**SUPPLEMENTARY MATERIALS**

**Table S1. PRISMA checklist**

|  |  |  |  |
| --- | --- | --- | --- |
| Section/Topic | Item # | Checklist Item | Comment |
| TITLE |  |  |  |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both | Yes |
| 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. | Yes |
| INTRODUCTION |  |  |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | Yes |
| Objectives | 4 | Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | Yes |
| METHODS |  |  |  |
| Protocol and registration | 5 | Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number. | No |
| 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. | Yes |
| 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. | Yes |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Yes |
| 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). | Yes |
| 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. | Yes |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | Yes |
| Risk of bias within 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. | Yes |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | Yes |
| 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 | Yes |
| 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). | No |
| Additional analyses | 16 | Describe methods of additional analyses (e.g. sensitivity or subgroup analyses, meta-regression), if done, indicating which were prespecified. | NA |
| 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. | Yes |
| 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. | Yes |
| 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). | Yes |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals, ideally with a forest plot. | Yes |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | NA |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see item 15). | No |
| Additional analyses | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses [see item 16]). | NA |
| 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., health care providers, researchers, and policymakers). | Yes |
| 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). | Yes |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | Yes |
| 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. | Yes |

NA: Not applicable

**Table S2. MEDLINE search strategy.**

|  |  |
| --- | --- |
| **#** | **Searches** |
| 1 | exp Lung Neoplasms/ |
| 2 | (lung\* adj3 (canc\* or carcinoma\* or tumo?r\* or neoplas\*)).tw. |
| 3 | ("non small cell" or "nonsmall cell").tw. |
| 4 | (1 or 2) and 3 |
| 5 | Carcinoma, Non-Small-Cell Lung/ |
| 6 | NSCLC.tw. |
| 7 | or/4-6 |
| 8 | exp chemotherapy, adjuvant/ |
| 9 | exp chemoradiotherapy, adjuvant/ |
| 10 | exp radiotherapy, adjuvant/ |
| 11 | exp neoadjuvant therapy/ |
| 12 | (adjuvant or neoadjuvant or periadjuvant).tw. |
| 13 | or/8-12 |
| 14 | exp Carcinoma, Non-small-cell Lung/su |
| 15 | exp Lung neoplasms/su |
| 16 | exp pneumonectomy/ |
| 17 | (operative or preoperative or postoperative or operable or surger\* or surgical\* or resect\* or pneumonectom\*).tw. |
| 18 | exp induction chemotherapy/ |
| 19 | exp combined modality therapy/ |
| 20 | exp chemoradiotherapy/ |
| 21 | exp radiotherapy/ |
| 22 | (((chemo or radio or immuno or target\* or induction) adj (therap\* or treatmen\*)) or chemotherap\* or radiotherap\* or chemoradiotherap\* or radiochemotherap\* or immunotherap\*).tw. |
| 23 | or/18-22 |
| 24 | (14 or 15 or 16 or 17) and 23 |
| 25 | 13 or 24 |
| 26 | 7 and 25 |
| 27 | Epidemiologic studies/ |
| 28 | exp case control studies/ |
| 29 | exp cohort studies/ |
| 30 | Case control.tw. |
| 31 | (cohort adj (study or studies)).tw. |
| 32 | Cohort analy$.tw. |
| 33 | (Follow up adj (study or studies)).tw. |
| 34 | (observational adj (study or studies)).tw. |
| 35 | Longitudinal.tw. |
| 36 | Retrospective.tw. |
| 37 | Cross sectional.tw. |
| 38 | Cross-sectional studies/ |
| 39 | (single arm adj (study or studies)).tw. |
| 40 | (treatment adj2 (pattern\* or path\* or paradigm)).tw. |
| 41 | or/27-40 |
| 42 | Randomized controlled trials as Topic/ |
| 43 | Randomized controlled trial/ |
| 44 | Random allocation/ |
| 45 | Double blind method/ |
| 46 | Single blind method/ |
| 47 | Clinical trial/ |
| 48 | clinical trial, phase i.pt. |
| 49 | clinical trial, phase ii.pt. |
| 50 | clinical trial, phase iii.pt. |
| 51 | clinical trial, phase iv.pt. |
| 52 | controlled clinical trial.pt. |
| 53 | randomized controlled trial.pt. |
| 54 | multicenter study.pt. |
| 55 | clinical trial.pt. |
| 56 | exp Clinical Trials as topic/ |
| 57 | or/42-56 |
| 58 | (clinical adj trial$).tw. |
| 59 | ((singl$ or doubl$ or tripl$ or treb$) adj (blind$3 or mask$3)).tw. |
| 60 | Placebos/ |
| 61 | Placebo$.tw. |
| 62 | randomly allocated.tw. |
| 63 | (allocated adj2 random$).tw. |
| 64 | or/58-63 |
| 65 | 57 or 64 |
| 66 | Case report.tw. |
| 67 | Letter/ |
| 68 | Historical article/ |
| 69 | or/66-68 |
| 70 | 65 not 69 |
| 71 | 41 or 70 |
| 72 | 26 and 71 |

**Table S3. EMBASE search strategy**

|  |  |
| --- | --- |
| **#** | **Searches** |
| 1 | exp lung tumor/ |
| 2 | (lung\* adj3 (canc\* or carcinoma\* or tumo?r\* or neoplas\*)).tw. |
| 3 | ("non small cell" or "nonsmall cell").tw. |
| 4 | (1 or 2) and 3 |
| 5 | exp non small cell lung cancer/ |
| 6 | NSCLC.tw. |
| 7 | or/4-6 |
| 8 | exp adjuvant therapy/ |
| 9 | exp neoadjuvant therapy/ |
| 10 | (adjuvant or neoadjuvant or periadjuvant).tw. |
| 11 | or/8-10 |
| 12 | exp non small cell lung cancer/su |
| 13 | exp lung tumor/su |
| 14 | exp lung resection/ |
| 15 | (operative or preoperative or postoperative or operable or surger\* or surgical\* or resect\* or pneumonectom\*).tw. |
| 16 | exp induction chemotherapy/ |
| 17 | exp multimodality cancer therapy/ |
| 18 | exp chemoradiotherapy/ |
| 19 | exp radiotherapy/ |
| 20 | (((chemo or radio or immuno or target\* or induction) adj (therap\* or treatmen\*)) or chemotherap\* or radiotherap\* or chemoradiotherap\* or radiochemotherap\* or immunotherap\*).tw. |
| 21 | or/16-20 |
| 22 | (12 or 13 or 14 or 15) and 21 |
| 23 | 11 or 22 |
| 24 | 7 and 23 |
| 25 | Clinical study/ |
| 26 | Case control study/ |
| 27 | Family study/ |
| 28 | Longitudinal study/ |
| 29 | Retrospective study/ |
| 30 | Prospective study/ |
| 31 | Randomized controlled trials/ |
| 32 | 30 not 31 |
| 33 | Cohort analysis/ |
| 34 | (Cohort adj (study or studies)).mp. |
| 35 | (Case control adj (study or studies)).tw. |
| 36 | (follow up adj (study or studies)).tw. |
| 37 | (observational adj (study or studies)).tw. |
| 38 | (epidemiologic$ adj (study or studies)).tw. |
| 39 | (cross sectional adj (study or studies)).tw. |
| 40 | (single arm adj (study or studies)).tw. |
| 41 | (treatment adj2 (pattern\* or path\* or paradigm)).tw. |
| 42 | or/25-29,32-41 |
| 43 | Clinical trial/ |
| 44 | Randomized controlled trial/ |
| 45 | controlled clinical trial/ |
| 46 | multicenter study/ |
| 47 | Phase 3 clinical trial/ |
| 48 | Phase 4 clinical trial/ |
| 49 | exp Randomization/ |
| 50 | Single blind procedure/ |
| 51 | Double blind procedure/ |
| 52 | Crossover procedure/ |
| 53 | Placebo/ |
| 54 | Randomi?ed controlled trial$.tw. |
| 55 | Rct.tw. |
| 56 | (random$ adj2 allocat$).tw. |
| 57 | Single blind$.tw. |
| 58 | Double blind$.tw. |
| 59 | ((treble or triple) adj blind$).tw. |
| 60 | Placebo$.tw. |
| 61 | Prospective study/ |
| 62 | or/43-61 |
| 63 | Case study/ |
| 64 | Case report.tw. |
| 65 | Abstract report/ or letter/ |
| 66 | Conference proceeding.pt. |
| 67 | Conference abstract.pt. |
| 68 | Editorial.pt. |
| 69 | Letter.pt. |
| 70 | Note.pt. |
| 71 | or/63-70 |
| 72 | 62 not 71 |
| 73 | 42 or 72 |
| 74 | 24 and 73 |
| 75 | conference.so. |
| 76 | conference paper/ |
| 77 | conference.pt. |
| 78 | or/75-77 |
| 79 | 74 not 78 |

**Table S4. Proportion of patients by treatment modality (without timing) in resected, stages I-III NSCLC**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study (year)** | **Country** | **Study period** | **N** | **Number of patients, n (%)** | | |
| **S (±RT)** | **S + CT** | **S + CRT** |
| **Stages I-II** |  |  |  |  |  |  |
| Gould (2017) | US | 2008-2013 | 1,291 | 1,076 (83.4) | 191 (14.8) | 24 (1.9) |
| Pinquié (2017) | France | 2010 | 465 | 337 (72.5) | 123 (26.5) | 5 (1.1) |
|  |  |  |  |  |  |  |
| **Stage III** |  |  |  |  |  |  |
| Gould (2017) | US | 2008-2013 | 242 | 80 (33.1) | 108 (44.6) | 54 (22.3) |
| Vinod (2012) | Canada | 2000-2007 | 250 | 148 (59.2) | 66 (26.4) | 36 (14.4) |
| Moore (2019) | Canada | 2005-2012 | 133 | 29 (21.8) | 44 (33.1) | 60 (45.1) |
| Pinquié (2017) | France | 2010 | 170 | 51 (30.0) | 93 (54.7) | 26 (15.3) |
| Lin (2017) | Taiwan | 2002-2012 | 558 | 177 (31.7) | 165 (29.6)\* | 216 (38.7)\* |
| Sonobe (2013) | Japan | 2000-2004 | 496 | 200 (40.3) | 182 (36.7)\* | 114 (23.0)\* |
|  |  |  |  |  |  |  |
| **Stages I-III** |  |  |  |  |  |  |
| Riquet (2012) | France | 2001-2006 | 1,195 | 612 (51.2) | 448 (37.5) | 135 (11.3) |
|  |  |  |  |  |  |  |
| **Stages I-IV** |  |  |  |  |  |  |
| Arnold (2016) | US | 2003-2009 | 45,933 | 34,527 (75.2) | 8,618 (18.7) | 2,788 (6.0) |
| Pinquié (2017) | France | 2010 | 635 | 388 (61.1) | 216 (34.0) | 31 (4.9) |

CRT: Chemoradiotherapy; CT: Chemotherapy; RT: Radiotherapy; S: Surgical resection; US: United States

\*Study did not report on neoadjuvant therapy, all data are for adjuvant CT or adjuvant CRT.

**Table S5. Internal and external Validity – assessment of generalizability of study population.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Author (year) | Target population | Selection bias relating to study population that may affect generalizability | | | | |
| Resectable population | Sampling frame-geography | Sampling frame-practice type | Sampling frame-study period | Missing clinical data |
| **North America** |  |  |  |  |  |  |
| Arnold (2016) | US | Some concern | No concern | No concern | Some concern | Some concern |
| Valle (2016) | US | No concern | Some concern | Some concern | Some concern | - |
| Gould (2017) | US | Some concern | Some concern | No concern | Some concern | Some concern |
| Buck (2015) | US | Some concern | Some concern | Some concern | Some concern | - |
| Rajaram (2016) | US | Some concern | No concern | No concern | Some concern | No concern |
| Booth (2012) | Canada | Some concern | Some concern | No concern | Concern | No concern |
| Vinod (2012) | Canada | No concern | Some concern | No concern | Concern | Some concern |
| Moore (2020) | Canada | No concern | Some concern | No concern | Some concern | No concern |
| Moore (2019) | Canada | No concern | Some concern | No concern | Some concern | No concern |
| Ramsden (2015) | Canada | No concern | Some concern | No concern | Some concern | No concern |
| **Europe** |  |  |  |  |  |  |
| Chouaid (2018) | EU3 | No concern | Some concern | Some concern | Some concern | - |
| Riquet (2012) | France | No concern | Concern | Concern | Concern | No concern |
| Pinquié (2017) | France | No concern | No concern | Some concern | Some concern | No concern |
| Couñago (2018) | Spain | Concern | Some concern | Some concern | Some concern | No concern |
| **Asia** |  |  |  |  |  |  |
| Sonobe (2013) | Japan | Some concern | No concern | No concern | Some concern | - |
| Maniwa (2018) | Japan | Concern | Concern | Concern | Some concern | - |
| Yoh (2019) | Japan | No concern | Some concern | Some concern | Some concern | No concern |
| Lee (20130 | Korea | Concern | Concern | Concern | Concern | Some concern |
| Lin (2017) | Taiwan | Some concern | No concern | No concern | Some concern | Some concern |
| Fan (2015) | China | No concern | Some concern | Some concern | Some concern | Concern |

EU3: France, Germany and UK; UK: United Kingdom; US: United States; RT: Radiotherapy.

Notes: Concern about eligible study population was assigned as follows: (1) no concern: there were no exclusions that affected generalizability, (2) some concern: there were minor exclusions that affected generalizability in a minor way, and (3) concern: there were many exclusions that affected generalizability. For resectable population, exclusions mean that there were exclusions of some disease subtypes (e.g. carcinoid tumor), treatment types (e.g. neoadjuvant RT), extent of resection (e.g. incomplete resection) or surgery types (e.g. wedge resection). For sampling frame – geography, exclusions mean that study selected a particular region (as opposed to selection of the whole country). For sampling frame – practice type, exclusions mean that there were exclusions of certain types of practice (e.g. community hospitals). For sampling frame – study period, exclusions here mean that study was conducted in early 2000s and thus lacked recent years.