**Supplementary material**

**Table 1: Search strategy**

|  |  |  |
| --- | --- | --- |
| **Database  (for example PubMed)** | **Search string (for example searching with [MesH] OR [tiab] in PubMed)** | **Number of hits** |
| **Pubmed** | ("Kidney Neoplasms"[Mesh:Noexp] OR "Carcinoma, Renal Cell"[Mesh] OR "renal mass\*"[Title/Abstract] OR "kidney neoplasm\*"[Title/Abstract] OR "renal neoplasm\*"[Title/Abstract] OR "kidney tumor\*"[Title/Abstract] OR "renal tumor\*"[Title/Abstract] OR renal cancer\*[tiab] OR kidney cancer\*[tiab] OR cancer of the kidney\*[tiab] OR kidney tumour\*[tiab] OR renal tumour\*[tiab] OR “small renal mass” OR “small renal masses” OR “SRM” )  AND  ("Watchful Waiting"[Mesh] OR "active surveillance"[Title/Abstract] OR "watchful waiting"[Title/Abstract] OR "conservative management"[Title/Abstract] OR "non-operative management"[Title/Abstract] OR expectant management[tiab] OR organ sparing treatment\*[tiab] OR nonsurgical treatment\*[tiab] OR non-surgical treatment\*[tiab] OR nonoperative treatment\*[tiab] OR conservative management\*[tiab]) | 916 |
| **Embase** | (exp Kidney tumor/ OR "renal mass\*".ti,ab,kf. OR "kidney neoplasm\*".ti,ab,kf.OR "renal neoplasm\*".ti,ab,kf.OR "kidney tumor\*".ti,ab,kf.OR "renal tumor\*".ti,ab,kf.OR renal cancer\*.ti,ab,kf. OR kidney cancer\*.ti,ab,kf. OR cancer of the kidney\*.ti,ab,kf. OR kidney tumour\*.ti,ab,kf. OR renal tumour\*.ti,ab,kf. OR SRM.ti,ab,kf. )  AND  (conservative treatment/ OR Watchful Waiting/ OR "active surveillance".ti,ab,kf.OR "watchful waiting".ti,ab,kf.OR "conservative management".ti,ab,kf.OR "non-operative management".ti,ab,kf.OR expectant management.ti,ab,kf. OR organ sparing treatment\*.ti,ab,kf. OR nonsurgical treatment\*.ti,ab,kf. OR non-surgical treatment\*.ti,ab,kf. OR nonoperative treatment\*.ti,ab,kf. OR conservative management\*.ti,ab,kf.) | 2209 (670 conference abstracts) |
| Cochrane | ([mh "Kidney Neoplasms"] OR ("renal" NEXT mass\*):ti,ab OR ("kidney" NEXT neoplasm\*):ti,ab OR ("renal" NEXT neoplasm\*):ti,ab OR ("kidney" NEXT tumor\*):ti,ab OR ("renal" NEXT tumor\*):ti,ab OR ("renal" NEXT cancer\*):ti,ab OR ("kidney" NEXT cancer\*):ti,ab OR ("cancer of the" NEXT kidney\*):ti,ab OR ("kidney" NEXT tumour\*):ti,ab OR ("renal" NEXT tumour\*):ti,ab OR ("small renal" NEXT mass\*):ti,ab OR SRM:ti,ab) AND ([mh "Watchful Waiting"] OR "active surveillance":ti,ab OR "watchful waiting":ti,ab OR "conservative management":ti,ab OR "non-operative management":ti,ab OR "expectant management":ti,ab OR ("organ sparing" NEXT treatment\*):ti,ab OR ("nonsurgical" NEXT treatment\*):ti,ab OR ("non-surgical" NEXT treatment\*):ti,ab OR ("nonoperative" NEXT treatment\*):ti,ab OR ("conservative" NEXT management\*):ti,ab) | 20 |

**Table 2: Case-control studies risk of bias assessment**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Source** | **Study design** | **Is the case definition adequate?** | **Representativeness of the cases** | **Selection of controls** | **Definition of controls** | **Comparability Based on design and analysis** | **Ascertainment of exposure** | **Same method of ascertainment for cases and controls** | **Non-response rate** | **Total score** |
| Rasmussen, 2022 | Case-control | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | 8/9 |

Table 2: CASE CONTROL. Selection. Is the case definition adequate? A) Yes, with independent validation (e.g. growth rate with subsequent CT or MRI, tumor related death) B) Yes, e.g. record linkage or based on self reports C) No description; Representiveness of the cases: a) Appropriate selection of cases (e.g. defined growth rate; appropriate criteria of cancer related death; defined, long enough follow-up period) b) potential for selection biases or not stated (growth rate not defined, cancer specific death not defined, criteria for delayed intervention not stated, definition of progression not stated, short follow-up); Selection of Controls a) community controls (i.e. same community as cases and would be cases if had outcome); b) hospital controls (i.e. controls are from a subgroup of patients) ; c) no description; Definition of Controls a) 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; b) no description of source; Comparability of cases and controls on the basis of the design or analysis: a) study controls for growth rate b) study controls for any additional factor (OS; CSS; MFS); 1) Ascertainment of exposure a) secure record (eg surgical records/follow-up imaging) 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) yesb) no 3) Non-Response rate a) same rate for both groups b) non respondents described c) rate different and no designation

**Table 3: cohort studies risk of bias assessment**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Source** | **Study design** | **Representativeness of the cases** | **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 the design or analysis** | **Assessment of outcome** | **Was follow-up long enough for outcomes to occur** | **Adequacy of follow up of cohorts** | **Total score** |
| Bazan et al., 2013 | Cohort | +1 (b) | +1 (a) | + 1 (a) | +1 (a) | +2 (a/b) | +1 (a) | +1 (a) | +1 (b) | 9/9 |
| Ajami et al., 2021 | Cohort | +0 (d) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (b) | 7/9 |
| McIntosh et al., 2018 | Cohort | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +2 (a/b) | +1 (a) | +1 (a) | +1 (b) | 9/9 |
| Schiavina et al., 2015 | Cohort | +1 (b) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1(a) | +0 (d) | 7/9 |
| Paterson et al., 2017 | Cohort | +0 (d) | +1 (a) | +1 (a) | +1 (a) | +2 (a/b) | +1 (a) | +1 (b) | +0 (d) | 7/9 |
| Youssif et al., 2007 | Cohort | +0 (d) | +1 (a) | +1 (a) | +1 (a) | +1 (b) | +1 (b) | +1(a) | +0 (c) | 6/9 |
| Brunocilla et al., 2014 | Cohort | +1 (b) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1(a) | +0 (d) | 7/9 |
| Kato et al., 2004 | Cohort | +0 (d) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +0 (b) | +0 (d) | 5/9 |
| Sugimoto et al., 2013 | Cohort | +0 (d) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +0 (b) | +0 (d) | 5/9 |
| Leonard et al., 2013 | Cohort | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (b) | +1 (a) | +0 (b) | +1 (b) | 7/9 |
| Zalimas et al., 2022 | Cohort | +0 (d) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +0 (b) | +1 (b) | 6/9 |
| Finelli et al., 2020 | Cohort | +1 (b) | +1 (a) | +1 (a) | +1 (a) | +2 (a/b) | +1 (a) | +1(a) | +1 (b) | 9/9 |
| Tang et al., 2022 | Cohort | +1(a) | +1 (a) | +1 (a) | +1 (a) | +1 (b) | +1 (a) | +1(a) | +0 (d) | 7/9 |
| Patel et al.,  2014 | Cohort | +1(a) | +1 (a) | +1 (a) | +1 (a) | +1 (b) | +1 (a) | +1(a) | +0 (d) | 7/9 |
| Jewett et al., 2011 | Cohort | +1 (b) | +1 (a) | +1 (a) | +1 (a) | +2 (a/b) | +1 (a) | +0 (b) | +1 (b) | 8/9 |
| Pierorazio et al., 2015 | Cohort | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +2 (a/b) | +1 (a) | +1(a) | +1 (b) | 9/9 |
| Uzosike et al., 2018 | Cohort | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1(a) | +1 (b) | 8/9 |
| Alam et al., 2023 | Cohort | +1 (b) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1 (a) | +1(a) | +1 (b) | 8/9 |

Table 3: COHORT Representativeness of the exposed cohort a) truly representative of the average SRMs patient in the community, b) somewhat representative of the average SRM patient in the community c) selected group of patients d) no description of the derivation of the cohort; 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; Ascertainment of exposure a) secure record (eg CT scan/surgical record) b) structured interview c) written self report d) no description; Demonstration that outcome of interest was not present at start of study a) yes b) no; Comparability of cohorts on the basis of the design or analysis a) study controls for growth rate b) study controls for survival outcomes; Assessment of outcome a) confirmation of the outcome by reference to secure records (CT scan/MRI/medical record) b) record linkage (e.g. identified through ICD codes on database records) c) self report (i.e. no reference to original medical records or CT to confirm) d) no description; Was follow-up long enough for outcomes to occur a) yes (more than 36 months) b) no; 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 > 95 % follow up, or description provided of those lost) c) follow up rate < 95% and no description of those lost d) no statement

**Table 4: Studies results**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Authors, Year** | **Age, median** | **Tumor size, cm** | **Comorbidity score, Median** | **Solid Cystic** | **Factors associated with GR, OS, CSS, and Metastasis** | **Factors NOT associated with GR, OS, CSS, and Metastasis** |
| **(range)** | **(range)** | **(range)** |
| Pierorazio, 2015 | 70.6 | 1.9 | ECOG 0 (69.2%); ECOG 1 (42%); ECOG 2-4 (14%) | solid | OS:  -Age (HR 1.1 (95% CI 1.04–1.1, p < 0.001)),  - CVI=1: (HR 2.6; 95% CI 0.9– 7.6, p = 0.09)  -CVI = 2: HR 3.0, (95% CI 1.7–13, p = 0.003).  GR:  -Age (HR: 1.03; 95% CI 1.003–1.1, p = 0.03)  -ECOG score ≥2 (HR 2.3 95% CI 1.1–4.7, p = 0.02) | OS  -Tumor size  - RENAL  -ECOG |
| 34-93 | 0.4-7.7 | 0 - 4 |
| Jewett, 2011 | 73 | 2.1 | NR | NS | NS | GR:  - The average GR of those with a malignant RMB was 0.14 cm/yr (p = 0.01) compared with 0.17 cm/yr if benign ( p = 0.10), which were not significantly different ( p = 0.8). |
| 41-96 | 0.4 - 4 |  |  |  |  |
| Leonard, 2013 | 70.6 | 2.4 | NS | Solid | NR | GR:  -tumor size  - socioeconomic status |
|  | NR | 0.6-4.0 |  |  |  |  |
| Bazan, 2021 | 77 | Solid: 2.3  Cystic: 2.6 | CCI 2 | Solid and cystic | NR |  |
|  | 47-93 | Solid: 0.8-3.8  Cystic: 1.2-4.0 | 0-7 |  |  |  |
| Finelli, 2020 | 70 | 2.5 | NR | Solid and cystic | METASTASIS:  -biopsy-proven clear cell histology  GROWTH RATE: - biopsy-proven clear cell histology |  |
|  | 41-87 | 2.2-3 |  |  |  |  |
| Zalimas, 2022 | 78 | 2.3 | CCI 5 | Solid | GROWTH:  -confirmed ccRCCC histology on RMB  - lower level of TFAP2B methylation on urines |  |
|  | 72-81 | 1.0-3.7 | 0-7 |  |  |  |
| Ajami, 2021 | 75.7 | 2.12 | CCI 6 | Solid |  | GROWTH: No statistical differences were found regarding the initial size, tumor heterogeneity, intratumoral vessels, irregular edge, intratumoral calcification, ratio of small/long axis, ratio of cortical/tumor density in unenhanced and enhanced (portal phase) CT, and angular interface, in the GR subgroups |
|  | NR | NR | 0-7 |  |  |  |
| Tang, 2022 | NS | NS | NS | NS | NS | 10y OVERALL MORTALITY: 52.1% in the ≤1 cm group; 76.8% in >3–4 cm group, and 10-year 10yCSM:12.8% in the ≤1 cm group to 31.3% in the >3–4 cm group |
| Patel, 2014 | 65-69y: 15.3%; 70-74y: 21.1%; 75-79y: 21.8%; 80-84%: 20.3%; >85y: 21.6% | <2cm: 17.8%; 2-3 cm: 34.3%; 3-4cm: 47.9% | CCI 0: 34.5%; CCI 1: 40.0%; CCI 2: 17.5%; CCI 3+: 16.1% | Solid and cystic | OS: decreased in case of CHF (HR 1.95, 95% CI 1.72–2.21); CKD (HR 1.67, 95% CI 1.40–2.01); worse CVI |  |
| McIntosh, 2018 | 70 | 2.1 | 1 | Solid and cystic | GROWTH RATE:  No correlation with initial tumor size.  CSM:  No correlations with any variables | OVERALL SURVIVAL:  -cystic masses performed better than solid |
|  | 60-78 | IQR 1.5-3.1 | 0-2 |  |  |  |
| Schiavina, 2015 | 76 | 2.1 | CCI 3 | SOLID AND CYSTIC | GROWTH RATE:  -age at presentation,  - CCI,  - tumor size,  - nephrometric scores,  - BMI | GROWTH RATE:  -Male sex (hazard ratio [HR], 1.70);  - Symptomatic presentation (HR, 1.85) |
|  |  | 1.8-3.7 | 1-6 |  |  |  |
| Alam, 2023 | 71.2 | 1.8 | CCI 0 (43.7%); CCI 1 (21.0%); CCI 2 (19.8%); CCI >3 (15.5%) |  | GROWTH RATE:  -age as a continuous variable (p=0.69)  -Black patients (lower GRi than White patients; p=0.02) | GROWTH RATE:  - ≥ 65 yr (faster GRi (0.151 cm/yr, 95% CI 0.002–0.300, p = 0.05))  - ≥ 70 yr (0.243 cm/yr, 95% CI 0.004–0.481, p = 0.05) |
|  | 63.2 – 78.1 |  | 0-7 |  |  |  |
| Rasmussen, 2022 | 65 | 1.7 | NS | Solid | GROWTH RATE:  - ccLS 4–5 SRMs:  faster growth than ccLS 1–2 and ccLS 3 SRMs (by diameter  and volume (*p* < .05)) |  |
|  | 55-74 | 1.3 – 2.5 | NS |  |  |  |
| Paterson, 2017 | 71.5 | 2.2 | NS | Solid and cystic | GROWTH RATE:  - (eGFR) of less than 60/min/1.73 m2 at baseline (HR 2.152, p<0.05)  -central tumour location (HR 0.559, p = 0.024)  -Presence of con-current co-morbidity  (HR 1.142, p = 0.02) | GROWTH RATE:  There does  not appear to be any significant differences in growth rate  between histologically confirmed benign and malignant  masses. |
|  | + o – 12.3 | 0.6 - 4 | NS |  |  |  |
| Uzosike, 2018 | 70.7 | 1.5 | CCI 0 (43.9%); CCI 1 (25.1%); CCI 2 (15.5%); CCI 3 (7.4%); 4+ (8.1%) | Solid | GROWTH RATE:  - RMB demonstrated RCC: higher GR than patients with oncocytoma (no statistical significance (p=0.11)). | GROWTH RATE:  GR  -as a binary variable (0.5 or greater and less  than 0.5 cm per year), no variables were significantly  associated with GR. |
|  | + O – 10.6 | NR | 0-7 |  |  |  |
| Youssid, 2007 | 71.8 | 2.2 | NR | Solid and cystic |  | GROWTH RATE:  no correlation between initial tumor dimension and size growth rate or initial tumor volume and volume growth rate. |
|  | 29-90 | 0.5-4 | NR |  |  |  |
| Brunocilla, 2014 | 75 | 2 | CCI 3 median | NS |  | GROWTH RATE:  No statistically signiﬁcant  correlations were found between initial tumor size of the SRMs and  their linear and volumetric growth rates |
|  | 65-90 | 1.6 – 4.3 | 1-6 |  |  |  |
| Kato, 2004 | 56.5 | 2 | NR | Solid | GROWTH RATE:  -TUNEL positive ratio (0.07% - 2.65%, mean 0.78%, SE 0.16%),  correlated (r = 0.681, p = 0.0013)  - Grade 3 tumors faster (mean 0.93 cm per year, Standard Error 0.34, p = 0.0110)  than grade 2 (mean 0.28 cm per year, Standard Error 0.05) | GROWTH RATE:  -Ki-67 positive ratio (0.41% - 8.94%; mean: 1.96%, SE 0.53%; r = 0.363, p = 0.141).  -No significant difference (p = 0.4764)  between grade 1 (mean 0.37 cm per year, SE 0.12)  and grade 2 tumors . |
|  | 37-71 | 1-3.4 |  |  |  |  |
| Sugimoto, 2013 | 64.4 | No size reported, volume: 6.2 cm3 | NR | NS |  | GROWTH RATE:  No significant difference of TTD according to histopathological grade and subtype. |
|  | 35-80 | 0.14 – 30.5 cm3 |  |  |  |  |

**Tabella 5: selection criteria**

|  |  |  |
| --- | --- | --- |
| **Authors, Year** | **Inclusion criteria** | **Exclusion criteria** |
| Pierorazio, 2015 | - ≥18 yr of age  - Clinically localized, solid enhancing renal mass ≤ 4 cm (cT1a) on axial imaging. | - Personal history of RCC,  - Familial RCC syndrome,  - Suspicion of a second malignancy metastatic to the kidney |
| Jewett, 2011 | -Unfit for surgery for advanced age or comorbidity,  -Refusal of treatment | -Estimated life expectancy ≤ 2 yrs,  -Concurrent systemic therapy for other malignancies,  -Known hereditary RCC condition. |
| Leonard, 2013 | None Specified | None specified |
| Bazan, 2021 | -≥18 years of age;  -Localized, solid, contrast-enhancing (>20 HU) renal mass ≤4 cm imaging,  -Or complex renal cysts (Bosniak IIF-IV) | -History of a hereditary RCC syndrome  -Suspicion of metastatic disease to the kidney |
| Finelli, 2020 | -cT1aN0M0 renal mass | -Estimated life expectancy of ≤ 2 yr,  -Concurrent systemic therapy,  - Hereditary renal cancer syndrome,  -Nondiagnostic or benign biopsy. |
| Zalimas, 2022 | -Older than 18 yr;  -Renal mass ≤ 4 cm histologically confirmed RCC by RMB;  -Inappropriate for active treatment for advanced age, co-morbidity,  -Choosing to avoid active treatment | -Estimated life expectancy of ≤ 1 yr;  -Simultaneous systemic therapy for malignancy;  -Hereditary renal cancer syndrome;  -Nondiagnostic RMB |
| Ajami, 2021 | -Contrast-enhanced SRMs.  -Elderly patients,  -Associated comorbidities,  -Surgical risks,  -Kidney failure in which active treatment could lead to a decline in renal function. | -Patients who lacked at least two contrast-enhanced CT or MRI with at least six months of time lapse between them,  -Cystic lesions,  -Tumors associated with hereditary syndromes. |
| Tang, 2022 | -cT1a RCC | -N+ or M+;  -Lacking detailed information on tumor size;  -Having a diagnosis made only at the time of death;  -Lacking follow-up information. |
| Patel, 2014 | -≥65 years  -Clinically localized, T1a (≤4 cm) renal cortical tumors | -Patients lacking Medicare A and/or B coverage or enrolled in managed care plans during treatment;  -Regional disease,  -Distant metastases,  -Unknown stage,  -Upper tract transitional cell carcinoma or ureteric, non-cortical renal tumors,  -Multiple procedures  -Bilateral tumors. |
| McIntosh, 2018 | -Localized (cT1-2N0M0) based on established radiographic  staging protocols.  Separate analysis for masses >4 cm | None specified |
| Schiavina, 2015 | -Diagnosis of SRMs  -Relevant comorbidities,  -Advanced age,  -Patient refusal of surgery. | -Von HippeleLindau syndrome,  -History of hereditary RCC,  -M+ at presentation |
| Alam, 2023 | None specified (DISSRM registry) | None specified (DISSRM registry) |
| Rasmussen, 2022 | -cT1a renal masses who underwent MRI. | -MRI performed without IV contrast;  -Histology of the renal mass known at the time of MRI;  -Mass ineligible for ccLS assignment;  -Mass size > 4 cm;  -Genetic predisposition;  -Imaging performed after a local intervention;  -Imaging showed a change in size for tumor  -Hemorrhage;  -Metastatic disease on initial MRI. |
| Paterson, 2017 | -Patients who opted for active surveillance for  SRMs after review at multidisciplinary meetings. | None specified |
| Uzosike, 2018 | -Clinically localized, solid, contrast enhancing SRMs;  - ≥18 yo; | -Prior RCC history,  -Presence of a concerning for metastatic disease  - RCC syndrome family history. |
| Youssid, 2007 | -Renal masses measuring ≤4 cm;  -Advanced age,  -Comorbidity,  -Fear of renal failure associated with surgical resection. | None specified |
| Brunocilla, 2014 | -Diagnosis of SRMs,  -Relevant comorbidities,  -Advanced age,  - Patient refusal of surgery. | -VHL,  -Hereditary RCC conditions,  -Metastatic disease |
| Kato, 2004 | -Clinically localized SRMs. All underwent DI after 12 months observation | None specified |
| Sugimoto, 2013 | -cT1a SRM | None specified |