Antepartum Dental Radiography and Infant Low Birth Weight

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Context Both high- and low-dose radiation exposures in women have been associated with low-birth-weight offspring. It is unclear if radiation affects the hypothalamus-pituitary-thyroid axis and thereby indirectly birth weight, or if the radiation directly affects the reproductive organs.

Objective To investigate whether antepartum dental radiography is associated with low-birth-weight offspring.

Design A population-based case-control study.

Participants and Setting Enrollees of a dental insurance plan with live singleton births in Washington State between January 1993 and December 2000. Cases were 1117 women with low-birth-weight infants (<2500 g), of whom 336 were term low-birth-weight infants (1501-2499 g and gestation ≥37 weeks). Four control pregnancies resulting in normal-birth-weight infants (≥2500 g) were randomly selected for each case (n=4468).

Main Outcome Measures Odds of low birth weight and term low birth weight by dental radiographic dose during gestation.

Results An exposure higher than 0.4 milligray (mGy) during gestation occurred in 21 (1.9%) mothers of low-birth-weight infants and, when compared with women who had no known dental radiography, was associated with an adjusted odds ratio (OR) for a low-birth-weight infant of 2.27 (95% confidence interval [CI], 1.11-4.66, *P*=.03). Exposure higher than 0.4 mGy occurred in 10 (3%) term low-birth-weight pregnancies and was associated with an adjusted OR for a term low-birth-weight infant of 3.61 (95% CI, 1.46-8.92, *P*=.005).

Conclusion Dental radiography during pregnancy is associated with low birth weight, specifically with term low birth weight.

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PREPUBERTAL, ADOLESCENT, AND pregnant females exposed to ionizing radiation may be at an increased risk for delivering a low-birth-weight (LBW) infant (<2500 g). In prepubertal girls, high-dose therapeutic radiation for childhood cancers has been associated with an increased risk for future LBW offspring, and a direct relationship has been reported between the radiation dose and LBW risk.[1-3] In adolescents, diagnostic radiation for idiopathic scoliosis was also associated with a dose-dependent increased LBW risk.[4] In pregnant women, medical x-ray radiation, not dental x-ray radiation, has been associated with an increased LBW risk,[5] and exposure to the atomic bomb explosion in Hiroshima during early pregnancy has been associated with offspring of small stature and head circumference.[6] These latter effects occurred at very low doses, the lowest yet known to produce grossly detectable effects in the offspring of exposed mothers.[6]

It is currently unclear whether radiation affects the reproductive organs directly, or thyroid function and thereby indirectly pregnancy outcomes, or whether factors unrelated to radiation are responsible for the LBW.[7] Because dental diagnostic radiography results in measurable radiation doses to the hypothalamus-pituitary-thyroid axis[8] and not the reproductive organs or the fetus,[9] it provides an opportunity to test the role of the hypothalamus-pituitary-thyroid axis in the radiation-LBW association. The goal of this study was to evaluate whether dental radiography influences the likelihood for a LBW infant in a population-based case-control study.

METHODS

Identification of Cases and Controls

We conducted a population-based case-control study linking dental utilization data from Washington Dental Service (WDS), a not-for-profit dental insurance company, and vital record birth certificates from Washington State. All women between the ages of 12 and 45 years, with a dental treatment between January 1, 1993, and December 31, 2000, were identified, and a client file was created that contained the first and last name, address, city, zip code, and birth date. This file was sent to the birth certificate data manager (with no affiliation to WDS) who created a unique identifier for each record and linked the data to the vital

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record birth certificates using both deterministic and probabilistic matching procedures. Only singleton births were included.

The combination of the mother's exact birth date along with the mother's first name and either the father's last name or mother's maiden name gave a conclusive match for 94.1% of the matched sample of women. Exact date of mother's birth, along with a partial name match (first 5 characters of last name and first character of first name) accounted for a further 2.7% of matches. Partial name matches (first 7 characters of last name and first 5 characters of first name) and either an address match (0.5%) or transposed date of mother's birth year, month, or day segment (2.7%) accounted for the remaining matches.

During this matching process, the WDS data manager only received infant birth dates from the birth certificate data manager, and the birth certificate data manager did not receive dental utilization data from WDS. All successful matches combined with infant birth dates (n=29 215) were sent back to WDS where it was determined whether eligibility for dental services existed during a period 40 weeks prior to birth and for how many months eligibility existed. Prior to 1995, eligibility for dental services could only be determined for those women who had at least 1 dental visit, whereas subsequent to 1995, eligibility could be determined regardless of whether a dental visit occurred. This change in method of determining eligibility did not affect the reported findings.

The unique identifiers of those women eligible for dental services during pregnancy were sent to the birth certificate data manager who then selected the case-control study population. The case group consisted of all pregnancies resulting in LBW infants. Four normal-birth-weight (NBW) infants (2500 g-5414 g) were randomly selected for each case without matching. Each NBW infant had an associated random number, which was generated using the "ranuni" function in SAS, version 8.2 (SAS Institute Inc, Cary, NC). The 4468 infants with the lowest random numbers were included in the sample. Both the WDS and birth certificate data managers subsequently stripped their respective data files of personal identifiers and sent them to the University of Washington where linking occurred using the patient unique identifier. Human subject approval was obtained from the Human Research Review Board of the Department of Health in the State of Washington.

Low birth weight was defined as any infant weighing less than 2500 g. Low-birth-weight infants were subdivided into 3 categories: very low-birth-weight (VLBW) infants (≤1500 g), preterm low-birth-weight (PLBW) infants (between 1501-2499 g and <37 weeks' gestation), and term low-birth-weight (TLBW) infants (1501-2499 g and ≥37 weeks' gestation). Sixteen infants with a birth weight between 1501 and 2499 g and of unknown gestational age could not be classified.

Dental Radiography Doses

Dental radiography can affect at least 3 organs in the head-and-neck region that are potentially involved in pregnancy outcomes: the hypothalamus, the pituitary, and the thyroid. Because of the evidence on thyroid susceptibility to radiation,[10] and because of the existing hypothesis that radiation-induced thyroid dysfunction causes LBW,[7] radiation doses to the thyroid were calculated. For each woman, the date and type of each dental radiograph taken was abstracted from the dental utilization data, doses were assigned to each type of radiographic exposure, and summed. Doses were estimated based on a nationwide 1993 dental survey evaluation of x-ray trends[11] and published thyroid radiation doses.[12] Given that mean skin exposure of a dental radiograph is typically 2.17 milligray (mGy),[11] that 90% of the sampled dental offices use D-speed film,[13] and that the mean kilovoltage in dental offices is approximately 70,[13] a full-mouth dental survey consisting of 21 radiographs can be expected to result in a typical dose to the thyroid of an adult female of 1.6 mGy.[8] The dose to the thyroid of a periapical dental radiograph, while dependent on the positioning of the x-ray unit, will on average equal 0.08 mGy. In a female patient, 4 bitewings is 14% of the total radiation dose of a full-mouth radiograph or 0.22 mGy.[12] A cephalometric radiograph was estimated as delivering a dose of 0.46 mGy to the thyroid[14] and a panoramic radiograph, 0.12 mGy.[15] Both are estimates to the central thyroid region. Doses to the left and right lobe of the thyroid can be substantially higher. We did not have information on thyroid shield use, but its use for intraoral films is reported to be low (Mike Odlaug, MPH, written communication, December 2003). The calculated cumulative radiation doses during gestation were categorized into 3 dose groups: 0 mGy (no known dental radiography), 0.1-0.4 mGy, and higher than 0.4 mGy. The value of 0.4 mGy corresponded to the 90th percentile of cumulative radiation doses among women with at least 1 dental x-ray. Radiation doses were also modeled as a continuous variable.

The WDS electronic database is validated both at treatment planning and completion phases by conducting random or data-driven patient record audits.[16] In addition, a recently concluded validation study indicated that the proportion agreement between chart audits and electronic records averaged almost 97% for all dental procedures and 93% for radiographic dental procedures.[16] For all analyses, the radiation dose since the last menstrual period prior to pregnancy was calculated. For 109 women (1.9%), the gestational length was not recorded, and an estimate of 40 weeks of gestational length was used. Sensitivity analyses indicated that the inclusion or exclusion of these 109 women did not affect the findings.

Confounding Variables

Both the birth certificate records and the dental utilization data provided information on the following variables: maternal age at the time of delivery (categorized into <20, 20-24, 25-29, 30-34, 35-39, ≥40 years), ethnicity (17 categories were condensed into white, black, Asian, and other ethnicities—the latter group included women of unknown ethnicity and women who refused to state ethnicity), education level of mother (unknown, ≤12 years of education, >12 years of education), the duration of eligibility for dental insurance during pregnancy, dental procedures during pregnancy, marital status, parity (categorized into 0, 1-2, and ≥3 prior pregnancies), self-reported maternal smoking during pregnancy, the presence of gestational or established diabetes, the Kessner Adequacy of Prenatal Care Index,[17] self-reported consumption of 1 or more alcoholic drinks per week during pregnancy, prepregnancy weight, weight gain during pregnancy, preeclampsia, and chronic hypertension.

Dental procedures other than radiography were also considered as confounders. The American Dental Association developed a code on dental procedures and nomenclature that is used by WDS and classifies dental procedures into diagnostic procedures (eg, radiographs, examinations), preventive procedures (eg, dental prophylaxis), restorative procedures (eg, fillings), periodontal procedures (eg, periodontal scaling or periodontal maintenance procedures), endodontic procedures (eg, root canal fillings), removable prosthodontic procedures, fixed prosthodontic procedures including implants, oral surgery procedures, and orthodontic procedures.

Statistical Analysis

Between 1993 and 2000, the 5719 women in the selected study sample had 1 singleton birth, 197 women had 2 singleton births, and 4 women had 3 singleton births. To take into account that the pregnancy outcomes for women with more than 1 birth are correlated events, generalized estimating equation models were used. Odds ratios (ORs) were calculated using generalized linear models with an exchangeable correlation structure, a logit link, and a binomial error distribution. Case-control differences in potential confounders were estimated using exchangeable correlation matrices, with the exception of prepregnancy weight where an independence correlation structure was used. Correlation coefficients and the respective *P* values describing the association between dental radiation and potential confounders were estimated ignoring within-subject correlation. The statistical significance level was set at .05.

The impact of missing values was assessed with multiple imputations of missing values using a sequential regression imputation method (Imputational and Variance Estimation software [IVEware], version 2.0, University of Michigan, Ann Arbor).[18] This method imputed values for each woman conditioned on the other values observed for that woman. The imputations were drawn from the posterior distribution specified by a regression model with a noninformative prior distribution. Values were imputed cyclically, each time overwriting previously drawn values. Subsequently, regression models were built using the jackknife repeated replication technique.

RESULTS

There were 1117 LBW infants born to women with WDS insurance between 1993 and 2000: 193 VLBW infants, 572 PLBW infants, 336 TLBW infants, and 16 of unknown gestational age (**TABLE 1**). A total of 4468 NBW controls were selected. The LBW rate among women with private dental insurance was 3.8%, or 0.7% lower than the LBW rate (4.5%) for Washington State during the same period (1993-2000). When compared with all women who had live births in Washington State, women who had private dental insurance were on average 1.5 years older (28.8 vs 27.3 years), more educated (14.3 years vs 12.9 years), smoked less (7.5% vs 14.6%), and were more likely to be white (81% vs 73%).

The use of dental diagnostic radiography was independent of several risk factors for LBW. Dental diagnostic radiation dose was not related to maternal age ($\rho = 0.00$, $P = .90$), diabetes ($\rho = 0.00$, $P = .88$), self-reported alcohol consumption ($\rho = 0.00$, $P = .79$), number of prenatal visits ($\rho = -0.02$, $P = .09$), chronic hypertension ($\rho = 0.01$, $P = .52$), or preeclampsia ($\rho = -0.01$, $P = .72$). Women reporting cigarette smoking had on average a 0.01 mGy higher radiation dose than women reporting not smoking ($P = .14$). Women with inadequate prenatal care had on average 0.05 mGy more radiation exposure than women with adequate prenatal care ($P = .13$). Ethnicity was related to dental radiation doses ($P = .01$), with women of Asian ethnicity having a mean radiation dose of 0.05 mGy, black women having a radiation dose of 0.04 mGy, and white women having a radiation dose of 0.03 mGy.

Dental radiation exposures were more common among women with LBW infants than among women with NBW infants. Among the women who delivered a LBW infant, 1.9% (n=21) had higher than 0.4 mGy radiation, as opposed to 1.0% of the women with NBW infants ($P = .02$) (**TABLE 2**). Among the women who delivered a TLBW infant, the prevalence of the higher than 0.4 mGy radiation dose was 3.0% (n=10), which was also significantly higher than among controls ($P = .002$). The prevalence of the higher than 0.4 mGy radiation dose among women with a PLBW infant and a VLBW infant was 1.6% and 1.0%, respectively, which was not significantly different from the prevalence in women with NBW infants ($P = .24$ and $P > .99$, respectively). Established risk factors for LBW such as maternal age, diabetes, smoking, ethnicity, preeclampsia, chronic hypertension, prepregnancy weight, maternal weight gain, and parity were significantly associated with LBW in the studied population (Table 1).

When compared with women with no known dental diagnostic radiography, a thyroid radiation dose of more than 0.4 mGy increased the adjusted odds for LBW by 2.27 (95% confidence interval [CI], 1.11-4.66) (**TABLE 3**). A thyroid radiation dose of 0.1 to 0.4 mGy was associated with an adjusted OR of 1.20

(95% CI, 0.88-1.63). When radiation dose was modeled as a continuous variable, a 1-mGy increase was associated with a 1.83 increased odds for a LBW infant (95% CI, 1.10-3.04). Further adjustment of the OR for the different types of dental procedures performed during pregnancy did not affect the radiation-LBW association (Table 3).

Table 1. Characteristics of Women Giving Birth to Low-Birth-Weight (LBW) Infants, Term Low-Birth-Weight (TLBW) Infants, and Normal-Birth-Weight (NBW) Infants*

Maternal Characteristics	LBW Infants (n = 1117)	TLBW Infants (n = 336)	NBW Infants (n = 4468)	*P* Value, LBW vs NBW†	*P* Value, TLBW vs NBW
Age, y					
<20	190 (17.0)	51 (15.2)	483 (10.8)	<.001	.01
20-24	200 (17.9)	64 (19.0)	750 (16.8)	.44	.31
25-29	192 (17.2)	65 (19.3)	1025 (22.9)	<.001	.13
30-34	282 (25.2)	82 (24.4)	1287 (28.8)	.04	.10
35-39	193 (17.3)	53 (15.8)	752 (16.8)	.98	.55
≥40	60 (5.4)	21 (6.3)	171 (3.8)	.02	.03
Ethnicity					
White	813 (72.8)	255 (75.9)	3644 (81.6)	<.001	.02
Black	83 (7.4)	17 (5.1)	142 (3.2)	.52	.05
Asian	96 (8.6)	26 (7.7)	298 (6.7)	.16	.08
Other	125 (11.2)	38 (11.3)	384 (8.6)	.01	.10
Education					
>12 y	620 (55.5)	195 (57.5)	2902 (65.0)	<.001	.008
Information unavailable	156 (14.0)	33 (9.8)	373 (8.4)	<.001	.35
Kessner Adequacy of Prenatal Care Index					
Adequate	677 (60.6)	237 (70.5)	3261 (73.0)	<.001	.31
Intermediate	299 (26.8)	70 (20.8)	876 (19.6)	<.001	.60
Inadequate	27 (2.4)	3 (0.9)	34 (0.8)	<.001	.79
Information unavailable	114 (10.2)	26 (7.7)	297 (6.6)	<.001	.39
Marital status					
Not married	295 (26.4)	85 (25.3)	843 (18.9)	<.001	.004
Information unavailable	2 (0.2)	1 (0.3)	6 (0.1)	.72	.46
Dental insurance eligibility during pregnancy, mean (SE), No. of wk	36.5 (0.3)	36.6 (0.5)	36.3 (0.1)	.54	.54
Weight gain during pregnancy, mean (SE), kg	12.1 (0.2)	12.7 (0.3)	14.8 (0.1)	<.001	<.001
Information unavailable	394 (35.3)	83 (24.7)	1147 (25.7)	<.001	.79
Prepregnancy weight, mean (SE), kg	64.0 (0.6)	62.0 (0.9)	66.3 (0.3)	<.001	<.001
Information unavailable	421 (37.7)	95 (28.3)	1199 (26.8)	<.001	.57
Diabetes					
Established or gestational	46 (4.1)	10 (3.0)	114 (2.6)	.005	.51
Information unavailable	105 (9.4)	20 (6.0)	371 (8.3)	.24	.13
Parity					
0	742 (66.4)	236 (70.2)	2393 (53.6)	<.001	<.001
1-2	280 (25.1)	76 (22.6)	1699 (38.0)	.08	<.001
≥3	45 (4.0)	10 (3.0)	210 (4.7)	.37	.14
Information unavailable	50 (4.5)	14 (4.2)	166 (3.7)	.28	.65
Self-reported No. of alcoholic drinks per wk					
≥1	19 (1.7)	5 (1.5)	63 (1.4)	.44	.76
Information unavailable	156 (14.0)	35 (10.4)	421 (9.4)	<.001	.51
Self-report of smoking during pregnancy					
Yes	140 (12.5)	52 (15.5)	325 (7.3)	<.001	<.001
Information unavailable	62 (5.6)	13 (3.9)	140 (3.1)	<.001	.46
Preeclampsia					
Yes	149 (13.3)	49 (14.6)	222 (5.0)	<.001	<.001
Information unavailable	105 (9.4)	20 (6.0)	371 (8.3)	.24	.13
Chronic hypertension					
Yes	39 (3.5)	11 (3.3)	28 (0.6)	<.001	<.001
Information unavailable	105 (9.4)	20 (6.0)	371 (8.3)	.24	.13

*Data are expressed as number (percentage) unless otherwise indicated. Weight categories: LBW, less than 2500 g; TLBW, 1501 to 2499 g and 37 or more menstrual weeks of gestation; NBW, at least 2500 g.
†All *P* values estimated using an exchangeable correlation matrix, except for prepregnancy weight where an independence correlation structure was used.

Table 2. Dental Procedure Characteristics of Women Giving Birth to Low-Birth-Weight (LBW) Infants, Term Low-Birth-Weight (TLBW) Infants, and Normal-Birth-Weight (NBW) Infants*

Dental Procedure Characteristics	LBW Infants (n = 1117)	TLBW Infants (n = 336)	NBW Infants (n = 4468)	*P* Value, LBW vs NBW	*P* Value, TLBW vs NBW
Estimated dental-related thyroid exposure					
>0.4 mGy (mean, 1.2 mGy)	21 (1.9)	10 (3.0)	46 (1.0)	.02	.002
0.1-0.4 mGy (mean, 0.2 mGy)	112 (10.0)	39 (11.6)	419 (9.4)	.52	.17
0 mGy (no known dental radiography)	984 (88.1)	287 (85.4)	4003 (89.6)	.16	.02
Full-mouth dental radiography	11 (1.0)	4 (1.2)	28 (0.6)	.20	.23
≥1 Panoramic radiograph†	21 (1.9)	7 (2.1)	42 (0.9)	.009	.05
Bitewings, mean (SE), No.	0.30 (0.03)	0.37 (0.06)	0.25 (0.01)	.12	.05
Periapical radiographs, mean (SE), No.	0.07 (0.01)	0.11 (0.02)	0.06 (0.01)	.27	.02
Total No. of dental procedures per 100 women per year	259.4	328.7	287.4	.02	.08
Diagnostic	108.0	130.6	116.9	.07	.10
Preventive	87.1	103.9	102.5	<.001	.83
Restorative	35.4	50.1	43.1	.13	.49
Endodontic	3.3	5.5	3.0	.68	.04
Periodontal	10.0	12.3	11.8	.41	.89
Removable prosthodontic	0.3	0.8	0.3	.88	.19
Implants and fixed prosthodontic	0.8	1.3	0.7	.91	.56
Oral surgery	6.7	12.7	5.6	.66	.17
Orthodontic	7.8	11.5	3.5	.05	.03

Abbreviation: mGy, milligray.
*Data are expressed as number (percentage) unless otherwise indicated. Weight categories: LBW, less than 2500 g; TLBW, 1501 to 2499 g and 37 or more menstrual weeks of gestation; NBW, at least 2500 g.
†One woman had 2 panoramic radiographs during gestation.

Table 3. Odds Ratios and 95% Confidence Intervals for Low Birth Weight (LBW) and Term Low Birth Weight (TLBW) Associated With Ionizing Radiation During Gestation and the Impact of Control for Competing Risk Factors*

	LBW		TLBW	
	>0.4 mGy	0.1-0.4 mGy	>0.4 mGy	0.1-0.4 mGy
Unadjusted	1.80 (1.09-2.97)	1.09 (0.87-1.36)	3.05 (1.53-6.08)	1.30 (0.92-1.85)
Adjusted	2.27 (1.11-4.66)†	1.20 (0.88-1.63)	3.61 (1.46-8.92)	1.66 (1.09-2.53)
	2.54 (1.23-5.21)‡	1.29 (0.95-1.76)	3.54 (1.40-8.96)	1.66 (1.08-2.56)

Abbreviation: mGy, milligray.
*Weight categories: LBW, less than 2500 g; TLBW, 1501 to 2499 g and 37 or more menstrual weeks of gestation. Reference group for odds ratios are those women with normal-birth-weight infants (≥2500 g).
†Adjusted for all variables listed in Table 1. Smoking, chronic hypertension, preeclampsia, alcohol use, marital status, and diabetic status were modeled as indicator variables; duration of dental insurance eligibility, weight gain, and prepregnancy weight were modeled as continuous variables.
‡In addition to variables described in Table 1, the following types of dental procedures were adjusted for: preventive, restorative, endodontic, periodontal, fixed prosthodontic, removable prosthodontic, oral surgery, and orthodontic. (The different types of procedures were modeled as the number of procedures performed during pregnancy.)

Subsequently, the association between diagnostic radiation and different types of LBW outcomes was evaluated. There was no significant association between a radiation dose higher than 0.4 mGy and the OR for VLBW infants (OR, 2.19; 95% CI, 0.21-22.49) or the OR for PLBW infant (OR, 1.77; 95% CI, 0.65-4.78).

There was a strong association between diagnostic radiation and TLBW infants (Table 3). When the thyroid radiation dose was higher than 0.4 mGy, the adjusted OR for a TLBW infant was 3.61 (95% CI, 1.46-8.92) when compared with women with no known dental radiography. When the radiation dose to the thyroid was 0.1 to 0.4 mGy, the adjusted OR for a TLBW infant was 1.66 (95% CI, 1.09-2.53). Further adjustment of the OR for the different types of dental procedures performed during pregnancy did not affect the OR (Table 3). When the cumulative radiation dose was modeled as a continuous variable, a 1-mGy increase was associated with a 2.59 increased odds for a TLBW infant (95% CI, 1.37-4.90) after adjustment for confounding variables. When values were imputed for missing confounders, the OR for a TLBW infant associated with a radiation dose to the thyroid higher than 0.4 mGy was 2.89 (95% CI, 1.32-6.33) when compared with women with no known dental radiography.

Subgroup analyses showed strong associations among women with adequate prenatal care or women reporting not smoking. Thyroid radiation higher than 0.4 mGy in nonsmokers was strongly associated with TLBW infants (naive OR, 4.81; 95% CI, 1.81-12.79). The naive OR estimate among women reporting smoking during pregnancy was 1.61 (95% CI, 0.15-17.34). Among women with adequate prenatal care, thyroid radiation higher than 0.4 mGy was associated with an OR for a TLBW infant of 4.38 (95% CI, 1.79-10.74) when compared with women with no known dental radiography.

Over two thirds of the total radiation doses (70.5%) were received in the first trimester. During the first trimester, a radiation dose higher than 0.4

mGy was associated with an OR for a LBW infant of 3.11 (95% CI, 1.44-6.73) and the OR for a TLBW infant was 5.49 (95% CI, 2.12 -14.17). During the second and third trimester, the confidence limits around the OR were too wide to make meaningful inferences.

COMMENT

In this study, antepartum dental radiography in pregnant women was associated with an increased risk for a LBW infant, especially a TLBW infant. The prevalence of dental radiography during pregnancy in this dentally insured population was approximately 10%. Since women may not always be aware of their pregnancy status, it may not be possible to eliminate all dental radiography during pregnancy, but if this goal could be achieved and if the identified association is causal, the prevalence of TLBW infants could be reduced by up to 5%. Current guidelines for diagnostic radiography,[19] which are based on the notion that only direct radiation to the reproductive organs is of concern during pregnancy, may need to be evaluated further.

While the findings of this study cannot determine which organ in the head-and-neck region may be responsible for the observed radiation-LBW association, epidemiological[20-22] and experimental evidence[23] point to the thyroid. Very low-dose radiation has been associated with thyroid dysfunction such as thyroid autoimmunity among young females, thyroid cysts in females of all ages,[24] and papillary thyroid cancer[25] among multiparous women. The thyroid's susceptibility to radiation has been hypothesized to be high during pregnancy.[26] In addition to the evidence on radiation-induced thyroid dysfunction, there is evidence that subtle, subclinical thyroid dysfunction decreases birth weight[20,21] and delays neurointellectual development of the offspring.[27,28] This raises the possibility that radiation-induced thyroid dysfunction may also affect the neurointellectual development of the offspring. Low-dose radiation in utero leads to poor performance on intelligence tests.[29] While those associations have typically been attributed to the direct effects of radiation on the development of the brain,[29] the potential role of radiation-induced thyroid dysfunction on brain development may need to be further explored.

Strengths of this study include the unbiased selection of cases and controls from registries, the individual radiation dosimetry data, the absence of recall bias with respect to radiation between cases and controls, the control for well-established risk factors of LBW, and the validation of the insurance records with respect to dental radiography information. Such rigor in design has often been difficult to achieve when studying the effects of radiation on pregnancy outcomes. In prior studies, birth weight was often assessed by maternal recall, selection bias was difficult to control due to nonresponse or survival bias, and bias due to confounding from the lack of information on other risk factors for LBW, such as diabetes, chronic hypertension, or smoking,[1,3-5,7] could not always be adjusted for.

Several factors reduced the potential for residual confounding. First, because all women had private dental insurance, the selected sample was of a higher and more homogeneous socioeconomic class (eg, higher education) and had better health awareness (eg, lower smoking prevalence) than the population of Washington State. Such restriction in subject selection is a useful tool to control confounding.[30] However, such restriction had the disadvantage that it limited the ability to assess effect modification—the number of women in certain subgroups, such as women reporting smoking or women with inadequate prenatal care, was too sparse to provide meaningful inferences. Second, dental radiography doses were not related to important risk factors of LBW such as maternal age, diabetes, preeclampsia, and chronic hypertension. Third, among women exposed during the first trimester, when radiation has been reported to have the greatest effect on infant growth,[6] the OR for TLBW was 5 and the lower limit of the 95% CI excluded 2. Odds ratios of such size are less likely to be the result of residual confounding.[31]

Weaknesses of the study include potential measurement errors of confounders such as smoking, the lack of thyroid function measures, the lack of information on nondental radiation exposures, bias in the linking process, the possibility of a chance finding, and missing data. It is possible that underreporting of the socially undesirable behavior of smoking during pregnancy biased the association between dental radiography and LBW. It is unclear to what extent restricting the analyses to women reporting not smoking minimized bias since attendants may be more likely to note smoking on a birth certificate for a LBW infant than for a NBW infant.[32] Some control for smoking was obtained by restricting the study population to those women of higher socioeconomic class in whom smoking prevalence is lower. The lack of thyroid function measures in the current study eliminated our ability to determine if indeed the thyroid is involved in explaining the observed association.

The likelihood of matching mothers' names may have depended on ethnicity, which may have induced selection biases because ethnicity was related to both radiation dose and birth weight. This bias may have been minimized, but not eliminated, by controlling for ethnicity and ethnicity-related risk factors for LBW, such as diabetes. The reported results may be a chance finding, but this is less likely given that prior studies also identified associations between diagnostic radiation and LBW.[4,5] The prevalence of missing data for certain confounders was moderately high. Even though imputation for missing values did not substantially influence the results, it is possible that the missing data biased the results.

The impact of nondental radiation or factors associated with dental radiography on the reported study findings is unknown. Additional analyses of data from a population-based case-control study on dental radiation[33] suggested that nondental therapeutic or diagnostic radiation during pregnancy is of low prevalence. It is possible that extensive dental radiography is associated with certain conditions such as facial trauma, tumors, or dental diseases, which in this study may have increased the risk for adverse pregnancy outcomes and caused a spurious association between radiation and LBW. Since adjustment for treatments of dental diseases did not affect the ORs, the possibility for dental diseases or treatments to confound the association is diminished but not eliminated. Furthermore, the observation that both orthodontic and endodontic therapies, 2 procedures where diagnostic radiation is common, were associated with TLBW is more suggestive of dental radiography being associated with LBW than dental diseases or procedures.

In summary, this study provides evidence that very low-dose radiation to the maternal head-and-neck region during pregnancy is associated with LBW offspring. If indeed the hypothalamus-pituitary-thyroid axis is somehow involved in the causal pathway, it is possible that a further understanding of disease mechanisms may lead to new intervention strategies for those circumstances where avoidance of very low-dose radiation is difficult. The notion that very low-dose radiation exposures to nonreproductive organs in expectant mothers are safe needs to be investigated further.[19]

Author Contributions: As principal investigator, Dr Hujoel had full access to all of the data in the study and takes full responsibility for the integrity of the data and the accuracy of the analyses.
Study concept and design: Hujoel, Bollen, del Aguila.
Acquisition of data: Hujoel, del Aguila.
Analysis and interpretation of data: Hujoel, Bollen, Noonan, del Aguila.
Drafting of the manuscript: Hujoel, Bollen.
Critical revision of the manuscript for important intellectual content: Hujoel, Bollen, Noonan, del Aguila.
Statistical expertise: Hujoel, Noonan, del Aguila.
Obtained funding: Hujoel.
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Supervision: Hujoel, Bollen.

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