**Supplementary Figure 1: Search Strategy**

Database(s): Embase 1988 to 2015 Week 14, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present, Cochrane Central Register of Controlled Trials November 2017

Search Strategy:

|  |  |
| --- | --- |
| **#** | **Searches** |
|  |  |
| 1 | pituitary.mp. or exp Pituitary Gland |
| 2 | hypophyse\*.mp. |
| 3 | sellar.mp. |
| 4 | 1 or 2 or 3 |
| 5 | adenoma\*.mp. or exp Adenoma/ |
| 6 | macroadenoma\*.mp. |
| 7 | neoplasm\*.mp. |
| 8 | tumo?r\*.mp. |
| 9 | mass\*.mp. |
| 10 | lesion\*.mp. |
| 11 | 5 or 6 or 7 or 8 or 9 or 10 |
| 12 | 4 and 11 |
| 13 | exp Pituitary Neoplasms/ or pituitary neoplasm\*.mp. |
| 14 | 12 or 13 |
| 15 | non?function\*.mp. |
| 16 | non?secret\*.mp. |
| 17 | inactiv\*.mp. |
| 18 | silen\*.mp. |
| 19 | asymptomatic.mp. |
| 20 | 15 or 16 or 17 or 18 or 19 |
| 21 | exp Recurrence/ or recurren\*.mp. |
| 22 | re?grow\*.mp. |
| 23 | enlarge\*.mp. |
| 24 | progress\*.mp. |
| 25 | increas\*.mp. |
| 26 | 21 or 22 or 23 or 24 or 25 |
| 27 | 14 and 20 and 26 |

**Supplementary Table 1: Characteristics of the studies including patients treated solely by surgery**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study**  **(first author and year)** | **Comparison**  **group in the article** | **Population** | **Recurrences/total number of patients (%)** |
| Watts *et al.,* 2017 (18) | Yes | SCAs | 3/8 (37.5%) |
| NFPAs | 33/115 (28.7%) |
| Alahmadi *et al.,* 2012 (12) | Yes | SCAs | 2/14 (14.3%) |
| NFPAs | 3/30 (10.0%) |
| Reddy *et al.,* 2011 (17) | Yes | SCAs | 5/16 (31.3%) |
| NFPAs | 49/139 (35.3%) |
| Cooper *et al.,* 2010 (8) | Yes | SCAs | 10/16 (62.5%) |
| NFPAs | 23/58 (39.7%) |
| Cho *et al.,* 2010 (15) | Yes | SCAs | 5/22 (22.7%) |
| NFPAs | 32/114 (28.1%) |
| Bradley *et al.,* 2003 (13) | Yes | SCAs | 8/22 (36.4%) |
| NFPAs | 20/60 (33.3%) |
| Tateno *et al.,* 2007 (31) | No | SCAs | 4/6 (66.7%) |
| Baldeweg *et al.,* 2005 (28) | No | SCAs | 1/9 (11.1%) |
| Lopez *et al.,* 2004 (30) | No | SCAs | 0/10 (0%) |
| Webb *et al.,* 2003 (32) | No | SCAs | 5/19 (26.3%) |

*SCAs: silent corticotroph adenomas, NFPAs: non-functioning pituitary adenomas (subtypes other than SCAs)*

**Supplementary Table 2:** **Characteristics of the studies including patients treated by surgery and adjuvant radiotherapy**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study**  **(first author and year)** | **Comparison group in the article** | **Population** | **Recurrences/total number of patients (%)** |
| Cho *et al.,* 2010 (15) | Yes | SCAs | 2/6 (33.3%) |
| NFPAs | 4/20 (20%) |
| Baldeweg *et al.,* 2005 (28) | No | SCAs | 4/6 (66.7%) |
| Bradley *et al.,* 2003 (13) | No | SCAs | 1/5 (20.0%) |
| Webb *et al.,* 2003 (32) | No | SCAs | 0/3 (0%) |

*SCAs: silent corticotroph adenomas, NFPAs: non-functioning pituitary adenomas (subtypes other than SCAs)*

**Supplementary Table 3: Risk of bias for the first review question**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study**  **(first author and year)** | **Type of study** | **Representativeness of the source population** | **Ascertainment of source population** | **Demonstration that outcome of interest was not present at start of study** | **Assessment of outcome** | **Follow-up long enough for outcome to occur** | **Adequacy of follow-up** | **Overall judgment** |
| Langlois *et al.,* 2018 (10) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (immunohistochemical study) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Watts *et al.,* 2017 (18) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (secure medical record) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Jahangiri *et al.,* 2013 (9) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (immunohistochemical study) | Low risk  (yes) | Low risk  (secure medical record with independent blind assessment) | Low risk  (yes) | High risk (follow-up rate less than 80%) | Low risk |
| Alahmadi *et al.,* 2012 (12) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (secure medical record) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Ioachimescu *et al.,* 2012 (16) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (immunohistochemical study) | Low risk  (yes-individuals with recurrent SCA were excluded from the analysis) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Reddy *et al.,* 2011 (17) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (secure medical record) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Hewedi *et al.,* 2011 (29) | Retrospective | Low risk  (somewhat representative - clinic based) | Low risk  (immunohistochemical study) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Cooper *et al.,* 2010 (8) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (immunohistochemical study) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | High risk (follow-up rate less than 80%) | Low risk |
| Cho *et al.,* 2010 (15) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk (secure medical record) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Tateno *et al.,* 2007 (31) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (immunohistochemical study) | Low risk  (yes) | High risk  (no description) | Low risk  (yes) | Low risk (complete follow-up) | Moderate risk |
| Baldeweg *et al.,* 2005 (28) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (immunohistochemical study) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Lopez *et al.,* 2004 (30) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (immunohistochemical study) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Bradley *et al.,* 2003 (13) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (secure medical record) | Low risk  (yes) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Webb *et al.,* 2003 (32) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (immunohistochemical study) | Low risk  (yes-individuals with recurrent SCA were excluded from the analysis) | Low risk (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |

*(SCA: silent corticotroph adenoma)*

**Supplementary Table 4: Risk of bias for the second review question**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study**  **(first author and year)** | **Type of study** | **Representativeness of the exposed cohort** | **Selection of the non-exposed cohort** | **Ascertainment of exposure** | **Demonstration that outcome of interest was not present at start of study** | **Comparability of cohorts on the basis of adjuvant radiotherapy (most important factor), extent of tumor removal and length of follow-up (additional factors)** | **Assessment of outcome** | **Follow-up long enough for outcome to occur** | **Adequacy of follow-up** | **Overall judgment** |
| Langlois *et al.,* 2018 (10) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk  (immunohistochemical study) | Low risk  (yes) | High risk  (no comparability) | Low risk (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | High risk |
| Watts *et al.,* 2017 (18) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk (secure medical record) | Low risk  (yes) | Moderate risk (study controls for the most important factor) | Low risk (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Moderate risk |
| Jahangiri *et al.,* 2013 (9) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk  (immunohistochemical study) | Low risk  (yes) | Low risk  (study controls for all factors) | Low risk (secure medical record with independent blind assessment) | Low risk  (yes) | High risk (follow-up rate less than 80%) | Low risk |
| Alahmadi *et al.,* 2012 (12) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk (secure medical record) | Low risk  (yes) | Moderate risk (study controls for the most important factor) | Low risk (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Moderate risk |
| Ioachimescu *et al.,* 2012 (16) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk  (immunohistochemical study) | Low risk  (yes - individuals with recurrent SCA were excluded from the analysis) | Low risk  (study controls for all factors) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Reddy *et al.,* 2011 (17) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk (secure medical record) | Low risk  (yes) | Moderate risk (study controls for the most important factor) | Low risk (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Moderate risk |
| Hewedi *et al.,* 2011 (29) | Retrospective | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk  (immunohistochemical study) | Low risk  (yes) | High risk  (no comparability) | Low risk  (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | High risk |
| Cooper *et al.,* 2010 (8) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk  (immunohistochemical study) | Low risk  (yes) | Low risk  (study controls for all factors) | Low risk  (secure medical record) | Low risk  (yes) | High risk (follow-up rate less than 80%) | Low risk |
| Cho *et al.,* 2010 (15) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk (secure medical record) | Low risk  (yes) | Low risk  (study controls for all factors) | Low risk (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | Low risk |
| Bradley *et al.,* 2003 (13) | Retrospective cohort | Low risk  (somewhat representative - clinic based) | Low risk  (drawn from the same source) | Low risk (secure medical record) | Low risk  (yes) | High risk  (no comparability) | Low risk (secure medical record) | Low risk  (yes) | Low risk (complete follow-up) | High risk |

*(SCA: silent corticotroph adenoma)*