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**Appendix A.** Database search strategy for article identification and inclusion

#1 "Tomography, X-Ray Computed/adverse effects"[Mesh] OR “Tomography, X-Ray Computed/contraindications” "[Mesh] OR “Tomography, X-Ray Computed/mortality"[Mesh] OR “Tomography, X-Ray Computed/pathology"[Mesh] OR “Tomography, X-Ray Computed/physiopathology"[Mesh] OR “Tomography, X-Ray Computed/radiation effects"[Mesh]

#2 “X-Rays/adverse effects"[Mesh] OR “X-Rays/complications"[Mesh]

#3 "Radiography/adverse effects"[Mesh] OR "Radiography/complications"[Mesh] OR "Radiography/contraindications"[Mesh] OR "Radiography/mortality"[Mesh] OR "Radiography/radiation effects"[Mesh] OR “radiography/pathology"[Mesh] OR “Radiography/physiopathology"[Mesh]

#4 "Diagnostic Imaging/adverse effects"[Mesh] OR "Diagnostic Imaging/complications"[Mesh] OR "Diagnostic Imaging/contraindications"[Mesh] OR "Diagnostic Imaging/mortality"[Mesh] OR "Diagnostic Imaging/pathology"[Mesh] OR "Diagnostic Imaging/physiopathology"[Mesh] OR “Diagnostic Imaging/radiation effects"[Mesh]

#5 Tomography, X-Ray Computed OR X-Rays OR Radiography OR CAT Scan OR CAT Scans OR PET Scan OR PET Scans

#6 Occupational Diseases OR Occupational Exposure OR radiologists OR radiologist

#7 (#1 OR #2 OR #3 OR #4 OR #5 OR #6)

#8 Neoplasms, Radiation-Induced OR Leukemia, Radiation-Induced OR Radiation-Induced Neoplasms OR Radiation-Induced Neoplasm OR Radiation-Induced Cancer OR Radiation-Induced Cancers OR “cancer death risk” OR Dose-Response Relationship, Radiation OR Radiation-induced effects OR Radiation Dosage OR Radiation Exposure OR radiation risk OR Dose-Response Relationship, Radiation [mh] OR Radiation Exposure OR Radioactive Hazard Release [mh]

#9 #7 OR #8

#10 “low dose” OR “low dosage” OR "low doses” OR “low dosing” OR “small dose” OR “small dosage” OR "small doses” OR “small dosing” OR "minimal dose" OR "minimal doses" OR "minimal dosing"

#11 #9 AND #10

#12 Risk assessment OR risk factors OR Risk [ti ab] OR risks [ti/ab]

#13 #9 AND #12

#14 #11 OR #13 Filters: Publication date from 1975/01/01; English

**Appendix B:** Newcastle - Ottawa Quality Assessment Scale

Case Control Studies

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

**Selection**

1) Is the case definition adequate?

a) yes, with independent validation ****

b) yes, eg record linkage or based on self-reports`

c) no description

2) Representativeness of the cases

a) consecutive or obviously representative series of cases ****

b) potential for selection biases or not stated

3) Selection of Controls

a) community controls ****

b) hospital controls

c) no description

4) Definition of Controls

a) no history of disease (endpoint) ****

b) no description of source

**Comparability**

1) Comparability of cases and controls on the basis of the design or analysis

a) study controls for \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (Select the most important factor.) ****

b) study controls for any additional factor **** (This criteria could be modified to indicate

 specific control for a second important factor.)

**Exposure**

1) Ascertainment of exposure

a) secure record (eg surgical records) ****

b) structured interview where blind to case/control status ****

c) interview not blinded to case/control status

d) written self report or medical record only

e) no description

2) Same method of ascertainment for cases and controls

a) yes ****

b) no

3) Non-Response rate

a) same rate for both groups ****

b) non respondents described

c) rate different and no designation

Cohort Studies

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

**Selection**

1) Representativeness of the exposed cohort

a) truly representative of the average \_\_\_\_\_\_\_\_\_\_\_\_\_\_(describe) in the community ****

b) somewhat representative of the average \_\_\_\_\_\_\_\_\_\_\_\_\_\_ in the community ****

c) selected group of users eg nurses, volunteers

d) no description of the derivation of the cohort

2) Selection of the non-exposed cohort

a) drawn from the same community as the exposed cohort ****

b) drawn from a different source

c) no description of the derivation of the non-exposed cohort

3) Ascertainment of exposure

a) secure record (eg surgical records) ****

b) structured interview ****

c) written self-report

d) no description

4) Demonstration that outcome of interest was not present at start of study

a) yes ****

b) no

**Comparability**

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for \_\_\_\_\_\_\_\_\_\_\_\_\_ (select the most important factor) ****

b) study controls for any additional factor **** (This criteria could be modified to indicate specific control for a second important factor.)

**Outcome**

1) Assessment of outcome

a) independent blind assessment ****

b) record linkage ****

c) self report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes (select an adequate follow up period for outcome of interest) ****

b) no

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for ****

b) subjects lost to follow up unlikely to introduce bias - small number lost - > \_\_\_\_ % (select an adequate % follow up, or description provided of those lost) ****

c) follow up rate < \_\_\_\_% (select an adequate %) and no description of those lost

d) no statement

**Appendix C.** Lower Quality Indicators

|  |  |
| --- | --- |
| Quality Indicator Number | Lower Quality Indicator Description  |
| 1 | Use of 90% Confidence Intervals |
| 2 | Use of 1-tailed tests of significance |
| 3 | Interview and/or questionnaire based |
| 4 | Potential confounding by internal contamination |
| 5 | Failure to address significant predisposing factors or confounding variables |
| 6 | Failure to address reverse causation |
| 7 | Use of methodological approaches that minimize or obscure detection of a threshold at low doses (analyzing low and high dose exposures together as one phenomenon, reporting cancers/Gy, use of a linear model) combined with failure to also explore non-linear mathematical models to depict the data relationships |
| 8 | Inclusion of data later invalidated |
| 9 | Failure to measure radiation dose directly or by a validated approximation |
| 10 | Making multiple statistical comparisons without adjusting confidence intervals or p-values for primary outcomes |
| 11 | Participation rate of less than 80% in survey study or dataset |

**Appendix D.** Articles and scores using NOS, lower quality indicators, and NIH assessment

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **Year** | **Total NOS** | **Selection** | **Comparability** | **Outcome** | **Low Quality Indicators** | **LNT** |
| Grant EJ, Brenner A | 2017 | 8 | 4 | 1 | 3 | 4, 7 | Supports |
| Kitahara CM, Linet MS | 2017 | 8 | 3 | 2 | 3 | 7, 11 | Refutes |
| Daniels RD, Bertke SJ | 2017 | 7 | 3 | 1 | 3 | 1, 4, 7 | Supports |
| Hsieh WH, Lin IF | 2017 | 7 | 4 | 0 | 3 | 1, 3, 5, 7 | Supports |
| De Gonzalez, AB, Salotti, JA | 2016 | 7 | 3 | 1 | 3 | 6, 7 | Supports |
| Wang, F, Sun, Q | 2016 | 6 | 3 | 0 | 3 | 3, 5, 9, 10 | Supports |
| Ohira, T, Takahashi, H | 2016 | 4 | 2 | 0 | 2 | 3, 4, 5, 11 | Refutes |
| Preston DL, Kitahara CM | 2016 | 8 | 3 | 2 | 3 | 7, 9, 11 | Supports |
| Smoll NR, Brady Z | 2016 | 8 | 4 | 1 | 3 | 1, 4, 5, 7 | Supports |
| Richardson DB, Cardis E | 2015 | 7 | 3 | 1 | 3 | 1, 2, 4, 7 | Supports |
| Leuraud K, Richardson DB | 2015 | 7 | 3 | 1 | 3 | 1, 2, 7 | Supports |
| Krille L, Dreger S | 2015 | 8 | 4 | 2 | 2 | 10  | Refutes |
| Journy N, Rehel J-L | 2015 | 8 | 4 | 2 | 2 |  | Refutes |
| Socol, Y, Dobrzyński, L | 2015 | 8 | 4 | 1 | 3 | 4 | Refutes |
| Lee, T, Sigurdson, AJ | 2015 | 6 | 2 | 2 | 2 | 3, 7, 9, 11 | Refutes |
| Schubauer-Berigan MK, Daniels RD | 2015 | 8 | 4 | 1 | 3 |  4, 7, 10 | Supports |
| Huang WY, Muo CH | 2014 | 8 | 4 | 2 | 2 | 6, 10 | Supports |
| White IK, Shaikh KA | 2014 | 6 | 3 | 0 | 3 | 5 | Refutes |
| Zablotska LB, Lane RSD | 2014 | 7 | 3 | 1 | 3 | 7  | Refutes |
| Sasaki MS, Tachibana A | 2014 | 8 | 4 | 1 | 3 | 4 | Refutes |
| Merzenich H, Hammer GP | 2014 | 8 | 4 | 1 | 3 | 5  | Refutes |
| Mathews JD, Forsythe AV | 2013 | 6 | 3 | 0 | 3 | 5, 6 | Supports |
| Cappa, M, Cambiaso, P | 2013 | 7 | 4 | 1 | 2 | 11 | Refutes |
| Metz-Flamant C, Laurent O | 2013 | 8 | 4 | 1 | 3 | 1, 2, 4, 7, 10 | Refutes |
| Samartzis D, Nishi N | 2013 | 8 | 4 | 1 | 3 | 4, 5, 7  | Supports |
| Choi KH, Ha M | 2013 | 7 | 4 | 1 | 2 | 5, 7, 10, 11 | Supports |
| Daniels RD, Bertke S | 2013 | 8 | 3 | 2 | 3 | 4 | Supports |
| Tao Z, Akiba S | 2012 | 7 | 3 | 1 | 3 | 4, 7 | Refutes |
| Hammer GP, Blettner M | 2012 | 7 | 3 | 1 | 3 | 5 | Refutes |
| Eisenberg MJ, Afilalo J | 2011 | 5 | 4 | 0 | 1 | 5 | Supports |
| Hammer GP, Seidenbusch MC | 2011 | 9 | 4 | 2 | 3 |  | Refutes |
| Pogoda, JM, Nichols, PW | 2011 | 6 | 3 | 1 | 2 | 3, 6, 11 | Refutes |
| Boice JD, Cohen S | 2011 | 9 | 4 | 2 | 3 | 2, 4  | Refutes |
| Yuan, M-K, Chien, C-W | 2010 | 3 | 2 | 0 | 1 | 5, 9, 10 | Refutes |
| Ronckers CM, Land CE | 2010 | 8 | 3 | 2 | 3 | 7, 9, 10, 11 | Supports |
| Jeong M, Jin YW | 2010 | 7 | 3 | 2 | 2 | 4 | Refutes |
| Muirhead CR, O’Hagan JA | 2009 | 8 | 4 | 1 | 3 | 1, 2, 4, 7 | Supports |
| Nair RRK, Rajan B | 2009 | 9 | 4 | 2 | 3 | 4, 7 | Refutes |
| Zielinski JM, Garner MJ | 2009 | 5 | 2 | 1 | 2 | 1, 4, 5, 10, 11 | Supports |
| Ronckers CM, Doody MM | 2008 | 6 | 3 | 1 | 2 | 2, 7, 11 | Supports |
| Vrijheid M, Cardis E | 2008 | 6 | 3 | 1 | 2 | 4, 7 | Refutes |
| Gun RT, Parsons J | 2008 | 7 | 3 | 1 | 3 | 4, 5 | Refutes |
| Cardis E, Vrijheid M | 2007 | 7 | 3 | 1 | 3 | 1, 2, 4, 7, 8, 10 | Supports |
| Yiin JH, Silver SR | 2007 | 7 | 2 | 2 | 3 | 7 | Refutes |
| Cardis E, Vrijheid M | 2005 | 7 | 3 | 1 | 3 | 4, 7, 8 | Supports |
| Lambe M, Hall P | 2005 | 6 | 4 | 0 | 2 | 5, 9 | Refutes |
| Zielinski JM, Garner MJ | 2005 | 5 | 2 | 0 | 3 | 1, 5 | Refutes |
| Sponsler R, Cameron JR | 2005 | 9 | 4 | 2 | 3 |  | Refutes |
| Engels H, Swaen GM | 2005 | 8 | 3 | 2 | 3 | 1, 4, 10 | Refutes |
| Howe GR, Zablotska LB | 2004 | 9 | 4 | 2 | 3 | 7  | Refutes |
| Langner I, Blettner M | 2004 | 6 | 2 | 1 | 3 | 5 | Refutes |
| Iwasaki T, Murata M | 2003 | 6 | 3 | 1 | 2 | 5 | Refutes |
| Artalejo FR, Lara SC | 1997 | 6 | 2 | 2 | 2 | 4 | Refutes |
| Matsuura M, Hoshi M | 1997 | 7 | 3 | 1 | 3 | 1, 4, 5, 7, 10, 11 | Supports |
| Howe GR, McLaughlin J | 1996 | 7 | 3 | 1 | 3 | 5, 7, 9 | Supports |
| Inskip PD, Ekbom A | 1995 | 8 | 4 | 1 | 3 | 5, 6 | Refutes |
| Cardis E, Gilbert ES | 1995 | 7 | 3 | 1 | 3 | 1, 2, 4, 7, 8 | Supports |
| Jablon S, Boice JD | 1993 | 5 | 3 | 0 | 2 | 4, 5  | Refutes |
| Boice JD Jr, Morin MM | 1991 | 7 | 3 | 1 | 3 | 5, 6 | Refutes |
| Hoffman DA, Lonstein JE | 1989 | 6 | 2 | 1 | 3 | 1, 2, 3, 5, 7 | Supports |
| Storm HH, Iversen E | 1986 | 7 | 3 | 2 | 2 | 7, 11 | Refutes |
| **Authors** | **Year** | **NIH Quality Assessment Score for Meta-Analyses** | **Positive Criteria** | **Low Quality Indicators** |  |
| Jansen-Van Der Weide, MC | 2010 | 5 out of 8 possible criteria | 1, 4, 5, 6, 7 | 5,9 | Supports |

**Appendix E.** Newcastle Ottawa Scale data collection tool

Coding Manual for Case-Control Studies

***SELECTION***

1. **Is the Case Definition Adequate?**
2. Requires some independent validation (e.g. >1 person/record/time/process to extract information, or reference to primary record source such as x-rays or medical/hospital records)
3. Record linkage (e.g. ICD codes in database) or self-report with no reference to primary record
4. No description
5. **Representativeness of the Cases**
6. All eligible cases with outcome of interest over a defined period of time, all cases in a defined catchment area, all cases in a defined hospital or clinic, group of hospitals, health maintenance organisation, or an appropriate sample of those cases (e.g. random sample)
7. Not satisfying requirements in part (a), or not stated.
8. **Selection of Controls**

This item assesses whether the control series used in the study is derived from the same population as the cases and essentially would have been cases had the outcome been present.

1. Community controls (i.e. same community as cases and would be cases if had outcome)
2. Hospital controls, within same community as cases (i.e. not another city) but derived from a hospitalised population
3. No description
4. **Definition of Controls**
5. If cases are first occurrence of outcome, then it must explicitly state that controls have no history of this outcome. If cases have new (not necessarily first) occurrence of outcome, then controls with previous occurrences of outcome of interest should not be excluded.
6. No mention of history of outcome

***COMPARABILITY***

1. **Comparability of Cases and Controls on the Basis of the Design or Analysis**

A maximum of 2 stars can be allotted in this category

Either cases and controls must be matched in the design and/or confounders must be adjusted for in the analysis. Statements of no differences between groups or that differences were not statistically significant are not sufficient for establishing comparability. Note: If the odds ratio for the exposure of interest is adjusted for the confounders listed, then the groups will be considered to be comparable on each variable used in the adjustment.

There may be multiple ratings for this item for different categories of exposure (e.g. ever vs. never, current vs. previous or never)

 Age = Other controlled factors =

***EXPOSURE***

1. **Ascertainment of Exposure**

Allocation of stars as per rating sheet

1. **Non-Response Rate**

Allocation of stars as per rating sheet