, which included 13 trials involving 6813 women, despite positive results reported by more than half of the included studies, the MAs conducted in 11 of the trials showed that NSPT had little to no effect on pregnancy outcomes. Similarly, Polyzos et al.<sup>15</sup> concluded that treatment of periodontal disease could not be considered an efficient way to reduce the incidence of preterm birth based on the results of 3 separate meta-analyses performed on the 11 included studies involving 6558 pregnant women. One interesting finding in this review was that low-quality studies tended to overestimate the treatment effect in contrast to the high-quality trials which showed no effect. The authors cautioned the interpretation of data from low-quality RCTs in making clinical decisions.

Lopez et al.<sup>22</sup> in their umbrella review of meta-analyses concluded that, in 4 of 5 MAs, periodontal treatment did not reduce preterm birth rates. However, one MA found that preterm birth rates were reduced following periodontal treatment but only for groups at high risk of preterm birth. This finding was also reported in the SRs conducted by Kim et al.<sup>15</sup> and Schwendicke et al.<sup>21</sup>

The umbrella review by Rangel-Rincón et al.<sup>18</sup> of 18 systematic reviews, 11 of which included a meta-analysis, identified numerous methodological and conceptual gaps such as sample size, sociodemographic characteristics, type of masking, and control for confounders. Other glaring issues were the lack of a standard definition for periodontal disease as well as the inconsistency in the type and frequency of treatment provided in each study. For example, although this review investigated the effects of the most commonly used treatment (scaling and root planing) on adverse pregnancy outcomes, the gestational timeframes, frequencies for delivery of treatment, and individuals delivering the treatment varied, thus making it more difficult to draw valid inferences. Since the outcome of this umbrella review clearly did not support the effectiveness of scaling and root planing as an effective means of reducing the risk for adverse pregnancy outcomes, future research should explore other types of treatment.

Additionally, use of different indices to measure the magnitude of periodontal disease, as well as use of different outcome measurement criteria, could potentially have a major effect on the results. When uniform criteria are not used to define gestational age (for example, use of sonograms versus use of last menstrual period), there is potential for random or non-differential measurement error. An underestimation of the true effect could occur if equal amounts of measurement error are found in both treatment and control groups, which would then bias the risk ratios towards the null value. Variability was also

Author (Country)	PRISMA score	Heterogeneity	Risk of bias	Quality assessment instrument	Comments	Included meta- analysis of the SR
Rangel-Rincón et al. 2018 <sup>18</sup> (Columbia)	N/A (umbrella review of SRs)	N/A (umbrella review of SRs)	N/A (umbrella review of SRs)	N/A (umbrella review of SRs)	Very thorough umbrella review	No (umbrella review)
Iheozor-Ejiofor et al. 2017 <sup>14</sup> (Cochrane Review)	25/27	High	High	Cochrane's risk of bias tool	15 RCTs (7161 participants) NSPT/PTB/LBW graded the evidence as low	Yes
da Silva 2017 <sup>20</sup> (Brazil)	24/27	Moderate	Moderate/High	Cochrane's risk of bias tool	4 RCTs included (2006, 2013, 2015, 2015) NSPT/PTB/LBW	Yes
Schwendicke et al. 2015 <sup>21</sup> (Germany, US, Denmark)	18/27	High	Unclear	Cochrane's risk of bias tool	13 RCTs included (6283 participants) NSPT/PTB/LBW	Yes
Lopez et al. 2015 <sup>22</sup>	18/27	Reported individually per clinical trial	Reported individually per clinical trial	Reported individually per clinical trial	Systematic review of 6 meta- analyses	No (SR of 6 MAs)
Shah et al. <b>2013</b> <sup>19</sup> (India)	12/27	High	Unclear	Cochrane's risk of bias tool	13 RCTs NSPT/PTB/LBW Poor Quality SR overall	Yes
Kim et al. 2012 <sup>16</sup> (US)	25/27	High	Low	Cochrane's risk of bias tool	12 RCTs SRP/PTB	Yes (11 studies included)
Chambrone et al. 2011 <sup>17</sup> (Brazil)	22/27	High	Low	Cochrane's risk of bias tool	13 RCTs SRP/SRP with antibiotics PTB/LBW	11 of the 13 studies included in MA
Polyzos et al. 2010 <sup>15</sup> (Greece)	24/27	High	Low	Cochrane's risk of bias tool	11 RCTs (6558 participants) SRP/PTB/LBW	Yes (3 separate MAs on 11 studies)

Table 4. Quality appraisal and summary of the systematic reviews/meta-analyses (n = 9)

noted in the definitions of adverse pregnancy outcomes, which makes comparisons difficult. In addition to the 3 adverse pregnancy outcomes explored in this review, other neonatal complications, such as still birth and spontaneous abortion, warrant futher exploration.

A summary of inconsistencies between studies identified by several authors of the included systematic reviews is found in Table 6. These issues and inconsistencies will need to be addressed in future studies as they can affect case selection leading to selection bias, the overall quality of the study, and the ability to make comparisons. The umbrella review authors recommended that future research studies follow the recommendations for epidemiological surveillance of periodontal diseases in population studies.<sup>18</sup>

Using the 9 Bradford Hill criteria for causation outlined in Table 1, it is clear that several of the criteria have not been met in these studies. Therefore one can conclude at this time there is not sufficient evidence to support a causal relationship between periodontal disease and adverse pregnancy outcomes. For example, beginning with "strength of association," although the highest levels of evidence (SRs & MAs) have been reviewed in this paper, none of the 9 SRs/MAs provided sufficient evidence of a strong enough association. The second criterion of "consistency" has definitely not been met as studies are inconsistent in their findings. Similarly, the criterion of "specificity" has not demonstrated that, in every instance, the outcome will be the same. The criterion of "temporality" has been met but only in some studies, where pregnant women in high-risk populations with periodontal disease have experienced adverse pregnancy outcomes. Studies investigated in this review also have not demonstrated a "dose-response" outcome comparing results with various magnitudes of periodontitis. The criterion of "biological plausibility," however, has been met as it is possible that elevated levels of inflammatory cytokines present during periodontitis could have an effect on premature rupture of the membranes leading to preterm birth. The criterion of "coherence" has not been demonstrated based on the inconsistencies and contradictory findings. The criterion of "experiment" also has failed to demonstrate consistent results through RCTs and SRs /MAs of these studies. Finally, the last criterion of "analogy," although the weakest, was not explored in this review. Thus, of the 9 criteria, only 2 can be said to have been fulfilled (Table 7).

## Table 5. Primary outcomes of retained studies

	Preterm Birth and Low Birth Weight	
Outcome 1 No relationship	Outcome 2 Possible relationship	Outcome 3 Positive relationship
Polyzos et al. 2010	Kim et al. 2012 (only in high risk groups)	None
da Silva et al. 2017	Schwendicke et al. 2015 (only in populations with	
Chambrone et al. 2011	high occurrence >20%)	
lheozor-Ejiofor et al. 2017 (preterm birth)	lheozor-Ejiofor et al. 2017 (low birth weight)	
Rangel-Rincón et al. 2018	Shah et al. 2013 BUT (better studies needed to demonstrate cause)	
Lopez et al. 2015		

Table 6. Summary of issues identified by authors of systematic reviews of RCTs

- 1. Inconsistency in defining periodontal disease and periodontal status
- 2. Inconsistency in the type of periodontal treatment provided, timing, frequency, clinician
- 3. Quality of studies (methodological shortcomings):
  - low quality supported a beneficial effect of treatment for PTB & LBW (high heterogeneity); overestimated treatment effect
  - high quality provided clear evidence that no effect of treatment exists
- 4. Publication bias: studies showing no/negative effect may not have been published
- 5. Evidence does not support SRP for reducing the rate of PTB
- 6. Gingivitis and periodontitis in the same meta-analysis; questionable
- 7. Treatment effectiveness should be measured
- 8. Selection criteria: high-risk & low-risk individuals combined; taking medication and other dental treatment not reported
- 9. Is SRP the preferred treatment (vs. mouth wash or antibiotics)?
- 10. Other conditions, e.g., smoking, not reported or evaluated

## CONCLUSION

Based on findings from the 9 SRs/MAs investigated in this current review, one can state with confidence that the answer to the PICO question: "For pregnant women in good general health who are diagnosed with periodontal disease, will receiving non-surgical periodontal therapy, as compared to not receiving non-surgical periodontal therapy, lower their risk for adverse pregnancy outcomes?" is "No." Numerous issues exist with published studies, which may have influenced these results. Future studies will need to focus on correcting these inconsistencies, particularly by identifying 1) a standard case definition of periodontal disease; 2) the type and frequency of the intervention; and 3) the target population. In addition, future studies should also investigate other types of interventions and measure their effectiveness.

It is interesting to note that, in August 2013, the American College of Obstetricians and Gynecologists Committee on Health Care of Underserved Women released an opinion piece entitled "Oral health care during pregnancy and through the lifespan."<sup>24</sup> This piece stated there was a lack of evidence that prenatal oral health care improves pregnancy outcomes. The college did, however, indicate that receiving oral health care during pregnancy is safe, and acknowledged that improvements in oral health improve general health by reducing the risk of transmission of cariogenic bacteria to children.

While 2 previous CDHA position papers on this topic have established associations between periodontal disease and adverse pregnancy outcomes, neither of those papers investigated a causal link. This position paper explored whether periodontal disease was causally related to adverse pregnancy outcomes. Its findings provide clear evidence that, although associations have been established, no causal link exists at this time between periodontal disease and adverse pregnancy outcomes. This evidence will enable the dental hygiene practitioner to clarify the nature of this relationship with their clients based on the most current research.

Bradford Hill criteria	Met	Not Met
Strength of association		Х
Consistency		Х
Specificity		Х
Temporality	X (in a few studies	;)
Dose-response		Х
Biological plausibility	Х	
Coherence		Х
Experiment		Х
Analogy	Not explored	Not explored

#### Table 7. Bradford Hill criteria analysis

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## CONFLICTS OF INTEREST

The authors have declared no conflicts of interest.

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