**APPENDIX A**

**Table S1: PRISMA checklist**

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic** | **#** | **Checklist item** | **Reported on page #** |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | |  |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3-4 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4 |
| **METHODS** | | |  |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 5 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 5 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 5 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 5 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 6 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 6 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 6 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 6 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 7 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis. | 7 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 7 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 7 |
| **RESULTS** | | |  |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 8 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 8 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 9 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 9 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 9 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 9 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 9-10 |
| **DISCUSSION** | | |  |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 10 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 11 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 12-13 |
| **FUNDING** | | |  |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 15 |

**Table S2: Literature search strategies**

|  |  |
| --- | --- |
| PUBMED: | **(((("firefighter"[mesh] OR "firefighter"[tiab] OR "firefighter"[ot] OR "fire"[mesh] OR "fire"[tiab] OR "fire"[ot] OR"firefighting"[mesh] OR "firefighting"[tiab] OR "firefighting"[ot] OR "first responder"[mesh] OR "first responder"[tiab] OR "first responder"[ot]) AND (("cancer"[mesh] OR "cancer"[tiab] OR "cancer"[ot] OR "lymphoma"[mesh] OR "lymphoma"[tiab] OR "lymphoma"[ot] OR "mesothelioma"[mesh] OR "mesothelioma"[tiab] OR "mesothelioma"[ot] OR "myeloma"[mesh] OR "myeloma"[tiab] OR "myeloma"[ot] OR "melanoma"[mesh] OR "melanoma"[tiab] OR "melanoma"[ot] OR "leukemia"[mesh] OR "leukemia"[tiab] OR "leukemia"[ot] OR "malignancy"[mesh] OR "malignancy"[tiab] OR "malignancy"[ot] OR "malignant"[mesh] OR "malignant"[tiab] OR "malignant"[ot] OR "tumor "[mesh] OR "tumor "[tiab] OR "tumor "[ot] OR "carcinoma"[mesh] OR "carcinoma"[tiab] OR "carcinoma"[ot])) AND (("2009/01/01"[PDAT] : "2020/04/30"[PDAT])) AND (English[lang])** |
| NIOSHTIC-2: | **fire OR firefighter OR firefighting AND cancer OR lymphoma OR mesothelioma OR myeloma OR melanoma OR leukemia OR malignancy OR malignant OR tumor OR carcinoma AND (2009/01/01 to 2020/04/30)** |
| GOOGLE SCHOLAR: | **fire OR firefighter OR firefighting OR ‘First Responder’ AND cancer OR lymphoma OR mesothelioma OR myeloma OR melanoma OR leukemia OR malignancy OR malignant OR tumor OR carcinoma AND (2009/01/01 to 2020/04/30)** |

**Table S3: Cancer types extracted from the studies included in the meta-analysis based on the ICD-10**

|  |  |
| --- | --- |
| **Code** | **Cancer Type** |
| C00-C97 | All cancers |
| C00-C14 | Buccal cavity and pharynx |
| C15 | Esophagus |
| C16 | Stomach |
| C17 | Small Intestine |
| C18 | Large intestine |
| C17-C18± | Colon |
| C19-C21 | Rectum |
| C22-C23 | Liver/Gallbladder |
| C25 | Pancreas |
| C32 | Larynx |
| C33-C34 | Lung |
| C40-C41 | Bone |
| C43 | Malignant Melanoma |
| C44 | Skin |
| C45 | Pleura (mesothelioma) |
| C49 | Soft tissue sarcoma |
| C50 | Breast |
| C60, C63 | Other male genital organs |
| C61 | Prostate |
| C62 | Testis |
| C64-C66 | Kidney |
| C67 | Bladder |
| C69 | Eye |
| C47, C70-C72 | Brain |
| C73 | Thyroid |
| C46.3, C82-C85, C88.0, C88.3, C91.4, C96 | Non-Hodgkin’s lymphoma |
| C81 | Hodgkin’s Disease |
| C88.7, C88.9, C90 | Multiple Myeloma |
| C91.0-C91.3, C91.5-C91.9, C92-C95 | Leukemia |

±If not specified as either large (C18) or small (C17) intestine

**Table S4: Extracted estimates on cancer incidence from case-control and cohort studies**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **First author, year** | **International Classification of Disease Code (ICD)-10** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| C00-C97 | C00-C14 | C15 | C16 | C17 | C18 | C17-C18 | C19-C21 | C22-C23 | C25 | C32 | C33-C34 | C40-C41 | C43 | C44 | C45 | C49 | C50 | C60, C63 | C61 | C62 | C64-C66 | C67-C68 | C69 | C47, C70-C72 | C73 | C46.3, C82-C85, C88.0, C88.3, C91.4, C96 | C81 | C88.7, C88.9, C90 | C91.0-C91.3, C91.5-C91.9, C92-95 | Other Cancer |
| **Case-Control** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kang, 2008 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Corbin, 2011 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Villeneuve, 2011 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Karami, 2012 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Paget-Bailly, 2013 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Tsai, 2015 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Bigert, 2016 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lee, 2019 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Langevin, 2020 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Cohort** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ahn, 2012 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Daniels, 2014\* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pukkala, 2014 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Glass, 2016\* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Kullberg, 2017 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Petersen, 2017 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Sritharan, 2018 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Harris, 2018 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\*Reported cancer incidence and mortality.

**Table S5: Extracted estimates on cancer mortality from case-control and cohort studies**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **First author, year** | **International Classification of Disease Code (IDC)-10** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| C00-C97 | C00-C14 | C15 | C16 | C17 | C18 | C17-C18 | C19-C21 | C22-C23 | C25 | C32 | C33-C34 | C40-C41 | C43 | C44 | C45 | C49 | C50 | C60, C63 | C61 | C62 | C64-C66 | C67-C68 | C69 | C47, C70-C72 | C73 | C46.3, C82-C85, C88.0, C88.3, C91.4, C96 | C81 | C88.7, C88.9, C90 | C91.0-C91.3, C91.5-C91.9, C92-95 | Other Cancer |
| **Case-Control** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Muegge, 2018 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Cohort** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Daniels, 2014\* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Brice, 2015 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ahn, 2015 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Glass, 2016\* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Petersen, 2018 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pinkerton, 2020 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\*Reported cancer incidence and mortality.

**Table S6: Characteristics of studies reporting on firefighting and cancer incidence**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **First Author, Year – Country\*** | **Time period** | **Sample size** | **Study design** | **Source of cancer data** | **Source of occupation data** | **Occupational focus** | **Exposure categories** | **Occupation identifier** | **Type of measure** | **Covariates** |
| Kang, 2008 – US | 1986-2003 | 2125 | Case-Control | Tumor registry | Tumor registry | Multiple occupations | AS, OT | Tumor registry | SMORs | Age, smoking status |
| Corbin, 2011 – New Zealand | 2007-2008 | 3 | Case-Control | Tumor registry | Interview | Multiple occupations | AS, DoE, OT | New Zealand Standard Classification of Occupations | OR | Age, gender, Māori ethnicity, smoking status |
| Villeneuve, 2011 – Canada | 1994-1997 | 22 | Case-Control | Tumor registry | Questionnaire | Multiple occupations | AS, CP, DoE, OT, TADE | Canadian Standard Occupational Classification, Canada Standard Industrial Classification | OR | Age, province, cigarette pack-years, exposure to secondhand smoke, exposure to silica and asbestos |
| Karami, 2012 – US | 2002-2007 | 8 | Case-Control | Tumor registry, Hospital records | Interview | Multiple occupations | AS, DoE, OT | Standard Industry Classification, Standard Occupational Classification | OR | Age, geographic area, alcohol consumption, tobacco consumption, smoking status |
| Paget-Bailly, 2013 – France | 2001-2007 | 25 | Case-Control | Tumor registry | Questionnaire information | Multiple occupations | DoE | ISCO, The Nomenclature | OR |  |
| Tsai, 2015 – US | 1988-2007 | 3,996 | Case-Control | Tumor registry | Tumor registry | Firefighters | OT | Code of Census Population | OR | Age, year of diagnosis, race |
| Bigert, 2016 – Europe, Canada, New Zealand, China | 1985-2010 | 190 | Case-Control | Previous study | Previous study | Firefighters | DoE, OT | ISCO | OR | Smoking status, work duration, cancer subtype |
| Lee, 2019 – US | 1982-2014 | 3,928 | Case-Control | Tumor registry, department information, LexisNexis | Employment records, Florida State Fire Marshall's Office, LexisNexis | Firefighters | AS | Florida State Fire Marshall's Office | OR | Age and year at cancer diagnosis |
| Langevin, 2020 – US | 1999-2011 | 25 | Case-Control | Tumor registry, hospital records | Questionnaire | Firefighters | AS, DoE | Questionnaire | OR | Age, race, smoking status, alcohol consumption, education |
| Ahn, 2012 – South Korea | 1980-2007 | 29,498 | Cohort | Tumor registry, Death certificate | Employment records | Multiple occupations | OT, DoE | Organizational classification | SIR, SRR | Age, calendar period |
| Daniels, 2014 – US | 1950-2009 | 29,993 | Cohort | Tumor registry, death certificate, employment records, previous study | Employment records, previous study | Firefighters | DoE | Employment records | SIR, SMR | Age, gender, race, calendar period |
| Pukkala, 2014 – Denmark, Finland, Iceland, Norway, Sweden | 1961-2005 | 16,422 | Cohort | Tumor registry | Census information | Firefighters | AS, CP, TADE | ISCO, National nomenclature | SIR | Age, calendar period |
| Glass, 2016 – Australian | 1980-2011 | 30,057 | Cohort | Tumor registry, death certificate | Department information | Firefighters | DoE, TADE, TSE | Employment records | SIR, SMR | Age, calendar period |
| Kullberg, 2017 –  Sweden | 1931-1958 | 1,080 | Cohort | Tumor registry | Employment records | Firefighters | AS, CP, DoE | Employment records | SIR | Age |
| Petersen, 2017 - Denmark | 1968-2014 | 9,061 | Cohort | Tumor registry | Employment records, Danish Supplementary Pension Fund Register | Firefighters | AS, DoE, TADE, TSE | Registration systems | SMR | Age, calendar period |
| Sritharan, 2018 – Canada | 1991-2010 | NA | Cohort | Tumor registry, mortality database | Census info | Multiple occupations | OT | NSCO | HR | Age, province, ethnicity, education, marital status |
| Harris, 2018 – Canada | 1992-2010 | 4,535 | Cohort | Tumor registry | Census info | Multiple occupations | OT | NSCO | HR | Age, region, education |

**Abbreviations:** AS = age-specific; CP = calendar period; DoE = duration of employment; HR = Hazard rate ratio; ISCO = International Standard Classification of Occupations; NSCO = National Institute for Occupational Safety and Health; OR = Odds ratio; OT = occupational title; RR = Risk ratio; SIR = Standard incidence ratio; SMR = Standard mortality ratio; TADE = task or activity during employment; TSE = time since employment

**Table S7: Characteristics of studies reporting on firefighting and cancer mortality**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **First Author, Year – Country\*** | **Time period** | **Sample size** | **Study design** | **Source of cancer data** | **Source of occupation data** | **Occupational focus** | **Exposure categories** | **Occupation identifier** | **Type of measure** | **Covariates** |
| Muegge, 2018 – US | 1982-2013 | 2,818 | Case-Control | Death certificate | Death certificate | Firefighters | OT | NSCO | OR | Age, gender, race/ethnicity |
| Daniels, 2014 – US | 1950-2009 | 29,993 | Cohort | SIR, SMR | Employment records, previous study | Firefighters | DoE | Employment records | SIR, SMR | Age, gender, race, calendar period |
| Brice, 2015 – Frace | 1979-2008 | 10,829 | Cohort | Death certificate | Department information | Firefighters | OT | Employment records, Registration systems | SMR | Age, calendar period |
| Ahn, 2015 – South Korea | 1980-2007 | 29,453 | Cohort | Death certificate | Employment records | Multiple occupations | OT, DoE | Organizational classification | SMR | Age, calendar period |
| Glass, 2016 – Australia | 1980-2011 | 30,057 | Cohort | Tumor registry, death certificate | Department information | Firefighters | DoE, TSE, TADE | Employment records | SIR, SMR | Age, calendar period |
| Petersen, 2018 – Denmark | 1970-2014 | 11,775 | Cohort | Death certificate | Employment records, Danish Civil Registration system | Firefighters | DoE | Registration systems | SMR | Age, calendar period |
| Pinkerton, 2020 – US | 1950-2016 | 29,992 | Cohort | Tumor registry, death certificate, employment records, previous study | Employment records, previous study | Firefighters | OT, DoE, TADE (included exposed-days, fire-runs, fire-hours, department location) | Organizational classification | SMR | Age, gender, race, calendar period |

**Abbreviations:** AS = age-specific; CP = calendar period; DoE = duration of employment; HR = Hazard rate ratio; ISCO = International Standard Classification of Occupations; NSCO = National Institute for Occupational Safety and Health; OR = Odds ratio; OT = occupational title; RR = Risk ratio; SIR = Standard incidence ratio; SMR = Standard mortality ratio; TADE = task or activity during employment; TSE = time since employment

**Table S8: Quality assessment of 22 individual studies on cancer incidence and mortality among firefighters**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **First author, Year** | **Selection** | **Comparability** | **Exposure or outcome** | **Total Score** | **Quality** |
| **Incidence** | | | | | |
| Kang, 2008 |  |  |  | 7 | Good |
| Corbin, 2011 |  |  |  | 7 | Good |
| Villeneuve, 2011 |  |  |  | 7 | Good |
| Karami, 2012 |  |  |  | 5 | Fair |
| Paget-Bailly, 2013 |  |  |  | 7 | Good |
| Tsai, 2015 |  |  |  | 7 | Good |
| Bigert, 2016 |  |  |  | 2 | Poor |
| Lee, 2019 |  |  |  | 7 | Good |
| Langevin, 2020 |  |  |  | 7 | Good |
| Ahn, 2012 |  |  |  | 9 | Good |
| Daniels, 2014\* |  |  |  | 7 | Good |
| Pukkala, 2014 |  |  |  | 8 | Good |
| Glass, 2016\* |  |  |  | 8 | Good |
| Kullberg, 2017 |  |  |  | 7 | Good |
| Petersen, 2017 |  |  |  | 8 | Good |
| Sritharan, 2018 |  |  |  | 8 | Good |
| Harris, 2018 |  |  |  | 9 | Good |
| **Mortality** | | | | | |
| Muegge, 2018 |  |  |  | 7 | Good |
| Daniels, 2014\* |  |  |  | 7 | Good |
| Brice, 2015 |  |  |  | 6 | Good |
| Ahn, 2015 |  |  |  | 8 | Good |
| Glass, 2016\* |  |  |  | 8 | Good |
| Petersen, 2018 |  |  |  | 8 | Good |
| Pinkerton, 2020 |  |  |  | 8 | Good |

\*Reported cancer incidence and mortality.