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Dental amalgams and risk of gestational hypertension in the MIREC study

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ABSTRACT

Background: The potential association between the presence or replacement of dental amalgams and gestational hypertension (GH) is unclear.
Objective: To assess the association between the presence or replacement of dental amalgams and the risk of GH in a prospective cohort study.
Methods: We assessed dental amalgam status (presence or replacement), blood mercury concentrations, and measured blood pressure (BP) in 1817 pregnant women recruited in 10 Canadian cities. BP was assessed in each trimester of pregnancy and mercury concentrations in 1st and 3rd trimesters. Logistic regression analysis was performed to estimate the adjusted odds ratios (aOR) and 95% confidence intervals (CI) for the associations between dental amalgam status and GH. Concurrent measures with systolic BP (SBP) and diastolic BP (DBP) were assessing through linear generalized estimating equations.
Results: Dental amalgam status was weakly statistically correlated with mercury concentrations but there was no evidence of an association with GH in women having 1–4 (aOR = 1.31 (0.92, 1.85)) or ≥ 5 dental amalgams (aOR = 1.32 (0.86, 2.04)), compared to women without amalgam reported at first trimester. Dental amalgam replacement reported in the first or third trimester was similarly not associated with GH (aOR = 0.75 (0.40, 1.42) and 0.73 (0.39, 1.34), respectively) but with SBP (beta = −1.58 (−2.95, −0.02)).
Conclusion: We found weak correlations between dental amalgams and blood mercury among pregnant women. However, the presence of dental amalgams or their replacement was not associated with GH but with decreased SBP for the replacement. Further studies are required.

1. Introduction

Gestational hypertension with or without preeclampsia (GH) [1] is presented in 10% of pregnancies [2]. Its etiology remains uncertain [3]. Exposure to metals has been reported to be associated with GH [4], however findings are not consistent [5,6]. In particular, previous studies have suggested that mercury might induce hypertension [4,7,8] through increased oxidative stress, reduced nitric oxide bioavailability, endothelial dysfunction and vasoconstriction [7,8]. Dental amalgams, restorative materials that have been used for more than 150 years [9], contain metals (approximately 50% of elemental mercury) [9]. They can release small amounts of elemental mercury into the body [10–12] for many years [13]. To date, no one has explored the possible association between dental amalgam status (presence or replacement) and the risk of GH.

Mercury has been found in the blood of pregnant women at variable levels [14,15]. The variability in blood mercury attributed to dental amalgams in pregnant women has been estimated at 6.47% compared to the 8.75% for seafood consumption [16]. One study has estimated that the majority (> 70%) of Hg in urine from individuals with < 10 dental amalgams is derived from ingestion of methyl mercury in fish [17]. In the Canadian Health Measures Survey (2007–2009), mean urinary mercury increased with the number of amalgam surfaces but was found to be significantly lower than the values considered to pose any risks for health [18]. Moreover, dental amalgam removal and replacement may be associated with higher prenatal exposure to mercury compared to new amalgam emplacement [19]. Some studies have suggested that dental amalgams can adversely impact health [20–25] including blood pressure [26]. Thus, our objective is to explore the potential association between dental amalgam status (presence or

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replacement) and the risk of GH.

2. Methods

2.1. Study design and population

Our analysis is based on data from the MIREC Study (Maternal-Infant Research on Environmental Chemicals) which is a prospective cohort study of 2001 pregnant women recruited between 2008 and 2011 in 10 Canadian cities (Vancouver, Edmonton, Winnipeg, Sudbury, Ottawa, Kingston, Hamilton, Toronto, Montreal, and Halifax). Full details of the MIREC study population have been published previously [27]. Briefly, generally healthy women were recruited in their first trimester of pregnancy and followed until after delivery. Maternal blood collected during the first and third trimesters were analyzed for total mercury. Blood pressure was measured during each trimester of pregnancy as well as after hospital admission for delivery. In addition, women completed a staff-administrated questionnaire at each visit in order to collect information on socio-demographic, exposure characteristics and other variables. Clinical data throughout pregnancy were abstracted from the medical charts. Of the 2001 consenting pregnant women, 18 withdrew from the study and requested that their data be destroyed. After recruitment, 74 women were excluded due to miscarriage or stillbirth, leaving 1909 women. Excluding women with chronic hypertension (58) or missing data on hypertension status (34), the final size for this analysis was 1817 women. The study was approved by Health Canada's Research Ethics Board and the Research Ethics Committee of Sainte-Justine University Hospital in Montreal, Quebec (Canada) as well as in all MIREC affiliated recruitment centers. All participants signed consent forms.

2.2. Dental amalgam information

Information on dental amalgams was obtained as part of a larger questionnaire administered at scheduled first and third trimester visits. More specifically, women were asked at each visit: "currently, how many mercury-silver dental fillings do you have?" In addition, at the first trimester visit, they were asked: "within the past 12 months, have you had any mercury-silver (also known as amalgam) dental fillings replaced?" and at the third trimester visit: "since visit 1, have you had any mercury-silver (also known as amalgam) dental fillings replaced?" The specific composition of the dental amalgams was not available.

2.3. Total mercury

Total mercury concentrations were measured in maternal blood collected at first and third trimester visits using a single-quadrupole inductively coupled plasma mass spectrometry (ICP-MS) Elan DRC-II system (Perkin Elmer, Norwalk CT, USA) with a limit of detection (LOD) of 0.1204 μg/l (0.6 nmol/l). The analysis was performed at the Centre de Toxicologie du Québec, Institut National de Santé Publique du Québec, Quebec, Canada. Concentrations below the LOD were assigned a value equivalent to half the LOD. < 12% of participants had blood mercury concentrations below the LOD.

2.4. Blood pressure and diagnosis of gestational hypertension

Systolic and diastolic blood pressure (SBP and DBP, respectively) were assessed in a sitting position by the study staff using a sphygmomanometer at each clinic visit. Two measures of blood pressure were taken about 1 min apart and averaged for each visit. The Korotkoff phase V (disappearance) was used for DBP measurement. The diagnostic criteria for GH are based on the Society of Obstetricians and Gynaecologists of Canada guidelines [1]. In the MIREC Study, the definition of GH in women with or without preeclampsia was the appearance of hypertension at ≥20 weeks of gestation based on the average of two measurements of SBP ≥140 mmHg and/or DBP ≥90 mmHg, taken at least 1 min apart. GH was measured between week 20 of pregnancy and the day of discharge from the hospital after delivery. Gestational age in weeks was based on last menstrual period and/or early ultrasound result. A total of 1630 (85.4%) of study participants were categorized as normotensive and 187 (9.8%) as having GH.

2.5. Covariates

Potential covariates for hypertension were derived from questionnaires at each trimester visit as well as from medical chart reviews. The following variables were analyzed as potential covariates: maternal age at delivery in years (continuous form), parity (multiparous, nulliparous), ethnicity (Caucasian, non-Caucasian), body mass index before pregnancy (BMI) in continuous form (weight in kg divided by height squared in meters), weight gain during pregnancy in continuous form (difference between last weight measured prior to delivery and weight measured at first trimester visit), education (graduate university, undergraduate university, college, less than college), household income ($ < 65,000, 65,000 – 90,000, > 90,000), maternal smoking (no, yes), and fish consumption (relative total quantity serving size per day, calculated from the food frequency questionnaire by Morisset [28]), coffee intake (no, yes), multiple child pregnancy (no, yes), women with autoimmune disease (no, yes). Because of the high proportion of missing data (35%) concerning gestational diabetes status, this covariate was not retained as a potential confounder.

2.6. Statistical analysis

Descriptive statistics for maternal characteristics were reported according to dental amalgam status (number of dental amalgams reported at first or third trimester visits, replacement of dental amalgams within the past 12 months reported at first trimester visit, and replacement during pregnancy reported at third trimester visit). Comparisons for continuous variables were conducted with Student's T-test, or univariate ANOVA, Mann-Whitney or Kruskal-Wallis tests and for categorical variables using chi-square tests. Medians (interquartile range (IQR)) and geometric means (GM) of mercury concentration were determined according to dental amalgam status and were compared using Mann-Whitney or Kruskal-Wallis. Finally, Spearman correlation was used to test the correlations between blood mercury, dental amalgam status and fish consumption.

Logistic regression models were created to explore the association between dental amalgam status and GH (yes or no). Presence of dental amalgams was assessed according to their number (categorized as 0, 1–4 and ≥ 5) and the time at which they were reported (first or third trimester visit). We also analyzed the impact of replacements according to data reported at first and third trimester visits, i.e. replacement within 12 months prior to first trimester visit and replacement during pregnancy (reported at third trimester visit). Crude and adjusted odds ratios (ORs) and 95% confident intervals (CI) were estimated using logistic regression models. Adjustment was made for covariates selected either *a priori* on the basis of evidence of potential confounding from the literature (maternal age) or empirically. We examined other covariates separately for a potential confounding bias using change-in-estimate method. Those that changed the ORs of the association between dental amalgam status and GH by ± 10% were considered as a confounder and included in the multivariable model. In order to optimize power in multivariable models, covariates were considered in a continuous form when possible and missing data were ignored. This may have reduced the number of women in certain multivariable models and may have some impact on our results. Each data point was statistically analysed according to the trimester in which it was reported (first or third trimester). Sensitivity analyses were conducted: (1) including covariates missing data in the model, and (2) excluding

Table 1
Participant characteristics according to dental amalgam status reported at recruitment.

Characteristics	Number of dental amalgam reported at 1st trimester visit[a]			Replacement within 12 months prior to 1st trimester visit[a]	
	0	1–4	≥ 5	No	Yes
Maternal age (years), mean ± SD	31.86 ± 5.01	33.33 ± 4.84*	34.42 ± 5.04*	32.71 ± 5.03	34.34 ± 4.94*
Weight gain (kg), mean ± SD	15.18 ± 6.31	15.07 ± 6.22	14.15 ± 6.24	15.03 ± 6.23	14.50 ± 0.55
BMI, median (IQR)	23.03 (20.83, 26.17)	23.30 (21.25, 26.71)*	24.33 (21.67, 27.83)*	23.33 (21.14, 26.58)	23.54 (21.59, 26.46)
***Ethnicity**, n (%)*[b]					
Caucasian	747 (86.7%)	510 (84.7%)	266 (87.8%)	1441 (86.6%)	122 (80.8%)*
Non-caucasian	115 (13.3%)	92 (15.3%)	37 (12.2%)	223 (13.4%)	29 (19.2%)*
Education					
Graduate University Undergraduate	228 (26.5%)	152 (25.3%)	79 (26.1%)	430 (25.9%)	45 (30.0%)
University	316 (36.7%)	221 (36.8%)	103 (34.0%)	605 (36.4%)	53 (35.3%)
College	225 (26.1%)	171 (28.5%)	81 (26.7%)	447 (26.9%)	40 (26.7%)
Less college	93 (10.8%)	56 (9.3%)	40 (13.2%)	181 (10.9%)	12 (8.0%)
Household income ($CAN)					
< 65,000	255 (31.0%)	169 (29.4%)	86 (29.4%)	484 (30.5%)	39 (27.3%)
65,000 – 90,000	237 (28.8%)	161 (28.0%)	90 (30.7%)	455 (28.7%)	43 (30.1%)
> 90,000	330 (40.1%)	245 (42.6%)	117 (39.9%)	649 (40.9%)	61 (42.7%)
Parity					
Multiparous	747 (56.6%)	510 (54.8%)	266 (62.7%)	942 (56.6%)	87 (58.0%)
Nulliparous	115 (43.4%)	92 (45.2%)	37 (37.3%)	721 (43.4%)	63 (42.0%)
Maternal smoking					
No	809 (93.9%)	568 (94.4%)	279 (92.1%)	1558 (93.6%)	145 (96.0%)
Yes	53 (6.1%)	34 (5.6%)	24 (7.9%)	106 (6.4%)	6 (4.0%)
Fish consumption (serving/day),					
median (IQR)	0.10 (0.03, 0.14)	0.09 (0.02, 0.14)	0.13 (0.03, 0.19)	0.10 (0.03, 0.14)	0.13 (0.03, 0.29)
Multiple child pregnancy					
No	827 (98.2%)	574 (96.8%)	292 (97.7%)	1592 (97.6%)	145 (96.7%)
Yes	15 (1.8%)	19 (3.2%)	7 (2.3%)	39 (2.4%)	5 (3.3%)
Coffee intake					
No	351 (43.1%)	252 (43.8%)	124 (43.1%)	679 (43.0%)	66 (45.2%)
Yes	464 (56.9%)	324 (56.3%)	164 (56.9%)	900 (57.0%)	80 (54.8%)
Autoimmune disease					
No	840 (97.4%)	598 (99.3%)*	298 (98.3%)*	1636 (98.3%)	148 (98.0%)
Yes	22 (2.6%)	4 (0.7%)*	5 (1.7%)*	28 (1.7%)	3 (2.0%)
GH					
No	784 (49.4%)	534 (33.6%)	269 (17.0%)	1488 (89.4%)	140 (92.7%)
Yes	78 (43.3%)	68 (37.8%)	34 (18.9%)	176 (10.6%)	11 (7.3%)

GH = gestational hypertension with or without preeclampsia. BMI = Body mass index. SD = standard deviation. IQR = interquartile range

[a] Association between dental amalgam status reported at first trimester visit and covariates using: T-test or Mann-Whitney, ANOVA or Kruskal-Wallis for continuous variables, Chi-square test for categorical variables

[b] Values are n (%), unless otherwise started

* $p < 0.05$

participants who reported data at first trimester but had missing data at third trimester.

We also used linear generalized estimating equations (GEE) to explore the relationship between dental amalgam status (repeated variable measured at first and third trimester) and SBP or DBP (repeated variable measured at first and third trimester). Linear GEEs take into account the clustering within each individual caused by the repeated-measurements design. Models incorporated a first-order autoregressive correlation pattern for the repeated events. This model considers automatically the value of first trimester when missing in the third trimester and vice versa. P-values (p) of < 0.05 indicated statistical significance. All statistical analyses were performed with IBM SPSS Statistics Version 22, SAS 9.4 for Windows and R for Windows 3.2.2.

3. Results

The majority of the participants were Caucasian, university educated, multiparous, non-smokers and had a household income more than $90,000 (Table 1). Mean maternal age was positively associated with number of dental amalgams and replacement status. BMI was significantly higher in women who reported dental amalgams (1–4 or ≥ 5) compared to those without amalgams. Autoimmune disease varied significantly by dental amalgam status.

As Table 2 reflects, blood mercury concentrations were higher in women who reported dental amalgams and also among those with any replacements within 12 months prior to the first trimester visit or replacement during pregnancy (all p-values < 0.05). First trimester mercury concentrations were significantly (but weakly) correlated with the presence of dental amalgams at both the first and third trimester visits (Spearman's rho (r) = 0.16, p < 0.001 and r = 0.15, p < 0.001; respectively) and to a lesser extent with the report of any replacements within the past 12 months (r = 0.07, p = 0.006) or replacement during pregnancy (reported in the 3rd trimester visit) (r = 0.06, p = 0.011) (data not shown). Similar results were found for the blood mercury concentrations measured on specimens obtained at the third trimester visit (r = 0.17, p < 0.001; r = 0.16, p < 0.001; r = 0.08, p = 0.001 and r = 0.07, p = 0.003; respectively). Mercury concentrations measured at first and third trimester visits were strongly correlated (r = 0.76, p < 0.001). Fish consumption was moderately correlated with mercury concentrations (r = 0.45, p < 0.001 at first trimester visit and r = 0.49, p < 0.001 at third trimester visit) and was not correlated to the presence and replacement of dental amalgams (data not shown).

In Table 3, dental amalgam status was not statistically associated with GH either in unadjusted or adjusted models. The adjusted ORs (aORs) (95% CI) for the outcome of GH according to the presence of dental amalgam reported in the first trimester visit were 1.31 (0.92, 1.85) and 1.32 (0.86, 2.04) for women with 1–4 amalgams and with ≥ 5 amalgams, respectively, compared to those without amalgam. Findings were similar for the presence of amalgams reported at the

Table 2
Mercury concentrations (μg/l) according to dental amalgam status.

Dental amalgam status	n	Mercury at 1st trimester visit		p	n	Mercury at 3rd trimester visit		p
		Median (IQR)	GM			Median (IQR)	GM	
Number reported at 1st trimester visit[a]				< 0.001				< 0.001
0	837	0.58 (0.24, 1.22)	0.50		756	0.46 (0.19, 0.91)	0.40	
1–4	593	0.74 (0.34, 1.40)	0.64		538	0.56 (0.28, 0.96)	0.51	
≥ 5	301	0.90 (0.56, 1.44)	0.87		269	0.70 (0.40, 1.24)	0.70	
Number reported at 3rd trimester visit[a]				< 0.001				< 0.001
0	787	0.60 (0.26, 1.24)	0.53		786	0.46 (0.19, 0.96)	0.41	
1–4	532	0.74 (0.34, 1.40)	0.64		514	0.54 (0.28, 0.94)	0.49	
≥ 5	286	0.90 (0.58, 1.48)	0.90		278	0.70 (0.40, 1.24)	0.71	
Replacement within 12 months prior to 1st trimester visit[b]				0.01				0.001
No	1627	0.68 (0.30, 1.36)	0.59		1471	0.54 (0.26, 0.98)	0.47	
Yes	150	0.88 (0.42, 1.38)	0.80		136	0.61 (0.36, 1.31)	0.68	
Replacement during pregnancy reported at 3rd trimester visit[b]								0.003
No					1456	0.55 (0.25, 0.98)	0.47	
Yes	NA	NA	NA	NA	152	0.58 (0.36, 1.18)	0.66	

IQR = interquartile range. GM = geometric mean. NA = not applicable
[a] Kruskal-Wallis test for the association between mercury and presence of dental amalgam.
[b] Mann-Whitney test for the association between mercury and dental amalgam replacement.

third trimester visit. Models considering fish consumption did not substantially change the associations between number of amalgams and odds ratio of GH in either 1st or 3rd trimesters (data not shown). Similarly no statistically significant associations were found for dental amalgam replacement. The aORs (95%CI) were 0.75 (0.40, 1.42) and 0.73 (0.39, 1.34) respectively for replacement within 12 months prior to the first trimester visit and replacement during pregnancy.

A sensitivity analysis including covariates missing data in the model showed minimal changes in the results (data not shown). Another sensitivity analysis (excluding participants who reported dental amalgams at first trimester but had missing data at third trimester) showed minimal changes in the GH results with the presence of dental amalgam in either trimester (aORs (95%CI) = 1.11 (0.74, 1.66) and 1.20 (0.73, 1.96) for women with 1–4 and with ≥ 5 amalgams, respectively, compared to those without amalgam as reference) (data not shown).

The results for the linear GEE models are presented in Table 4. The replacement of dental amalgam before or during pregnancy was associated with decreased SBP while the associations with DBP remained non-significant. There is no evidence of an association between the number of dental amalgams (the first and third trimester measure taken together) and SBP or DBP.

4. Discussion

No statistically significant associations between dental amalgam status and risk of GH were found in our study although blood mercury concentrations were slightly higher as the number of amalgams increased or with amalgam replacement. However, the replacement of dental amalgam before or during pregnancy was associated with decreased SBP.

To our knowledge, no other study has analyzed the association between dental amalgam and GH or blood pressure in pregnant women. A cross-sectional study of 263 pregnant women at delivery did not find an association between inorganic mercury (GM = 0.13 μg/l (0.10, 0.17) in cord blood and DBP, but did find an association with decreased SBP, while total mercury in cord blood was associated with a non-significant increase in SBP during labor and delivery [29]. Studies in the general population are not consistent on the association between dental amalgams and cardiovascular disease. A prospective study with 1462 Swedish women reported no association between dental amalgams and cardiovascular diseases [30,31]. In contrast, another study in the USA general population (women and men) [26] found a positive association between mercury from dental amalgam and cardiovascular disorders including high blood pressure.

In this study, mercury concentrations were weakly correlated with the presence or replacement of dental amalgam. On the other hand,

Table 3
Crude and adjusted Odds Ratios for the association between dental amalgam status and GH.

Dental amalgam status	GH					
	n	Unadjusted OR (95%CI)	p	n	Adjusted OR (95%CI)	p
Number reported at 1st trimester visit[a]	1767			1726		
0		Reference			Reference	
1–4		1.28 (0.91, 1.80)	0.16		1.31 (0.92, 1.85)	0.13
≥ 5		1.27 (0.83, 1.95)	0.27		1.32 (0.86, 2.04)	0.21
Number reported at 3rd trimester visit[b]	1634			1516		
0		Reference			Reference	
1–4		1.27 (0.89, 1.82)	0.19		1.26 (0.85, 1.88)	0.25
≥ 5		1.18 (0.75, 1.85)	0.47		1.03 (0.63, 1.70)	0.90
Replacement within 12 months prior to 1st trimester visit[c]	1815	0.66 (0.35, 1.25)	0.21	1724	0.75 (0.40, 1.42)	0.38
Replacement during pregnancy reported at 3rd trimester visit[d]	1816	0.65 (0.36, 1.20)	0.17	1725	0.73 (0.39, 1.34)	0.31

GH = gestational hypertension with or without preeclampsia. OR = odds ratio. CI = confident interval.
Logistic regression between dental amalgam status and GH:
[a] adjusted for maternal age
[b] adjusted for maternal age, BMI
[c,d] adjusted for maternal age, fish consumption

Table 4
Associations[a] between concurrent measures of dental amalgam status and systolic or diastolic blood pressure (SBP or DBP) at 1st and 3rd trimester visits among pregnant women.

Dental amalgam status	SBP			DBP		
	n	Adjusted beta (95% CI)	p	n	Adjusted beta (95% CI)	p
Number of dental amalgam	1582	−0.52 (−1.32, 0.29)[b]	0.21	1531	0.06 (−0.57, 0.69)[c]	0.85
Replacement before or during pregnancy	1474	−1.58 (−2.95, −0.02)[d]	0.02	1472	−0.21 (−1.39, 0.99)[e]	0.74

SBP = systolic blood pressure. DBP = diastolic blood pressure. CI = confident interval.
[a] linear generalized estimating equations between dental amalgam status and SBP or DBP
[b] adjusted for maternal age, BMI, household income.
[c] adjusted for maternal age, BMI, fish consumption, weight gain, coffee intake.
[d] adjusted for maternal age, BMI, education, household income, ethnicity, fish consumption, weight gain, coffee intake, multiple child pregnancy, maternal smoking.
[e] adjusted for maternal age, BMI, fish consumption, weight gain, coffee intake, education, household income, ethnicity, parity, multiple child pregnancy, maternal smoking.

some studies have demonstrated a moderate or high correlation between mercury and dental amalgams using different types of matrices such as cord blood (r = 0.46) [15], saliva (r = 0.93) [32,33] or hair (r = 0.92) [33]. Thus, although there was a weak correlation between blood mercury concentrations and dental amalgam status in our study, other biological matrices might be better suited to explore the magnitude of the association between dental amalgam and mercury concentrations.

The concentrations of blood mercury measured in the first trimester (0.51, 0.64, and 0.86 μg/l for women with 0, 1–4 and ≥ 5 dental amalgams, respectively) were statistically higher than the concentrations of mercury measured at third trimester (0.40, 0.51 and 0.71 μg/l, respectively). This difference may be explained by the capacity of mercury to bind to haemoglobin [34], the concentration of which decreases over the course of pregnancy as blood volumes increase [35]. Haemoglobin concentrations are higher in cord blood than in maternal blood [36], which could result in higher mercury concentrations in cord blood compared to maternal blood, which we previously reported in the same study population [37]. Similar results on mercury concentrations in cord blood were found by others authors [14,38-44]. Furthermore, plasma volume expansion during pregnancy, which can increase approximately 45% [45] may also impact the concentration of mercury measured in blood later in pregnancy.

Autoimmune disease has been associated with dental amalgams [46] and hypertension in pregnancy [47,48]. In our study, the percentage of women reporting an autoimmune disease was significantly lower in women with dental amalgams compared to those without dental amalgams. Some studies have shown an association between dental amalgam and autoimmune disease [46,49] and others not [21,50,51]. A recent health technology assessment of the evidence reported no clinically important differences in the safety of amalgam compared with composite resin dental restorations [52].

4.1. Strengths and limitations of the study

To our knowledge this is the first study to examine the association between dental amalgams and risk of GH. This study had a number of strengths, including laboratory mercury measurements were performed in a national reference laboratory and cases of GH were identified by clinical staff. The prospective cohort design increases the validity of study findings. Whild study has a relatively large sample size (n = 1817) the power of our study to detect small effects of dental amalgam status on the risk of GH is limited, if such an effects were to be present. Missing data reduced the number of women in certain multivariable models which might also have impacted our results. However, sensitivity analysis including or excluding missing data showed minimal changes. In addition, blood mercury may not be the best indicator of body burden, especially as it relates to associations with presence or replacement of dental amalgams, as urinary mercury is widely used as the biomarker for assessing chronic mercury vapor exposure [53]. Furthermore, we did not collect information on what those fillings were replaced with, which could have been another amalgam, or with composite resin, gold, or ceramic. The number of dental amalgams (and their replacement) was based on self-report by each participant (versus measured by direct clinical examination by a licensed dentist and may be subject to recall bias. As the study population on average was from a higher socio-economic group, our results may not be generalizable to the Canadian population. Confounding variables were conservatively controlled; however, residual confounding may have been present.

4.2. Perspectives

The presence of or replacement of dental amalgams, although positively associated with blood mercury concentrations, was not significantly associated with an increased risk of GH in our study population. However, the replacement of dental amalgam before or during pregnancy was associated with decreased SBP. Additional studies in pregnant women may help to confirm these results.

4.3. Sources of Funding

Funding was provided by Health Canada's Chemicals Management Plan, the Canadian Institute of Health Research (grant MOP-81285), and the Ontario Ministry of the Environment. RLC received a PhD scholarship from the MIREC study and the QTNPR (Quebec Training Network in Perinatal Research). HT holds a salary award (chercheur-boursier) from the Fonds de la recherche du Québec en santé (FRQ-S) and from CIHR (New investigator salary award). WDF holds a Tier 1 CIHR Canada Research Chair.

4.4. Novelty and significance

1) What Is New: Dental amalgams status (presence or replacement), was not significantly associated with an increased risk of GH. However, the replacement of dental amalgam before or during pregnancy was associated with decreased SBP.
2) What Is Relevant? The replacement of dental amalgam before or during pregnancy was associated with decreased SBP.

Declaration of competing interest

The authors declare no actual or potential competing financial interests.

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