Canadian Agency for Drugs and Technologies in Health

RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

TITLE: **Dental X-rays and Cancer: A Review of the Evidence on Safety**

DATE: 25 May 2012

CONTEXT AND POLICY ISSUES

There is an international trend of increasing population exposure to medical diagnostic sources of radiation.[1,2] In 2006, conventional diagnostic x-rays and fluoroscopy accounted for 74% of medical radiation exposures in the US.[2] This represented only 11% of the cumulative dose of medical radiation exposure due to the fact that the dose per exam is relatively small.[2] In comparison, computed tomography (CT) represents 47% of the cumulative dose.[2] Computed tomography scans deliver approximately 100 times the effective dose of conventional x-rays, and it is the increasing use of CT that is responsible, in a large part, for the increase in population mean dose over the last several years.[1]

Radiation doses are measured in millisieverts (mSv), which is the amount of energy absorbed per gram of tissue.[3] Some examples of radiation doses are as follows:

Head, neck, face, upper spine x-ray[4]	0.01 to 0.03 mSV
Skull x-ray[5]	0.03 to 0.20 mSv
CT head[4,5]	2.0 to 2.6 mSv
Pediatric CT scan to abdomen[6]	25 mSV
Background dose due to natural radiation[6]	3 mSv/year

Dental x-rays are the most common type of conventional x-ray examination worldwide and account for <1% of the global annual per capita effective radiation dose.[2] There are several types of dental x-rays and they vary in the dose of radiation delivered. Bitewings involve two to four individual films usually taken of the molars. Full mouth x-rays involve 10 to 22 individual films of all the teeth. With panoramic x-rays, the x-ray machine rotates around the patient's head and images of all teeth are captured on one film.[7] The effective radiation dose per dental x-ray is estimated to be 0.02 mSv,[2,4] or 0.09 mSv for a panoramic x-ray.[4] The absorbed dose to the brain is 20% to 60% less with panoramic than full mouth x-rays.[7]

Over the years, the dose of radiation per x-ray has decreased with the use of newer technology, such as digital radiography and fast speed radiographic films, and the ALARA principle (as low as reasonably achievable), which became part of medical practice in the 1970's.[4,5,7] It is estimated that the mean patient dose from dental x-rays decreased by 40% from the late 1980's to the late 1990's.[8] Better radiation protection measures such as routine shielding of the patient's neck (thyroid) has also contributed to a reduction in exposure.[8] A substantial decrease in occupational radiation exposure among dental workers was also observed in the 1970's and 1980's in Canada.[3]

Although the radiation exposure with dental x-rays is low, any increased risk associated with dental x-rays would be an important public health concern due to the high prevalence and frequency of these exams. Ionizing radiation is a known risk factor for cancer.[2,3,6,9] Studies of low dose radiation exposure from atomic bomb survivors and patients who received radiation therapy for tinea capitis have shown a dose related increase in the risk of cancer, and that children are more radiosensitive than adults.[1] Atomic bomb survivors who were exposed to mean dose 34 mSv or higher, show a statistically significant increased risk of mortality from solid cancers, compared to those exposed to less than 5 mSv.[1,6] Non-significant increased risk was observed for mean doses as low as 20 mSv.[1,6]

This report will review the available evidence on the risk of cancer associated with exposure to dental x-rays.

RESEARCH QUESTIONS

1. What is the clinical evidence for the risk of developing cancer in patients receiving dental x-rays?

KEY MESSAGE

Based on data from eight case-control studies, there is a possible association between exposure to dental x-rays and meningioma, thyroid cancer, breast cancer, and pediatric rhabdomyosarcoma. This finding must be interpreted in light of the limitations of the studies and is not proof of cause and effect.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 4), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and abbreviated lists of major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between Jan 1, 2002 and Apr 26, 2012. Reference lists of relevant articles were hand searched.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection, according to the selection criteria presented in Table 1.

Table 1: Selection Criteria

Population	Any age group
Exposure	Dental X-rays
Comparator	No exposure to dental X-rays
Outcomes	Any cancer, meningioma, thyroid cancer
Study Designs	HTAs, systematic reviews, meta-analyses, RCTs, non-randomized studies

HTA=health technology assessment; RCT=randomized controlled trial

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria, were duplicate publications, or were published prior to 2002.

Critical Appraisal of Individual Studies

Non-randomized studies were assessed for validity using the JAMA User's Guide for articles about harm.[10]

SUMMARY OF EVIDENCE:

Quantity of Research Available

The selection of studies is summarized in Appendix 1. The literature search yielded 531 citations. Four additional reports were identified by searching the grey literature or hand searching. After screening of abstracts, 23 potentially relevant studies were selected for full text review. Of these, eight non-randomized studies met the inclusion criteria.[4,5,7,8,11-14]

No health technology assessments, systematic reviews, meta-analysis, or randomized controlled trials met the inclusion criteria.

Summary of Study Characteristics

All eight reports were case-control studies that assessed the association between exposure to dental x-rays and brain tumors,[4,5,7,11,14] thyroid cancer,[12] breast cancer,[13] or pediatric rhabdomyosarcoma[8] (Appendix 2). Case-control studies are designed so that patients who have already developed cancer (i.e., cases) are matched to controls, who do not have cancer, but are similar to cases with respect to other determinants of the outcome.[10] Cases and controls are then compared with respect to the frequency of past exposure to the potentially harmful agent (i.e., dental x-rays).

In the included studies, the number of cases per study ranged from 200 to 1742, and these patients were matched to population-based controls in five studies,[5,7,8,11,14] or friend controls,[4] neighborhood controls,[13] or primary care clinic attendees.[12] Except for the friend control study,[4] controls were matched to cases by age and gender, and in some reports, by residence or race. The average age of participants was 49 to 59 years for the brain tumor studies, 35 to 39 years for the thyroid cancer study, 43 years for the breast cancer study, and 7.5 years for the rhabdomyosarcoma study. One study was conducted in Germany,[5] one in Kuwait,[12] and all others were from the US.

In all studies, information on exposures to dental and other sources of radiation was self-reported by participants, and was gathered through in-person, telephone or web-based interviews. One study validated the dental exposure information for 25% of participants by contacting the participants' dentists and abstracting data from dental records.[7] In three reports, detailed information on the number and type of dental x-rays was reported.[4,7,11] This included data on bitewing, full-mouth series, panoramic x-rays, and in one report,[7] lateral cephalometric exams. Six studies included dental x-ray exposures received over the participants lifetime,[5,7,11-14] one study limited to exposures as an adult,[4] and one limited to exposure in utero.[8] In four studies, recent exposures (two[4,5,14] or five years[13]) were excluded from the analysis. Because of the long latency period of most cancers, these recent exposures were not expected to impact on cancer incidence.

Summary of Critical Appraisal

Appendix 3 summarizes the validity assessment of the included studies.

Cases and controls were selected using acceptable methods and sources. In four studies there were imbalances between groups with respect to education attainment or income, which may be related to access to medical care and medical radiation exposure.[5,7,8,11] Limited information on the characteristics of the control participants was available in one report.[12] All exposure data was self-reported using structured questionnaires. None of the interviewers were blinded to case or control status. Objective verification of exposure information was completed for 25% of patients in one study.[7] Only exposures preceding the disease were considered, and the time period of exposures captured was sufficiently long to account for the long latency period of most cancers.

Summary of Findings

The results of the studies are summarized in Appendix 4.

Meningioma

Three studies evaluated the association between dental x-rays and meningioma (Appendix 4 Table 1).[5,7,11] The report by Blettner et al.[5] found no statistically significant association between dental x-rays and meningioma [odds ratio (OR) 0.9 (95% confidence interval (CI) 0.6 to 1.2)].[5]

Claus et al.[11] reported that patients with meningioma were twice as likely to have been exposed to bitewing x-rays, than controls [OR 2.0 (95% CI 1.4 to 2.9)].[11] An increased risk of exposure was found across the age groups evaluated, although the analyses reached statistical significance for those exposed at 10 to 19 years of age, and 20 to 49 years of age only. Yearly or more frequent exposure to bitewings were associated with statistically significant risks of meningioma across the age groups.[11]

No association was found between meningioma and any exposure to full mouth or panoramic x-rays. However, with panoramic x-rays there were some statistically significant age and dose effects found. Exposure before age 10, or between ages 10 and 19 were associated with statistically significant increased risks of meningioma. In addition, increased risks were noted with exposure to yearly or more frequent panoramic x-rays in the different age groups.[11]

The study by Longstreth et al.[7] found that cases were more likely to have been exposed to 6 or more full-mouth x-rays, and this association was statistically significant [OR 2.06 (95% CI 1.03 to 4.17)].[7] None of the other analyses, or dose trends for bitewing, panoramic or lateral cephalometric x-rays showed statistically significant associations with meningioma. The authors analyzed the aggregated full-mouth x-ray exposures for each individual using sliding 10 year intervals to investigate the variation in risk according to timing of dental x-rays. They found an increased risk (i.e., OR >1) starting with the period 15 years prior to diagnosis that became statistically significant beginning 22 to 30 years before diagnosis.[7] No association was found between age of exposure and meningioma.[7] The analysis of the sliding 10 year exposure window for bitewings or panoramic x-rays showed no increase in risk.[7]

Other brain tumors
No association was found between dental x-rays and glioma[4,5,14] or acoustic neuroma (Appendix 4 Table 2).[5]

Thyroid cancer
The study conducted in Kuwait found a statistically significant association between thyroid cancer and dental x-rays [OR 2.1 (95% CI 1.1 to 3.1)], with increasing risk as the number of x-rays increased (Appendix 4 Table 3).[12] The authors reported that shielding of the patient's neck was not common practice when this study was conducted.

Rhabdomyosarcoma
Children with rhabdomyosarcoma were more likely to have had mothers who were exposed to dental, sinus, neck or lower extremity x-rays during their pregnancy, than children without the disease [OR 2.1 (95% CI 1.4 to 7.7)].[8]

Breast cancer
Women with breast cancer were statistically significantly more likely to have had a dental x-ray while not wearing a lead apron, compared to women without breast cancer [OR 2.9 (95% CI 1.5 to 5.4)].[13] No statistically significant association was found between breast cancer and dental x-rays among women who always wore a lead apron, across the range of exposures examined.[13]

Limitations

We conducted a literature search focused on exposure to dental x-rays and it is possible that relevant studies may have been missed if dental related terms were not stated in the abstracts or subject headings.

All of the studies used self-reported information on dental x-ray exposures and only one study[7] validated these data for a subset of patients, using dental records. The possibility of bias due to differential recall of exposures between cases and controls cannot be ruled out. If cases expended more effort than controls to remember exposures that may have contributed to their disease, this recall bias could overestimate the association between x-rays and cancer. Another potential issue related to recall is the effect of the disease on the cognitive function of the participants. In the studies of patients with brain tumors in particular, the disease, or disease treatment may have had an impact on cognitive function. Cases may have been unable to recall exposures or may differentially recall exposures as a result. Some of the studies examined the frequency of different types of dental x-rays and it may have been difficult for patients to distinguish between each type of x-ray (for example, bitewing versus full mouth x-rays). In general, the number and type of x-rays received decades earlier may be difficult to recall, leading to miss-classification of exposures. If cases and controls failed to recall x-ray exposures equally, this non-differential miss-classification may bias the results towards no effect (i.e., OR closer to 1).

The validation sub-study by Longstreth et al,[7] provides some information on the accuracy of the self-reported exposure data. There is some evidence of differential recall, as cases were more likely to over report more recent full mouth x-rays than controls. Recall for bitewings and panoramic x-rays were more accurate than full mouth series. Few dental records were available to validate the most remote x-ray exposures when participants were young.[7]

The use of a proxy (for example a patient's relative) to gather exposure and other data is another source of bias. In the included studies the use of proxies were limited except for one report.[14] In this study 45% of case interviews were completed by a proxy, however analyses of data with, and without, proxy information yielded similar findings.[14] In addition, when interpreting the dose effects, it should be noted that the number of x-rays is a crude estimate of the radiation dose. The dose of radiation for the same exam has been shown to vary depending on the machine used, and doses of radiation per exam have decreased substantially over time.[5] In the Claus et al report,[11] no association between full mouth x-rays and meningioma was found in any analysis. Considering that full mouth series are thought to deliver a higher radiation dose than either bitewing or panoramic x-rays, the observed results are inconsistent with the expected dose gradient.

Within the studies, the cases and controls seemed to be similar with respect to important determinants, although limited information was available to assess similarity in one report.[12] Only three studies adjusted for, or excluded, patients exposed to other important sources of radiation, for example CT scans or radiation therapy.[5,11,12] There were some imbalances in income or education (markers for socioeconomic status) in four studies[5,7,8,11] which could have had an impact on access to medical care and medical radiation exposure. In all four studies, cases had a lower income or education level, which could bias the results towards no effect. In all but one study,[12] known imbalances were adjusted for in the analysis, although the possibility of unmeasured confounding or selection bias remains.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

A dental x-ray is an important diagnostic tool to maintain oral health. X-ray machines have become safer over the years, but due to the prevalence and frequency of dental x-rays, dental radiation exposure is an important public health concern. We identified eight case-control studies that assessed the association between exposure to dental x-rays and brain tumors (5 reports), thyroid cancer (1 report), breast cancer (1 report) or pediatric rhabdomyosarcoma (1 report).

There is some evidence of an association between exposure to dental x-rays and meningioma, and thyroid cancer or breast cancer, when shielding with a lead apron is not used. An association between pediatric rhabdomyosarcoma and maternal exposure to x-rays was also detected. No association between gliomas or acoustic neuromas and dental x-rays were detected. These findings should be interpreted with caution, as there was only one study available for some cancers. The exposure information was collected from self-reports which is prone to recall bias, and the possibility of selection bias or residual confounding that could influence the results of these case-control studies cannot be ruled out. Furthermore, the lack of or inconsistent dose response gradient in some studies brings further uncertainty to the results. Finally, a positive association in an epidemiological study is not proof of cause and effect.

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca

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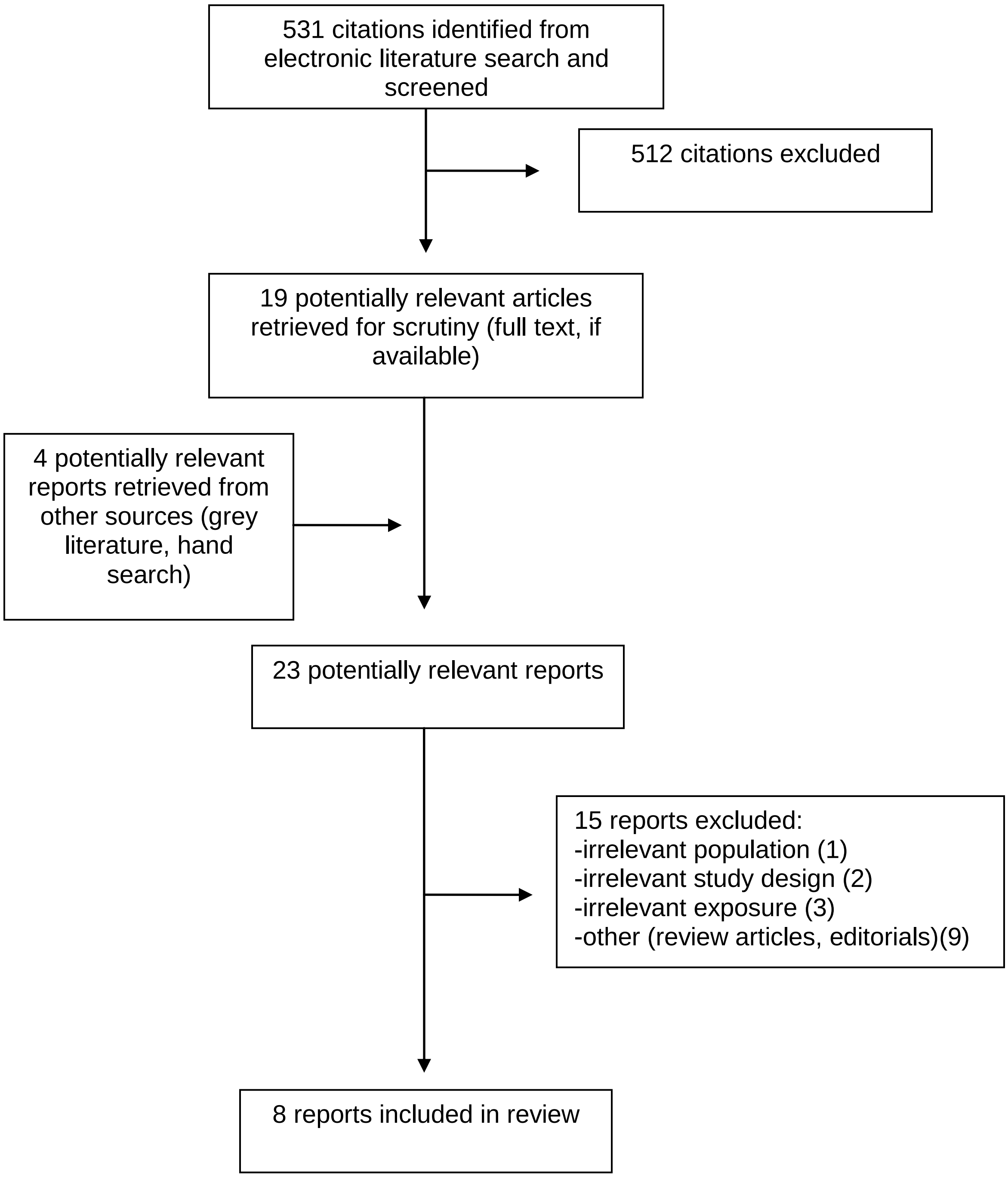
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Characteristics of Included Studies

Author, Year, Country	Objective	Characteristics of cases, N	Characteristics of controls, N	Radiation exposures investigated
Brain tumors				
Claus 2012[11] US	To determine the association between dental x-rays and intracranial meningioma	Histologically confirmed intracranial meningioma diagnosed between 2006 and 2011 (aged 20-79 years at diagnosis). -identified through rapid case ascertainment systems or state cancer registries N=1433	Matched to cases by 5-year age intervals, sex and state of residence. -excluded those with a previous history of meningioma or brain lesion of unknown outcome -identified through random digit dialing N=1350	Dental x-rays throughout lifetime, other therapeutic and diagnostic radiation procedures (self-report)
Davis 2011[4] US	To determine the association between medical diagnostic radiation exposure and gliomas	Adults (≥18 years old) newly diagnosed with glioma between 2003 and 2007, recruited from two referral centers N=205	Friend(s) of cases used as controls N=333	Diagnostic radiation exposure as an adult including x-rays, CT scans, MRI of upper body (self-report)
Blettner 2007[5] Germany	To determine the association between medical or occupational ionizing radiation, EMF, and brain tumors	Newly diagnosed patients with histologically confirmed glioma, meningioma, or acoustic neuroma (between 2000 and 2003), aged 30 to 69 years, admitted to one of four referral centers. N=798	Randomly selected from population registries for the four study regions according to age, sex and regional distribution of cases. -post-hoc 1:2 matching by gender and age ± 2 years. N=1682	Diagnostic x-rays, CT scans, angiography, scintigrams or radiotherapy treatments, occupational exposures to radiation over lifetime (self-report)
Ruder 2006[14] US	To investigate the association between farm and rural exposures and intracranial gliomas	Adults (aged 18 to 80 years) with histologically confirmed primary intracranial gliomas (1995 to 1997) living in non-metropolitan counties -identified through a rapid ascertainment system through physician offices N=798	Adults without glioma living in the same non-metropolitan counties -frequency matched by sex and 10 year age groups -identified through state driver's license, and Health Care Financing Administration registries N=1175	Panoramic dental x-rays exposure over lifetime (self-report)

Author, Year, Country	Objective	Characteristics of cases, N	Characteristics of controls, N	Radiation exposures investigated
Brain tumors				
Longstreth 2004[7] US	To determine the association between dental x-rays and intracranial meningioma	Adults (≥18 years old) newly diagnosed with histologically confirmed intracranial meningioma between 1995 and 1998. -identified through population based cancer registry N=200	Residents of same area, matched to cases based on age (within 5 years) and sex. -identified through random digit dialing and random selection from Medicare eligibility lists (for those ≥65 years) N=400	Dental x-rays, radiation therapy over lifetime (self-report, validation with dental records for 25% of patients)
Thyroid cancer				
Memon 2010[12] Kuwait	To determine the association between dental x-rays and thyroid cancer	History of primary thyroid cancer, alive and aged≤ 70 years at time of study. - identified through population based cancer registry (diagnosis dates not reported) N=313	Matched to cases by age (± 3 years), sex, nationality, and district of residence -identified when visiting or accompanying persons at a primary care clinic N=313	Any diagnostic or dental x-rays to head and chest, or radiotherapy exposure over lifetime (self-report)
Other cancers				
Grufferman 2009[8] US	To determine the association between in utero x-ray exposure and rhabdomyosarcoma in children	Persons 0 to 20 years diagnosed with rhabdomyosarcoma between 1982 and 1988 (surviving and dying patients) N=319	Matched to cases by age (within 1 to 3 year age intervals), sex and race -identified through random digit dialing N=319	X-rays during pregnancy (self-report)
Ma 2008[13] US	To determine the association between medical radiation exposure and breast cancer	Females aged 20 to 49 years when diagnosed with histologically confirmed primary breast cancer (diagnosed between 1998 and 2003) -identified through a population based cancer registry N=1742	Matched to a subset of cases diagnosed between 2000 and 2003, by age (within 5 years) and race -identified from neighborhood where cases resided when diagnosed N=441	Any medical radiation exposure including x-rays, upper gastrointestinal exams, CT exams, angiogram, fluoroscopy and radiation therapy over lifetime (self-report)

CT=computed tomography; EMF=electromagnetic field; MRI=magnetic resonance imaging

APPENDIX 3: Validity Assessment of Case-control Studies

	Claus 2012[11]	Davis 2011[4]	Blettner 2007[5]
Cancer type	Meningioma	Glioma	Meningioma, glioma, acoustic neuroma
Were comparison groups similar with regards to important determinants?	Cases less likely to have annual dental visit, had lower education and income than controls.	Cases and controls were similar with respect to age, race, income and family history of cancer; more males in the case group.	Cases had lower SES than controls.
Were differences adjusted for in analysis?	Adjusted for education, age, sex, race and history of CT of the head.	Adjusted for age, gender; interaction between exposure and family of history of cancer was included in model	Adjusted for age, sex, study center, SES, urban/rural residence, occupational exposure to radiation
Were exposures measured in the same way in the groups?	Telephone interview with structured questionnaire -unclear if interviewer was blinded to case or control status. -no validation with objective source of exposure data. -proxy <1% cases, 0% controls	Web-based or telephone survey. -resurvey of a subset of questions showed responses were reasonably reliable. -unclear if interviewer was blinded to case status -patients had to have mental capacity to consent (based on MMSE)	In-person interview using computer assisted interview program. -interviewer was not blinded to case status -no validation with objective sources -proxy interviewed for 6% of cases, <1% controls. -authors reported glioma patients had difficulty completing questions
Was follow up sufficiently long and complete?	Exposure information collected over lifetime of participant.	Exposure as an adult only	Exposure over lifetime up to 2 years prior
Is the temporal relationship correct?	Analysis included exposures up until date of interview (controls) or diagnosis (cases)	Included exposures as an adult, up to 2 years prior to diagnosis	Included exposures up to 2 years prior to diagnosis for cases, or equivalent reference date for matched case.
Is there a dose response gradient?	Dose gradient inconsistent	Yes, for CT scans but not for other radiation exposures	Not assessed
Comments	Controlled for CT head and excluded those who had undergone radiation therapy		Analysis did not separate dental x-rays from other x-rays of head and neck. Controlled for occupational radiation exposure

CT=computed tomography; MMSE=Mini-Mental State Examination; SES=socioeconomic status

	Ruder 2006[14]	Longstreth 2004[7]
Cancer type	Glioma	Meningioma
Were comparison groups similar with regards to important determinants?	Cases selected represent 78% of all glioma patients in the study area. Cases and controls were similar in most variables reported.	Fewer cases had attended college than the controls. Past dental procedures and years of dental care were similar between groups.
Were differences adjusted for in analysis?	Adjusted for age, sex, education	Adjusted for education
Were exposures measured in the same way in the groups?	In person or telephone interview using structured questionnaire -interviewer was not blinded to case status but was unaware of the study hypothesis and received training on interview methods -study coordinator re-interviewed 10% of participants for key exposure questions. Interviewers were re-trained if inconsistencies were found. -proxies were interviewed for 45% of cases and 3% of controls	In-person interview using structured questionnaire -interviewer not blinded to case status -case patients interviewed on average 212 days after reference date (date of surgery) and controls were interviewed 870 days after (same date as matched case). -validation sub-study (n=147) using dental records found over-reporting of full mouth, under reporting of cephalometric x-rays, and more accurate recall of bitewing and panoramic x-rays. -multiple imputation was used to fill in gaps in exposure history -proxies interviewed for 7% of cases
Was follow up sufficiently long and complete?	Exposure over lifetime up to 1993 (2 to 4 years prior to diagnosis)	Exposure over lifetime analyzed
Is the temporal relationship correct?	Exposures up to Jan 1993 considered in analysis	Analysis included exposures up to reference date.
Is there a dose response gradient?	Not assessed	No dose response detected
Comments	Dental x-ray exposure not the focus of study	Analysis excluding those with history of radiation therapy showed strengthened results for full mouth series.

	Memon 2010[12]	Grufferman 2009[8]	Ma 2008[13]
Cancer type	Thyroid	Rhabdomyosarcoma	Breast cancer
Were comparison groups similar with regards to important determinants?	Cases were survivors of thyroid cancer (year of diagnosis not reported). No details on controls provided.	Cases had lower family income levels. Cases and controls had similar obstetric histories except for premature birth, and vaginal bleeding during pregnancy, which was more likely in cases. Controls were more likely to have an overdue birth.	Cases were different from controls on a number of factors related to breast cancer (for example family history of breast cancer, early menarche, parity,).
Were differences adjusted for in analysis?	Adjusted for exposure to head, neck or chest x-rays	Adjustment for obstetric history or SES did not change results.	Adjusted for differences in breast cancer risk factors
Were exposures measured in the same way in the groups?	In person interview with structured questionnaire -interviewer unblinded but was unaware of epidemiology of thyroid cancer. -no validation with objective source of exposure data. Consistency of responses assessed by re-survey of a random subset of participants.	Telephone interview with mothers using structured questionnaire -unclear if interviewer was blinded to case or control status. -no validation with objective source of exposure data.	In-person interview using structured questionnaire -unclear if interviewer was blinded to case or control status. -no validation with objective source of exposure data.
Was follow up sufficiently long and complete?	Radiation exposures over lifetime were collected.	Limited to duration of pregnancy.	Exposure information collected over lifetime of participant
Is the temporal relationship correct?	Any exposure prior to diagnosis or reference date (when the control the same age as matched case) included in analysis.	Yes, exposure during pregnancy.	Any exposure prior to diagnosis or reference date (when controls first contacted). Analyses excluded exposures within 5 years of reference date.
Is there a dose response gradient?	Dose gradient observed	Not assessed	Not for dental x-rays but gradient was detected for chest x-ray or mammogram exposure
Comments	Lead aprons were not commonly used during the study period.	Analysis did not separate dental x-rays from other x-ray exposures	

SES=socioeconomic status

APPENDIX 4: Association between exposure to dental x-rays and cancer

Table 1. Meningioma

Author, year, subgroup	Exposure group/ frequency	Bitewing x-ray Adj OR (95% CI)	Full mouth x-ray Adj OR (95% CI)	Panoramic x-ray Adj OR (95% CI)	Any dental x-ray Adj OR (95% CI)
Meningioma					
Claus 2012[11] [a]	Exposure at any age (yes/no)	2.0 (1.4 to 2.9)	1.0 (0.9 to 1.3)	1.0 (0.8 to 1.2)	NR
	Age < 10 years	1.3 (1.0 to 1.7)	1.2 (0.8 to 1.7)	4.9 (1.8 to 13.2)	
	Age 10 to 19 years	1.4 (1.1 to 1.7)	1.1 (0.9 to 1.4)	1.5 (1.1 to 2.1)	
	Age 20 to 49 years	1.7 (1.3 to 2.2)	1.0 (0.9 to 1.2)	0.9 (0.7 to 1.1)	
	Age ≥ 50 years	1.2 (0.9 to 1.6)	1.1 (0.9 to 1.4)	1.2 (0.9 to 1.5)	
Sub-groups					
Age<10 years	None (reference)	1.0	1.0	1.0	NR
	< 1 yearly	1.3 (1.0 to 1.8)	1.2 (0.8 to 1.7)	4.9 (1.8 to 13.2)**	
	Yearly or more frequent	1.4 (1.0 to 1.8)	1.3 (0.8 to 2.3)	--	
Age 10-19 years	None (reference)	1.0	1.0	1.0	NR
	< 1 yearly	1.3 (1.1 to 1.6)	1.1 (0.9 to 1.4)	1.3 (0.9 to 1.9)	
	Yearly or more frequent	1.6 (1.2 to 2.0)	1.2 (0.9 to 1.8)	3.0 (1.2 to 7.8)	
Age 20-49 years	None (reference)	1.0	1.0	1.0	NR
	< 1 yearly	1.6 (1.2 to 2.1)	1.0 (0.8 to 1.2)	0.9 (0.7 to 1.0)	
	Yearly or more frequent	1.9 (1.4 to 2.6)	1.1 (0.8 to 1.5)	2.7 (1.4 to 5.3)	
Age≥50 years	None (reference)	1.0	1.0	1.0	NR
	< 1 yearly	1.1 (0.8 to 1.4)	1.1 (0.9 to 1.4)	1.0 (0.8 to 1.3)	
	Yearly or more frequent	1.5 (1.1 to 2.0)	1.1 (0.8 to 1.6)	3.0 (1.6 to 5.6)	

Author, year, subgroup	Exposure group/ frequency	Bitewing x-ray Adj OR (95% CI)	Full mouth x-ray Adj OR (95% CI)	Panoramic x-ray Adj OR (95% CI)	Any dental x-ray Adj OR (95% CI)
Meningioma					
Blettner 2007[5] [b]	Ever exposed to dental or other x-ray to head or neck (yes/no)	NR	NR	NR	0.9 (0.6 to 1.2)
Longstreth 2004[7] [c]	No exposure (reference)	1.0	1.0	1.0	Lateral cephalometric x-ray 1.0
	Lower exposure †	1.6 (0.7 to 3.5)	0.9 (0.6 to 1.3)	0.9 (0.4 to 1.6)	0.9 (0.6 to 1.3)
	Higher exposure †	1.0 (0.5 to 2.1)	2.1 (1.03 to 4.17)	0.8 (0.4 to 1.6)	--

Adj=adjusted; CI=confidence interval; NR=not reported; OR=odds ratio

[a] Adjusted for age, sex, education, race (white versus nonwhite), and history of head CT

[b] Exposure defined as at least one plain x-ray of the head or neck, including panorama/full mouth dental series but not x-rays of individual teeth. Adjusted for or stratified by gender, age, study center, SES, living in urban area, and occupational radiation exposure.

[c] Adjusted for education. P values for dose trend were not statistically significant for any type of x-ray.

** OR for ever being exposed to panoramic x-ray

† Exposure frequency as follows: bitewing, lower=1 to 10 x-rays, higher=11 or more x-rays; full-mouth, lower=1 to 5 x-rays, higher=6 or more x-rays; panoramic, lower=1 to 2 x-rays, higher=3 or more x-rays; lateral cephalometric, lower=1 or more x-rays.

Table 2. Glioma or Acoustic Neuroma

Author, year	Group/ Frequency	Panoramic x-ray OR (95% CI)	Any dental x-ray OR (95% CI)
Glioma			
Davis 2011[4 a]	*Total number of exams*		
	none (reference)	1.0	NR
	1 to 2 exams	0.95 (0.6 to 1.6)	
	3+ exams	0.7 (0.4 to 1.2)	
	Frequency		
	none (reference)	NR	1.0
	< 1 yearly		0.6 (0.2 to 1.7)
	Yearly or more frequent		0.6 (0.2 to 1.7)
Blettner 2007[5 b]	Ever exposed to dental or other x-ray to head or neck (yes/no)	NR	0.6 (0.4 to 0.8)
Ruder 2006[14 c]	Ever exposed (yes/no) Including proxy interviews	0.8 (0.6 to 0.9)	NR
	Excluding proxy interviews	0.7 (0.5 to 0.9)	NR
Acoustic neuroma			
Blettner 2007[5 b]	Ever exposed to dental or other x-ray to head or neck (yes/no)	NR	0.8 (0.4 to 1.6)

Adj=adjusted; CI=confidence interval; NR=not reported; OR=odds ratio
[a] Adjusted for age and gender. P values for dose trend were not statistically significant for panoramic or dental x-rays.
[b] Exposure defined as at least one plain x-ray of the head or neck, including panorama/full mouth dental series but not x-rays of individual teeth. Adjusted for, or stratified by gender, age, study center, SES, living in urban area, and occupational radiation exposure.
[c] Adjusted for age, age group, education, state and sex

Table 3. Other cancers

Author, year	Exposure group/ frequency	Adjusted OR (95% CI)
Thyroid cancer		
Memon 2010[12 a]	Ever had dental x-ray (yes/no)	2.1 (1.4 to 3.1)
	Frequency of exposure	
	No exposure	1.0 (reference)
	1 to 4 x-rays	2.2 (1.4 to 3.5)
	5 to 9 x-rays	4.6 (1.4 to 14.7)
	≥ 10 x-rays	5.4 (1.1 to 26.7) p value for dose trend<0.0001
Rhabdomyosarcoma		
Grufferman 2009[8 b]	Dental/upper or lower body x-rays at any time during pregnancy (yes/no)	2.9 (1.1 to 7.7)
	Trimester of exposure	
	First trimester	NE
	Second trimester	0.8 (0.2 to 3.1)
	Third trimester	4.8 (0.5 to 45.6)

Author, year	Exposure group/ frequency	Adjusted OR (95% CI)	
Breast cancer			
Ma 2008[13] [c]	Always wore lead apron during dental x-rays or had no dental x-rays	1.0 (reference)	
	Did not always wear apron - age <20 years	1.5 (0.9 to 2.5)	
	- age >20 years	1.4 (0.8 to 2.7)	
	- before and after 20 years old	2.9 (1.5 to 5.4)	
	Lead apron use unknown	1.3 (0.9 to 1.7)	
		Age at exposure	
	Women who always wore lead apron during dental x-rays	**Before age 20**	**After age 20**
	- Less than 1 x-ray every 5 years	1.0 (reference)	1.0 (reference)
	- At least 1 x-ray every 5 years	1.2 (0.8 to 2.0)	1.0 (0.7 to 1.6)
	- At least 1 x-ray every 3 years	1.4 (1.0 to 2.0)	0.8 (0.5 to 1.2)
	- About one x-ray per year	1.0 (0.7 to 1.5)	1.0 (0.6 to 1.4)
	Women who did not always wear lead apron	1.8 (1.1 to 2.9)	1.3 (0.8 to 2.2)
	Lead apron use unknown	1.2 (0.8 to 1.9)	1.7 (0.9 to 3.1)

Adj=adjusted; CI=confidence interval; NE=not estimable; OR=odds ratio

[a] Adjusted for upper-body x-rays (head, neck or chest)

[b] Includes cases and controls exposed to dental (n=15) , sinus (n=1), neck (n=1) and lower extremity (n=7) x-rays. Adjusted for age, sex, race, length of pregnancy, delivery type, presence of spotting or cramping during pregnancy

[c] Adjusted for age group, race, education, family history of breast or ovarian cancer, age at menarche, parity, age at first term pregnancy, BMI, alcohol consumption, menopause/hormone status, history of benign breast disease.