National Institute for Health and Care Excellence

Kidney cancer: diagnosis and management

[E] Evidence review for monitoring of untreated renal lesions using active surveillance

NICE guideline NG256

Evidence underpinning recommendations 1.4.1 to 1.4.9, 1.5.12 to 1.5.21, and a research recommendation in the NICE guideline

March 2026

Final

NICE National Institute for Health and Care Excellence®

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

ISBN: 978-1-4731-9344-4

Contents

1 Monitoring of untreated renal lesions using active surveillance

1.1 Review question

For adults with small or suspected benign renal lesions that have not been treated, what are the most clinically and cost-effective approaches to active surveillance (including method, duration and frequency), based on the type of renal lesion, for the early detection of disease progression?

1.1.1 Introduction

Management options for renal cell carcinoma (RCC) include surgical interventions such as partial or radial nephrectomy, non-surgical interventions such as ablative therapies and stereotactic ablative radiotherapy (SABR), and active surveillance. This review focuses on active surveillance for small or suspected benign renal lesions that have not undergone prior treatment.

Active surveillance is currently used in practice most commonly for people with very small lesions, or those with small lesions who decline active treatment. It involves a set programme of imaging to monitor the development of the lesion, often using imaging such as ultrasound (US), computed tomography (CT) or magnetic resonance imaging (MRI), with an option for intervention if there is growth above a threshold during the period of monitoring or if the person with RCC decides that they would like to discuss treatment. However, there is no universally agreed protocol for active surveillance.

This review aims to evaluate and compare the clinical and cost-effectiveness of different active surveillance approaches (for example different methods, durations, and frequencies) for early detection of disease progression in adults who have not been actively treated for small renal lesions (without histological assessment), small renal cell carcinomas, Bosniak 2F, 3 and 4 cysts and oncocytomas.

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria

Population	Adults (18 years or over) with renal lesions that have not been treated with surgery, non-surgical interventions or systemic anti-cancer therapy (SACT) divided into the following categories:
	• Small renal lesions and complex cysts (<4cm):
	  ○ small renal lesions (without histological assessment) or
	  ○ small renal cell carcinomas or
	• grade 3 and 4 Bosniak complex cysts
	• Grade 2F Bosniak cysts and oncocytomas (of any size)

Interventions	Approaches to active surveillance that might include: • Frequency and type of imaging

	• Frequency and type of testing to monitor renal function and cardiovascular outcomes • Different durations of active surveillance
Comparator	Different active surveillance approaches compared to each other.

Outcomes	Survival outcomes:
	  ○ Overall survival
	  ○ Disease-specific survival
	• Local or distant progression of disease
	• Time to discharge from active surveillance
	• Need for treatment including time to intervention or numbers of people needing the treatment
	• Quality of life using:
	  ○ EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30)
	  ○ EuroQol-5 dimensions (EQ-5D)

Study type	• Randomised controlled trials (RCTs) • Any controlled, non-randomised studies • Systematic reviews of the above studies

EORTC: European Organisation for Research and Treatment of Cancer

For the full protocol see appendix A.

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.3.1 Search methods

The searches for the effectiveness evidence were run on 19/08/2024 and re-run on 16/04/2025. The following databases were searched: Cochrane CENTRAL (Wiley), Cochrane CDSR (Wiley), Embase (Ovid), Epistemonikos (Epistemonikos), Medline ALL (Ovid). Limits were applied to remove animal studies, conference abstracts, editorials, letters, news items and commentaries, as well as papers not published in the English language. Filters were used to limit to OECD countries, observational studies, systematic reviews and randomised controlled trials.

The searches for the cost effectiveness evidence were run on 29/08/2024 and 05/09/2024 and re-run on 07/05/2025. The following databases were searched: Econlit (Ovid), Embase (Ovid), NHS EED (CRD York), International Health Technology Assessment Database (INAHTA), Medline ALL (Ovid). Limits were applied to remove animal studies, conference abstracts, editorials, letters, news items and commentaries, as well as papers not published in the English language. Filters were used to limit to cost utility studies.

A NICE senior information specialist (SIS) conducted the searches. The MEDLINE strategy was quality assured by another NICE SIS. All translated search strategies were peer

reviewed to ensure their accuracy. Both procedures were adapted from the 2015 PRESS Guideline Statement. Further details and full search strategies for each database are provided in appendix B.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 1,225 references (see appendix B for the literature search strategy).

These 1,225 references were screened at title and abstract level against the review protocol, with 1,142 excluded at this level. 10% of references were screened separately by two reviewers with 85.5% agreement. Discrepancies were most often due to conservative screening by the main reviewer and so were unlikely to miss any relevant studies. All discrepancies were resolved by discussion.

The full texts of 22 systematic reviews and 61 primary non-randomised studies were ordered for closer inspection. No studies were identified that met the criteria specified in the review protocol (appendix A).

The clinical evidence study selection is presented as a PRISMA diagram in appendix C.

1.1.4.2 Excluded studies

Details of studies excluded at full text, along with reasons for exclusion are given in appendix J.

1.1.5 Summary of studies included in the effectiveness evidence

No studies were identified which were applicable to this review question (and so there are no evidence tables in appendix D). No meta-analysis was conducted for this review (and so there are no forest plots in appendix E).

1.1.6 Summary of the effectiveness evidence

No studies were identified which were applicable to this review question, and so there are no GRADE tables in appendix F.

1.1.7 Economic evidence

A literature search was conducted to identify published economic evaluations of relevance to this review question (see appendix B). This search retrieved 119 studies, and based on title and abstract screening, one study was considered for full text screening, but was further excluded (see appendix G for the economic evidence study selection diagram and appendix J for a list of studies and reasons for exclusion).

1.1.8 Summary of included economic evidence

No economic evaluations were included for this review question.

1.1.9 Economic model

Costs around active surveillance were estimated as part of the costing analysis conducted for evidence reviews A, B and C. Full details of the analysis are included in the accompanying costing report.

Active surveillance costs were based on the schedule of monitoring and types of scans in the Getting It Right First Time (GIRFT) guidelines and committee opinion, and scenarios with different imaging modalities were discussed. One scenario included cross-sectional imaging with CT with contrast of chest, abdomen and pelvis (CT CAP) in the first year, and then annually thereafter. The second scenario included CT CAP in the first year, and then further imaging on an annual basis alternating between ultrasound and CT CAP. The third scenario included an MRI with contrast of three areas in the first year, followed by annual imaging alternating between ultrasound and MRI. Total first year costs and subsequent annual costs of the active surveillance scenarios are presented in Table 2.

Table 2: Imaging scenario annual costs

Scenario	First year cost	Mean subsequent annual cost
CT CAP only	£123	£123
Alternating CT CAP and ultrasound	£123	£88
Alternating MRI and ultrasound	£202	£128

1.1.10 Unit costs

Unit costs of each of the types of scans are summarised in Table 3.

Table 3: Unit costs of imaging modalities

Resource	Unit cost	Source
CT-CAP with contrast	£123.03	NHS Cost Collection (2024). RD26Z Computerised Tomography Scan of Three areas with contrast
CT-CAP without contrast	£100.74	NHS Cost Collection (2024). RD25Z Computerised Tomography Scan of Three areas without contrast
MRI with contrast	£202.40	NHS Cost Collection (2024). RD05Z Magnetic Resonance Imaging Scan of Two or Three areas with contrast
MRI without contrast	£153.84	NHS Cost Collection (2024). RD04Z Magnetic Resonance Imaging Scan of Two or Three areas without contrast
Ultrasound <20 minute duration with contrast	£53.32	NHS Cost Collection (2024). RD41Z Ultrasound Scan with duration of less than 20 minutes with contrast

Resource	Unit cost	Source
Ultrasound >20 minute duration with contrast	£29.96	NHS Cost Collection (2024). RD43Z Ultrasound Scan with duration of more than 20 minutes with contrast
Ultrasound <20 minute duration without contrast	£66.95	NHS Cost Collection (2024). RD40Z Ultrasound Scan with duration of less than 20 minutes without contrast
Ultrasound >20 minute duration without contrast	£88.18	NHS Cost Collection (2024). RD42Z Ultrasound Scan with duration of more than 20 minutes without contrast

CT-CAP: computed tomography scan of chest, abdomen and pelvis. MRI: magnetic resonance imaging

1.1.11 The committee's discussion and interpretation of the evidence

1.1.11.1. The outcomes that matter most

The committee discussed the outcomes specified in the protocol. They agreed that the most important outcomes to assess the effectiveness of active surveillance as a management option were survival, disease progression, time to discharge and need for treatment. In their experience, concerns about survival (overall and cancer-specific), the likelihood of lesion progression (local or distant) if not removed, duration of being on active surveillance and needing treatment in the future are usually at the forefront of people's minds when considering active surveillance as a treatment option.

Of importance, but less so than the outcomes above, were quality of life and health status in the short and long term, which play an important role in deciding which management option is best for the individual.

1.1.11.2 The certainty of the evidence

No studies were identified which met the inclusion criteria for this review question. The committee were not surprised by this and agreed that to their knowledge there is unlikely to be any evidence that directly answers it. The committee made a research recommendation that matched this current review question to try to stimulate research into this area.

1.1.11.3 Benefits and harms

The committee noted that the terms 'active surveillance' and 'follow-up' are sometimes conflated, leading to a lack of clarity for people with renal cell carcinoma (RCC). Active surveillance refers to the monitoring of lesion size and characteristics instead of, or before, treatment, when treatment is possible, whereas follow-up is monitoring undertaken after treatment for RCC. Both types of monitoring involve regular imaging.

In the absence of evidence about the most effective methods and duration of active surveillance, the committee made recommendations based on consensus, using their knowledge, experience of current practice and awareness of the recommendations in the Getting It Right First Time (GIRFT) guide Urology: Towards better care for patients with kidney cancer and European Association of Urology (EAU) guidelines. They noted that

current practice for active surveillance in the UK varies widely and there is no single standard of practice. Active surveillance protocols will usually depend on the type and size of the renal lesion, comorbidities of the patient (for example, existing health conditions that may affect choice of imaging) and access to imaging facilities.

To help with drafting recommendations the committee split the process of active surveillance into several sequential stages: determining who is suitable for active surveillance; how this is carried out (types of imaging and frequency) and when to stop active surveillance by discharging someone or offering them active treatment (such as surgery) instead.

Active surveillance for oncocytomas

A separate review (evidence review B comparing surgical and non-surgical management options for localised RCC) covers when active surveillance should be offered or considered for people with localised small renal lesions. However, evidence review B did not cover people with Bosniak 2F cysts or oncocytomas. The committee discussed when active surveillance should be offered to these groups as part of the current review.

As oncocytomas are benign, the committee recommended that active surveillance should be offered to people with a renal lesion likely to be an oncocytoma. They highlighted that this may not be appropriate if there is suspicion, based on pathology, of a malignant diagnosis. This could be due to hybrid features in the lesion. For example, hybrid oncocytic chromophobe tumours (HOCT) have two different components – the oncocytoma and chromophobe RCC. While oncocytomas are benign, HOCTs are more concerning as they may be malignant due to the chromophobe RCC component and may therefore be managed as a chromophobe RCC. The committee also noted that oncocytomas can sometimes cause symptoms such as bleeding or pain which may necessitate treatment, and they therefore included the absence of symptoms in the recommendation about when active surveillance should be offered for people with oncocytomas. They noted that a person may decline active surveillance and agreed that treatment for the oncocytoma should be offered in such situations. The committee did not review evidence about treatment options for oncocytomas and so were unable to draft recommendations on this. However, they noted that in their experience these would likely involve surgery to remove the oncocytoma or thermal ablation to destroy it.

The committee noted that when someone with a lesion likely to be an oncocytoma is experiencing symptoms like haematuria (blood in the urine), treating the lesion might be the most appropriate way to stop the bleeding. If left untreated, bleeding may cause other problems and affect quality of life. They made a recommendation to offer treatment for the oncocytoma if symptoms are present and only to offer active surveillance if the person declines this.

The committee agreed that where a lesion likely to be an oncocytoma is fast growing, further tests may be necessary to confirm the diagnosis, and that biopsy would be the best test to do this. This should be discussed with the person. If biopsy results show that the lesion is malignant, the committee agreed that due to the fast-growing nature of the lesion, progression to treatment for RCC would be appropriate. If the lesion is found to be benign, or if the person chooses not to have or cannot have biopsy, they agreed that either staying on active surveillance or moving to treatment to remove or destroy the lesion would be appropriate. The committee made recommendations to cover these points.

The committee were aware of a different category of oncocytic lesions affecting the kidney classed as 'oncocytic renal neoplasms of low malignant potential, not otherwise specified'. They noted that these lesions are low risk due to their low malignant potential and should usually be managed in the same way as oncocytomas. Therefore, they made a recommendation to reflect this.

Active surveillance for Bosniak 2F cysts

The committee noted that Bosniak 2F, 3 and 4 cysts can usually be characterised by imaging, and treatment decisions can be made based on these imaging results. Bosniak 2F cysts are usually benign but have a 5 to 10% risk of harbouring malignancy, which will usually become apparent during a period of active surveillance. Therefore, the committee recommended that active surveillance should be offered to people with Bosniak 2F cysts. They agreed that treatment is not necessary for Bosniak 2F cysts unless they progress to a Bosniak 3 or 4 cyst, or more rarely to an advanced RCC, and included cross references to the relevant sections of the guideline for treatment options.

Discharging people with oncocytomas or Bosniak 2F cysts from active surveillance

The committee agreed that where treatments for local symptoms, or RCC if developed in the future, are no longer an option for a person, active surveillance should be discontinued because the purpose of this monitoring is to detect lesion changes that could warrant treatment. Examples of where the person may be unable to have treatment could include if they are very frail or have multiple comorbidities. The committee agreed that it was important to explain to the person why they are being discharged from the active surveillance pathway.

The committee noted the low probability that Bosniak 2F cysts and oncocytomas harbour malignancy. They therefore also agreed that if these lesions remained stable for at least 5 years, for example if a Bosniak 2F cyst does not progress to a Bosniak 3 or 4 cyst or an oncocytoma has a growth rate below 5 mm in diameter in any 12-month period, then discharge should be considered. They noted that this decision should take into account the person's clinical characteristics such as age and fitness, and their preferences.

The committee noted the impact of long-term active surveillance on a person's mental well-being, and that discharge from active surveillance, where appropriate, may be welcomed by some people. However, they acknowledged that other people find active surveillance reassuring and agreed that there should be discussion about discharge with the person who has an oncocytoma or Bosniak 2F cyst if their lesion has remained stable for 5 years. This should include information about why they are being discharged, reassurance that if there was a malignancy present, it would most likely have been detected within the 5-year active surveillance period, and examples of symptoms that the person should contact primary care about (such as if they have blood in their urine or persistent abdominal pain).

Information to provide during active surveillance

Active surveillance is managed by secondary care. The committee recommended that all people who are undergoing active surveillance have a written care plan including details of their active surveillance imaging schedule, and the name of a designated healthcare

professional who can be the point of contact if, for example, the person experiences symptoms (such as blood in their urine or persistent abdominal pain).

Active surveillance imaging types

The committee discussed the types of imaging that could be used for active surveillance. They acknowledged the lack of evidence about the most effective active surveillance regimen and duration, and using their knowledge and experience decided what an active surveillance plan should entail. They agreed that the types of imaging and imaging schedule they recommended would be suitable as a starting point for people with all types of renal lesions (including oncocytomas, Bosniak 2F cysts, Bosniak 3 or 4 cysts and solid renal masses less than 4 cm in diameter).

They noted that the main aim of active surveillance is to detect a change in the lesion size or character. This is important because treatment options may reduce when lesions cross certain size thresholds (e.g. 4 cm for solid renal masses) or characteristics (e.g. Bosniak stages for cysts). The committee therefore recommended that as part of active surveillance, imaging is offered at regular interval to detect changes in lesion size or other characteristics.

The committee discussed the types of imaging tests currently used in practice (CT, MRI and ultrasound), and the benefits and harms associated with them. They noted that:

- Cross-sectional imaging (CT and MRI) produces more detailed images of a tumour than ultrasound. They noted that the imaging quality from an ultrasound may be insufficient to use in making an informed judgement about the characteristics of some lesions.
- MRI scans can be unpleasant for people who experience claustrophobia and cannot be offered to people with metal implants.
- Not all hospitals in the UK have an MRI machine and hospitals which do may have only one. This may result in longer waiting times for MRI or require referral to a different department or another hospital. Some people may struggle to access MRI scans depending on location. Contrast-enhanced ultrasound is not available everywhere in the UK and will usually not be used for active surveillance.
- Costs differ between imaging types and ultrasounds have the lowest unit costs. However, there may be increased inter-user variability and difficulty comparing scans when using ultrasounds.
- There are potential harms from the agents used in contrast-enhanced CT or contrast-enhanced MRI. People with renal insufficiencies may be unable to use contrast agents.
- Repeated radiation from CT could be harmful and so MRI without contrast or ultrasounds may be preferred for some groups, for example women or people of childbearing age, who could be or get pregnant.

The committee therefore recommended that CT, MRI or ultrasound imaging should be used as part of an active surveillance approach, with choice based on lesion and the individual's clinical characteristics, and that ultrasound or MRI could be alternated with CT to reduce radiation exposure. To try to reduce the risk of kidney damage arising when iodine-based contrast media is used in imaging the committee included a cross reference to relevant recommendations of the NICE guideline on Acute kidney injury: Assessing risk factors in

adults having iodine-based contrast media and Preventing acute kidney injury in adults having iodine-based contrast media.

The active surveillance imaging schedule

The committee agreed that imaging for active surveillance should be offered at regular intervals. In their experience, this imaging is usually carried out at 3-, 6- or 12-month intervals or a combination of these, for example every 6 months in the first year and then every 12 months afterwards. The committee noted that the timing of active surveillance scans will depend on the behaviour of the lesion. They agreed that imaging scans should be offered more regularly if there are major changes to the lesion, and less frequently if the lesion is more stable or slowly growing. However, lay members highlighted that following a decision to participate in active surveillance, patients may be very anxious as they wait for their next scan in case the lesion has grown. This level of anxiety is highest at the start of active surveillance and may decrease over time if the lesion size and characteristics remain constant.

The committee took these issues into account when recommending a schedule that could be used for active surveillance. However, they noted that it is impossible to provide an active surveillance protocol for every possible scenario and that this schedule should be adapted if more intensive imaging is required based on the lesion and the individual's clinical characteristics. The committee recommended that the first imaging scan after the decision for active surveillance should be in the first 3 to 6 months to pick up changes and reassure people. They also agreed that subsequent scans should be offered at 12 months from initiation of active surveillance and at least annually thereafter up to 5 years, and that the person's wishes should also be taken into account when this schedule is agreed. At 5 years they recommended that there be a discussion with the person about the benefits and risks of continuing active surveillance or being discharged (see below for more information about discharge.) However, the committee recommended that should the lesion's size, growth rate or characteristic change (but not enough to trigger a discussion about possible treatment) then more frequent imaging should be considered.

The committee noted that changes to lesions may occur within a short time or over a longer period. They agreed that baseline imaging is necessary to provide information about the size, shape and characteristics of the tumour at the start of management for comparison to the new imaging results. They agreed that to properly monitor changes in lesion size, shape or characteristics, and the rate at which the changes occur, each imaging scan should be compared both to the most recent scan and to the baseline imaging and made a recommendation to reflect this. This could be particularly important if, for example, a change is minimal from the last scan but significant from the baseline scan.

Moving to treatment for lesions 4 cm in diameter and smaller (including solid renal masses, and Bosniak 3 or 4 cysts)

The committee agreed that people with Bosniak 3 and 4 cysts have an increased chance of malignancy compared with Bosniak 2F cysts, and that in many cases management should be similar to management of solid renal masses that are suspected to be RCC. Therefore, they chose to include people with Bosniak 3 and 4 cysts and people with solid renal masses in the same recommendations here and in the section on discharge below.

The committee discussed the changes that may result in a decision to move to treatment from active surveillance. They highlighted a change in size or growth rate of the lesion as the

main triggers to move to active treatment but also recognised changes to the appearance or shape as factors to consider. They noted that there is no universally accepted threshold for change in lesion size but based on their experiences were aware that they can increase and decrease in diameter over time. Therefore, they made a recommendation that a discussion to move to active treatment should be had with people when observed changes to the lesion include any of the following:

- the growth rate of the lesion (or the growth rate of the solid component for Bosniak 4 cysts) exceeds 5 mm in diameter in a year
- the lesion is likely to exceed 4 cm in diameter at the next scan based on the observed trajectory of growth in diameter at the next scan
- progression (in clinical TNM stage for solid renal masses, and in Bosniak classification / characteristics for cysts).

In addition, they highlighted the possibility that a person may have a change in the clinical circumstance that affected their preoperative risk or competing clinical priorities (comorbidities and renal function) and as a result may become eligible for treatments that were not previously suitable. For example, comorbidities may have been controlled or optimised making treatment an option, or a person with end stage renal failure may be moved to transplant list and need a nephrectomy. The committee also highlighted that people's preferences should be taken into account as people who previously opted for active surveillance may decide that they would like to change to a treatment plan, and that any suitable treatment options should be discussed with the person. Therefore, they recommended that a discussion about moving to active treatment should also cover these points and emphasised that this is a shared decision to be made with the person.

Moving to discharge for lesions 4 cm in diameter and smaller (including solid renal masses, and Bosniak 3 or 4 cysts)

The decision about when to stop active surveillance when no changes are observed was discussed. The committee noted the difficulty in giving a precise duration for active surveillance as renal lesions can behave unpredictably. However, the committee identified some situations where it may be suitable to discharge people from active surveillance. They noted that for some people, a change in condition during active surveillance - for example an increase in frailty, comorbidities or other competing causes of mortality - will mean that they are no longer suitable for active treatments such as surgery, thermal ablation or stereotactic ablative radiotherapy (SABR) and should therefore be discharged from active surveillance. Similarly, they noted that for people with lesions that are small (4 cm or smaller) and remain stable or with minimal changes for 5 years discharge might be suitable. The patient committee members added that remaining on active surveillance for a long time and having repeated imaging can be experienced as an extended period of uncertainty and cause of anxiety that is relieved by being discharged. Therefore, the committee made a recommendation to consider discharging the person from active surveillance if the lesion remains stable for 5 or more years but that this decision should take the person's preferences and clinical characteristics (such as age and fitness) into account. They made another recommendation to discharge people if they are no longer eligible for treatment of the RCC.

The committee explained that ultimately, the decision to discharge a person from active surveillance will be based on a combination of clinical judgement and patient choice. The

committee highlighted the importance of applying the recommendations in NICE's shared decision-making guideline during discussions with the person with a renal lesion. They also highlighted the importance of ensuring that people understand why they are being discharged, that there is a lack of evidence around how long active surveillance should last and the need to provide examples of symptoms that the person should contact primary care about (such as if they have blood in their urine or persistent abdominal pain).Therefore, they recommended that the discussion with the person should include these points.

1.1.11.4 Cost effectiveness and resource use

No relevant published health economic analyses were identified for this review, and it was not prioritised for original economic modelling. Annual costs of active surveillance were estimated as part of a costing analysis and the unit cost of the different types of scans used for monitoring people in active surveillance were presented to aid committee consideration of cost effectiveness. The unit cost of undertaking CT of the chest, abdomen and pelvis was cheaper than the unit cost of MRI, and ultrasound was cheaper than either of these options. The annual costs of different scenarios for active surveillance were between £421 and £501 for the first year which included biopsy and cross-sectional imaging. In subsequent years, the annual cost of this ranges between £88 and £128, where people receive an annual CT scan or annual scans alternating between CT or MRI and ultrasound.

The committee discussed how practice in the UK varies widely and there is no standard practice for active surveillance. Active surveillance protocols as currently practiced will usually depend on the type and size of the renal lesion, comorbidities of the patient (for example, existing health conditions that may affect choice of imaging) and access to imaging facilities. Access to MRI nationwide is thought to be highly variable. Active surveillance is commonly undertaken at least annually using a CT scan, for at least five years but sometimes up to ten years. MRI are associated with less radiation exposure, so they are usually preferred for younger patients, but the cost is higher than a CT scan and they are usually more difficult to access. Ultrasound is the least expensive type of scan; they are not as accurate as CT or MRI, but may be used to limit radiation exposure.

The recommendations have been made on what is considered to be best practice based on committee consensus, while emphasising shared decision making between the patient and multidisciplinary team and are broadly consistent with recommendations in other widely used kidney cancer guidelines. This allows for standardisation of practice across the country and more optimal use of resources for managing people undergoing active surveillance. The recommendations could increase imaging, but this may be balanced by a reduction in the number of people undergoing other treatments such as surgery.

1.1.11.5 Other factors the committee took into account

The committee discussed whether any specific equality issues applied to active surveillance and whether any specific population groups could be disadvantaged by the recommendations. Most of the issues identified in the EHIA were societal in nature and focused on non-kidney cancer specific issues such as accessibility of some imaging machines for populations such as older people, people with disability and people with lower socio-economic status. They noted that reduced accessibility to imaging machines (for example, MRI) may result in longer waiting times, especially where alternative imaging types are not suitable.

Pregnancy will impact on decisions about imaging for active surveillance. The committee recognised that some types of imaging, particularly CT, are likely to be delayed until after pregnancy, but that other safer alternatives like ultrasound or MRI may be suitable after consideration by the individual, with support from the clinician, about the benefits and risks.

The committee also noted that CT and MRI scanners have an upper weight limit due to safety concerns and the design of the equipment, therefore people with very high weight may have reduced options available for imaging. In these cases, the committee agreed that an ultrasound scan would be the best available alternative, but with the awareness that ultrasounds may not produce images as detailed as CT or MRI.

1.1.12 Recommendations supported by this evidence review

This evidence review supports recommendations 1.4.1 to 1.4.9, 1.5.12 to 1.5.21 and the research recommendation on active surveillance.

1.1.13 References – included studies

1.1.13.1 Effectiveness

No studies were identified which were applicable to this review question.

1.1.13.2 Economic

No studies were identified which were applicable to this review question.

1.1.14 References – other

NHS England. National Cost Collection for the NHS 2023/24. Available from: https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ [online, accessed 10 July 2025]

Appendices

Appendix A – Review protocols

Effectiveness review protocol

ID	Field	Content
1.	Review title	Active surveillance approaches for early detection of disease progression in adults who have not been treated for small (<4cm) or suspected benign renal lesions.
2.	Review question	For adults with small or suspected benign renal lesions that have not been treated, what are the most clinically and cost-effective approaches to active surveillance (including method, duration and frequency), based on the type of renal lesion, for the early detection of disease progression?
3.	Objective	To evaluate and compare the effectiveness, safety, and cost-effectiveness of different active surveillance approaches (e.g., different methods, duration, and frequency) for early detection of disease progression in adults who have not been actively treated for small renal lesions (without histological assessment), small renal cell carcinomas (RCC), grade 3 and 4 Bosniak complex cysts. Grade 2F Bosniak cysts and oncocytomas will also be assessed.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE ALL • Epistemonikos For the economics review the following databases will be searched: • Embase • MEDLINE • Econlit • HTA (legacy records) • NHS EED (legacy records) • INAHTA Database functionality will be used, where available, to exclude: • Non-OECD countries • Animal studies • Editorials, letters, news items and commentaries

		• Conference abstracts and posters • Registry entries for ongoing clinical trials or those that contain no results • Theses and dissertations • Papers not published in the English language Search filters and classifiers • The following standard NICE filters will be used to limit results by study type: cost effectiveness studies / cost utility studies/ systematic reviews / randomised controlled trials and observational studies. • The full search strategies for all databases will be published in the final review.
5.	Condition or domain being studied	1. Small renal lesions and complex cysts (<4cm) 2. Grade 2F Bosniak cysts and oncocytomas (of any size)
6.	Population	Adults (18 years or over) with renal lesions that have not been treated with surgery, non-surgical interventions or systemic anti-cancer therapy (SACT) divided into the following categories: 1. Small renal lesions and complex cysts (<4cm): o small renal lesions (without histological assessment) or o small renal cell carcinomas or o grade 3 and 4 Bosniak complex cysts 2. Grade 2F Bosniak cysts and oncocytomas (of any size) Exclusion: • Renal lesions which have been actively treated.
7.	Intervention	Approaches to active surveillance that might include: • Frequency and type of imaging • Frequency and type of testing to monitor renal function and cardiovascular outcomes • Different durations of active surveillance
8.	Comparator	Different active surveillance approaches compared to each other.
9.	Types of study to be included	Systematic reviews of RCTs and RCTs If RCTs are not available, systematic reviews of non-randomised comparative studies and primary non-randomised comparative studies will be considered. Where good quality systematic reviews of non-randomised studies are identified, these may be used completely or as a source of references, depending on applicability.
10.	Other exclusion criteria	None

11.	Context	There is currently no national guideline in the UK on the diagnosis and treatment of kidney cancer and audit data indicates variation in the clinical practice within NHS. Stakeholders identified this gap and NICE was commissioned to develop a guideline on kidney cancer by NHSE. Active surveillance of renal lesions, which includes serial imaging with the possibility of delayed treatment, has emerged as a viable alternative to immediate therapeutic intervention in selected patients. There is uncertainty around the intensity required for active surveillance approaches (e.g. different methods, duration, and frequency) and how this might differ depending on risk of disease progression and the person undergoing active surveillance. In the lower risk category which includes small renal lesions (without histological assessment), small renal cell carcinomas (RCC), grade 3 and 4 Bosniak complex cysts and the benign lesions grade 2F Bosniak cysts and oncocytomas, there may be further variation in active surveillance methods required. Therefore, an evidence review is needed to identify the most clinically and cost effective active surveillance approaches suitable for different types of lower-risk renal lesions.
12.	Outcomes	Survival outcomes: • Overall survival (time to event data) • Disease-specific (cancer-specific) survival (time to event data) Some studies may report all-cause mortality instead of overall survival or they may report cancer-related mortality instead of disease-specific survival. These will be extracted as proxy outcomes where the preferred outcome is not available. • Local or distant progression of disease, (defined as a linear growth rate greater than 0.5 cm per year, diameter greater than 4 cm, or metastasis) (dichotomous outcome) • Time to discharge from active surveillance (continuous outcome) • Need for treatment* including time to intervention (continuous outcome) or numbers of people needing the treatment (dichotomous outcomes) *(Treatment include types of surgery or non-surgical interventions such as SABR, thermal ablation or systemic anti-cancer therapy.) • Quality of life using: o EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30) o EuroQol-5 dimensions (EQ-5D) **Minimal important differences** Any statistically significant difference will be used for the following outcomes: • Survival outcomes

		• Local and distant progression of disease • Time to discharge from active surveillance • Need for/time to intervention • Quality of life using EORTC QLQ-C30 MIDs for the following quality of life measure was identified in the literature: EQ-5D: 0.08 for UK-based scores and 0.07 for VAS scores
13.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.2). Study investigators may be contacted for missing data where time and resources allow. This review may make use of the priority screening functionality within the EPPI-reviewer software. If priority screening is used, the following rules will be adopted to determine when to stop screening: • at least 50% of the identified abstracts (or 1,000 records, if that is a greater number) will be screened • After this point, screening is only terminated if a threshold of 750 is met for a number of abstracts being screened without a single new include being identified. if sifting is terminated before the full database has been looked at additional checks will be carried out to ensure that relevant studies have not been missed.
14.	Risk of bias (quality) assessment	Risk of bias will be carried out using the preferred checklists as described in Appendix H of Developing NICE guidelines: the manual The risk of bias for RCTs will be assessed using the Cochrane Risk of Bias v.2.0 checklist and for systematic reviews, the Risk of Bias in Systematic Reviews (ROBIS) tool will be used. The risk of bias for non-RCT studies will be assessed using the Cochrane Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tool.
15.	Strategy for data synthesis	Where possible, meta-analyses will be conducted to combine the results of quantitative studies for each outcome. RCT and non-RCT data will be pooled separately. Where data can be disambiguated it will be separated into the subgroups identified in section 16 (below).

		Pairwise meta-analyses will be performed in Cochrane Review Manager V5.3. Continuous outcomes will be analysed as pooled mean differences (using the inverse variance method) unless multiple scales are used to measure the same factor. In these cases, standardised mean differences will be used instead. Where different studies present continuous data measuring the same outcome but using different numerical scales (e.g. a 0-10 and a 0-100 visual analogue scale), these outcomes will all converted to the same scale before meta-analysis is conducted on the mean differences. Pooled relative risks will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event. Absolute risks will be presented where possible. Hazard ratios will be pooled using the generic inverse-variance method. Adjusted, unadjusted and partially adjusted hazard ratios will be pooled. Sensitivity analysis will be carried out to look at the effect of removing partially and unadjusted studies. For survival outcomes, time-to-event data is preferred. Where this data is not available, relative risks will be calculated for proxy outcomes as described in section 12. Fixed- and random-effects models (der Simonian and Laird) will be fitted for all outcomes, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models will be deemed to be inappropriate if one or both of the following conditions are met: Significant between-study heterogeneity in methodology, population, intervention, or comparator was identified by the reviewer in advance of data analysis. The presence of significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$. GRADE will be used to assess the quality of the outcomes. Data from randomised controlled trials and non-randomised comparative trials will be initially rated as high quality where they come from: RCTs and systematic reviews of RCTs (where individual studies have been quality assessed using Cochrane risk of bias) non-randomised comparative trials and systematic reviews of non-randomised studies (where individual studies have been quality assessed using the ROBINS-I assessment tool) The quality of the evidence for each outcome will then be downgraded or not from this starting point based on the other GRADE domains. To assess imprecision, where there are no defined MIDs we will set the MID as the line of no effect for all outcomes (1.0 for dichotomous outcomes and 0 for continuous outcomes). A second

<table>
<tr><td></td><td></td><td colspan="3">decision threshold will be applied where the sample size is sufficiently small that it is not plausible any realistic effect size could have been detected.

Where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically (visually) assess the potential for publication bias.</td></tr>
<tr><td>16.</td><td>Analysis of sub-groups</td><td colspan="3">Where the data allows, subgroup analyses may be conducted to explore heterogeneity considering the following:
• components of active surveillance,
• type of renal lesion e.g. solid mass or Bosniak cyst
• age,
• tumour size,
• by primary RCC type e.g. clear cell, papillary, chromophobe
• renal function, and
• performance status of the person.</td></tr>
<tr><td>17.</td><td>Type and method of review</td><td colspan="3">X Intervention
Diagnostic
Prognostic
Qualitative
Epidemiologic
Service Delivery
Other (please specify)</td></tr>
<tr><td>18.</td><td>Language</td><td colspan="3">English</td></tr>
<tr><td>19.</td><td>Country</td><td colspan="3">England</td></tr>
<tr><td>20.</td><td>Anticipated or actual start date</td><td colspan="3">October 2024</td></tr>
<tr><td>21.</td><td>Anticipated completion date</td><td colspan="3">March 2026</td></tr>
<tr><td rowspan="8">22.</td><td rowspan="8">Stage of review at time of this submission</td><td>Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td>Preliminary searches</td><td></td><td>X</td></tr>
<tr><td>Piloting of the study selection process</td><td></td><td>X</td></tr>
<tr><td>Formal screening of search results against eligibility criteria</td><td></td><td>X</td></tr>
<tr><td>Data extraction</td><td></td><td>X</td></tr>
<tr><td>Risk of bias (quality) assessment</td><td></td><td>X</td></tr>
<tr><td>Data analysis</td><td></td><td>X</td></tr>
<tr><td>23.</td><td>Named contact</td><td colspan="3">Named contact
Centre for Guidelines, NICE</td></tr>
</table>

		Named contact e-mail kidneycancerguideline@nice.org.uk **Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and Guideline Development Team.
24.	Review team members	From the Guideline Development Team: • Marie Harrisingh, Topic Lead • Olivia Crane, Senior technical analyst • Adefisayo Abba-Abba, Technical analyst • Lindsay Claxton, Health economics adviser • Hannah Tebbs, Senior health economist • Yuanyuan Zhang, Senior health economist • Amy Finnegan, Senior Information specialist
25.	Funding sources/sponsor	This systematic review is being completed by the Guideline Development Team which receives funding from NICE.
26.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: Kidney Cancer (GID-NG10398).
28.	Other registration details	None
29.	Reference/URL for published protocol	None
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.

31.	Keywords	Localised renal cell carcinoma, thermal ablation, stereotactic ablative radiotherapy, active surveillance
32.	Details of existing review of same topic by same authors	Not applicable
33.	Current review status	Ongoing Completed but not published X Completed and published Completed, published and being updated Discontinued
34..	Additional information	None
35.	Details of final publication	www.nice.org.uk

Economic review protocol

ID	Field	Content
1.	Review title	For adults with small or suspected benign renal lesions that have not been treated, what are the most clinically and cost-effective approaches to active surveillance (including method, duration and frequency), based on the type of renal lesion, for the early detection of disease progression?
2.	Objective	To identify economic studies for active surveillance approaches for early detection of disease progression in adults who have not been treated for small (<4cm) or suspected benign renal lesions
3.	Inclusion criteria	• Populations, interventions and comparators as specified in the effectiveness review protocol. • Relevant comparative economic study design: cost–utility analysis • Decision analytic model-based or within-trial economic analyses • OECD countries (except USA) • Healthcare and personal social services cost perspective • Studies published from 2010 – this cut off has been applied to restrict the review to more recent studies which will have more applicable resource use and costs High-quality studies in line with the NICE reference case (recent UK NHS/PSS cost-utility analyses using the QALY as the measure of outcome) are the most applicable to NICE decision making. Not all studies meeting the inclusion criteria will therefore necessarily be used in decision-making - see Review strategy below for details.
4.	Exclusion criteria	• Conference posters or abstract only studies – these do not provide sufficient information for quality assessment. • Studies published before 2010 – this cut off has been applied to restrict the review to more recent studies which will have more applicable resource use and costs

		• Studies from non-OECD countries or the USA – these are considered unlikely to be applicable to the UK NHS setting due to substantial differences in healthcare delivery and unit costs. • Non-comparative economic analyses including cost-of-illness studies. • Letters, editorials or commentaries, study protocols or reviews of economic evaluations (recent reviews will be ordered and the bibliographies will be checked for relevant individual economic studies, which will then be ordered and checked for eligibility). • Non-English language papers. • Studies considering exclusively intervention costs, e.g. medicine acquisition costs, without considering wider healthcare costs associated with the management of renal cell carcinoma. • Studies comparing costs of branded versus generic forms of the same medicine. • Studies only focussing on productivity losses or gains.
5.	Search strategy	An economic study search will be undertaken covering review questions relating to the active surveillance of untreated renal cell carcinoma, using guideline population-specific terms and a health economic study filter. For search details see appendix B below. The following databases will be searched: • MEDLINE All, Ovid • Embase, Ovid • International HTA database, International Network of Agencies for Health Technology Assessment (INAHTA) • Econlit • NHS EED
6.	Review strategy	• Studies meeting the inclusion and exclusion criteria will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist in appendix H of Developing NICE guidelines: the manual. • The NICE economic evaluation checklist assesses: ○ Applicability to the NICE guideline decision making context with consideration of the NICE reference case relevant to the guideline. Recent UK studies that use the NICE reference case methods are the most applicable when considering cost effectiveness. ○ Methodological limitations. • The aim is to present the best available economic evidence to inform committee decision-making in the context of the guideline, the current UK NHS setting and NICE methods. Therefore, the health economist may not present all studies that meet inclusion criteria. If recent high quality, UK cost-utility analyses are available for a question, it is often not deemed informative to present studies that are less applicable or lower quality such as older UK analyses or analyses from other countries. A similar principle is deemed to apply more generally when considering applicability and methodological limitations. Some specific examples are given below: ○ If multiple versions of a model are available for the UK and other countries it is usually reasonable to only present the UK version.

		○ If multiple versions of the same UK model are available, it is usually reasonable to present only the most recent. ○ If there has been a NICE MTA or guideline model that informs current NHS practice it is usually reasonable not to present older studies, unless they address a different subpopulation or other specific issue. ○ If a UK model that includes all interventions in the decision space is available it may be reasonable not to present studies that only include individual or fewer interventions, if the analysis is sufficiently applicable and of good methodological quality. • Quality and relevance of effectiveness data used in the economic analysis: the more closely the clinical effectiveness data used in the economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. • Hierarchy of economic evaluation evidence based on quality assessment ○ 'Directly applicable' and 'Minor limitations' (only recent UK CUAs can get this rating). Usually presented and used in decision-making. ○ Directly or partially applicable combined with minor or potentially serious limitations (other than 1). Discretion over whether these are presented and used in decision-making, depending on the availability of more relevant evidence. ○ 'Not applicable' or 'Very serious limitations'. Typically not presented and not used in decision-making. The health economist will make a decision based on the relative applicability and quality of the available evidence for each question, in discussion with the guideline committee if required. All decisions will be transparently reported in the evidence report. Studies that are presented to the committee and used in decision-making when formulating recommendations will be included in the summary tables and will have an evidence extraction. Other studies may not be presented to the committee in detail but will be listed, with the reason for not being presented to the committee and thus not used in decision-making being provided. Committee members can review and query the decision not to present studies with the health economist and will be provided with full details of these studies where requested.

Appendix B – Literature search strategies

Background and development

Search design and peer review

A NICE Senior Information Specialist (SIS) conducted the literature searches. The MEDLINE strategies below were quality assured (QA) by another NICE SIS. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the Peer Review of Electronic Search Strategies Guideline Statement (for further details see: McGowan J et al. PRESS 2015 Guideline Statement. *Journal of Clinical Epidemiology*, 75, 40-46).

The principal search strategies were developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

This search report is based on the requirements of the PRISMA Statement for Reporting Literature Searches in Systematic Reviews (for further details see: Rethlefsen M et al. PRISMA-S. *Systematic Reviews*, 10(1), 39).

Review management

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess "low-probability" matches. All decisions made for the review can be accessed via the deduplication history.

Search limits and other restrictions

Formats

Limits were applied in adherence to standard NICE practice (as set out in the Identifying the evidence chapter of the manual) and the eligibility criteria listed in the review protocol to exclude:

- Animal studies
- Editorials, letters, news items and commentaries
- Conference abstracts and posters
- Registry entries for ongoing clinical trials or those that contain no results
- Theses and dissertations
- Papers not published in the English language.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from:

Dickersin K, Scherer R & Lefebvre C. (1994) Systematic Reviews: Identifying relevant studies for systematic reviews. *BMJ*, 309(6964), 1286.

Date limits

No date limits were applied, in adherence to the review protocol.

Search filters and classifiers

Effectiveness searches

Systematic reviews filters:

Lee, E. et al. (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. BMC Medical Research Methodology, 12(1), 51.

- In MEDLINE, the standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.
- In Embase, the standard NICE modifications were used: pubmed.tw added to line medline.tw.

Randomised control trial filters:

The MEDLINE RCT filter was McMaster Therapy – Medline - "best balance of sensitivity and specificity" version.

The standard NICE modifications were used: the MeSH heading *randomized controlled trial/*, which is equivalent *to randomized controlled trial.pt* was exploded to capture newer, narrower *terms equivalence trial/ and pragmatic clinical trial*. The free-text term *randomized.mp* was also changed to the (more inclusive) alternative *randomi?ed.mp.* to capture both UK and US spellings.

Haynes RB et al. (2005) Optimal search strategies for retrieving scientifically strong studies of treatment from Medline: analytical survey. *BMJ*, 330, 1179-1183.

The Embase RCT filter was McMaster Therapy – Embase "best balance of sensitivity and specificity" version.

Wong SSL et al. (2006) Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE. *Journal of the Medical Library Association*, 94(1), 41-47.

Observational filter:

The terms used for observational studies are standard NICE practice that have been developed in house.

OECD countries filter:

The MEDLINE and Embase searches were limited to evidence from Organisation for Economic Co-operation and Development (OECD) member states using the validated NICE filter.

The OECD countries filters were used without modification:

Ayiku, L., Hudson, T., Williams, C., Levay, P., & Jacob, C. (2021). The NICE OECD countries' geographic search filters: Part 2 - Validation of the MEDLINE and Embase (Ovid) filters. *Journal of the Medical Library Association*, 109(4), 583–589.

Cost effectiveness searches

In line with the review protocol, the sensitive version of the validated NICE cost utility filter was used in the MEDLINE and Embase strategies without amendment.

> Hubbard W et al. (2022) Development and validation of paired MEDLINE and Embase search filters for cost-utility studies. *BMC Medical Research Methodology*, 22(1), 310.

Key decisions

The search strategy was based on the population terms used in review questions A, B, C, H1 and H2 (review A: surgical interventions for localised RCC, review B: non-surgical interventions for localised RCC, review C: nephrectomy or stereotactic ablative radiotherapy for locally advanced RCC, reviews H1 and H2: non-pharmacological management of advanced RCC) for this guideline. The population was amended to remove nephrectomy and stage three and stage four terms as these were out of scope for this review question (review E).

Clinical searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	19/08/2024	Wiley	Issue 7 of 12, July 2024	56
Cochrane Database of Systematic Reviews (CDSR)	19/08/2024	Wiley	Issue 7 of 12, July 2024	1
Embase	19/08/2024	Ovid	1974 to 2024 August 16	799
Epistemonikos	19/08/2024	Epistemonikos	n/a	147

MEDLINE ALL	19/08/2024	Ovid	1946 to August 15, 2024	760

Rerun search database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	16/04/2025	Wiley	Issue 3 of 12, March 2025	18
Cochrane Database of Systematic Reviews (CDSR)	16/04/2025	Wiley	Issue 3 of 12, March 2025	1
Embase	16/04/2025	Ovid	1974 to 2025 April 15	846
Epistemonikos	16/04/2025	Epistemonikos	n/a	172
MEDLINE ALL	16/04/2025	Ovid	1946 to April 15, 2025	792

No date limit was applied to the rerun searches due to technical issues with OVID. Instead the duplication of records was managed in EPPI Reviewer 5.

Search strategy history

Database name: Cochrane CENTRAL and CDSR

Searches
#1 MeSH descriptor: [Kidney Neoplasms] explode all trees 1977
#2 (Kidney* NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-1 or stage-I)):ti,ab 957
#3 (collecting-duct* NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumour* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma*)):ti,ab 14
#4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*):ti,ab 3884
#5 (Kidney* NEAR/2 (Transitional-cell* or cell or urothelial* or duct or advanc*) NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumour* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma*)):ti,ab 69
#6 {or #1-#5} 4938
#7 MeSH descriptor: [Adenoma, Oxyphilic] this term only 10
#8 (oncocytom* or Oxyphilic*):ti,ab 20
#9 (((small* or benign* or suspect* or solid*) NEAR/3 (lesion* or mass* or non-treat* or tumo?r* or cyst*)) or SRM*):ti,ab 11595

Searches
#10 (Complex* NEAR/3 (cyst* or lesion*)):ti,ab 563
#11 ((before or prior or naive) NEAR/3 (treat* or therap* or interven* or medicat*)):ti,ab 99702
#12 (t1 or t1a or t1b or tb or ct1 or ct1a or ct1b or ctb):ti,ab 29815
#13 (1cm or "1-cm" or 2cm or "2-cm" or 3cm or "3-cm" or 4cm or "4-cm"):ti,ab 17237
#14 {or #7-#13} 153088
#15 #6 and #14 1370
#16 (bosniak* or bosniac*):ti,ab 4
#17 #15 or #16 1372
#18 MeSH descriptor: [Watchful Waiting] this term only 543
#19 MeSH descriptor: [Early Detection of Cancer] this term only 2593
#20 ((activ* or watch* or schedul* or routin* or close*) NEAR/3 (wait* or monitor* or observ* or watch*)):ti,ab 20695
#21 ((activ* or watch* or monitor* or routin* or schedul* or close*) NEXT (wait* or monitor* or observ*)):kw 847
#22 ((early or earlier or initial*) NEAR/3 (detect* or diagnos* or catch*)):ti,ab 11122
#23 (surveillan* or (expect* NEXT manag*) or (conservat* NEXT manag*) or "wait and see"):ti,ab,kw 13950
#24 ((defer* or delay* or postpone) NEAR/1 (treat* or therap* or interven* or medicat*)):ti,ab 3549
#25 {or #18-#24} 50287
#26 #17 and #25 56
#27 #17 and #25 in Cochrane Reviews 1
#28 "conference":pt or (clinicaltrials or trialsearch):so 770307
#29 #26 NOT #28 in Trials 19

Database name: Embase

Searches
1 exp kidney tumor/ (175080)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-1 or stage-I)).ti,ab. (24645)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (756)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (109572)
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (1238)
6 or/1-5 (203892)
7 exp oncocytoma/ (6319)
8 (oncocytom* or Oxyphilic*).ti,ab. (5042)

Searches
9 (((small* or benign* or suspect* or solid*) adj3 (lesion* or mass* or non-treat* or tumo?r* or cyst*)) or SRM*1).ti,ab. (364120)
10 (Complex* adj3 (cyst* or lesion*)).ti,ab. (13625)
11 ((before or prior or naive) adj3 (treat* or therap* or interven* or medicat*)).ti,ab. (426624)
12 (t1 or t1a or t1b or tb or ct1 or ct1a or ct1b or ctb).ti,ab. (310276)
13 (<1cm or <1-cm or <= 1cm or <= 1-cm or <2cm or <2-cm or <=2cm or <= 2-cm or <3cm or <3-cm or <=3cm or <= 3-cm or <4cm or <4-cm or <=4cm or <= 4-cm).ti,ab. (169605)
14 (("or less" or less-than) adj1 (1cm or 1-cm or 2cm or 2-cm or 3cm or 3-cm or 4cm or 4-cm)).ti,ab. (9485)
15 or/7-14 (1238880)
16 6 and 15 (34746)
17 (bosniak* or bosniac*).ti,ab. (864)
18 16 or 17 (35157)
19 watchful waiting/ or early cancer diagnosis/ (21977)
20 ((activ* or watch* or schedul* or routin* or close*) adj3 (wait* or monitor* or observ* or watch*)).ti,ab. (265452)
21 (activ*-wait* or activ*-monitor* or activ*-observ* or watch*-wait* or watch*-monitor* or watch*-observ* or routin*-wait* or routin*-monitor* or routin*-observ* or schedul*-wait* or schedul*-monitor* or schedul*-observ* or close*-wait* or close*-monitor* or close*-observ*).kw. (1974)
22 ((early or earlier or initial*) adj3 (detect* or diagnos* or catch*)).ti,ab. (499298)
23 (surveillan* or expect*-manag* or conservat*-manag* or "wait and see").ti,ab,kw. (392047)
24 ((defer* or delay* or postpone) adj1 (treat* or therap* or interven* or medicat*)).ti,ab. (24919)
25 or/19-24 (1155428)
26 18 and 25 (3578)
27 limit 26 to english language (3400)
28 27 not (letter or editorial).pt. (3373)
29 nonhuman/ not (human/ and nonhuman/) (5512857)
30 28 not 29 (3350)
31 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or

Searches
mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (1801408)
32 exp "organisation for economic co-operation and development"/ (3076)
33 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (3917782)
34 european union/ (32596)
35 developed country/ (36434)
36 or/32-35 (3952914)
37 31 not 36 (1640544)
38 30 not 37 (3305)
39 random:.tw. (2111491)
40 placebo:.mp. (544575)
41 double-blind:.tw. (255237)
42 or/39-41 (2396497)
43 (MEDLINE or pubmed).tw. (460971)
44 exp systematic review/ or systematic review.tw. (573485)
45 meta-analysis/ (327626)
46 intervention$.ti. (288345)
47 or/43-46 (1071487)
48 clinical study/ (167556)
49 observational study/ (388528)
50 exp cohort analysis/ (1208873)
51 exp comparative study/ (1750788)
52 (observational adj (study or studies)).tw. (285053)
53 ((follow up* or followup* or concurrent* or incidence* or population* or control*) adj3 (study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab. (1597482)
54 Longitudinal study/ or Retrospective study/ or comparative study/ or Prospective study/ (3623394)
55 (longitudinal* or prospective* or retrospective* or cohort*).ti,ab. (4409443)

Searches
56 or/48-54 (6220781)
57 42 or 47 or 56 (8394955)
58 38 and 57 (1425)
59 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6006324)
60 58 not 59 (799)

Database name: Epistemonikos

Searches
(title:((title:((Kidney* AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma* OR stage-1 OR "stage 1" OR stage-I OR "stage I")) OR ((collecting-duct* OR "collecting duct" OR "collecting ducts") AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*)) OR ((renal-cell* OR "renal cell" OR "renal cells" OR RCC OR ccRCC OR Renal-mass* OR "Renal mass" OR "Renal masses" OR renal-tumor* OR renal-tumour* OR "renal tumor" OR "renal tumors" OR "renal tumour" OR "renal tumours" OR grawitz* OR hypernephroma* OR nephrocarcinoma*)) OR (Kidney* AND (Transitional-cell* OR cell OR urothelial* OR duct OR advanc*) AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*))) OR abstract:((Kidney* AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma* OR stage-1 OR "stage 1" OR stage-I OR "stage I")) OR ((collecting-duct* OR "collecting duct" OR "collecting ducts") AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*)) OR ((renal-cell* OR "renal cell" OR "renal cells" OR RCC OR ccRCC OR Renal-mass* OR "Renal mass" OR "Renal masses" OR renal-tumor* OR renal-tumour* OR "renal tumor" OR "renal tumors" OR "renal tumour" OR "renal tumours" OR grawitz* OR hypernephroma* OR nephrocarcinoma*)) OR (Kidney* AND (Transitional-cell* OR cell OR urothelial* OR duct OR advanc*) AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*))))) AND (title:((oncocytom* OR oxyphilic*) OR ((small* OR benign* OR suspect* OR solid*) AND (lesion* OR mass* OR non-treat* OR tumor* OR tumour* OR cyst*)) OR (SRM OR SRMs) OR (Complex* AND (cyst* OR lesion*)) OR ((before OR prior OR naive) AND (treat* OR therap* OR interven* OR medicat*)) OR (t1 OR t1a OR t1b OR tb OR ct1 OR ct1a OR ct1b OR ctb) OR (1cm OR "1-cm" OR "1 cm" OR 2cm OR "2-cm" OR "2 cm" OR 3cm OR "3-cm" OR "3 cm" OR 4cm OR "4-cm" OR "4 cm")) OR abstract:((oncocytom* OR oxyphilic*) OR ((small* OR benign* OR suspect* OR solid*) AND (lesion* OR mass* OR non-treat* OR tumor* OR tumour* OR cyst*)) OR (SRM OR SRMs) OR (Complex* AND (cyst* OR lesion*)) OR ((before OR prior OR naive) AND (treat* OR therap* OR interven* OR medicat*)) OR (t1 OR t1a OR t1b OR tb OR ct1 OR ct1a OR ct1b OR ctb) OR (1cm OR "1-cm" OR "1 cm" OR 2cm OR "2-cm" OR "2 cm" OR 3cm OR "3-cm" OR "3 cm" OR 4cm OR "4-cm" OR "4 cm"))) AND (title:(((activ* OR watch* OR schedul* OR routin* OR close*) AND (wait* OR monitor* OR observ* OR watch*)) OR ((early OR earlier OR initial*) AND (detect* OR diagnos* OR catch*)) OR (surveillan* OR (expect* AND manag*) OR (conservat* AND manag*) OR "wait AND see" OR wait-and-see) OR ((defer* OR delay* OR postpone) AND (treat* OR therap* OR interven* OR medicat*))) OR abstract:(((activ* OR watch* OR schedul* OR routin* OR close*) AND (wait* OR monitor* OR observ* OR watch*)) OR

Searches
((early OR earlier OR initial*) AND (detect* OR diagnos* OR catch*)) OR (surveillan* OR (expect* AND manag*) OR (conservat* AND manag*) OR "wait AND see" OR wait-and-see) OR ((defer* OR delay* OR postpone) AND (treat* OR therap* OR interven* OR medicat*))))) OR abstract:((title:((Kidney* AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma* OR stage-1 OR "stage 1" OR stage-I OR "stage I")) OR ((collecting-duct* OR "collecting duct" OR "collecting ducts") AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*)) OR ((renal-cell* OR "renal cell" OR "renal cells" OR RCC OR ccRCC OR Renal-mass* OR "Renal mass" OR "Renal masses" OR renal-tumor* OR renal-tumour* OR "renal tumor" OR "renal tumors" OR "renal tumour" OR "renal tumours" OR grawitz* OR hypernephroma* OR nephrocarcinoma*)) OR (Kidney* AND (Transitional-cell* OR cell OR urothelial* OR duct OR advanc*) AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*))) OR abstract:((Kidney* AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma* OR stage-1 OR "stage 1" OR stage-I OR "stage I")) OR ((collecting-duct* OR "collecting duct" OR "collecting ducts") AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*)) OR ((renal-cell* OR "renal cell" OR "renal cells" OR RCC OR ccRCC OR Renal-mass* OR "Renal mass" OR "Renal masses" OR renal-tumor* OR renal-tumour* OR "renal tumor" OR "renal tumors" OR "renal tumour" OR "renal tumours" OR grawitz* OR hypernephroma* OR nephrocarcinoma*)) OR (Kidney* AND (Transitional-cell* OR cell OR urothelial* OR duct OR advanc*) AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*)))) AND (title:((oncocytom* OR oxyphilic*) OR ((small* OR benign* OR suspect* OR solid*) AND (lesion* OR mass* OR non-treat* OR tumor* OR tumour* OR cyst*)) OR (SRM OR SRMs) OR (Complex* AND (cyst* OR lesion*)) OR ((before OR prior OR naive) AND (treat* OR therap* OR interven* OR medicat*)) OR (t1 OR t1a OR t1b OR tb OR ct1 OR ct1a OR ct1b OR ctb) OR (1cm OR "1-cm" OR "1 cm" OR 2cm OR "2-cm" OR "2 cm" OR 3cm OR "3-cm" OR "3 cm" OR 4cm OR "4-cm" OR "4 cm")) OR abstract:((oncocytom* OR oxyphilic*) OR ((small* OR benign* OR suspect* OR solid*) AND (lesion* OR mass* OR non-treat* OR tumor* OR tumour* OR cyst*)) OR (SRM OR SRMs) OR (Complex* AND (cyst* OR lesion*)) OR ((before OR prior OR naive) AND (treat* OR therap* OR interven* OR medicat*)) OR (t1 OR t1a OR t1b OR tb OR ct1 OR ct1a OR ct1b OR ctb) OR (1cm OR "1-cm" OR "1 cm" OR 2cm OR "2-cm" OR "2 cm" OR 3cm OR "3-cm" OR "3 cm" OR 4cm OR "4-cm" OR "4 cm"))) AND (title:(((activ* OR watch* OR schedul* OR routin* OR close*) AND (wait* OR monitor* OR observ* OR watch*)) OR ((early OR earlier OR initial*) AND (detect* OR diagnos* OR catch*)) OR (surveillan* OR (expect* AND manag*) OR (conservat* AND manag*) OR "wait AND see" OR wait-and-see) OR ((defer* OR delay* OR postpone) AND (treat* OR therap* OR interven* OR medicat*))) OR abstract:(((activ* OR watch* OR schedul* OR routin* OR close*) AND (wait* OR monitor* OR observ* OR watch*)) OR ((early OR earlier OR initial*) AND (detect* OR diagnos* OR catch*)) OR (surveillan* OR (expect* AND manag*) OR (conservat* AND manag*) OR "wait AND see" OR wait-and-see) OR ((defer* OR delay* OR postpone) AND (treat* OR therap* OR interven* OR medicat*)))))) Total: 1700 Limit to SRs: 147

Database name: Medline ALL

Searches
1 exp Kidney Neoplasms/ (87582)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-1 or stage-I)).ti,ab. (16669)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (503)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (72931)
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (862)
6 or/1-5 (120665)
7 Adenoma, Oxyphilic/ (2355)
8 (oncocytom* or Oxyphilic*).ti,ab. (3527)
9 (((small* or benign* or suspect* or solid*) adj3 (lesion* or mass* or non-treat* or tumo?r* or cyst*)) or SRM*1).ti,ab. (248771)
10 (Complex* adj3 (cyst* or lesion*)).ti,ab. (8685)
11 ((before or prior or naive) adj3 (treat* or therap* or interven* or medicat*)).ti,ab. (241513)
12 (t1 or t1a or t1b or ct1 or ct1a or ct1b or ctb).ti,ab. (148786)
13 (<1cm or <1-cm or <= 1cm or <= 1-cm or <2cm or <2-cm or <=2cm or <= 2-cm or <3cm or <3-cm or <=3cm or <= 3-cm or <4cm or <4-cm or <=4cm or <= 4-cm).ti,ab. (100095)
14 (("or less" or less-than) adj1 (1cm or 1-cm or 2cm or 2-cm or 3cm or 3-cm or 4cm or 4-cm)).ti,ab. (6380)
15 or/7-14 (727513)
16 6 and 15 (16721)
17 (bosniak* or bosniac*).ti,ab. (530)
18 16 or 17 (16989)
19 "Watchful Waiting"/ or "Early Detection of Cancer"/ (46726)
20 ((activ* or watch* or schedul* or routin* or close*) adj3 (wait* or monitor* or observ* or watch*)).ti,ab. (192669)
21 (activ*-wait* or activ*-monitor* or activ*-observ* or watch*-wait* or watch*-monitor* or watch*-observ* or routin*-wait* or routin*-monitor* or routin*-observ* or schedul*-wait* or schedul*-monitor* or schedul*-observ* or close*-wait* or close*-monitor* or close*-observ*).kw. (1349)
22 ((early or earlier or initial*) adj3 (detect* or diagnos* or catch*)).ti,ab. (338906)
23 (surveillan* or expect*-manag* or conservat*-manag* or "wait and see").ti,ab,kw. (282458)
24 ((defer* or delay* or postpone) adj1 (treat* or therap* or interven* or medicat*)).ti,ab. (15652)
25 or/19-24 (837532)
26 18 and 25 (1606)
27 limit 26 to english language (1461)

Searches
28 limit 27 to (letter or historical article or comment or editorial or news or case reports) (225)
29 27 not 28 (1236)
30 animals/ not humans/ (5215368)
31 29 not 30 (1230)
32 remove duplicates from 31 (1229)
33 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ (1362672)
34 exp "organisation for economic co-operation and development"/ (622)
35 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ (3582616)
36 european union/ (18128)
37 developed countries/ (21607)
38 or/34-37 (3599082)
39 33 not 38 (1271243)
40 31 not 39 (1225)
41 exp Randomized Controlled Trial/ (620769)
42 randomi?ed.mp. (1135803)
43 placebo.mp. (259089)

Searches
44 or/41-43 (1204046)
45 (MEDLINE or pubmed).tw. (370931)
46 systematic review.tw. (312737)
47 systematic review.pt. (270325)
48 meta-analysis.pt. (206366)
49 intervention$.ti. (219128)
50 or/45-49 (767302)
51 Observational Studies as Topic/ (9971)
52 Observational Study/ or exp Cohort Studies/ (2695873)
53 Comparative Study.pt. (1924412)
54 (observational adj (study or studies)).tw. (183381)
55 ((follow up* or followup* or concurrent* or incidence* or population*) adj3 (study* or studies* or analy* or observation* or design* or method* or research*)).ti,ab. (511510)
56 (longitudinal* or prospective* or retrospective* or cohort*).ti,ab. (2775547)
57 or/51-56 (5634627)
58 44 or 50 or 57 (6801581)
59 40 and 58 (760)
60 ("clinical conference" or congress* or overall* or consensus*).pt. or (conference* or proceeding*).jn. or (conference* not (video* or confere

Cost-effectiveness searches

Database results

Database	Date searched	Database Platform	Database segment or version
EconLit	29/08/2024	OVID	1886 to August 22, 2024
Embase	29/08/2024	Ovid	1974 to 2024 August 28
International Health Technology Assessment Database from INAHTA	29/08/2024	https://database.inahta.org/	n/a
MEDLINE ALL	29/08/2024	Ovid	1946 to August 27, 2024
NHS EED	05/09/2024	CRD	n/a

Rerun search database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	07/05/2025	Ovid	1886 to May 01, 2025	1
Embase	07/05/2025	Ovid	1974 to 2025 May 06	97
International Health Technology Assessment Database from INAHTA	07/05/2025	https://database.inahta.org/	n/a	12
MEDLINE ALL	07/05/2025	Ovid	1946 to May 06, 2025	41

No date limit was applied to the rerun searches due to technical issues with OVID. Instead the duplication of records was managed in EPPI Reviewer 5. NHS EED was not included in the rerun searches as the database contains legacy information and is not updated.

Search strategy history

Database name: Econlit

Searches
1 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-1 or stage-I)).ti,ab. (8)
2 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (0)
3 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (24)
4 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (0)
5 or/1-4 (32)
6 (oncocytom* or Oxyphilic*).ti,ab. (0)
7 (((small* or benign* or suspect* or solid*) adj3 (lesion* or mass* or non-treat* or tumo?r* or cyst*)) or SRM*1).ti,ab. (184)
8 (Complex* adj3 (cyst* or lesion*)).ti,ab. (0)
9 ((before or prior or naive) adj3 (treat* or therap* or interven* or medicat*)).ti,ab. (447)

Searches
10 (t1 or t1a or t1b or ct1 or ct1a or ct1b or ctb).ti,ab. (113)
11 (<1cm or <1-cm or <= 1cm or <= 1-cm or <2cm or <2-cm or <=2cm or <= 2-cm or <3cm or <3-cm or <=3cm or <= 3-cm or <4cm or <4-cm or <=4cm or <= 4-cm).ti,ab. (45)
12 (("or less" or less-than) adj1 (1cm or 1-cm or 2cm or 2-cm or 3cm or 3-cm or 4cm or 4-cm)).ti,ab. (0)
13 or/6-12 (787)
14 5 and 13 (2)
15 (bosniak* or bosniac*).ti,ab. (4)
16 14 or 15 (6)
17 ((activ* or watch* or schedul* or routin* or close*) adj3 (wait* or monitor* or observ* or watch*)).ti,ab. (3240)
18 (activ*-wait* or activ*-monitor* or activ*-observ* or watch*-wait* or watch*-monitor* or watch*-observ* or routin*-wait* or routin*-monitor* or routin*-observ* or schedul*-wait* or schedul*-monitor* or schedul*-observ* or close*-wait* or close*-monitor* or close*-observ*).kw. (0)
19 ((early or earlier or initial*) adj3 (detect* or diagnos* or catch*)).ti,ab. (398)
20 (surveillan* or expect*-manag* or conservat*-manag* or "wait and see").ti,ab,kw. (2301)
21 ((defer* or delay* or postpone) adj1 (treat* or therap* or interven* or medicat*)).ti,ab. (53)
22 or/17-21 (5929)
23 16 and 22 (1)

Database name: NHS EED

Searches		
1	MESH DESCRIPTOR Kidney Neoplasms EXPLODE ALL TREES	201
2	(Kidney* NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-1 or stage-I))	191
3	(collecting-duct* NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumour* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma*))	1
4	(renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*)	204
5	(Kidney* NEAR2 (Transitional-cell* or cell or urothelial* or duct or advanc*) NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumour* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma*))	3
6	#1 or #2 or #3 or #4 or #5	259
7	MESH DESCRIPTOR Adenoma, Oxyphilic	3
8	(oncocytom* or Oxyphilic*)	3
9	(((small* or benign* or suspect* or solid*) NEAR3 (lesion* or mass* or non-treat* or tumor* or tumour* or cyst*)) or SRM*)	478
10	(Complex* NEAR3 (cyst* or lesion*))	20
11	((before or prior or naive) NEAR3 (treat* or therap* or interven* or medicat*))	1191
12	(t1 or t1a or t1b or tb or ct1 or ct1a or ct1b or ctb)	431
13	(1cm or "1-cm" or 2cm or "2-cm" or 3cm or "3-cm" or 4cm or "4-cm")	334
14	#7 or #8 or #9 or #10 or #11 or #12 or #13	2382
15	#6 and #14	52
16	(bosniak* or bosniac*)	0
17	#15 or #16	52
18	MESH DESCRIPTOR Watchful Waiting	38
19	MESH DESCRIPTOR Early Detection of Cancer	277
20	((activ* or watch* or schedul* or routin* or close*) NEAR3 (wait* or monitor* or observ* or watch*))	414
21	((early or earlier or initial*) NEAR3 (detect* or diagnos* or catch*))	1049
22	((surveillan* or (expect* NEAR1 manag*) or (conservat* NEAR1 manag*) or (wait NEAR1 see)))	1414
23	(((defer* or delay* or postpone) NEAR1 (treat* or therap* or interven* or medicat*)))	158
24	#18 OR #19 OR #20 OR #21 OR #22 OR #23	2870
25	#17 and #24	8
26	(#17 and #24) IN NHSEED	4

Database name: Embase

Searches
1 exp kidney tumor/ (175312)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-1 or stage-I)).ti,ab. (24695)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (756)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (109722)
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (1241)
6 or/1-5 (204160)
7 exp oncocytoma/ (6326)
8 (oncocytom* or Oxyphilic*).ti,ab. (5046)
9 (((small* or benign* or suspect* or solid*) adj3 (lesion* or mass* or non-treat* or tumo?r* or cyst*)) or SRM*1).ti,ab. (364523)
10 (Complex* adj3 (cyst* or lesion*)).ti,ab. (13653)
11 ((before or prior or naive) adj3 (treat* or therap* or interven* or medicat*)).ti,ab. (427109)
12 (t1 or t1a or t1b or tb or ct1 or ct1a or ct1b or ctb).ti,ab. (310824)
13 (<1cm or <1-cm or <= 1cm or <= 1-cm or <2cm or <2-cm or <=2cm or <= 2-cm or <3cm or <3-cm or <=3cm or <= 3-cm or <4cm or <4-cm or <=4cm or <= 4-cm).ti,ab. (169767)
14 (("or less" or less-than) adj1 (1cm or 1-cm or 2cm or 2-cm or 3cm or 3-cm or 4cm or 4-cm)).ti,ab. (9485)
15 or/7-14 (1240472)
16 6 and 15 (34784)
17 (bosniak* or bosniac*).ti,ab. (867)
18 16 or 17 (35198)
19 watchful waiting/ or early cancer diagnosis/ (22026)
20 ((activ* or watch* or schedul* or routin* or close*) adj3 (wait* or monitor* or observ* or watch*)).ti,ab. (265833)
21 (activ*-wait* or activ*-monitor* or activ*-observ* or watch*-wait* or watch*-monitor* or watch*-observ* or routin*-wait* or routin*-monitor* or routin*-observ* or schedul*-wait* or schedul*-monitor* or schedul*-observ* or close*-wait* or close*-monitor* or close*-observ*).kw. (1980)
22 ((early or earlier or initial*) adj3 (detect* or diagnos* or catch*)).ti,ab. (500231)
23 (surveillan* or expect*-manag* or conservat*-manag* or "wait and see").ti,ab,kw. (392737)
24 ((defer* or delay* or postpone) adj1 (treat* or therap* or interven* or medicat*)).ti,ab. (24952)
25 or/19-24 (1157408)
26 18 and 25 (3582)
27 limit 26 to english language (3404)

Searches
28 27 not (letter or editorial).pt. (3377)
29 nonhuman/ not (human/ and nonhuman/) (5519769)
30 28 not 29 (3354)
31 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (1804349)
32 exp "organisation for economic co-operation and development"/ (3088)
33 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (3920724)
34 european union/ (32646)
35 developed country/ (36451)
36 or/32-35 (3955906)
37 31 not 36 (1643264)
38 30 not 37 (3309)
39 cost utility analysis/ (13158)
40 quality adjusted life year/ (38290)
41 cost*.ti. (204250)
42 (cost* adj2 utilit*).tw. (13581)

Searches
43 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (411026)
44 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (71004)
45 (qualit* adj2 adjust* adj2 life*).tw. (29251)
46 QALY*.tw. (28690)
47 (incremental* adj2 cost*).tw. (30618)
48 ICER.tw. (14132)
49 utilities.tw. (16012)
50 markov*.tw. (42645)
51 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (76741)
52 ((utility or effective*) adj2 analys*).tw. (40389)
53 (willing* adj2 pay*).tw. (16014)
54 (EQ5D* or EQ-5D*).tw. (28414)
55 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (5840)
56 (european* adj2 quality adj3 ("5" or five)).tw. (1093)
57 or/39-56 (674435)
58 38 and 57 (98)

Database name: INAHTA

Searches		
	Search query	Hits
#1	((Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-1 or stage-I)) OR ((collecting-duct* OR "collecting duct*") AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or "renal cell*" or RCC or ccRCC or Renal-mass* or "Renal mass*" or renal-tumor* or renal-tumour* or "renal tumor*" or "renal tumour*" or grawitz-tumor* or grawitz-tumour* or "grawitz tumor*" or "grawitz tumour*" or hypernephroma* or nephrocarcinoma*)) OR (Kidney* AND (Transitional-cell* or "Transitional cell*" or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*)))	150
#2	((oncocytom* OR oxyphilic*) OR ((small* OR benign* OR suspect* OR solid*) AND (lesion* OR mass* OR non-treat* OR tumor* OR tumour* or cyst*)) OR (SRM or SRMs) OR (Complex* AND (cyst* OR lesion*)) OR ((before OR prior OR naive) AND (treat* OR therap* OR interven* OR medicat*)) OR (t1 OR t1a OR t1b OR tb OR ct1 OR ct1a OR ct1b OR ctb) OR (1cm OR "1-cm" OR "1 cm" OR 2cm OR "2-cm" OR "2 cm" OR 3cm OR "3-cm" OR "3 cm" OR 4cm OR "4-cm" or "4 cm"))	1380

Searches		
#3	(((activ* OR watch* OR schedul* OR routin* OR close*) AND (wait* OR monitor* OR observ* OR watch*)) OR ((early OR earlier OR initial*) AND (detect* OR diagnos* OR catch*)) OR (surveillan* OR (expect* AND manag*) OR (conservat* AND manag*) OR "wait AND see" OR wait-and-see) OR ((defer* OR delay* OR postpone) AND (treat* OR therap* OR interven* OR medicat*)))	2103
#4	#1 and #2 and #3	10
	Searched as: ((((activ* OR watch* OR schedul* OR routin* OR close*) AND (wait* OR monitor* OR observ* OR watch*)) OR ((early OR earlier OR initial*) AND (detect* OR diagnos* OR catch*)) OR (surveillan* OR (expect* AND manag*) OR (conservat* AND manag*) OR "wait AND see" OR wait-and-see) OR ((defer* OR delay* OR postpone) AND (treat* OR therap* OR interven* OR medicat*))))) AND (((oncocytom* OR oxyphilic*) OR ((small* OR benign* OR suspect* OR solid*) AND (lesion* OR mass* OR non-treat* OR tumor* OR tumour* or cyst*)) OR (SRM or SRMs) OR (Complex* AND (cyst* OR lesion*)) OR ((before OR prior OR naive) AND (treat* OR therap* OR interven* OR medicat*)) OR (t1 OR t1a OR t1b OR tb OR ct1 OR ct1a OR ct1b OR ctb) OR (1cm OR "1-cm" OR "1 cm" OR 2cm OR "2-cm" OR "2 cm" OR 3cm OR "3-cm" OR "3 cm" OR 4cm OR "4-cm" or "4 cm"))) AND (((Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-1 or stage-I)) OR ((collecting-duct* OR "collecting duct*") AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or "renal cell*" or RCC or ccRCC or Renal-mass* or "Renal mass*" or renal-tumor* or renal-tumour* or "renal tumor*" or "renal tumour*" or grawitz-tumor* or grawitz-tumour* or "grawitz tumor*" or "grawitz tumour*" or hypernephroma* or nephrocarcinoma*)) OR (Kidney* AND (Transitional-cell* or "Transitional cell*" or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))))	

Database name: Medline ALL

Searches
1 exp Kidney Neoplasms/ (87631)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-1 or stage-I)).ti,ab. (16693)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (504)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (73020)

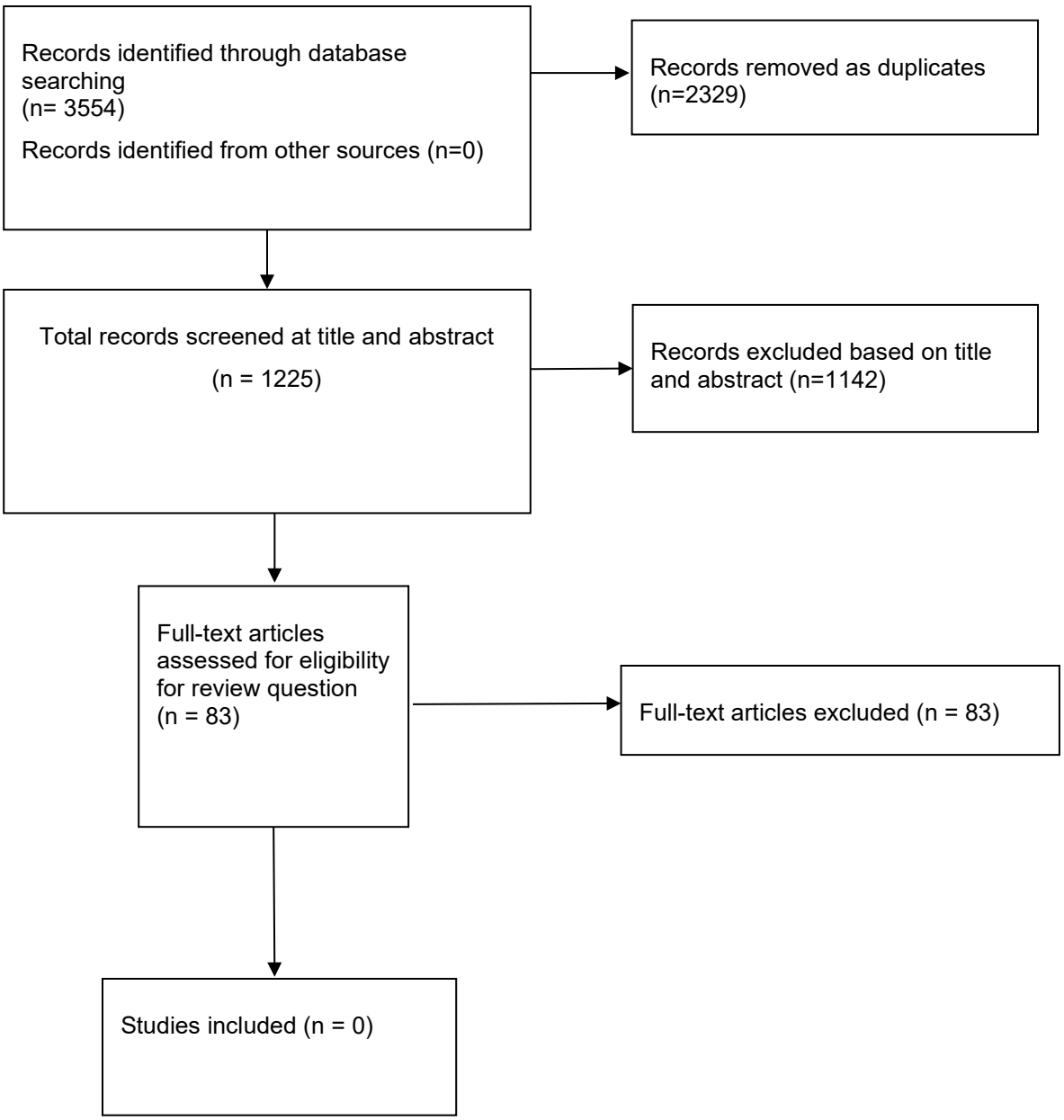
Searches
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (861)
6 or/1-5 (120784)
7 Adenoma, Oxyphilic/ (2358)
8 (oncocytom* or Oxyphilic*).ti,ab. (3530)
9 (((small* or benign* or suspect* or solid*) adj3 (lesion* or mass* or non-treat* or tumo?r* or cyst*)) or SRM*1).ti,ab. (249141)
10 (Complex* adj3 (cyst* or lesion*)).ti,ab. (8702)
11 ((before or prior or naive) adj3 (treat* or therap* or interven* or medicat*)).ti,ab. (241877)
12 (t1 or t1a or t1b or ct1 or ct1a or ct1b or ctb).ti,ab. (149088)
13 (<1cm or <1-cm or <= 1cm or <= 1-cm or <2cm or <2-cm or <=2cm or <= 2-cm or <3cm or <3-cm or <=3cm or <= 3-cm or <4cm or <4-cm or <=4cm or <= 4-cm).ti,ab. (100220)
14 (("or less" or less-than) adj1 (1cm or 1-cm or 2cm or 2-cm or 3cm or 3-cm or 4cm or 4-cm)).ti,ab. (6387)
15 or/7-14 (728648)
16 6 and 15 (16739)
17 (bosniak* or bosniac*).ti,ab. (532)
18 16 or 17 (17009)
19 "Watchful Waiting"/ or "Early Detection of Cancer"/ (46838)
20 ((activ* or watch* or schedul* or routin* or close*) adj3 (wait* or monitor* or observ* or watch*)).ti,ab. (192959)
21 (activ*-wait* or activ*-monitor* or activ*-observ* or watch*-wait* or watch*-monitor* or watch*-observ* or routin*-wait* or routin*-monitor* or routin*-observ* or schedul*-wait* or schedul*-monitor* or schedul*-observ* or close*-wait* or close*-monitor* or close*-observ*).kw. (1354)
22 ((early or earlier or initial*) adj3 (detect* or diagnos* or catch*)).ti,ab. (339679)
23 (surveillan* or expect*-manag* or conservat*-manag* or "wait and see").ti,ab,kw. (283066)
24 ((defer* or delay* or postpone) adj1 (treat* or therap* or interven* or medicat*)).ti,ab. (15693)
25 or/19-24 (839238)
26 18 and 25 (1609)
27 limit 26 to english language (1464)
28 limit 27 to (letter or historical article or comment or editorial or news or case reports) (225)
29 27 not 28 (1239)
30 animals/ not humans/ (5218519)
31 29 not 30 (1233)
32 remove duplicates from 31 (1231)
33 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/

Searches
or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ (1364748)
34 exp "organisation for economic co-operation and development"/ (621)
35 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ (3585930)
36 european union/ (18153)
37 developed countries/ (21608)
38 or/34-37 (3602408)
39 33 not 38 (1273262)
40 31 not 39 (1228)
41 Cost-Benefit Analysis/ (95525)
42 Quality-Adjusted Life Years/ (16757)
43 Markov Chains/ (16394)
44 exp Models, Economic/ (16488)
45 cost*.ti. (151972)
46 (cost* adj2 utilit*).tw. (8240)
47 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (298573)
48 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (50822)
49 (qualit* adj2 adjust* adj2 life*).tw. (19135)
50 QALY*.tw. (15533)
51 (incremental* adj2 cost*).tw. (18639)

Searches
52 ICER.tw. (6636)
53 utilities.tw. (10015)
54 markov*.tw. (33834)
55 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (57014)
56 ((utility or effective*) adj2 analys*).tw. (26856)
57 (willing* adj2 pay*).tw. (10772)
58 (EQ5D* or EQ-5D*).tw. (14851)
59 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (4342)
60 (european* adj2 quality adj3 ("5" or five)).tw. (789)
61 or/41-60 (534752)
62 40 and 61 (40)

Appendix C – Effectiveness evidence study selection

Figure 1: PRISMA diagram



Appendix D – Effectiveness evidence

No studies were identified which were applicable to this review question.

Appendix E – Forest plots

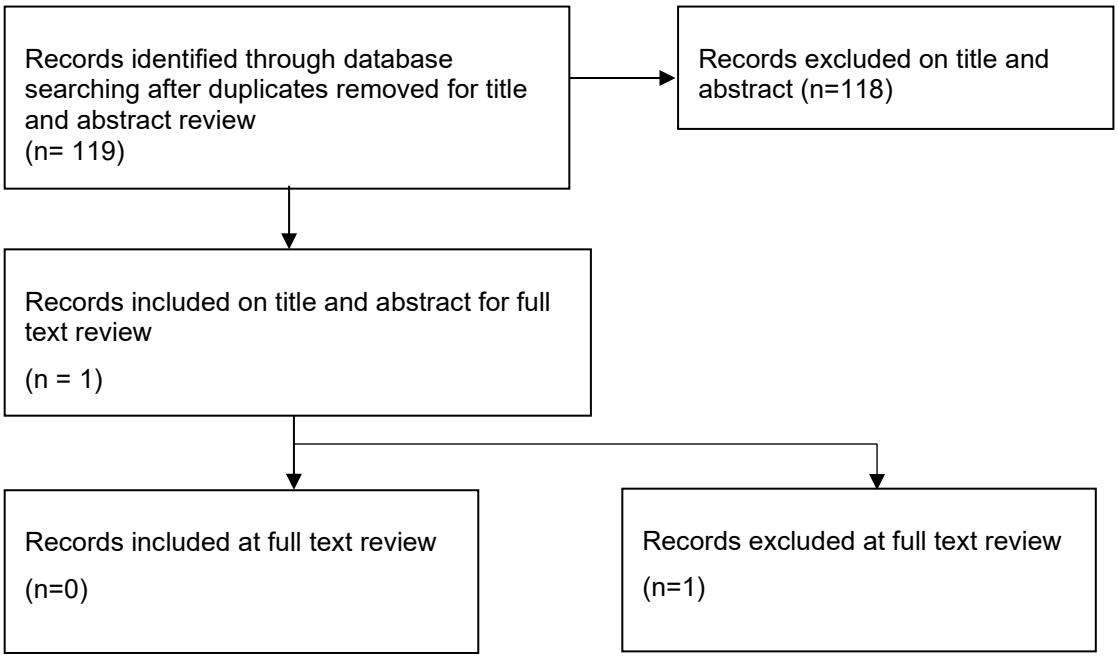
No studies were identified which were applicable to this review question.

Appendix F – GRADE tables

No studies were identified which were applicable to this review question.

Appendix G – Economic evidence study selection

Figure 2: Economic evidence study selection



Appendix H – Economic evidence tables

No economic evidence was identified for this review question.

Appendix I – Health economic model

No economic modelling was conducted for this review question.

Appendix J – Excluded studies

Effectiveness references excluded at full text (n = 83)

Table 4: Excluded effectiveness studies

Study	Reason for exclusion
Abou Youssif, Tamer, Kassouf, Wassim, Steinberg, Jordan et al. (2007) Active surveillance for selected patients with renal masses: updated results with long-term follow-up. Cancer 110(5): 1010-4	- Study design *Non-comparative single-arm study of patients undergoing active surveillance. Outcomes were compared among those who underwent delayed intervention (surgery) or those who died*
Ajami, Tarek, Sebastia, Carmen, Corominas, Daniel et al. (2021) Clinical and radiological findings for small renal masses under active surveillance. Urologic oncology 39(8): 499e9-499e14	- Comparison *Cohort study comparing delayed intervention after AS with those who remained on AS.*
Alam, Ridwan, Patel, Hiten D, Osumah, Tijani et al. (2019) Comparative effectiveness of management options for patients with small renal masses: a prospective cohort study. BJU international 123(1): 42-50	- Comparison *Compares active surveillance with other active interventions*
Ambani, Sapan N, Morgan, Todd M, Montgomery, Jeffrey S et al. (2016) Predictors of Delayed Intervention for Patients on Active Surveillance for Small Renal Masses: Does Renal Mass Biopsy Influence Our Decision?. Urology 98: 88-96	- Comparison *Comparison was between active surveillance and patients undergoing delayed intervention*
Baboudjian, Michael, Moser, Daniel, Yanagisawa, Takafumi et al. (2022) Benefit and Harm of Active Surveillance for Biopsy-proven Renal Oncocytoma: A Systematic Review and Pooled Analysis. European urology open science 41: 8-15	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Included studies were either noncomparative studies, comparing AS versus PN or comparing AS in oncocytomas versus AS in other RCCs*
Bahouth, Zaher, Halachmi, Sarel, Meyer, Gil et al. (2015) The natural history and predictors for intervention in patients with small renal mass undergoing active surveillance. Advances in urology 2015: 692014	- Comparison *Study compares active surveillance with Nephron-sparing surgery*
Bazan, Alfredo Aguilera, Carrion, Diego M, Rivas, Juan Gomez et al. (2021) Active surveillance in renal tumors: Clinical and	- Study design *Single-armed cohort study assessing active surveillance on solid or cystic renal lesions*

Study	Reason for exclusion
oncological outcomes. Journal of cancer research and therapeutics 17(2): 414-419	
Beisland, C., Hjelle, K.M., Reisaeter, L.A.R. et al. (2009) Observation Should be Considered as an Alternative in Management of Renal Masses in Older and Comorbid Patients. European Urology 55(6): 1419-1429	- Study design *Non-comparative single-arm study. Delayed intervention was observed in a subset of the population*
Bertelli, Elena, Palombella, Alberto, Sessa, Francesco et al. (2021) Contrast-enhanced ultrasound (CEUS) imaging for active surveillance of small renal masses. World journal of urology 39(8): 2853-2860	- Study design *Non-comparative single-arm study with CEUS and CT administered to patients in the same group.*
Bhan, Sasha N, Pautler, Stephen E, Shayegan, Bobby et al. (2013) Active surveillance, radiofrequency ablation, or cryoablation for the nonsurgical management of a small renal mass: a cost-utility analysis. Annals of surgical oncology 20(11): 3675-84	- Study design *Not an intervention study. A cost-utility analysis*
Borgbjerg, Jens, Larsen, Nis Elbrond, Salte, Ivar Mjaland et al. (2023) Radiation dose in CT-based active surveillance of small renal masses may be reduced by 75%: A retrospective exploratory multiobserver study. Research in diagnostic and interventional imaging 5: 100019	- Intervention *Intervention was not focused on active surveillance. Patients on active surveillance were included in the study but study focused on assessing whether low dose CT is comparable to normal dose CT in determining tumour size at a single time point*
Brunocilla, E, Borghesi, M, Schiavina, R et al. (2014) Active surveillance for small renal masses diagnosed in elderly or comorbid patients: looking for the best treatment strategy. Actas urologicas espanolas 38(1): 1-6	- Language other than English *Study not in English. Italian*
Brunocilla, Eugenio, Borghesi, Marco, Monti, Carlo et al. (2013) Surveillance for small renal masses: retrospective analysis of a cohort of 42 patients with long-term follow-up. International urology and nephrology 45(2): 307-12	- Study design *Non-comparative single-arm study. All participants underwent active surveillance and comparisons were made between those that underwent delayed intervention versus those that remained on active surveillance after a follow-up period*
Brunocilla, Eugenio, Borghesi, Marco, Schiavina, Riccardo et al. (2014) Small renal masses initially managed using active surveillance: results from a retrospective	- Study design *Non-comparative single-arm study. All participants underwent active surveillance and comparisons were made between those that underwent delayed intervention*

Study	Reason for exclusion
study with long-term follow-up. Clinical genitourinary cancer 12(3): 178-81	*versus those that remained on active surveillance after a follow-up period*
Campbell, Steven, Uzzo, Robert G, Allaf, Mohamad E et al. (2017) Renal Mass and Localized Renal Cancer: AUA Guideline. The Journal of urology 198(3): 520-529	- Study design *Not a research article. The paper is a guideline summary*
Castaneda, Crystal V, Danzig, Matthew R, Finkelstein, Julia B et al. (2015) The natural history of renal functional decline in patients undergoing surveillance in the DISSRM registry. Urologic oncology 33(4): 166e17-20	- Study design *Non-comparative single-arm study assessing active surveillance on small renal masses and measuring outcomes of glomerular filtration rate, which do not match protocol criteria*
Celtik, Kenan E, Shah, Paras H, Patel, Vinay R et al. (2017) Active surveillance for incidental renal mass in the octogenarian. World journal of urology 35(7): 1089-1094	- Study design *Non-comparative single-arm study. All participants underwent active surveillance and comparisons were made between those that underwent delayed intervention versus those that remained on active surveillance after a follow-up period*
Chan, Vinson Wai-Shun, Tan, Wei Shen, Leow, Jeffrey J et al. (2021) Delayed surgery for localised and metastatic renal cell carcinoma: a systematic review and meta-analysis for the COVID-19 pandemic. World journal of urology 39(12): 4295-4303	- Systematic review used as source of primary studies *Systematic review with no relevant studies for inclusion. Included studies compared AS or delayed intervention/surgery versus PN or RN.*
Cheung, Douglas, Frankel, Jed, Tut, Pavinder et al. (2022) Treatment on active surveillance of small renal masses: Progression vs. preference. Canadian Urological Association journal = Journal de l'Association des urologues du Canada 16(4): 97-101	- Study design *Non-comparative single-arm study assessing patients who were on active surveillance and then underwent delayed intervention*
Crispen, Paul L, Viterbo, Rosalia, Fox, Eric B et al. (2008) Delayed intervention of sporadic renal masses undergoing active surveillance. Cancer 112(5): 1051-7	- Study design *Non-comparative single-arm study*
Crispen, Paul L, Wong, Yu-Ning, Greenberg, Richard E et al. (2008) Predicting growth of solid renal masses under active surveillance. Urologic oncology 26(5): 555-9	- Study design *Non-comparative single-arm study*
Danzig, M.R., Ghandour, R.A., Chang, P. et al. (2017) Active surveillance is superior to radical nephrectomy and equivalent to partial nephrectomy for preserving renal	- Study design *Commentary*

Study	Reason for exclusion
function in patients with small renal masses: Results from the DISSRM registry. Urologic Oncology: Seminars and Original Investigations 35(3): 116	
Danzig, Matthew R, Ghandour, Rashed A, Chang, Peter et al. (2015) Active Surveillance is Superior to Radical Nephrectomy and Equivalent to Partial Nephrectomy for Preserving Renal Function in Patients with Small Renal Masses: Results from the DISSRM Registry. The Journal of urology 194(4): 903-9	- Comparison *Comparison was treatment interventions including partial nephrectomy, radical nephrectomy and cryoablation*
Deledalle, Francois-Xavier, Ambrosetti, Damien, Durand, Mathieu et al. (2021) Active Surveillance for Biopsy Proven Renal Oncocytomas: Outcomes and Feasibility. Urology 156: 185-190	- Study design *Non-comparative single-arm study assessing rate of conversion from active surveillance to treatment*
Dorin, Ryan, Jackson, Max, Cusano, Antonio et al. (2014) Active surveillance of renal masses: an analysis of growth kinetics and clinical outcomes stratified by radiological characteristics at diagnosis. International braz j urol : official journal of the Brazilian Society of Urology 40(5): 627-36	- Study design *Non-comparative single-arm study*
Ellimoottil, Chandy, Greco, Kristin A, Hart, Spencer et al. (2014) New modalities for evaluation and surveillance of complex renal cysts. The Journal of urology 192(6): 1604-11	- Review article but not a systematic review *Checked for studies relating to surveillance and no relevant studies were identified for inclusion*
Ellis, E.E. and Messing, E. (2021) Active Surveillance of Small Renal Masses: A Systematic Review. Kidney Cancer 5(3): 139-152	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Seventeen included studies but were not clearly reported/labelled so unable to determine which studies were included.*
Fernandez-Pello, Sergio, Hora, Milan, Kuusk, Teele et al. (2020) Management of Sporadic Renal Angiomyolipomas: A Systematic Review of Available Evidence to Guide Recommendations from the European Association of Urology Renal Cell Carcinoma Guidelines Panel. European urology oncology 3(1): 57-72	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Studies were either single-armed or did not have comparisons relevant to the protocol.*
Finelli, Antonio, Ismaila, Nofisat, Bro, Bill et al. (2017) Management of Small Renal	- Study design

Study	Reason for exclusion
Masses: American Society of Clinical Oncology Clinical Practice Guideline. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 35(6): 668-680	*Not a review article. Paper is a summary of guideline document.*
Furrer, MA, Spycher, SCJ, Büttiker, SM et al. (2019) Comparison of the Diagnostic Performance of Contrast-enhanced Ultrasound with That of Contrast-enhanced Computed Tomography and Contrast-enhanced Magnetic Resonance Imaging in the Evaluation of Renal Masses: A Systematic Review and Meta-analysis. European urology oncology 3(4): 464-473	- Systematic review used as source of primary studies *Review focused on diagnosis of benign and malignant cystic and solid renal mass using ultrasound or CT. No relevant studies identified for inclusion*
Gabr, Ahmed H, Gdor, Yehoshua, Roberts, William W et al. (2009) Radiographic surveillance of minimally and moderately complex renal cysts. BJU international 103(8): 1116-9	- Study design *Non-comparative single-arm study*
Ghavamian, R. (2011) Management of the small renal mass: What is the most reasonable option?. Expert Review of Anticancer Therapy 11(7): 979-982	- Review article but not a systematic review
Graversen, Joseph A, Mues, Adam C, Perez-Lanzac de Lorca, Alberto et al. (2011) Active surveillance of renal cortical neoplasms: a contemporary review. Postgraduate medicine 123(1): 105-13	- Review article but not a systematic review
Griebling, T.L. (2010) Is surveillance of small renal masses safe in the elderly?. Journal of Urology 184(5): 1927-1928	- Study design *Editorial comment*
Gupta, Mohit, Alam, Ridwan, Patel, Hiten D et al. (2019) Use of delayed intervention for small renal masses initially managed with active surveillance. Urologic oncology 37(1): 18-25	- Study design *Editorial*
Gupta, Mohit, Blute, Michael L Jr, Su, Li-Ming et al. (2017) Delayed Intervention of Small Renal Masses on Active Surveillance. Journal of kidney cancer and VHL 4(2): 24-30	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Included studies were single-arm studies assessing factors associated with treatment after a period of active surveillance*
Hobarth, K, Klingler, H C, Kuber, W et al. (1993) Value of routine sonography in the diagnosis and conservative management of	- Study design *Non-comparative single-arm study*

Study	Reason for exclusion
renal angiomyolipoma. European urology 24(2): 239-43	
Jakubowicz, Deborah, Dariane, Charles, Correas, Jean-Michel et al. (2022) Disease Progression in Older Patients With Renal Tumor Assigned to an Active Surveillance Protocol. Clinical genitourinary cancer 20(1): e53-e60	- Study design *Non-comparative single-arm study*
Jewett, Michael A S, Mattar, Kamal, Basiuk, Joan et al. (2011) Active surveillance of small renal masses: progression patterns of early stage kidney cancer. European urology 60(1): 39-44	- Study design *Non-comparative single-arm study*
Kang, Stella K, Turan, Ekin A, Eisenberg, Jonathan D et al. (2014) Microsimulation model of CT versus MRI surveillance of Bosniak IIF renal cystic lesions: should effects of radiation exposure affect selection of imaging strategy?. AJR. American journal of roentgenology 203(6): w629-36	- Study does not contain a relevant outcome *Study outcome was life expectancy following surveillance and the study was a hypothetical study*
Kassiri, Borna; Cheaib, Joseph G; Pierorazio, Phillip M (2019) Patients with Small Renal Masses Undergoing Active Surveillance-Is Yearly Chest Imaging Necessary?. The Journal of urology 201(6): 1061-1063	- Study design *Conference abstract*
Kawaguchi, S., Fernandes, K.A., Finelli, A. et al. (2011) Most renal oncocytomas appear to grow: Observations of tumor kinetics with active surveillance. Journal of Urology 186(4): 1218-1222	- Study design *Not an intervention study. Study follows the disease course of patients with oncocytomas*
Klatte, Tobias, Berni, Alessandro, Serni, Sergio et al. (2021) Intermediate- and long-term oncological outcomes of active surveillance for localized renal masses: a systematic review and quantitative analysis. BJU international 128(2): 131-143	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Included studies were single-armed studies assessing use of active surveillance for localised renal masses.*
Kouba, Erik, Smith, Angela, McRackan, Daniel et al. (2007) Watchful waiting for solid renal masses: insight into the natural history and results of delayed intervention. The Journal of urology 177(2): 466-470	- Intervention *Study assessed watchful waiting (no intervention), not active surveillance*
Kowalczyk, Keith J, Choueiri, Toni K, Hevelone, Nathanael D et al. (2013) Comparative effectiveness, costs and	- Study design *Not an intervention study. Comparative and cost analysis study*

Study	Reason for exclusion
trends in treatment of small renal masses from 2005 to 2007. BJU international 112(4): e273-80	
Kunkle, David A; Egleston, Brian L; Uzzo, Robert G (2008) Excise, ablate or observe: the small renal mass dilemma--a meta-analysis and review. The Journal of urology 179(4): 1227-4	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Included studies were single-armed studies assessing either treatments for SRMs or active surveillance for SRMs*
Laguna, M.P. (2019) Re: Use of Delayed Intervention for Small Renal Masses Initially Managed with Active Surveillance. Journal of Urology 202(2): 207	- Study design *Editorial comment*
Liu, Shuo, Lee, Stephen, Rashid, Prem et al. (2016) Active surveillance is suitable for intermediate term follow-up of renal oncocytoma diagnosed by percutaneous core biopsy. BJU international 118suppl3: 30-34	- Study design *Non-comparative single-arm study*
Lodder, JJ, Remmers, S, van den Bergh, RCN et al. (2025) A Personalized, Risk-Based Approach to Active Surveillance for Prostate Cancer with Takeaways from Broader Oncology Practices: A Mixed Methods Review. Journal of personalized medicine 15(3)	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Systematic review focused on prostate cancer and the kidney cancer narrative did not include studies comparing active surveillance approaches*
Mason, Ross J, Abdolell, Mohamed, Trottier, Greg et al. (2011) Growth kinetics of renal masses: analysis of a prospective cohort of patients undergoing active surveillance. European urology 59(5): 863-7	- Study design *Non-comparative single-arm study*
Mawi, Hatem; Narine, Rishi; Schieda, Nicola (2021) Adequacy of Unenhanced MRI for Surveillance of Small (Clinical T1a) Solid Renal Masses. AJR. American journal of roentgenology 216(4): 960-966	- Study design *Non-comparative single-arm study*
Mendhiratta, Neil, Hong, Benjamin D, Johnson, David et al. (2023) Contemporary care patterns in the management of small renal masses. The American journal of managed care 29(5): e143-e148	- Comparison *Study assessed patterns of care (active treatment or surveillance) for patients newly diagnosed with SRMs and did not include a comparison group for patients undergoing active surveillance*
Menon, Arun R, Hussein, Ahmed A, Attwood, Kristopher M et al. (2021) Active	- Study design *Non-comparative single-arm study*

Study	Reason for exclusion
Surveillance for Risk Stratification of All Small Renal Masses Lacking Predefined Clinical Criteria for Intervention. The Journal of urology 206(2): 229-239	
Metcalf, Meredith R, Cheaib, Joseph G, Biles, Michael J et al. (2021) Outcomes of Active Surveillance for Young Patients with Small Renal Masses: Prospective Data from the DISSRM Registry. The Journal of urology 205(5): 1286-1293	- Comparison *Comparison group not relevant to protocol. Study compared active surveillance with treatment*
Mir, Maria Carmen, Capitanio, Umberto, Bertolo, Riccardo et al. (2018) Role of Active Surveillance for Localized Small Renal Masses. European urology oncology 1(3): 177-187	- Systematic review used as source of primary studies *No relevant studies identified for inclusion.*
Nayyar, Megha, Cheng, Phillip, Desai, Bhushan et al. (2016) Active Surveillance of Small Renal Masses: A Review on the Role of Imaging With a Focus on Growth Rate. Journal of computer assisted tomography 40(4): 517-23	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Included studies were non-comparative studies assessing active surveillance in maintenance of SRMs*
Neves, Joana B, Varley, Rebecca, Agnesi, Stefano et al. (2021) Growth and renal function dynamics of renal oncocytomas in patients on active surveillance. BJU international 128(6): 722-727	- Study design *Non-comparative single-arm study*
O'Connor, Kevin M, Davis, Niall, Lennon, Gerry M et al. (2009) Can we avoid surgery in elderly patients with renal masses by using the Charlson comorbidity index?. BJU international 103(11): 1492-5	- Study design *Non-comparative single-arm study*
Ouzaid, Idir, Autorino, Riccardo, Fatica, Richard et al. (2014) Active surveillance for renal angiomyolipoma: outcomes and factors predictive of delayed intervention. BJU international 114(3): 412-7	- Study design *Non-comparative single-arm study. Study assessed outcomes for patients undergoing active surveillance and predictive factors of delayed intervention*
Patel, Hiten D, Riffon, Mark F, Joice, Gregory A et al. (2016) A Prospective, Comparative Study of Quality of Life among Patients with Small Renal Masses Choosing Active Surveillance and Primary Intervention. The Journal of urology 196(5): 1356-1362	- Comparison *Comparison was primary intervention (active treatment)*
Patel, Nilay, Cranston, David, Akhtar, M Zeeshan et al. (2012) Active surveillance of	- Comparison

Study	Reason for exclusion
small renal masses offers short-term oncological efficacy equivalent to radical and partial nephrectomy. BJU international 110(9): 1270-5	*Comparisons included active treatments such as partial nephrectomy and radical nephrectomy*
Paterson, C, Yew-Fung, C, Sweeney, C et al. (2017) Predictors of growth kinetics and outcomes in small renal masses (SRM <=4 cm in size): Tayside Active Surveillance Cohort (TASC) Study. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 43(8): 1589-1597	- Study design *Non-comparative single-arm study*
Petros, Firas G, Venkatesan, Aradhana M, Kaya, Diana et al. (2019) Conditional survival of patients with small renal masses undergoing active surveillance. BJU international 123(3): 447-455	- Study design *Non-comparative single-arm study*
Pierorazio, Phillip M, Johnson, Michael H, Ball, Mark W et al. (2015) Five-year analysis of a multi-institutional prospective clinical trial of delayed intervention and surveillance for small renal masses: the DISSRM registry. European urology 68(3): 408-15	- Comparison *Comparison was primary intervention (active treatment)*
Pierorazio, Phillip M, Johnson, Michael H, Patel, Hiten D et al. (2016) Management of Renal Masses and Localized Renal Cancer: Systematic Review and Meta-Analysis. The Journal of urology 196(4): 989-99	- Systematic review used as source of primary studies *No relevant study was identified for inclusion. Majority of the included studies assessed treatment interventions and those assessing active surveillance were single-armed studies*
Prins, Fieke M, Kerkmeijer, Linda G W, Pronk, Anne A et al. (2017) Renal Cell Carcinoma: Alternative Nephron-Sparing Treatment Options for Small Renal Masses, a Systematic Review. Journal of endourology 31(10): 963-975	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Included studies which focussed on active surveillance were single-armed studies*
Pruthi, Deepak K, Liu, Qianqian, Kirkpatrick, Iain D C et al. (2018) Long-Term Surveillance of Complex Cystic Renal Masses and Heterogeneity of Bosniak 3 Lesions. The Journal of urology 200(6): 1192-1199	- Study design *Non-comparative single-arm study*
Rebez, Giacomo; Pavan, Nicola; Mir, M Carmen (2021) Available active surveillance	- Systematic review used as source of primary studies

Study	Reason for exclusion
follow-up protocols for small renal mass: a systematic review. World journal of urology 39(8): 2875-2882	*No relevant studies identified for inclusion. Included studies which focussed on active surveillance were single-armed studies*
Rini, Brian I, Dorff, Tanya B, Elson, Paul et al. (2016) Active surveillance in metastatic renal-cell carcinoma: a prospective, phase 2 trial. The Lancet. Oncology 17(9): 1317-24	- Population does not meet protocol criteria *Population included patients diagnosed with metastatic renal cell carcinoma, including those who had undergone some treatment. Study was also a single-arm study*
Ristau, Benjamin T, Kutikov, Alexander, Uzzo, Robert G et al. (2016) Active Surveillance for Small Renal Masses: When Less is More. European urology focus 2(6): 660-668	- Review article but not a systematic review
Rodger, Flora E, Brown, Keiran, Leung, Steve et al. (2022) Real world outcomes of biopsy-proven oncocytic neoplasm of the kidney managed by surveillance. BJUI compass 3(4): 291-297	- Comparison *Study compared active surveillance with immediate treatment*
Schiavina, Riccardo, Borghesi, Marco, Dababneh, Hussam et al. (2015) Small renal masses managed with active surveillance: predictors of tumor growth rate after long-term follow-up. Clinical genitourinary cancer 13(2): e87-92	- Study design *Non-comparative single-arm study*
Shaish, Hiram, Ahmed, Firas, Schreiber, Jessica et al. (2019) Active Surveillance of Small (< 4 cm) Bosniak Category 2F, 3, and 4 Renal Lesions: What Happens on Imaging Follow-Up?. AJR. American journal of roentgenology 212(6): 1215-1222	- Study design *Non-comparative single-arm study. Outcomes reported were also not relevant to protocol criteria*
Siu, Wendy, Hafez, Khaled S, Johnston, William K 3rd et al. (2007) Growth rates of renal cell carcinoma and oncocytoma under surveillance are similar. Urologic oncology 25(2): 115-9	- Study design *Non-comparative single-arm study*
Smaldone, Marc C, Kutikov, Alexander, Egleston, Brian L et al. (2012) Small renal masses progressing to metastases under active surveillance: a systematic review and pooled analysis. Cancer 118(4): 997-1006	- Systematic review used as source of primary studies *No relevant studies identified for inclusion. Included studies were non-comparative single-armed studies*
Smith, Andrew Dennis, Allen, Brian C, Sanyal, Rupan et al. (2015) Outcomes and complications related to the management of Bosniak cystic renal lesions. AJR. American journal of roentgenology 204(5): w550-6	- Comparison *Study compared outcomes in patients treated with surgery or ablation against those undergoing active surveillance*

Study	Reason for exclusion
Sotimehin, Ayodeji E, Patel, Hiten D, Alam, Ridwan et al. (2019) Selecting Patients with Small Renal Masses for Active Surveillance: A Domain Based Score from a Prospective Cohort Study. The Journal of urology 201(5): 886-892	- Comparison *Study compared active surveillance with primary intervention*
Tse, Justin R, Shen, Luyao, Shen, Jody et al. (2022) Growth Kinetics and Progression Rate of Bosniak Classification Version 2019 Class III and IV Cystic Renal Masses on Imaging Surveillance. AJR. American journal of roentgenology 219(2): 244-253	- Study design *Non-comparative single-arm study*
Volpe, Alessandro (2016) The role of active surveillance of small renal masses. International journal of surgery (London, England) 36(ptc): 518-524	- Review article but not a systematic review
Weibl, P., Hora, M., Kollarik, B. et al. (2017) A practical guide and decision-making protocol for the management of complex renal cystic masses. Arab Journal of Urology 15(2): 115-122	- Comparison *Study compared outcomes in patients undergoing active surveillance with those undergoing surgery*
Whelan, Emily A, Mason, Ross J, Himmelman, Jeffrey G et al. (2019) Extended Duration of Active Surveillance of Small Renal Masses: A Prospective Cohort Study. The Journal of urology 202(1): 57-61	- Study design *Non-comparative study assessing outcomes in patients undergoing active surveillance*
Woskowiak, Piotr, Lewicka, Katarzyna, Bureta, Adrianna et al. (2020) Active surveillance and focal ablation for small renal masses: a better solution for comorbid patients. Archives of medical science : AMS 16(5): 1111-1118	- Review article but not a systematic review
Yasuda, Y., Zhang, J.J.H., Attawettayanon, W. et al. (2023) Comprehensive Management of Renal Masses in Solitary Kidneys. European Urology Oncology 6(1): 84-94	- Comparison *Comparison included treatments such as partial or radical nephrectomy, or cryoablation*

AS: active surveillance; CT: computed tomography; CEUS: contrast enhanced ultrasound; PN: partial nephrectomy; RCC: renal cell carcinoma; RN: radial nephrectomy; SRM: small renal mass

Excluded economic studies (n=1)

Table 5: Excluded economic studies

Study	Reason
Oh, Aaron, Bhardwaj, Lokesh, Cacciamani, Giovanni et al. (2023) Cost-effectiveness of Contrast-Enhanced Ultrasound for Diagnosis and Active Surveillance of Complex Cystic Renal Lesions. Urology practice 10(1): 11-19	- US third-party payer perspective

Appendix K– Research recommendations – full details

K1.1 Research recommendation

For people with small renal lesions (whether benign, malignant or unknown) that have not been treated, what are the most clinically and cost-effective approaches to active surveillance (including method, duration, appropriate frequency of imaging and when to discharge), for the early detection of disease progression in people with localised RCC?

K1.1.1 Why this is important

Due to the risks associated with surgery and the possible impact on quality of life thereafter, people with small renal masses which can safely be offered active treatment as a management option without the risk of increased oncological consequences may benefit from knowledge of the effectiveness of active surveillance as a management option for RCC.

K1.1.2 Rationale for research recommendation

Table 6: Rationale for research recommendation

Importance to 'patients' or the population	There is no evidence on the most effective active surveillance approaches and any risks associated. There is no standard protocol for an active surveillance regimen or duration.
Relevance to NICE guidance	Effectiveness of active surveillance approaches has been considered in this guideline and there was no evidence on any standard protocols.
Relevance to the NHS	The outcome would affect the types of treatment options made available for people with renal cell carcinoma and may reduce the long-term consequences of having surgery when not entirely necessary.
National priorities	Low
Current evidence base	Limited evidence available
Equality considerations	These may include: • Age • Disability • Pregnancy and maternity • Socio-economic and geographical factors

K1.1.3 Modified PICO table

Table 7: Modified PICO table

Population	Adults (18 years or over) with localised renal lesions that have not been treated with surgery, non-surgical interventions or systemic anti-cancer therapy (SACT) divided into the following categories: 1. Small renal lesions and complex cysts (<4cm): • small renal lesions (without histological assessment) or • small renal cell carcinomas or • grade 3 and 4 Bosniak complex cysts 2. Grade 2F Bosniak cysts and oncocytomas (of any size)
Intervention	Approaches to active surveillance that might include: • Frequency and type of imaging • Frequency and type of testing to monitor renal function and cardiovascular outcomes • Different durations of active surveillance
Comparator	Different active surveillance approaches compared to each other

Outcome	• Survival outcomes:
	  ○ Overall survival
	  ○ Disease-specific (cancer-specific) survival
	• Local or distant progression of disease, (defined as a linear growth rate greater than 0.5 cm per year, diameter greater than 4 cm, or metastasis)
	• Time to discharge from active surveillance
	• Need for treatment* including time to intervention or numbers of people needing the treatment
	• Quality of life using a validated tool
	• Cost effectiveness
	*(Treatment include types of surgery or non-surgical interventions such as SABR, thermal ablation or systemic anti-cancer therapy.)

Study design	RCTs Comparative non-randomised studies
Timeframe	Long term
Additional information	None