**Table A1.** General characteristics of included studies.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Lead author, Publication date** | **Country** | **Study design** | **Study period** | **Setting** | **Sample size** | **Female** | **Papillary thyroid cancer** | **Micropapillary thyroid cancer** |
| Russo et al. 2018 | Argentina | Retrospective cohort study | January 2003 to December 2012 | Population-based study | 176 | 158 | 166 | Not reported |
| Iwata et al. 2018 | United States | Retrospective cohort study | January 2006 to December 2010 | Single center | 128 | Not reported | Not reported | Not reported |
| Seifert et al. 2017 | Germany | Retrospective cohort study | October 2009 to September 2015 | Single center | 103 | 78 | 68 | 13 |
| Marina et al. 2017 | Italy | Retrospective cohort study | January 1998 to December 2015 | Single center | 281 | 220 | 259 | Not reported |
| Zagzag et al. 2017 | United States | Retrospective cohort study | 2004 to 2010 | Multicenter in one country | 473 | 352 | 427 | 100 |
| Shakil et al. 2017 | United States | Retrospective cohort study | 2005 to 2014 | Single center | 172 | 131 | 160 | 54 |
| Provenzale et al. 2016 | Italy | Prospective cohort study | March 2013 to March 2014 | Single center | 374 | Not reported | 374 | 159 |
| González-Sánchez-Migallón et al. 2016 | Spain | Retrospective cohort study | 2000 to 2014 | Single center | 259 | 208 | 225 | 92 |
| Brito et al. 2015 | United States | Retrospective cohort study | 2000 to 2012 | Population-based study | 213 | 149 | 199 | Not reported |
| Choi et al. 2015 | Canada | Retrospective cohort study | January 2000 to January 2013 | Single center | 168 | 126 | 168 | Not included |
| Bahl et al. 2014 | United States | Retrospective cohort study | January 2003 to December 2012 | Single center | 675 | 499 | 566 | 206 |
| Malone et al. 2014 | United States | Retrospective cohort study | January 2007 to August 2010 | Single center | 473 | 345 | 451 | 156 |
| Minuto et al. 2013 | Italy | Retrospective cohort study | February 2002 to November 2003 | Single center | 188 | 139 | 181 | Not reported |
| Kahn et al. 2012 | Australia | Cross-sectional study | May 2006 to August 2008 | Population-based study | 419 | 321 | 359 | Not reported |
| Davies et al. 2010 | United States | Retrospective cohort study | 2006 to 2007 | Multicenter in one country | 95 | Not reported | 86 | Not reported |
| Roti et al. 2006 | Italy | Retrospective cohort study | 1993 to 2002 | Single center | 243 | 197 | 243 | 243 |
| Ruggieri et al. 2001 | Italy | Retrospective cohort study | 1991 to 2000 | Single center | 30 | Not reported | 28 | 30 |

**Table A2.** Quality of evidence.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Authors/Publication Year** | **Design** | **Score** | | | | |
| **Newcastle-Ottawa Scale for Cohort Studies** | | **Selection/\*\*\*\*** | **Comparability/\*\*** | **Outcome/\*\*\*** | **Total** | **Overall risk of bias** |
| Russo et al. 2018 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*** | 7 | moderate risk |
| Iwata et al. 2018 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*** | 7 | moderate risk |
| Seifert et al. 2017 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Marina et al. 2017 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Zagzag et al. 2017 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Shakil et al. 2017 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Provenzale et al. 2016 | Prospective cohort study | **\*\*\*** | **\*\*** | **\*\*** | 7 | moderate risk |
| González-Sánchez-Migallón et al. 2016 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Brito et al. 2015 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Choi et al. 2015 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Bahl et al. 2014 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Malone et al. 2014 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Minuto et al. 2013 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*** | 7 | moderate risk |
| Davies et al. 2010 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*** | 7 | moderate risk |
| Roti et al. 2006 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| Ruggieri et al. 2001 | Retrospective cohort study | **\*\*\*** | **\*\*** | **\*\*\*** | 8 | low risk |
| **Newcastle-Ottawa Scale adapted for Cross-Sectional Studies** | | **Selection/\*\*\*\*\*** | **Comparability/\*\*** | **Outcome/\*\*\*** | **Total** | **Overall risk of bias** |
| Kahn et al. 2012 | Cross-sectional study | **\*\*\*\*** | **\*** | **\*\*** | 7 | moderate risk |

**Table A3.** Definition of the triggers of thyroid cancer diagnosis of each study.

|  |  |  |
| --- | --- | --- |
| **Lead author, Publication date** | **Definition of the triggers of thyroid cancer diagnosis in each study** | **Reasons** |
| Russo et al. 2018 | **Incidental imaging**: Unexpected finding of thyroid cancer in an asymptomatic patient during a routine examination, imaging study, or surgical procedure, or a pathological examination of a surgical specimen in a patient with no thyroid mass, no benign thyroid disease, and no family history of thyroid cancer including ultrasounds performed during a multiphase check-up module.  **Non-incidental**:   * Detection of thyroid cancer by the patient or people outside the healthcare system. This category includes patients with and without symptoms related to the nodule that harbored thyroid cancer. * Clinical evaluation with a presumptive diagnosis of thyroid cancer including a physical exam or diagnostic workup of a cervical mass or lymph node detected by a physician belonging to the healthcare system. This category also included findings by a diagnostic cascade for benign thyroid disease.\* | **Not reported** |
| Iwata et al. 2018 | **Incidental imaging:** Nodules within the thyroid gland that are discovered during diagnostic imaging, which is performed for reasons unrelated to the thyroid gland.  **Non-incidental:** Palpable nodule. | **Not reported** |
| Seifert et al. 2017 | **Incidental histological:** The patients underwent thyroid surgery with an indication of benign thyroid disease, not for suspicion of differentiate thyroid cancer.  **Non-incidental:** Patients with differentiated thyroid cancer that presented in the pre-surgical diagnosis local symptoms and/or hard nodules.\* | **Not reported** |
| Zagzag et al. 2017 | **Incidental imaging:** Included patients for whom further diagnostic workup was indicated because of a nodule that was initially detected on an imaging study. The indications for these imaging studies were unrelated to the thyroid tumor.  **Non-incidental**: Included those patients in whom further diagnostic studies were initiated because a physician had noted an abnormality on physical examination or because the patient or another nonprofessional had noted a mass in the neck. | **Not reported** |
| Shakil et al. 2017 | **Incidental imaging:** histologically proven thyroid cancer initially discovered on imaging not intended for evaluation of the thyroid by computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), or ultrasonography (US)**.**  **Incidental histological:** thyroid cancers discovered histologically after thyroidectomy for benign thyroid diseases, such as Graves’ disease or multinodular goiter.  **Non-incidental:** cancer that had been first discovered due to clinical signs or symptoms or imaging done specifically to evaluate thyroid anatomy | **Not reported** |
| Marina et al. 2017 | **Incidental imaging**: This group of subjects was represented by asymptomatic subjects in whom the thyroid nodule harboring thyroid cancer was incidentally discovered during thyroid imaging not related to the clinical context.  **Incidental histological:** this group was represented by patients affected by different thyroid disorders in whom for some reasons thyroid imaging was done with the results of an incidental finding of a thyroid nodule harboring thyroid cancer or thyroidectomized patients in whom thyroid cancer was incidentally found at the thyroid histological examination.  **Non-incidental:** Patients in whom a nodule harboring thyroid cancer was discovered because of a self-report of a visual finding or a self-palpation of a neck lump or a complain of compressive sumptoms. | **Incidental imaging by ultrasound:**   * General screening in asymptomatic subject (n=23). * During gynecological visit (n=6). * During cardiologic visit (n=7). * Neck US for salivary glands or lymphnode studies (n=32). * Carotid power duplex (n=25). |
| González-Sánchez-Migallón et al. 2016 | **Incidental histological:** Malignant neoplasms of thyroid origin, not detected clinically or by preoperative imaging tests, and that are evidenced in the pathological study of the surgical piece removed by an a priori benign process (goiter or hyperthyroidism).  **Non-incidental:** When the diagnosis of thyroid cancer was established based on clinical, ultrasound, and fine needle aspiration cytology. | **Not reported** |
| Provenzale et al. 2016 | **Incidental histological:** identified postoperatively at histological examination of thyroid in patients submitted to surgery for large multinodular goiter with compressive symptoms and/or incidentally detected in the extra-nodular parenchyma of thyroid gland of patients submitted to surgery for nodules with an ‘indeterminate’ cytological diagnosis and with a final histological diagnosis of benign nodules.  **Non-incidental:**   * Diagnosed before surgery as small thyroid nodule incidentally detected at thyroid ultrasound and submitted to FNAC because of the presence of suspicious signs at ultrasound.\* * Papillary thyroid cancer larger than 1 cm. | **Not reported** |
| Brito et al. 2015 | **Incidental imaging**:   * When a thyroid nodule harboring thyroid cancer is found during an imaging test requested for reasons unrelated to a thyroid disorder or symptom. This category, however, also includes patients who had an imaging test for possible palpable or symptomatic nodule but the nodule harboring thyroid cancer is not related to any of these symptoms. * When a thyroid nodule harboring thyroid cancer is found during the work up of non-nodular thyroid disease (e.g., patient with hyperthyroidism who has a thyroid ultrasound positive for a nodule).   **Incidental histological**: Thyroid cancer is found incidentally in the histological examination of the thyroid gland removed for a benign condition (e.g., Graves disease).  **Non-incidental:**   * When a thyroid nodule harboring thyroid cancer is found during a physical exam (thyroid palpation) or imaging study in a symptomatic patient. * When a thyroid nodule harboring thyroid cancer is found during a physical exam (thyroid palpation) of an asymptomatic patient\* | **Incidental imaging by ultrasound:**   * Palpated nodule or symptoms not associated with nodule harboring thyroid cancer (n=37). * Hypothyroidism (n=5). * Unknown (n=12). |
| Choi et al. 2015 | **Incidental imaging:** The detection of thyroid nodule by imaging performed for indications unrelated to the thyroid mass.  **Non-incidental:**   * The patient presents with complaints possibly related to the thyroid mass such as dysphagia, dysphonia, neck pain, selfdetection of a neck mass, or self-requested screening for thyroid cancer. * The thyroid nodule detected by a clinician during an evaluation for complaints not related to a thyroid mass. | **Not reported** |
| Bahl et al. 2014 | **Incidental imaging:** Incidental cancers were detected on imaging studies performed for other reasons in patients without any clinical symptoms, examination findings, or suspicion for thyroid cancer.  **Incidental histological:** An incidental cancer on pathology was found on the surgical specimen when surgery was performed for benign disease or resection of another nodule that was subsequently found to be benign.  **Non-incidental:**   * A clinical cancer was defined as a palpable nodule. * A clinical cancer was defined as a nodule discovered in the workup of abnormal thyroid function test or in the context of suspicion for thyroid cancer\*. | **Not reported** |
| Malone et al. 2014 | **Incidental Imaging**: patients in whom the indication for surgery was a suspicious or malignant cytological finding on fine needle aspiration biopsy (FNAB) of a tumor that was initially detected on an imaging study.  **Incidental histological:** patients in whom incidental cancers were found on pathological study of the surgical specimen that were not related to the indication for thyroidectomy, the indications for surgery included nodules with suspicious cytology that proved to be benign, symptomatic or enlarging nodules with benign cytology, multinodular goiters, and thyrotoxicosis.  **Non-incidental:** patients in whom the indication for surgery was a suspicious or malignant cytological finding on FNAB and in whom the patient stated that further diagnostic studies were initiated because a physician had noted an abnormality on physical examination or because the patient or another non-professional had noted a mass in the neck | **Incidental imaging by ultrasound:**   * **Hashimoto’s thyroiditis (n=17).** * **Family history of thyroid cancer (n=11).** * **Hyperthyroidism (n=11).** * **Nonspecific neck symptoms (n=10).** * **Hypothyroidism (n=9).** * **Nonspecific constitutional symptoms (n=6).** * **Gynecological exam (n=4).** * **History of radiation exposure (n=4).** * **Hyperparathyroidism (n=4).** * **Goiter (n=3).** * **Previous thyroid surgery (no malignancy) (n=2).** * **Hypercalcemia (n=2).** * **‘‘Routine’’ sonogram (n=2).** * **Self-sonography (n=2).** * **Other lab abnormalities (n=2).** * **Surveillance of another thyroid nodule (n=1).** * **Unknown (n=8)** |
| Minuto et al. 2013 | **Incidental histological:**  Patients who underwent surgery for presumed benign disease and demonstrated at least 1 focus of thyroid cancer on final histology.  **Non-incidental:** Patients with clinically evident thyroid cancer. | **Not reported** |
| Kahn et al. 2012 | **Incidental imaging**: Tumor incidentally found during diagnostic imaging for another health problem.  **Incidental histological**: Cancer diagnosed after surgery for a benign thyroid disorder.  **Non-incidental:**   * Initially presented due to patient’s concern about a mass in their neck or obstructive symptom. * A doctor noticed a lump in the patient’s neck of which they were unaware. | **Not reported** |
| Davies et al. 2010 | **Incidental imaging**:   * The patient specifically requested a thyroid test or evaluation. * When the identification of a thyroid finding was through a radiologic test done for an indication unrelated to the thyroid gland, such as a computed tomography scan of the chest done for a trauma workup or a chest x-ray done during a preoperative visit. * When the diagnostic cascade stated when a thyroid finding was revealed during a laboratory or other non-radiologic workup for a patient complaint but the thyroid finding did not plausibly explain the patient’s presenting complaint.   **Non-incidental**:   * When a thyroid nodule or other finding had been known about for some time but had been managed expectantly. * When the person had no complaints referable to the neck or thyroid function and was identified as having a thyroid finding during a routine physical exam performed by a primary care practitioner in a primary care setting. * A patient was said to be ‘‘symptomatic’’ if the patient’s presenting complaint was clearly referable to the region of the thyroid gland or the soft tissues of the neck. | **Not reported** |
| Roti et al. 2006 | **Incidental histological:** Thyroid cancer diagnosed incidentally during thyroid surgery for benign thyroid disordes such as Graves’ disease and nodular goiter.  **Non-incidental:** were thyroid nodules detected by neck ultrasonography conducted for other reasons, because of a family history of thyroid disease and/or presence of altered laboratory test results (TSH, FT4, and thyroid peroxidase antibodies).\* | **Incidental imaging by ultrasound:**   * **Family history of thyroid disease and/or presence of altered laboratory test results (TSH, FT4, and thyroid per-oxidase antibodies) (n=103).** |
| Ruggieri et al. 2001 | **Incidental histological**: Patients in whom the histological diagnosis of cancer was incidental after an operation performed for benign disease.  **Non-incidental**:   * Patients with a clinically suspicious neoplastic lesion diagnosed before surgical treatment. * Patients in whom a neck lymph node metastases were clinically found before diagnosis of an occult papillary carcinoma in thyroid gland. | **Not reported** |

\*The information given by the article allow us to take some non-incidental thyroid cancers as incidental imaging.

Ovid

Database(s): Embase 1974 to 2020 June 02, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to June 02, 2020   
Search Strategy:

|  |  |  |
| --- | --- | --- |
| **#** | **Searches** | **Results** |
| 1 | exp Thyroid Neoplasms/di, dg [Diagnosis, Diagnostic Imaging] | 15940 |
| 2 | exp thyroid cancer/di [Diagnosis] | 24061 |
| 3 | (thyroid\* adj3 (cancer\* or neoplasm\* or carcinoma\*)).ti,ab,hw,kw. | 139248 |
| 4 | (diagnos\* or detect\* or identify\* or identified or identification\*).ti,ab,hw,kw. | 17002808 |
| 5 | 1 or 2 or (thyroid\* adj3 (cancer\* or neoplasm\* or carcinoma\*) adj3 (diagnos\* or detect\* or identify\* or identified or identification\*)).ti,ab,hw,kw. | 36818 |
| 6 | exp incidental findings/ | 27510 |
| 7 | exp Mass Screening/ | 367938 |
| 8 | exp Palpation/ | 26410 |
| 9 | (((diagnos\* or detect\* or event or events or identify\* or identified or identification\*) adj5 (trigger\* or chance)) or incidental or incidentally or palpabl\* or palpat\* or screen\* or serendipit\* or subclinical).ti,ab,hw,kw. | 2473978 |
| 10 | 6 or 7 or 8 or 9 | 2484354 |
| 11 | 5 and 10 | 4847 |
| 12 | exp comparative study/ | 3262555 |
| 13 | exp Cohort Studies/ | 2580088 |
| 14 | exp longitudinal study/ | 274713 |
| 15 | exp retrospective study/ | 1741673 |
| 16 | exp prospective study/ | 1144154 |
| 17 | exp population research/ | 106991 |
| 18 | (cohort\* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal\* or ((retrospective or "ex post facto") adj3 (study or survey or analysis or design)) or retrospectiv\* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv\* or (population adj3 (stud\* or survey\* or analys\* or research)) or "incidence study" or "incidence survey" or "incidence analysis" or (("follow-up" or followup) adj (stud\* or survey or analysis)) or (compar\* and (study or trial))).mp,pt. | 14626951 |
| 19 | or/12-18 | 14739985 |
| 20 | 11 and 19 | 2002 |
| 21 | limit 20 to (editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] | 8 |
| 22 | 20 not 21 | 1994 |
| 23 | remove duplicates from 22 | 1565 |

Scopus

1 TITLE-ABS-KEY(thyroid\* W/3 (cancer\* or neoplasm\* or carcinoma\*) W/3 (diagnos\* or detect\* or identify\* or identified or identification\*))

2 TITLE-ABS-KEY(((diagnos\* or detect\* or event or events or identify\* or identified or identification\*) W/5 (trigger\* or chance)) OR incidental OR incidentally OR palpabl\* OR palpat\* OR screen\* OR serendipit\* OR subclinical)

3 TITLE-ABS-KEY(cohort\* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal\* or ((retrospective or "ex post facto") W/3 (study or survey or analysis or design)) or retrospectiv\* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv\* or (population W/3 (stud\* or survey\* or analys\* or research)) or "incidence study" or "incidence survey" or "incidence analysis" or (("follow-up" or followup) W/1 (stud\* or survey or analysis)) or (compar\* and (study or trial)))

4 1 and 2 and 3

5 DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)

6 4 and not 5

7 INDEX(embase) OR INDEX(medline) OR PMID(0\* OR 1\* OR 2\* OR 3\* OR 4\* OR 5\* OR 6\* OR 7\* OR 8\* OR 9\*)

8 6 and not 7