National Institute for Health and Care Excellence

Kidney cancer: diagnosis and management

[J] Evidence review for renal biopsy

NICE guideline [number]
Evidence review underpinning recommendations 1.3.1 to 1.3.13 in the NICE guideline

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Draft for consultation

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1.1 Review questions

1. What is the clinical and cost effectiveness of core biopsy (compared with no biopsy) for suspected renal cell carcinoma? (clinical effectiveness)

2. In adults with suspected renal cell carcinoma, what is the diagnostic accuracy and cost effectiveness of core biopsy for diagnosing renal masses? (diagnostic accuracy)

1.1.1 Introduction

Renal cell carcinoma (RCC) and benign mass forming lesions in the kidney can present as solid renal masses or cysts. Management of renal lesions in the case of RCC is often by surgery or ablation, or the person undergoes active surveillance. Some renal lesions are difficult to diagnose on imaging, which can lead to overtreatment of a benign lesion if they are removed surgically. A minimally invasive procedure such as a core biopsy of the lesion may be able to distinguish between malignant and benign lesions and prevent unnecessary surgery. This review aims to assess the diagnostic ability, and clinical and cost effectiveness of core biopsy at detecting RCC in renal lesions.

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria for question 1 on clinical effectiveness

Population	Adults (18 years or over): • with solid renal masses or complex cystic renal lesions with a solid component
Index test	Core biopsy of renal lesions guided by: • CT • Ultrasound • MRI
Comparison	No biopsy. RCC confirmed by: Pathology diagnosis after surgical intervention Follow-up (if no surgery)

Outcomes	Clinical outcomes (for test and treat studies):
	• Progression of disease
	• Recurrence of disease
	• Overall survival
	• Need for repeat biopsy
	• Quality of life using:
	  ○ EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30)
	  ○ EuroQol-5 dimensions (EQ-5D)
	• Adverse events from biopsy

Study type	• Test and treat RCTs and systematic reviews of test and treat RCTs.

Table 2: PICOS inclusion criteria for question 2 on diagnostic accuracy

Population	Adults (18 years or over): • with solid renal masses or complex cystic renal lesions with a solid component
Index test	Core biopsy of renal lesions guided by: • CT • Ultrasound • MRI
Reference standard	Pathology diagnosis after surgical intervention Follow-up (if no surgery)
Outcomes	Diagnostic accuracy outcomes: • Positive and negative likelihood ratios • Sensitivity and Specificity
Study type	• Diagnostic accuracy cross-sectional studies and cohort studies. • Systematic reviews of diagnostic accuracy cross-sectional studies.

CT: computed tomography; **MRI**: magnetic resonance imaging

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.

As this review is a diagnostic accuracy review, the decision thresholds as described by Jaeschke et al. (1994) were used for positive and negative likelihood ratios. These are described in the methods chapter.

1. Judgement for imprecision was based on likelihood ratios. The evidence was downgraded by one level when the confidence interval around the point estimate crossed one of the decision-making thresholds and by two levels when the confidence interval around the point estimate crossed 2 or more thresholds. The value 2 for LR+ and 0.5 for LR- were used as one threshold, and the line of no effect (being 1.0) as the second clinical decision line in both cases.

2. Heterogeneity (inconsistency) was assessed by visual inspection of the point estimates and confidence intervals of the included studies. Heterogeneity was independently assessed by two reviewers and discrepancies resolved. The evidence was downgraded if these varied widely between studies, for example, point estimates for some studies lying outside the CIs of other studies. Weighted subjective judgement was used to downgrade once for heterogeneity if <50% were inconsistent, or twice for heterogeneity if ≥50% were inconsistent (serious and very serious heterogeneity).

1.1.3.1 Search methods

The searches for the effectiveness evidence were run on 15/11/2024 and re-run on 09/04/2025. 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. The validated NICE OECD countries limit was also applied. Filters were used to limit to OECD countries, randomised controlled trials, observational studies and diagnosis studies.

The searches for the cost effectiveness evidence were run on 15/11/2024 and re-run on 08/05/2025. The following databases were searched: Econlit (Ovid), Embase (Ovid), 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 OECD countries, cost utility, health state utility and cost effectiveness 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.

1.1.3.2 Protocol deviations

- An additional reference standard (follow-up) was added to the protocol where surgery was not carried out in cases where biopsy was negative or active surveillance was chosen.
- MetaDTA based on the R glmer package was used instead of the mada package due to NICE methods changing after the protocol was written.

1.1.4 Clinical effectiveness and diagnostic evidence

1.1.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 2429 references (see appendix B for the literature search strategy).

These 2,544 references were screened at title and abstract level against the review protocol, with 2,444 excluded at this level. 100% of references were screened separately by two reviewers with 100% agreement. Discrepancies were resolved by discussion.

The full texts of 100 retrospective and prospective studies were ordered for closer inspection. No test and treat studies were found to answer question 1. Twelve studies met the criteria specified in the review protocol for question 2 on diagnostic accuracy (appendix A). For a summary of the 12 included studies see Table 3.

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

See section 1.1.14 references for the full references of the included studies.

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 diagnostic evidence

Table 3 Summary of studies included in the diagnostic evidence

Study details	Setting and location	Population	Index test	Reference test	Risk of bias
Bernhard (2015) N=117 Study type: Prospective cohort Follow up time: Time between tests not reported.	Setting: Surgical practices Location: France	Patients who had a preoperative biopsy followed by nephrectomy	Biopsy performed under US or CT guidance	Surgical specimen following nephrectomy	Moderate
Blumenfeld (2010) N=79 Study type: Retrospective cohort Follow up time: Time between tests not reported.	Setting: Not reported Location: USA	Patients who had a preoperative biopsy followed by nephrectomy	Biopsy performed under US or CT guidance	Surgical specimen following nephrectomy	High
Cazzato (2021) N=43 Study type: Retrospective cohort Follow up time: 12 month follow up for benign biopsies. Time between tests not reported	Setting: Hospital Location: France	Patients referred for percutaneous MRI-guided biopsy of indeterminate solid renal mass	Biopsy performed under MRI guidance	Surgery or follow-up of benign biopsies	Low
Chyhrai (2010) N=21	Setting: Not reported Location: Germany	Patients who underwent biopsy for small	Biopsy performed under US guidance	Surgery or follow-up	High

Study details	Setting and location	Population	Index test	Reference test	Risk of bias
Study type: Retrospective cohort Follow up time: 24 months for non-surgery patients. Time between tests not reported		homogenous and non-cystic renal masses of ≤4cm, or old (age threshold not reported) and multimorbid patients			
Doganca (2019) N=13 Study type: Prospective cohort Follow up time: 26.4 days: time between tests	Setting: Not reported Location: Turkey	Patients with renal mass <5cm and candidates for extirpative surgery	Biopsy performed under US guidance	Surgery	Moderate
Eshed (2004) N=16 Study type: Retrospective cohort Follow up time: Time between tests not reported	Setting: Not reported Location: Israel	Patients with indeterminate renal mass, referred for CT guided biopsy	Biopsy performed under CT-guidance	Surgery or follow-up	High
Gao (2023) N=63 Study type: Retrospective study Follow up time: 3.4 months from biopsy to resection	Setting: Not reported Location: USA	Renal mass 4cm or less	Biopsy performed under CT or US guidance	Resection	Moderate
Lee (2013) N=17	Setting: Hospital Location: Korea	Patients with a predominantly solid lesion	Biopsy performed under US guidance	Surgery	Moderate

Study details	Setting and location	Population	Index test	Reference test	Risk of bias
Study type: Retrospective cohort Follow up time: Time between tests not reported		suspicious for malignancy on CT			
Maturen (2007) N=148 Study type: Retrospective cohort Follow up time: Time between tests not reported. 2 year follow-up for benign biopsy	Setting: Hospital Location: USA	Patients who underwent a renal mass biopsy	Biopsy performed under CT or US guidance	Surgery or follow-up for benign biopsy	High
Schmidbauer (2008) N=76 Study type: Prospective cohort Follow up time:	Setting: Hospital Location: Austria	Patients who underwent renal mall biopsy followed by removal of the mass	Biopsy performed under CT guidance	Surgery	High
Shannon (2008) N=136 Study type: Retrospective cohort Follow up time: 18 months follow-up for benign biopsy. Time between tests not reported.	Setting: Hospital Location: Australia	Patients with renal biopsy of solid mass <5cm suspicious for malignancy on imaging	Biopsy performed under CT or US guidance	Surgery or follow-up for benign biopsy	Moderate
Sofikerim (2010) N=42	Setting: Not reported Location: Turkey	Suspicious masses on imaging: tumour <4cm and	Biopsy performed under US guidance	Surgery	High

Study details	Setting and location	Population	Index test	Reference test	Risk of bias
Study type: Prospective cohort Follow up time: 44.8 months		one or more criteria not present			

CT: computed tomography; **US**: ultrasonography

See appendix D for full evidence tables.

1.1.6 Summary of the diagnostic evidence

Table 4: Summary of findings for diagnostic accuracy of core biopsy for renal carcinoma

Number of studies	Outcome	Sample size	Sensitivity (95% CI)	Specificity (95% CI)	Effect estimate (95% CI)	Certainty	Interpretation of diagnostic ability
12	Diagnostic accuracy	753	0.976 (0.936, 0.991)	0.995 (0.527, 1.000)	LR + 198.55 (1.16, 35045.76)	VERY LOW	Very large increase in the probability of disease
					LR - 0.024 (0.009, 0.065)	LOW	Very large decrease in the probability of disease

CI: confidence interval; **LR**: likelihood ratio
Reasons for downgrading can be found in the full GRADE tables in appendix F.

See appendix F for full GRADE tables.

1.1.7 Economic evidence

1.1.7.1 Included studies

A search was performed to identify published economic evaluations of relevance to this review question. See the literature search strategy in appendix B.

Two economic studies were identified which were applicable to this review question (see appendix G).

One Canadian study compared sequential biopsy and ablation with concurrent biopsy and ablation in people with small renal masses measuring 1–3 cm (Florea et al. 2024). Another Canadian study compared active surveillance or biopsy alongside possible radiofrequency ablation or cryoablation in people with small renal masses measuring ≤4 cm (Bhan et al. 2013).

1.1.7.2 Excluded studies

See appendix J for a list of excluded economic studies, with reason for exclusion.

1.1.8 Summary of included economic evidence

Table 5 provides summary details of the included studies. See appendix H for a full evidence table and assessment of applicability and limitations.

Table 5 Economic evidence profile

Study	Applicability and limitations	Key details	Cost (£) [1]	Effects (QALYs)	ICER (£/QALY)	Uncertainty
Bhan (2013) (Canada)	Partially applicable[2] Potentially serious limitations[3]	• Interventions: 1) biopsy + RFA if required, 2) biopsy + cryoablation if required, 3) active surveillance and RFA if required, 4) active surveillance and cryoablation if required, 5) immediate RFA, 6) immediate cryoablation. • Population: men aged 67 with small renal mass (≤4cm) who are not candidates for surgery. • Decision analytic model (Markov). Payer perspective. • Effectiveness: systematic review. • Time horizon: lifetime.	4) £6,813 6) £8,525 2) £8,775 3) £8,650 5) £10,123 1) £10,451 Cost year: 2010	4) 8.463 6) 8.454 2) 8.447 3) 8.239 5) 8.234 1) 8.225	4) Dominant 6) Dominated 2) Dominated 3) Dominated 5) Dominated 1) Dominated	Probabilistic sensitivity analysis was not conducted. Active surveillance plus cryoablation was dominant for both men and women, and across the age ranges considered. Immediate cryoablation would become the favoured strategy at higher rates of progression to early and late metastatic disease under an active surveillance strategy.
Florea (2024) (Canada)	Partially applicable[4] Potentially serious limitations[5]	• Interventions: 1) biopsy and ablation if required, 2) concurrent biopsy and ablation. • Population: men aged 65 with small renal mass (1-3cm) amenable to radiofrequency ablation • Decision analytic model (decision tree and Markov). Payer perspective. • Effectiveness: systematic review. • Time horizon: lifetime.	1) £160,583 2) £160,805 Cost year: 2022	1) 13.009 2) 13.054	£4,891	Almost all results demonstrated cost effectiveness (72%) or dominance (25%) for the concurrent strategy, at a threshold of £28,790 per QALY. The concurrent strategy was the dominant strategy for a prevalence of benign mass of <5%. Sequential biopsy and ablation was only cost-effective when LYs were not quality-adjusted and ablation cost was >£6,795 or benign mass prevalence was >28%.

Abbreviations: ICER=incremental cost-effectiveness ratio; QALY=Quality-adjusted life-year; RFA=radiofrequency ablation; LY=life year

1. Other currencies were converted to pound sterling using IMF Purchasing Power Parities: https://eppi.ioe.ac.uk/costconversion/default.aspx.

2. Canadian setting and reflects only a subgroup of the people who may get biopsy in practice. 3. Discount rate 5%, some transition probabilities relating to progression of disease, and treatment-related disutility were based on author opinion due to lack of data.

4 Canadian setting and reflects only a subgroup of the people who may get biopsy in practice. 5. Discount rate 1.5%, interpretation of results lacked transparency.

1.1.9 Economic model

Original economic modelling was prioritised for this review question. However, no economic modelling was undertaken for this review because a recent economic study was identified that explored the cost-effectiveness of renal biopsy compared with empiric surgery for diagnosing solid T1 tumours of size 2-7cm.

The cost-effectiveness analysis was part of a broader piece of work that evaluated the feasibility and acceptability of 99m Tc-SestaMIBI SPECT/CT across a number of sites in the UK NHS. This comparator is out of scope of this review, but the analysis was still considered relevant as it contained a comparison between two relevant comparators, biopsy and empiric surgery.

At the time of the evidence consideration by the committee, the analysis was still unpublished. Since this was an area where the committee was considering making a recommendation, they agreed that it was essential to understand the analysis. As a result, the committee invited an expert witness from University College London (UCL) to present the analysis. Details of the expert testimony are provided in appendix L.

1.1.10 Unit costs

The unit cost of biopsy is provided below to aid committee deliberations around cost effectiveness.

Table 6: Unit costs of biopsy

Resource	Unit costs	Source
Biopsy day case procedure	£1,045	NHS Cost Collection (2024). Code YL20A Percutaneous Needle Biopsy of Lesion of Kidney, 19 years and over, Service code 101 Urology service day case

1.1.11 Evidence statements

Economic evidence statements

- One cost-utility analysis from Canada (Bhan et al. 2012) found that in men with small renal masses (≤4cm), strategies with biopsy plus either radiofrequency ablation or cryoablation if required were unlikely to be an effectiveness use of NHS resources as they were found to be more costly and less effective than a strategy of active surveillance and cryoablation if required.
- One cost-utility analysis from Canada (Florea et al. 2024) found that in men with small renal masses (1-3cm), a strategy with concurrent biopsy and ablation was more effective but more expensive than a strategy with biopsy in advance of ablation. It was likely to be an effective use of NHS resources as it was associated with a cost per QALY of £4,891.
- One unpublished cost-utility analysis from the UK, presented through expert testimony (Appendix L), found that in people with T1 kidney tumours, biopsy for diagnosing renal tumours was more effective and less expensive than empiric surgery, and was therefore likely to be an effective use of NHS resources.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

The committee agreed that the diagnostic accuracy outcomes were the critical outcomes for this review. They agreed that likelihood ratios and specificity and sensitivity would be the most useful outcome measures. They noted that the magnitude of the positive (higher better) and negative LRs (lower better) give an indication of how good the index test is at determining how likely it is that the person has (positive LRs) or does not have (negative LRs) renal cell carcinoma (RCC), compared to a person who does not have RCC. They also noted that sensitivity and specificity would provide information about how good the index test was at identifying those with the RCC and those without, respectively. The committee agreed to use LRs to make their decisions with reference to sensitivity and specificity as a secondary measure of test accuracy.

The committee discussed the different implications of false positives and false negatives. They noted that a false positive biopsy test could lead to overtreatment by surgery to remove the tumour, but that a false negative could lead to a missed diagnosis especially if the person was not monitored further following the test. They discussed that in practice it could be more detrimental to the person if a biopsy revealed a false positive test, as a nephrectomy could have long term implications on renal health and quality of life and the person could also experience complications from the surgery. Following a negative biopsy, there would usually be some monitoring of the tumour to ensure that it does not grow in size and therefore the likelihood of a false negative biopsy leading to a completely missed malignant lesion, or one which progressed into a more aggressive or metastatic cancer is very low. The committee agreed that both false positive and false negative results have important implications and so patient involvement, and shared decision making were crucial to consider throughout.

The committee also discussed clinical outcomes that were important to the review that could be reported in test and treat studies. They agreed that progression and recurrence of disease, and overall survival would be important outcomes as they would give an indication of the implications in practice of continuing with treatment following a positive index test. However, there were no test and treat studies identified for inclusion in the review.

1.1.12.2 The certainty of the evidence

The evidence was rated low to very low certainty and was downgraded due to risk of bias as assessed by QUADAS-2. There were concerns around selection bias for some studies, when only those who had a nephrectomy were included. There were also some concerns over studies not reporting the time interval between the index test and reference standard. If the length of this interval was too long there could be inaccuracies in the results if the disease developed over time. The evidence was also downgraded for inconsistency due to heterogeneity in results between studies (some of the point estimates for some studies were outside the CIs for other studies). Some of the evidence was downgraded for imprecision where the confidence intervals crossed 2 or more decision making thresholds.

The committee noted that the evidence included studies with different reference standards to the one listed in the protocol, which was histopathology following surgery. They discussed that some studies included people who went on to have follow-up without surgery following a negative result on biopsy as their reference standard. They agreed that this was likely to represent situations in clinical practice, as where possible, a biopsy would have been used

with the aim of avoiding an unnecessary nephrectomy in those with benign lesions. They agreed that the use of this reference standard was commonly observed throughout the literature and were not concerned that this would affect the certainty of the included studies or the usefulness of their results for decision making. Therefore, this reference standard was included as a deviation from the protocol.

Relevance of the evidence

The committee discussed the evidence in the review. They noted that none of the studies were from a UK population, however agreed that the evidence was still applicable as the studies were from OECD countries. The committee discussed whether the diagnostic ability of the biopsy was operator dependent. They noted that the quality of the sample was an important factor to consider, but noted that although some studies did not specify, most studies reported that the biopsies were performed by an interventional radiologist or an experienced urologist. They noted this was in line with practice in the UK and agreed that it was likely that the operator would not have impacted the quality of the sample in the evidence in this review, as they would all be expected to have adequate experience.

1.1.12.3 Benefits and harms

Diagnostic accuracy of biopsy

The likelihood ratios showed that biopsy was good at identifying people who were likely to have RCC, and that those who tested negative were unlikely to have RCC. They noted that the positive likelihood ratio showed a very large increase in the probability of a person having the disease if the biopsy was positive, and that the small negative likelihood ratio showed that there was a very large decrease in the probability of having the disease if the biopsy showed a negative result. The sizes of the likelihood ratios were above the thresholds (less than or equal to 0.5 for LR-, and greater than or equal to 2 for LR+) that were chosen as the decision thresholds for recommending a diagnostic test. There were very wide 95% confidence intervals (CIs) around the positive likelihood ratio leading to uncertainty around the magnitude of the result. Looking at sensitivity and specificity, the results were both above 95% which suggests a good ability for a biopsy to detect RCC, although the specificity result was associated with very wide 95% CIs. The committee agreed that this was in line with their experience in practice regarding the diagnostic accuracy of biopsy.

The committee noted that there was heterogeneity between the results of the included studies and the 95% CIs of some of these did not overlap with other studies. They agreed that the reasons for heterogeneity could not be easily explained with the information provided by the studies. However, looking across the point estimates of the individual studies, most had positive likelihood ratios classified as being associated with a large increase in the probability of having the disease (the remaining 3 out of 12 were classified as moderate), and small negative likelihood ratios (most classified as being associated with a very low probability of having the disease) and so the committee were confident that the evidence was consistent with their conclusion that biopsy is an accurate test for diagnosing RCC.

Populations for biopsy

<u>Suspected localised or locally advanced RCC</u>

Since the evidence supported biopsy as an accurate test for diagnosing RCC, the committee agreed that the results of this test could be used to support a diagnosis and inform decisions

around the management of benign lesions and malignant RCC. This information would be particularly useful when decisions are being made about whether surgery or another treatment is needed at all. For people with benign oncocytomas, for example, having biopsy results to support this diagnosis could prevent unnecessary surgery and the associated side effects and long-term consequences of having this. Biopsy results supporting a specific diagnosis are also important to help determine suitable treatment options and inform the choice between them, for example, choosing between a radical nephrectomy that will have long term renal consequences or more renal function-preserving treatments such as partial nephrectomy, thermal ablation or SABR. For people with benign oncocytomas or very small renal lesions active surveillance may be the most appropriate clinical option.

The committee discussed the population of the studies in the evidence review to determine who would benefit from a biopsy. They noted that the evidence was relevant to solid renal masses and that there were no studies specific to cystic renal lesions with a solid component. However, they agreed that cystic renal lesions with a solid component are common, and that if there is a substantial solid component to take a sample from, the evidence could be applied to this population group too. The committee agreed that a biopsy would not be performed on a cystic renal lesion that did not have a solid component as this could cause a spillage of the fluid and might lead to unintended harm. The committee then discussed the size of the lesions in the evidence. They noted that evidence was mainly for small (solid) renal masses of 4 cm or smaller, and agreed the evidence, along with their experience in practice, supported a recommendation for biopsy of renal lesions under 4cm with a solid component where it is possible to obtain a useful sample. (The term renal lesions include solid renal masses and cysts.)

The evidence included a range of lesion sizes of up to 17cm. The committee acknowledged that some people with renal lesions over 4cm, that have a solid component, will undergo SABR treatment or thermal ablation, instead of a nephrectomy, and that as these treatments damage the tissue, interpretation of biopsy results may be challenging and unreliable if carried out after these treatments. To allow for a histological diagnosis in this situation, they made a consider recommendation for a biopsy prior to these treatments, and to avoid unnecessary treatment in cases where imaging suggests the lesion could be benign. The committee also highlighted the importance of individual choice. They noted that a person may prefer to have a biopsy to avoid a potential nephrectomy if their lesion is determined to be benign.

Based on their clinical expertise, the committee then discussed the occasions when biopsy should not be performed. These fell into 2 groupings: where biopsy is not going to change management and is therefore unnecessary, or where it is not possible. They noted that a CT scan would be able to identify those with locally advanced renal cell carcinoma, specifically those where the tumour has grown into the renal vein or the inferior vena cava. For this group of people, if surgery is an option, biopsy is unnecessary because treatment options would not change based on a biopsy result and moreover, a delay in treatment is undesirable. Another situation where a biopsy is not recommended include where a person cannot have any treatment, perhaps due to the presence of comorbidities or if they are frail. The committee also discussed situations when management will not change following biopsy such as when the person has decided to have active treatment regardless of the biopsy results, and they agreed a biopsy should not be performed in these situations. The committee discussed situations that would make it difficult to obtain an adequate sample of tissue, such as if the location of the lesion was not accessible by biopsy, the needle had far to travel through the skin, or if the tumour size was smaller than 2cm. They agreed that

where a tumour is inaccessible, or acquisition of a representative sample is not possible then a biopsy is not recommended. The committee agreed that an interventional radiologist would have the expertise to decide when it would not be feasible to perform a biopsy.

The committee also noted that in practice not everyone is offered a biopsy, but people do not always understand why this happens. This creates confusion when these people find out about the biopsy procedure from other people having investigations for suspected RCC. The committee agreed that it is important when someone is not offered a biopsy to explain the reason for this decision. It could be, for example, that the results of a biopsy would not change the management of their RCC, so a biopsy is unnecessary, or that a biopsy is not feasible if they have a cyst that lacks a solid component.

The committee noted that there may be occasions where a sample is non-diagnostic, for example, if not enough tissue was obtained. A repeat biopsy could be an option in these cases if the interventional radiologist thought they could obtain a better sample, and this might involve using a different imaging modality to guide the biopsy. They made a recommendation in support of repeat biopsies that highlighted these points. In practice an ultrasound is usually the first imaging modality, and a repeat biopsy could be carried out using either CT or MRI.

The committee discussed the importance of ensuring that people are given the option to have a biopsy if they have previously declined one. There may be people who are on active surveillance without a histological diagnosis, and the committee agreed that they should be given the opportunity for a biopsy if it is still suitable for them and if the results could provide useful information to inform management decisions. They agreed that it was important to highlight this in a recommendation as people may not be aware that they can request a biopsy if previously declined.

Biopsy for people with suspected metastatic RCC

The committee noted that the evidence for the diagnostic accuracy in this review was limited to renal biopsy. However, as well as having renal lesions, people with suspected metastatic RCC also have lesions in other places (the metastases). These could be in the brain or spinal cord, for example. The committee agreed that it would be confusing for clinicians not to mention biopsy of the metastases as well as of the renal lesion in this section of the guideline. They therefore drafted recommendations for both biopsy of the renal lesions and metastases, but also included cross references to other NICE guidelines for specific metastases that mention biopsy: Investigation of suspected brain metastases in NICE's guidance on Brain tumours (primary) and brain metastases in over 16s and Timing of invasive interventions (where biopsy is mentioned) in NICE's guidance on Spinal metastases and metastatic spinal cord compression.

The committee discussed the use of biopsy in people with suspected metastatic RCC. These people fell into 2 groupings: people with suspected metastatic RCC at first presentation and those who had previously been treated for RCC with no distant disease who now have suspected metastatic deposits. For the first group they agreed that biopsy may be useful as part of diagnosis to inform decisions around systemic anticancer therapy (SACT) or other treatment options, but it is not necessary if the person is having surgery as their first treatment option because the pathology information can be obtained from the tissue removed during surgery. However, in the committee's experience, the decision whether to biopsy the renal lesion or metastases is based on their location, and size. In addition, they agreed that this decision may be affected by the technical skills of the local radiologists and referrals may

be required in difficult cases where more expertise is needed. They drafted recommendations to reflect these points but agreed that the specific details of the decision-making process about whether to biopsy the renal lesion or metastases are too complex and linked to individual circumstances to be captured in more detail in a recommendation. The committee were also aware of the NICE guidance on Metastatic malignant disease of unknown primary origin in adults: diagnosis and management (CG104) which provides more information on diagnosis in people with metastases of unknown primary origin and agreed to cross refer to this guidance.

The committee then discussed the situation where people with suspected metastatic RCC who have previously been treated for RCC with no distant disease now have suspected new metastatic deposits. They agreed that it may be unnecessary to do a biopsy in this group providing that a histological diagnosis has already been obtained from a previous biopsy or post-surgery as part of the initial treatment, as the metastasis is likely to be the same cancer as the RCC. However, if the metastases occurred many years later (for example, over 2 years later), or there were other clinical suspicions that the metastases could be from another malignancy (for example, in cases where the person has had another type of cancer as well) then a biopsy of these metastases could provide useful information to inform SACT or other treatment decisions. They agreed that it should be up to clinical judgement to determine whether to carry out a biopsy of the metastatic deposits for each individual case.

The committee agreed that where SACT or other treatments are not suitable for people with suspected metastatic RCC, a biopsy would not provide any useful information and so the risks of carrying out a biopsy would outweigh any potential benefits. They therefore recommended that biopsy should not be performed in these situations.

Biopsy for people with suspected RCC and a heritable RCC predisposition syndrome

There was no evidence specifically about biopsy of renal lesion in people with suspected RCC who have a heritable RCC predisposition syndrome, so the committee used their clinical expertise to draft consensus recommendations. They agreed that there was no reason the biopsy should be less diagnostically accurate in these people but that there were additional considerations, due to the nature of the RCC associated with these syndromes, that might make biopsy less advisable for people with some heritable RCC predisposition syndromes.

The committee noted that it would be inappropriate to perform a biopsy in people with hereditary leiomyomatosis and renal cell carcinoma (HLRCC) due to the aggressive nature of the lesion. They recommended that a biopsy is not carried out in this group of people. The committee noted that in people with Von Hippel-Lindau (VHL) syndrome the renal lesions are invariably clear cell RCC, and a routine biopsy to confirm malignancy may therefore be unnecessary. However, they agreed that a biopsy to provide information on lesion histology might be useful when there was uncertainty about the lesion type so recommended that biopsy in VHL is not routinely carried out.

The committee agreed that biopsy results could support the diagnosis of RCC and determine the type of lesion before treatment for people with Birt-Hogg-Dubé syndrome (BHD) who have a suspicious renal lesion and therefore made a consider recommendation for biopsy for these people. They noted that people with tuberous sclerosis (TSC) syndrome tend to have benign angiomyolipomas (AML), but that in some rare cases people have aggressive epithelioid AML. They also noted that some AMLs do not show typical features on scans and a biopsy could provide further information for a diagnosis. They agreed therefore that a

biopsy could be useful to determine the nature of the lesion for people with TSC and also included them in the recommendation.

Biopsy specific information

The committee discussed the evidence from review D which explored the information needs of people with suspected or confirmed RCC (see this review for more information about the qualitative evidence base supporting the recommendations on information about biopsy).They focused on the theme about information needs specific to biopsy during diagnosis, which was rated as having moderate confidence in the findings. This highlighted that people valued having information about biopsy, such as information on the procedure itself, the risks associated with it and about side-effects. The committee agreed that the finding reflected their experiences in practice. In addition, they noted that there is often a feeling of fear surrounding the biopsy procedure and concluded that access to more information regarding the benefits of biopsy would help to alleviate these concerns and facilitate informed decision-making.

The committee discussed the benefits of having a biopsy. These included the possibility of ruling out RCC and therefore avoiding an unnecessary nephrectomy, which could lead to a long-term reduction in renal function. There can also be complications from surgery and both problems can be avoided by not having surgery if it's known that the lesion is benign. In addition, biopsy can identify whether a lesion is low-risk based on the grading and tumour type and could be conservatively managed by active surveillance. The committee agreed that informing people of this would help them to understand that a biopsy is an extension of the diagnostic pathway and provides useful information to guide treatment choices. The committee agreed it was important to make a recommendation covering the information that should be discussed with the person with suspected RCC when they are deciding whether to have a biopsy and that it should highlight these benefits.

The committee agreed that performing a biopsy was not risk free or without some potential drawbacks. They noted that although complications associated with the procedure such as pain and bleeding are common, they are usually minor, and that the likelihood of experiencing severe complications is low. They agreed that it was important for people to be aware of this. They also acknowledged that some people were concerned about the risk of seeding of the tumour along the biopsy tract during the biopsy and that this was a reason for some people not taking up a biopsy when offered. (This fear was raised in the qualitative evidence.) The committee noted that available evidence in the literature to support this hypothesis is based on a small number of case series and that in practice, the risk of this is thought to be extremely rare. They agreed that it was important that this was conveyed to the person when discussing biopsy as a diagnostic option.

The committee then discussed the anxiety that people can experience regarding the length of time they have to wait for the biopsy procedure and results and that this would delay surgery or other treatments. They noted that the availability of biopsy depended on local capacity and resources, and that the total time for waiting for a biopsy appointment, and the additional waiting time for the results could take around 3 to 4 weeks, but may be longer in some areas. They therefore included in the recommendation that the person should be told the expected wait time at their centre to have the biopsy and get their results.

The committee acknowledged the anxiety surrounding the wait for biopsy results came from not knowing the outcome of the biopsy (whether the lesion is malignant or not) and concerns that the lesion would grow during that time. The committee agreed that a lesion is unlikely to

progress in a way that would lead to negative consequences (in terms of limiting treatment options or leading to poorer outcomes) during the waiting period and included this information in the recommendation. The committee also highlighted the importance of letting the person know that in some cases a biopsy may show an inconclusive result and might need to be repeated.

The committee agreed that the benefits and risks of biopsy would differ for each person, and that even though it would be a useful tool for diagnosis for some lesions, the clinical status of the patient, and their preferences would still be factors to consider. They recommended that people should be reassured that it may be possible to have a biopsy later if they choose not to have one at diagnosis and they choose to undergo active surveillance. (It would not be possible to do a biopsy if the person has had treatment to remove or destroy the renal lesion.)

1.1.12.4 Cost effectiveness and resource use

The committee reviewed economic evidence on the cost effectiveness of renal mass biopsy from the existing literature. The evidence from the literature came from two cost-effectiveness analyses, both of which took a Canadian payer perspective (Florea et al. 2024 and Bhan et al. 2013). Both studies were assessed as partially applicable (due to the Canadian setting and reflecting only a subgroup of the people who may get biopsy in practice) and with potentially serious limitations.

The committee noted that the differences in costs and QALYs were very small in both studies, especially in relation to the total cost and QALYs, and that it was possible that the overall conclusions of the analysis might differ should an alternative set of assumptions be made (e.g. to convert the model to a UK setting). Therefore, the results of the studies were not used for decision making.

The committee considered the greatest economic and patient benefit of biopsy would be for the purpose of avoiding unnecessary surgery, which can be associated with a risk of complications and decreased renal function over the lifetime. However, there was no relevant economic evidence comparing strategies containing biopsy and surgical options for treatment. Therefore, the committee reached a consensus that this review question should be prioritised for health economic analysis to support a change in practice. There is potentially a high resource impact given the cost of biopsy and likely large population size who may benefit. Supportive evidence from economic modelling would optimise the use of biopsy and associated patient benefits, preventing misdiagnosis or delayed treatment, and can support business cases for its uptake.

The committee were aware of an ongoing study that modelled the cost-effectiveness of renal biopsy compared with empiric surgery to diagnose T1 tumours. The committee received expert testimony on this health economic model and considered that it was directly relevant and applicable to the decision problem in the review. The model evaluated outcomes over the patient lifetime, from a UK NHS and PSS perspective.

In the model, sensitivity and specificity for biopsy was taken from a published systematic review and meta-analysis, Marconi et al. (2016), which estimated a 99.1% sensitivity and 99.7% specificity. While some studies included in the Marconi et al. (2016) study were excluded for this review conducted for this guideline (see Appendix J), the results were relatively consistent with each other. The prevalence of malignant tumours in patients with renal lesions (median size 3.4cm, range 0.8-30cm) was taken from a UK audit of partial

nephrectomy procedures, Fernando et al. (2016), which estimated that 18% of tumours were benign. This value is lower than the 30.9% reported by another study (Kim et al. 2019) highlighted by the committee, which evaluated 18,060 partial nephrectomy patients in the US between 2007 and 2014. The Kim et al. (2019) study was noted by the committee to be less likely to have reporting bias and be a true reflection of the actual rate, but that it is difficult to make direct comparisons between the results as they did not have access to tumour size in the dataset. Higher numbers of benign tumours being biopsied would be associated with greater numbers of avoided unnecessary nephrectomies, and so biopsy would be expected to be more cost effective if the higher benign tumour rate was used in the analysis.

Both the Marconi et al. (2016) systematic review of biopsy accuracy and the Fernando et al. (2016) audit of partial nephrectomies in the UK included people with renal tumours over a range of sizes. The committee noted how larger lesions were more likely to be malignant and the decision to proceed to surgery was less contentious and therefore less likely to require confirmatory results of a biopsy. They considered that it would be useful to conduct an economic analysis based on different tumour sizes to determine at which threshold biopsy would be cost effective, but it was not possible do so due to the data not being reported in this way.

The model predicted that empiric surgery was associated with 180 unnecessary surgeries and 820 surgeries of malignant tumours per 1,000 patients with renal lesions, while biopsy only resulted in 2 unnecessary surgeries per 1,000 patients but slightly fewer surgeries of malignant tumours (813 per 1,000 patients). The biopsy strategy was associated with greater benefits and lower cost over the patient lifetime than the empiric surgery strategy, due to the lower number of surgeries, and so was concluded to be an effective use of NHS resources. On the basis of the clinical and cost effectiveness evidence, the committee recommended the use of biopsy in people with lesions less than 4cm.

The effectiveness review found biopsy to a have high sensitivity and high specificity. False negative results would be associated with a large impact to the patient and to NHS resources due to a missed tumour, but due to the high sensitivity of the test the numbers of these results would be expected to be low. Similarly, a false positive biopsy result would also have a large patient and NHS resource impact as these are associated with unnecessary surgical treatment, and increased risk of reduced renal function which may require substantial management e.g. dialysis, but due to the high specificity of the test, the numbers of these results are also low.

Since one of the primary benefits of biopsy is to avoid unnecessary surgical management, the committee did not recommend biopsy if it would not change the pre-biopsy decision for ongoing management (such as someone who has decided to have surgery regardless of the biopsy results), or if biopsy was considered more likely to be non-diagnostic. In these instances, biopsy would not be associated with the same benefit to the patient and was not considered to merit the additional use of resources.

The unit cost of biopsy was presented to the committee in order to understand the resource impact of their recommendations. It was noted that for people with suspected kidney cancer, a biopsy is usually a day case. Patients typically remain in hospital between 3 to 6 hours following biopsy and rest in a hospital bed whilst being monitored, and then are discharged the same day unless complications occur. NHS Cost Collection reports costs of biopsy of £1,045 for a day case procedure.

While the delay in treatment due to biopsy has a large impact on the person awaiting results from their test, the committee advised that it would be unlikely to have negative clinical consequences, and as such, is unlikely to be associated with increased management and resources above those related to doing the biopsy and analysing and communicating the results.

The most frequent complications of biopsy are pain and bleeding. These are typically self-limiting and may only require analgesia and early outpatient review, but rarely some bleeding complications may require embolization, blood transfusion or ultimately nephrectomy, which are more costly and have greater impact to the patient.

Biopsy has not been routinely adopted everywhere and the committee reported great variation in practice across the country. While the recommendations represent practice in many tertiary centres, many local centres do not presently have the capacity or capability to offer biopsy or can only offer a limited number of biopsy procedures. As a result of the recommendation for biopsy in people with lesions less than 4cm, there would be a change in practice and a corresponding resource impact associated with its adoption. The committee advised that there would be a requirement for additional interventional radiology provision, including greater numbers of staff, and that this would constitute a change in the ways of working as patients would need to be monitored for several hours following the procedure. In order to offer this service to more people, there may be additional referrals to specialist centres, or some local centres that do not currently offer biopsy would require additional training in order to be able to offer this procedure. There would also be additional histopathology support required to process the results of the biopsy, which includes consultants to analyse and report the biopsies, and laboratory resources to process the biopsies. In centres where the pathologists are not familiar with reporting biopsies, there may also be additional training requirements.

However, the committee considered that the benefit of avoiding unnecessary surgical procedures and their large associated cost due to biopsy supported their recommendation, and this was supported by the clinical and cost effectiveness evidence.

1.1.12.5 Other factors the committee took into account

The committee were aware of a consensus statement (Bernstein et al. 2025) produced by people with RCC and clinicians that support the use of biopsy for diagnosis of small renal masses. They noted that the study design did not meet the criteria set out in the review for inclusion but nonetheless felt reassured that other pieces of guidance supported the use of biopsy and that the recommendations in the consensus statement about when to recommend biopsy were broadly consistent with the recommendations they made. Some of the committee members had also contributed to the development of the consensus statement.

The committee discussed some of the equality considerations that were specific to the recommendations for biopsy. They noted that the main concern would be geographical inequalities for people living in rural areas if biopsy was only available in tertiary centres. They noted that increasing the availability of biopsy in local centres would resolve this potential inequality and that the recommendations for biopsy in the guideline could be used to support a business case to provide resources to do so.

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.3.1 to 1.3.13. Other evidence supporting these recommendations can be found in evidence review D on information needs.

1.1.14 References – included studies

1.1.14.1 Diagnostic

Bernhard, J. C., Bigot, P., Pignot, G. et al. (2015) The accuracy of renal tumor biopsy: analysis from a national prospective study. World journal of urology 33(8): 1205-11

Blumenfeld, Aaron J., Guru, Khurshid, Fuchs, Gerhard J. et al. (2010) Percutaneous biopsy of renal cell carcinoma underestimates nuclear grade. Urology 76(3): 610-3

Cazzato, Roberto Luigi, De Marini, Pierre, Auloge, Pierre et al. (2021) Diagnostic accuracy and safety of percutaneous MRI-guided biopsy of solid renal masses: single-center results after 4.5 years. European radiology 31(2): 580-590

Chyhrai, Aliaksei, Sanjmyatav, Jimsgene, Gajda, Mieczyslaw et al. (2010) Multi-colour FISH on preoperative renal tumour biopsies to confirm the diagnosis of uncertain renal masses. World journal of urology 28(3): 269-74

Doganca, Tunkut and Obek, Can (2019) Evaluation of Diagnostic Accuracy of Percutaneous Biopsy for Small Renal Masses and First Report of Post-Biopsy Adhesions: A Prospective Study. Urology journal 16(4): 357-360

Eshed, I.; Elias, S.; Sidi, A. A. (2004) Diagnostic value of CT-guided biopsy of indeterminate renal masses. Clinical radiology 59(3): 262-7

Gao, Haijuan, Nowroozizadeh, Behdokht, Zepeda, Joaquin Ponce et al. (2023) The success rate of small renal mass core needle biopsy and its impact on lowering benign resection rate. BMC urology 23(1): 189

Lee, Seung Woo, Lee, Min Ho, Yang, Hee Jo et al. (2013) Experience of ultrasonography-guided percutaneous core biopsy for renal masses. Korean journal of urology 54(10): 660-5

Maturen, Katherine E., Nghiem, Hanh V., Caoili, Elaine M. et al. (2007) Renal mass core biopsy: accuracy and impact on clinical management. AJR. American journal of roentgenology 188(2): 563-70

Schmidbauer, Joerg, Remzi, Mesut, Memarsadeghi, Mazda et al. (2008) Diagnostic accuracy of computed tomography-guided percutaneous biopsy of renal masses. European urology 53(5): 1003-11

Shannon, Beverley A., Cohen, Ronald J., de Bruto, Hildemarie et al. (2008) The value of preoperative needle core biopsy for diagnosing benign lesions among small, incidentally detected renal masses. The Journal of urology 180(4): 1257-1261

Sofikerim, Mustafa, Tatlisen, Atila, Canoz, Ozlem et al. (2010) What is the role of percutaneous needle core biopsy in diagnosis of renal masses?. Urology 76(3): 614-8

1.1.14.2 Economic

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. Ann Surg Oncol 20:3675–3684

Florea Alexandru, Zaric Gregory S, Kang Ziru, et al. (2024) Cost-Effectiveness Analysis Comparing Biopsy in Advance of Ablation with Concurrent Biopsy and Ablation for Small Renal Masses Measuring 1–3 cm. J Vasc Interv Radiol 35(9):1388-1396.e5.

1.1.15 References – other

Bernstein DE, Warren H, Santiapillai J, Fox G, Wildgoose WH, Stewart GD, et al. (2025) A modified Delphi consensus statement on the role of biopsy in small renal masses. BJUI Compass. 6(4):e70018

Fernando A, Fowler S, O'Brien T (2016). Nephron-sparing surgery across a nation - outcomes from the British Association of Urological Surgeons 2012 national partial nephrectomy audit. BJU Int. 117(6):874-82

Jaeschke, R., Guyatt, G. H., & Sackett, D. L. et al. (1994). Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? JAMA, 271(9), 703–707

Kim JH, Li S, Khandwala Y, et al. (2019). Association of Prevalence of Benign Pathologic Findings After Partial Nephrectomy With Preoperative Imaging Patterns in the United States From 2007 to 2014. JAMA Surg, 154(3):225-231

Marconi L, Dabestani S, Lam TB, et al. (2016). Systematic Review and Meta-analysis of Diagnostic Accuracy of Percutaneous Renal Tumour Biopsy. Eur Urol. 69(4):660-673

NHS England. National Cost Collection for the NHS 2023/24. Available from: https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/

Appendices

Appendix A – Review protocols

Review protocol for effectiveness and diagnostic accuracy of core biopsy

Table 7: Review protocol

ID	Field	Content
1.	Review title	Accuracy and cost effectiveness of core biopsy for diagnosis of renal cell carcinoma (RCC)
2.	Review questions	What is the clinical and cost effectiveness of core biopsy (compared with no biopsy) for suspected renal cell carcinoma? (clinical effectiveness) If no test and treat studies are identified, the following question on diagnostic accuracy will be reviewed: In adults with suspected renal cell carcinoma, what is the diagnostic accuracy and cost effectiveness of core biopsy for diagnosing renal masses? (diagnostic accuracy)
3.	Objective	To evaluate and compare the accuracy, safety, and cost effectiveness of biopsy versus no biopsy for diagnosis (e.g. malignancy, histology, and grade) of suspected RCC.
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 ALL • 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	Suspected renal cell carcinoma
6.	Population	Adults (18 years or over): • with solid renal masses or complex cystic renal lesions with a solid component
7.	Index text	Core biopsy of renal masses guided by: • CT • Ultrasound • MRI
8.	Reference standard	• Pathological diagnosis after surgical intervention
9.	Types of study to be included	• Test and treat RCTs and SRs of test and treat RCTs. If no test and treat studies identified: • Diagnostic accuracy cross-sectional studies and cohort studies. • Systematic reviews of diagnostic accuracy cross-sectional studies. • Where there are no cross-sectional or cohort studies identified, case-control studies will be included.
10.	Other exclusion criteria	• Diagnostic accuracy studies that do not report sufficient information to allow a 2*2 table (TP, FP, TN, FN) to be constructed will be excluded
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. There are uncertainties regarding the accuracy, safety, and cost effectiveness of biopsy compared with no biopsy in adults with suspected RCC.

		Therefore, an evidence review is needed to evaluate the accuracy and cost effectiveness of biopsy versus no biopsy (pathological diagnosis after surgical intervention) for diagnosing adults with suspected RCC and to identify how the accuracy and cost effectiveness varies based on the characteristics of the tumour and the person.

12.	Outcomes	Clinical outcomes (for test and treat studies):
		• Progression of disease (dichotomous outcome)
		• Recurrence of disease (dichotomous outcome)
		• Overall survival
		Some studies may report overall survival as death or mortality. These will be extracted as proxy outcomes where survival data is not reported in the studies.
		• Need for repeat biopsy (dichotomous outcome)
		• Quality of life using:
		  ○ EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30; continuous or dichotomous outcomes)
		  ○ EuroQol-5 dimensions (EQ-5D; continuous or dichotomous outcomes)
		• Adverse events from biopsy (dichotomous outcome)
		
		Diagnostic accuracy outcomes:
		• Positive and negative likelihood ratios
		• Sensitivity and Specificity
		
		Minimal important differences
		Any statistically significant difference will be used for the following outcomes:
		• Progression of disease
		• Recurrence of disease
		• Overall survival
		• Need for repeat biopsy
		• Quality of life using EORTC QLQ-C30
		• Number of hospital admissions
		• Adverse events of biopsy
		
		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 will make use of the priority screening functionality within the EPPI-reviewer software. 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 pre-specified threshold is met for a number of abstracts being screened without a single new include being identified. This threshold is set according to the expected proportion of includes in the review (with reviews with a lower proportion of includes needing a higher number of papers without an identified study to justify termination) and is a minimum of 250.
14.	Risk of bias (quality) assessment	The risk of bias for diagnostic test studies will be assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 tool (QUADAS-2) and for systematic reviews, the Risk of Bias in Systematic Reviews (ROBIS) tool will be used, as described in Developing NICE guidelines: the manual. The risk of bias for test and treat 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, as described in Developing NICE guidelines: the manual.
15.	Strategy for data synthesis	Diagnostic test accuracy (DTA) data will be used to generate a 2x2 classification of true positives and false negatives (in people who, according to the reference standard, truly have the condition) and false positives and true negatives (in people who, according to the reference standard, do not). Where possible, meta-analyses of diagnostic accuracy data will be conducted with reference to the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy Version 2.1 (Deeks et al. 2022). When five or more studies are available for all included strata, a bivariate model will be fit using the mada package in R v3.4.0, which accounts for the correlations between positive and negative likelihood ratios, and between sensitivities and specificities. Where sufficient data were not available (2-4 studies), separate independent pooling will be performed for positive likelihood ratios, negative likelihood ratios, sensitivity and specificity, using R. This approach is conservative as it is likely to somewhat underestimate test accuracy, due to failing to account for the correlation and trade-off between sensitivity and specificity (see Deeks 2010).

		Random-effects models (der Simonian and Laird) will be fit for all syntheses, as recommended in the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (Deeks et al. 2010). Evidence from diagnostic accuracy studies will be initially rated as high-quality, and then downgraded according to the standard GRADE criteria. Where data can be disambiguated it will be separated into the subgroups identified in section 16 (below). In all cases, the downstream effects of diagnostic accuracy on patient-important outcomes will be considered based on the evidence. If there is no or limited evidence for downstream effects of diagnostic accuracy, considerations for this will be explicitly discussed during committee deliberations and reported as part of the discussion section of the review detailing the likely consequences of true positive, true negative, false positive and false negative test results. For RCT evidence: 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. All outcomes in this review which come from RCTs and systematic reviews will be rated as high quality initially and downgraded from this point. 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 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.
16.	Analysis of sub-groups	Where the data allows, subgroup analyses may be conducted to explore heterogeneity considering the following:

<table>
<tr><td></td><td></td><td colspan="3">• biopsy technique,
• age,
• tumour size,
• location and complexity of the tumours,
• renal function at baseline, and
• performance status of the person at baseline (e.g., ECOG and Karnofsky).</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">December 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>X</td><td>X</td></tr>
<tr><td>Piloting of the study selection process</td><td>X</td><td>X</td></tr>
<tr><td>Formal screening of search results against eligibility criteria</td><td>X</td><td>X</td></tr>
<tr><td>Data extraction</td><td>X</td><td>X</td></tr>
<tr><td>Risk of bias (quality) assessment</td><td>X</td><td>X</td></tr>
<tr><td>Data analysis</td><td>X</td><td>X</td></tr>
<tr><td></td><td></td><td></td><td></td></tr>
<tr><td>23.</td><td>Named contact</td><td colspan="3">5a. Named contact
Centre for Guidelines, NICE

5b Named contact e-mail</td></tr>
</table>

		kidneycancerguideline@nice.org.uk **5e 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: • Steve Sharp, Technical adviser • Marie Harrisingh, Technical adviser • Sarah Boyce, Senior technical analyst • Fernando Zanghelini, Technical analyst • Olivia Crane, Technical analyst • Lindsay Claxton, Health economics adviser • Hannah Tebbs, Health economist • Yuanyuan Zhang, 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, partial nephrectomy, radical nephrectomy
32.	Details of existing review of same topic by same authors	Not applicable
33.	Current review status	X Ongoing Completed but not published Completed and published Completed, published and being updated Discontinued
34.	Additional information	None
35.	Details of final publication	www.nice.org.uk

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; CT: computed tomography; DTA: diagnostic test accuracy; EQ-5D: EuroQol-5 dimensions; FN: false negative; FP: false positive; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally importance difference; MRI: magnetic resonance imaging; OECD: Organisation for Economic Co-operative and Development; RCC: renal cell carcinoma; RCT: randomised controlled trial; ROBIS: Risk of Bias in Systematic Reviews; SR: systematic review; TN: true negative; TP: true positive;

1 Economic review protocol

2 Table 8: Economic review protocol

ID	Field	Content
1.	Review title	What is the clinical and cost effectiveness of core biopsy (compared with no biopsy) for suspected renal cell carcinoma?
2.	Objective	To identify economic studies of biopsy versus no biopsy for diagnosis of suspected renal cell carcinoma
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 only focussing on productivity losses or gains.
5.	Search strategy	An economic study search will be undertaken covering the review question relating to the use of biopsy for diagnosis of suspected 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

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.

1

2

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.

Prior work

The search strategy was based on the population terms used in previous review questions for this guideline. The stage terms were removed from this version of the population.

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

Randomised control trial filters:

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

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:

A modified version of the observational filter was applied to Medline and Embase. 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.

Diagnosis filter:

The Medline and Embase searches were limited to diagnosis evidence using the optimal filter. Additional terms were added to the filter.

Haynes RB, Wilczynski NL. Optimal search strategies for retrieving scientifically strong studies of diagnosis from MEDLINE: analytical survey. *BMJ*. 2004;328:1040-2.

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.

The following search filters were applied to the search strategies in MEDLINE and Embase to identify cost-effectiveness studies:

Health state utility balanced filter was used without modification:

> Arber, M et al (2017) Performance of Ovid MEDLINE search filters to identify health state utility studies. International Journal of Technology Assessment in Health Care 33(4):472-80

The following search filters were applied to the search strategies in MEDLINE and Embase to identify cost-effectiveness studies:

> Glanville J et al. (2009) Development and Testing of Search Filters to Identify Economic Evaluations in MEDLINE and EMBASE. Alberta: Canadian Agency for Drugs and Technologies in Health (CADTH)

Note: Several modifications have been made to these filters over the years that are standard NICE practice.

Key decisions

The population terms have been used throughout the guideline. For this review question 'stage' was removed from the free-text terms to reduce results of kidney disease, which is out of scope of this guideline.

Epistemonikos was searched for systematic reviews, therefore a filter was not applied to Medline or Embase for systematic reviews. This is in line with current in-house practice.

The biopsy terms were limited to core needle biopsy. Fine needle aspiration was considered out of scope.

Clinical searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	15/11/2024	Wiley	Issue 10 of 12, October 2024	37
Cochrane Database of Systematic Reviews (CDSR)	15/11/2024	Wiley	Issue 10 of 12, October 2024	0
Embase	15/11/2024	Ovid	1974 to 2024 November 14	1801
Epistemonikos	15/11/2024	Epistemonikos	N/A	47
MEDLINE ALL	15/11/2024	Ovid	1946 to November 14, 2024	1099

Re-run search results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	29/04/2025	Wiley	Issue 3 of 12, March 2025	62
Cochrane Database of Systematic Reviews (CDSR)	29/04/2025	Wiley	Issue 3 of 12, March 2025	36
Embase	29/04/2025	Ovid	1974 to 2025 April 28	1884
Epistemonikos	29/04/2025	Epistemonikos	n/a	52

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
MEDLINE ALL	29/04/2025	Ovid	946 to April 28, 2025	1127

Date limits were not applied to the rerun searches due to technical issues in OVID. The duplication of records was managed in EPPI Reviewer 5.

Search strategy history

Database name: Cochrane CDSR and Cochrane CENTRAL

Searches
#1 MeSH descriptor: [Kidney Neoplasms] explode all trees 1999
#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*)):ti,ab,kw 3415
#3 (collecting-duct* NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)):ti,ab,kw 15
#4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*):ti,ab,kw 4228
#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 tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)):ti,ab,kw 115
#6 {OR #1-#5} 5675
#7 MeSH descriptor: [Biopsy] this term only 4350
#8 MeSH descriptor: [Biopsy, Needle] this term only 1126
#9 MeSH descriptor: [Biopsy, Large-Core Needle] this term only 90
#10 MeSH descriptor: [Image-Guided Biopsy] this term only 275
#11 ((core* or guid* or percutan*) NEAR/3 biops*):ti,ab,kw 3643
#12 {OR #7-#11} 8452
#13 #6 AND #12 in Cochrane Reviews 0
#14 #6 AND #12 in Trials 61
#15 "conference":pt or (clinicaltrials or trialsearch):so 789605
#16 #14 NOT #15 37

Database name: Embase

Searches
1 exp kidney tumor/ (177008)
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*)).ti,ab. (24740)
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. (760)

Searches
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (110826)
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. (1259)
6 or/1-5 (205931)
7 large core needle biopsy/ or thin core needle biopsy/ or exp image guided biopsy/ or biopsy/ or biopsy needle/ or core biopsy needle/ or kidney biopsy/ (272720)
8 ((core* or guid* or percutan*) adj3 biops*).ti,ab,kw. (64467)
9 or/7-8 (312185)
10 6 and 9 (8360)
11 nonhuman/ not (human/ and nonhuman/) (5565298)
12 10 not 11 (8260)
13 limit 12 to english language (7872)
14 13 not (letter or editorial).pt. (7597)
15 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6063172)
16 14 not 15 (4659)
17 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/ (1825559)
18 exp "organisation for economic co-operation and development"/ (3226)
19 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/

Searches
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/ (3946820)
20 european union/ (32918)
21 developed country/ (36532)
22 or/18-21 (3982322)
23 17 not 22 (1663032)
24 16 not 23 (4617)
25 Clinical study/ (168075)
26 Case control study/ (226360)
27 Retrospective study/ (1711658)
28 comparative study/ (1088333)
29 Prospective study/ (949397)
30 Randomized controlled trials/ (285019)
31 29 not 30 (937704)
32 Cohort analysis/ (1244476)
33 cohort analy$.tw. (22410)
34 (Cohort adj (study or studies)).tw. (535792)
35 (Case control$ adj (study or studies)).tw. (185351)
36 (cross sectional adj (study or studies)).tw. (395630)
37 case series.tw. (163783)
38 prospective.tw. (1199635)
39 retrospective.tw. (1411447)
40 or/25-28,31-39 (5611300)
41 sensitiv*.tw. (2232853)
42 diagnostic accuracy.sh. (330085)
43 diagnostic.tw. (1345846)
44 ((likelihood adj ratio*) or lr or plr or nlr).ti,ab. (89048)
45 or/41-44 (3523654)
46 random:.tw. (2141979)
47 placebo:.mp. (548760)
48 double-blind:.tw. (257532)
49 or/46-48 (2428317)
50 40 or 45 or 49 (10161899)
51 24 and 50 (1801)

Database name: Epistemonikos

Searches
(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 (collecting-duct* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumour* or tumor* or mass or metastat* or malignan* or sarcoma* or

Searches
parenchyma*)) OR (renal-cell* or rcc or ccrcc or renal-mass* or (renal and mass*) or "renal-tumour" or "renal-tumours" or "renal tumour" or "renal tumours" or "renal-tumor" or "renal-tumors" or "renal tumor" or "renal tumors" or "grawitz-tumour" or "grawitz-tumours" or "grawitz tumour" or "grawitz tumours" or "grawitz-tumor" or "grawitz-tumors" or "grawitz tumor" or "grawitz tumors" or hypernephroma* or nephrocarcinoma*) OR (kidney* AND (transitional-cell* or (transitional and cell) or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumour* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma*)) AND (core* or guid* or percutan*) AND biops* Systematic reviews - 47

1 **Database name: Medline ALL**

Searches
1 exp Kidney Neoplasms/ (88149)
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*)).ti,ab. (16762)
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. (507)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (73767)
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. (878)
6 or/1-5 (121639)
7 biopsy/ or biopsy, needle/ or biopsy, large-core needle/ or Image-Guided Biopsy/ (246678)
8 ((core* or guid* or percutan*) adj3 biops*).ti,ab,kw. (37577)
9 or/7-8 (265078)
10 6 and 9 (3478)
11 animals/ not humans/ (5241545)
12 10 not 11 (3437)
13 limit 12 to english language (2998)
14 limit 13 to (letter or historical article or comment or editorial or news or case reports) (1279)
15 13 not 14 (1719)
16 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

Searches
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/ (1381449)
17 "organisation for economic co-operation and development"/ (637)
18 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/ (3610125)
19 european union/ (18251)
20 developed countries/ (21664)
21 or/17-20 (3626724)
22 16 not 21 (1289453)
23 15 not 22 (1693)
24 (sensitiv: or predictive value:).mp. or accurac:.tw. (2776783)
25 ((likelihood adj ratio*) or lr or plr or nlr).ti,ab. (60553)
26 diagnos*.ti. (730281)
27 or/24-26 (3388126)
28 exp Randomized Controlled Trial/ (627195)
29 randomi?ed.mp. (1151295)
30 placebo.mp. (261724)
31 or/28-30 (1219997)
32 exp Case-Control Studies/ (1552041)
33 exp Cohort Studies/ (2672320)
34 Cross-Sectional Studies/ (521131)
35 Comparative Study.pt. (1932359)
36 case control$.tw. (171141)
37 (cohort adj (study or studies)).tw. (372006)
38 cohort analy$.tw. (13858)
39 prospective.tw. (781033)

Searches	
40	longitudinal.tw. (359131)
41	retrospective.tw. (852787)
42	cross sectional.tw. (591682)
43	or/32-42 (5722868)
44	23 and (27 or 31 or 43) (1099)

Cost-effectiveness searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Econlit	15/11/2024	Ovid	1886 to November 11, 2024	0
Embase	15/11/2024	Ovid	1974 to 2024 November 14	92
International Health Technology Assessment Database from INAHTA	15/11/2024	https://database.inahta.org/	n/a	4
Medline ALL	15/11/2024	Ovid	1946 to November 14, 2024	38

Re-run search results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	08/05/2025	Ovid	1886 to May 01, 2025	0
Embase	08/05/2025	Ovid	1974 to 2025 May 07	96
International Health Technology Assessment	08/05/2025	https://database.inahta.org/	n/a	4

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Database from INAHTA				
MEDLINE ALL	08/05/2025	Ovid	1946 to May 07, 2025	39

Date limits were not applied to the rerun searches due to technical issues in OVID. The duplication of records was managed in EPPI Reviewer 5.

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*)).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. (25)
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 (33)
6 ((core* or guid* or percutan*) adj3 biops*).ti,ab,kw. (1)
7 5 and 6 (0)

Database name: Embase

Searches
1 exp kidney tumor/ (177008)
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*)).ti,ab. (24740)
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. (760)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (110826)
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. (1259)
6 or/1-5 (205931)
7 large core needle biopsy/ or thin core needle biopsy/ or exp image guided biopsy/ or biopsy/ or biopsy needle/ or core biopsy needle/ or kidney biopsy/ (272720)

Searches
8 ((core* or guid* or percutan*) adj3 biops*).ti,ab,kw. (64467)
9 or/7-8 (312185)
10 6 and 9 (8360)
11 nonhuman/ not (human/ and nonhuman/) (5565298)
12 10 not 11 (8260)
13 limit 12 to english language (7872)
14 13 not (letter or editorial).pt. (7597)
15 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6063172)
16 14 not 15 (4659)
17 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/ (1825559)
18 exp "organisation for economic co-operation and development"/ (3226)
19 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/ (3946820)
20 european union/ (32918)
21 developed country/ (36532)
22 or/18-21 (3982322)

Searches
23 17 not 22 (1663032)
24 16 not 23 (4617)
25 cost utility analysis/ (13316)
26 quality adjusted life year/ (38779)
27 cost*.ti. (205964)
28 (cost* adj2 utilit*).tw. (13733)
29 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (416964)
30 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (71946)
31 (qualit* adj2 adjust* adj2 life*).tw. (29631)
32 QALY*.tw. (29023)
33 (incremental* adj2 cost*).tw. (30947)
34 ICER.tw. (14312)
35 utilities.tw. (16180)
36 markov*.tw. (43152)
37 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (77599)
38 ((utility or effective*) adj2 analys*).tw. (40893)
39 (willing* adj2 pay*).tw. (16249)
40 (EQ5D* or EQ-5D*).tw. (28922)
41 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (5962)
42 (european* adj2 quality adj3 ("5" or five)).tw. (1119)
43 or/25-42 (683407)
44 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kf. (29747)
45 (illness state$1 or health state$1).ti,ab,kf. (15881)
46 (hui or hui1 or hui2 or hui3).ti,ab,kf. (3462)
47 (multiattribute$ or multi attribute$).ti,ab,kf. (1723)
48 (utility adj3 (score$1 or valu$ or health$ or cost$ or measur$ or disease$ or mean or gain or gains or index$)).ti,ab,kf. (35163)
49 (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or euroqol or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol).ti,ab,kf. (35108)
50 (euro$ adj3 (5 d or 5d or 5 dimension$ or 5dimension$ or 5 domain$ or 5domain$)).ti,ab,kf. (10079)
51 (sf36$ or sf 36$ or sf thirtysix or sf thirty six).ti,ab,kf. (48633)
52 (time trade off$1 or time tradeoff$1 or tto or timetradeoff$1).ti,ab,kf. (3827)
53 quality of life/ and ((quality of life or qol) adj (score$1 or measure$1)).ti,ab,kf. (36436)
54 quality of life/ and ec.fs. (69509)
55 quality of life/ and (health adj3 status).ti,ab,kf. (22943)
56 (quality of life or qol).ti,ab,kf. and Cost-Benefit Analysis/ (7321)
57 or/44-56 (252901)

Searches
58 Health economics/ (36903)
59 exp health care cost/ (360560)
60 exp Fee/ (45875)
61 exp Budget/ (35369)
62 Funding/ (82693)
63 budget*.ti,ab. (50645)
64 (economic* or pharmaco?economic*).ti. (81755)
65 (price* or pricing*).ti,ab. (79050)
66 (cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab. (315408)
67 (financ* or fee or fees).ti,ab. (253958)
68 (value adj2 (money or monetary)).ti,ab. (4405)
69 or/58-68 (1071373)
70 43 or 57 or 69 (1503855)
71 24 and 70 (92)

1 **Database name: INAHTA**

Searches

Line	Search query	Hits
#1	"Kidney Neoplasms"[mhe]	129
#2	((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*)))	51
#3	(("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*))	1
#4	("renal cell" or "renal cells" or rcc or ccrcc or renal-mass* or "renal tumor" or "renal tumors" or "renal tumours" or "renal tumour" or "grawitz tumor" or "grawitz tumors" or "grawitz tumour" or "grawitz tumours" or hypernephroma* or nephrocarcinoma*)	115
#5	(kidney* AND ("transitional cell" or "transitional cells" 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*))	22
#6	((kidney* AND ("transitional cell" or "transitional cells" 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 (("renal cell" or "renal cells" or rcc or ccrcc or renal-mass* or "renal tumor" or "renal tumors" or "renal tumours" or "renal tumour" or "grawitz tumor" or "grawitz tumors" or "grawitz tumour" or "grawitz tumours" or hypernephroma* or nephrocarcinoma*)) OR ((("collecting duct" or "collecting ducts") AND (cancer* or carcinoma* or	172

Searches		
	carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))) OR (((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 ("Kidney Neoplasms"[mhe])	
#7	"Biopsy"[mh]	126
#8	"Biopsy Needle"[mh]	16
#9	"Biopsy Large-Core Needle"[mh]	0
#10	"Image-Guided Biopsy"[mh]	16
#11	(core* or guid* or percutan*) AND biops*	102
#12	((core* or guid* or percutan*) AND biops*) OR ("Image-Guided Biopsy"[mh]) OR ("Biopsy Large-Core Needle"[mh]) OR ("Biopsy Needle"[mh]) OR ("Biopsy"[mh])	189
#13	(((core* or guid* or percutan*) AND biops*) OR ("Image-Guided Biopsy"[mh]) OR ("Biopsy Large-Core Needle"[mh]) OR ("Biopsy Needle"[mh]) OR ("Biopsy"[mh])) AND (((kidney* AND ("transitional cell" or "transitional cells" 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 (("renal cell" or "renal cells" or rcc or ccrcc or renal-mass* or "renal tumor" or "renal tumors" or "renal tumours" or "renal tumour" or "grawitz tumor" or "grawitz tumors" or "grawitz tumour" or "grawitz tumours" or hypernephroma* or nephrocarcinoma*)) 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 (((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 ("Kidney Neoplasms"[mhe]))	4

1 **Database name: Medline ALL**

Searches
1 exp Kidney Neoplasms/ (88149)
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*)).ti,ab. (16762)
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. (507)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (73767)
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. (878)

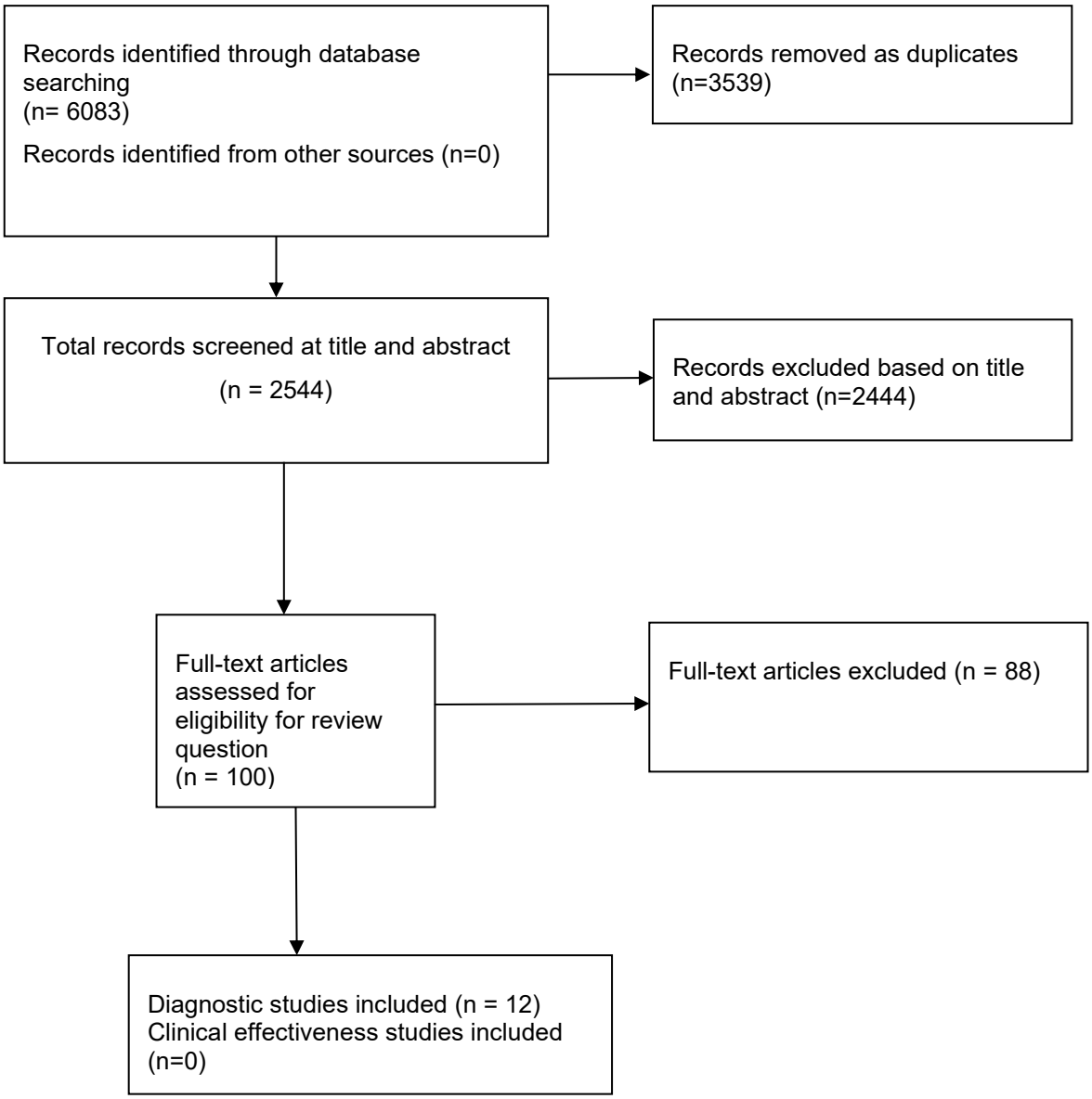
Searches
6 or/1-5 (121639)
7 biopsy/ or biopsy, needle/ or biopsy, large-core needle/ or Image-Guided Biopsy/ (246678)
8 ((core* or guid* or percutan*) adj3 biops*).ti,ab,kw. (37577)
9 or/7-8 (265078)
10 6 and 9 (3478)
11 animals/ not humans/ (5241545)
12 10 not 11 (3437)
13 limit 12 to english language (2998)
14 limit 13 to (letter or historical article or comment or editorial or news or case reports) (1279)
15 13 not 14 (1719)
16 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/ (1381449)
17 "organisation for economic co-operation and development"/ (637)
18 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/ (3610125)
19 european union/ (18251)
20 developed countries/ (21664)
21 or/17-20 (3626724)

Searches
22 16 not 21 (1289453)
23 15 not 22 (1693)
24 Cost-Benefit Analysis/ (96131)
25 Quality-Adjusted Life Years/ (17053)
26 Markov Chains/ (16579)
27 exp Models, Economic/ (16574)
28 cost*.ti. (153505)
29 (cost* adj2 utilit*).tw. (8385)
30 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (304082)
31 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (51719)
32 (qualit* adj2 adjust* adj2 life*).tw. (19473)
33 QALY*.tw. (15802)
34 (incremental* adj2 cost*).tw. (18920)
35 ICER.tw. (6792)
36 utilities.tw. (10163)
37 markov*.tw. (34331)
38 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (57634)
39 ((utility or effective*) adj2 analys*).tw. (27306)
40 (willing* adj2 pay*).tw. (10992)
41 (EQ5D* or EQ-5D*).tw. (15175)
42 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (4454)
43 (european* adj2 quality adj3 ("5" or five)).tw. (807)
44 or/24-43 (542956)
45 (quality adjusted or adjusted life year$).ti,ab,kf. (26718)
46 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kf. (16243)
47 (illness state$1 or health state$1).ti,ab,kf. (9118)
48 (hui or hui1 or hui2 or hui3).ti,ab,kf. (2151)
49 (multiattribute$ or multi attribute$).ti,ab,kf. (1526)
50 (utility adj3 (score$1 or valu$ or health$ or cost$ or measur$ or disease$ or mean or gain or gains or index$)).ti,ab,kf. (22368)
51 (sf36$ or sf 36$ or sf thirtysix or sf thirty six).ti,ab,kf. (28419)
52 (time trade off$1 or time tradeoff$1 or tto or timetradeoff$1).ti,ab,kf. (2582)
53 quality of life/ and ((quality of life or qol) adj (score$1 or measure$1)).ti,ab,kf. (17142)
54 quality of life/ and ec.fs. (11130)
55 quality of life/ and (health adj3 status).ti,ab,kf. (12756)
56 (quality of life or qol).ti,ab,kf. and Cost-Benefit Analysis/ (18236)
57 or/45-56 (115551)
58 Economics/ (27540)
59 Value of life/ (5833)
60 exp "Costs and Cost Analysis"/ (274343)

Searches	
61	exp Economics, Hospital/ (26028)
62	exp Economics, Medical/ (14452)
63	Economics, Nursing/ (4013)
64	Economics, Pharmaceutical/ (3150)
65	exp "Fees and Charges"/ (31562)
66	exp Budgets/ (14278)
67	budget*.ti,ab. (38497)
68	(economic* or pharmaco?economic*).ti. (65739)
69	(price* or pricing*).ti,ab. (58186)
70	(financ* or fee or fees).ti,ab. (177038)
71	(value adj2 (money or monetary)).ti,ab. (3308)
72	or/58-71 (590597)
73	44 or 57 or 72 (996285)
74	23 and 73 (38)

Appendix C –Diagnostic evidence study selection

Figure 1: PRISMA diagram



Appendix D –Diagnostic evidence

Bernhard, 2015

Bibliographic Reference	Bernhard, J. C.; Bigot, P.; Pignot, G.; Baumert, H.; Zini, L.; Lang, H.; Crepel, M.; Monod, P.; Salomon, L.; Bellec, L.; Roupret, M.; Schneider, M.; Xylinas, E.; Paparel, P.; Bruyere, F.; Berger, J.; Ansieau, J. P.; Gimel, P.; Salome, F.; Castagnola, C.; Pfister, C.; Legraverend, J. M.; Timsit, M. O.; Le Pellec, L.; Auberget, J. L.; Rolland, E.; Mallet, R.; Mejean, A.; Patard, J. J.; The accuracy of renal tumor biopsy: analysis from a national prospective study; World journal of urology; 2015; vol. 33 (no. 8); 1205-11

Study Characteristics

Study type	Prospective cohort study
Study details	Study location France Setting Multicentre - surgical practices Study dates June to December 2010 Sources of funding Baxter provided financial support
Inclusion criteria	• Underwent a nephrectomy between study dates • had a preoperative biopsy • comparison available between renal tumour biopsy and nephrectomy specimen.
Exclusion criteria	Not reported
Number of participants	N=117
Length of follow-up	Not reported
Loss to follow-up	Not reported

Index test(s)	Renal tumour biopsy performed under ultrasonography or CT guidance using local anaesthesia to attain 18-gauge needle cores for pathological analyses. Urologists participated in the study, but not specified who performed biopsy. Pathologists trained to genitourinary malignancies evaluated the specimens.
Reference standard (s)	Surgical specimen following nephrectomy
Additional comments	TP: 112 FP: 2 TN: 3 FN: 0

Population characteristics

Study-level characteristics

Characteristic	Study (N = 117)
% Female Sample size	n = 41 ; % = 35
Age Custom value	Median (range): 60 (21-83)
Tumour size (cm) Mean (SD)	4.8 (2.8)
Ethnicity	NR

Critical appraisal - Critical Appraisal - QUADAS-2

Question	Answer
Risk of Bias	Moderate *(Unclear whether patient selection was consecutive or random, and potential inappropriate exclusions)*
Directness	Directly applicable

1 **Blumenfeld, 2010**

Bibliographic Reference	Blumenfeld, Aaron J.; Guru, Khurshid; Fuchs, Gerhard J.; Kim, Hyung L.; Percutaneous biopsy of renal cell carcinoma underestimates nuclear grade; Urology; 2010; vol. 76 (no. 3); 610-3

2

3 **Study Characteristics**

Study type	Retrospective cohort study
Study details	Study location USA Setting Not reported Study dates July 2004 to May 2008 Sources of funding Not reported
Inclusion criteria	• Patients who underwent nephrectomy and had a preoperative biopsy • indications for biopsy: prior history of nonrenal malignancy, tumour in solitary kidney, a central tumour suspicious for urothelial carcinoma • tumour suspicious for malignancy on contrast CT or MRI.
Exclusion criteria	Exclusion criteria not specifically reported. Participants with benign tumour on biopsy who chose observation were not included in this study.
Number of participants	N=81 N= 79 after removing non-diagnostic biopsy
Length of follow-up	Time between biopsy and surgery not reported.
Loss to follow-up	Not reported.
Index test(s)	• Renal biopsy performed under ultrasound or CT guidance, by experienced interventional radiologist • percutaneous biopsy core obtained with an 18 gauge needle • at least 2 core tumours obtained.

Reference standard (s)	• Surgery: radical or partial nephrectomy, or nephroureterectomy.
Additional comments	TP: 77 FP: 1 TN: 1 FN: 0

Population characteristics

Study-level characteristics

Characteristic	Study (N = 81)
Sample size Sample size	n = 81
% Female Sample size	n = 29 ; % = 36
Age Custom value	Mean 64, range (35-85)
Tumour size (cm) Custom value	mean (range): 5.3 (1-17)
Ethnicity - White	n = 61 ; % = 75
Ethnicity – African American	n = 10 ; % = 25 (n doesn't add up but as study reported)

Critical appraisal - Critical Appraisal - QUADAS-2

Question	Answer
Risk of Bias	High *(Unclear whether patient selection was consecutive or random, potential for exclusion of biopsy who underwent follow-up only. Time between biopsy and surgery unclear.)*
Directness	Directly applicable

Cazzato, 2021

Bibliographic Reference	Cazzato, Roberto Luigi; De Marini, Pierre; Auloge, Pierre; Leclerc, Loic; Tricard, Thibault; Linder, Veronique; Jost, Marion; Ramamurthy, Nitin; Lang, Herve; Garnon, Julien; Gangi, Afshin; Diagnostic accuracy and safety of percutaneous MRI-guided biopsy of solid renal masses: single-center results after 4.5 years; European radiology; 2021; vol. 31 (no. 2); 580-590

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location France Setting Hospital Study dates April 2014 and October 2018 Sources of funding No funding received
Inclusion criteria	• Referred for percutaneous MRI-guided biopsy of radiologically indeterminate solid renal mass.
Exclusion criteria	• Diagnostic benign finding on the first biopsy and absence of sufficient follow-up • non-diagnostic on the first biopsy and absence of sufficient follow-up.
Number of participants	N=101 N=88 following exclusions, and N=43 when removing those who had cryoablation
Length of follow-up	12 month follow-up for those with benign tumour on biopsy
Loss to follow-up	N=13

Index test(s)	• Percutaneous MRI-guided renal mass biopsy • performed by five interventional radiologists with 5+ years' experience in the procedure • 18-G needle used to obtain one or more needle-core samples.
Reference standard (s)	Surgery or follow-up
Additional comments	TP (malignant histopathology): 26 TN (benign/non-diagnostic histopathology and renal mass stability/regression on minimum 12 months MRI follow-up): 14 FP (zero based on TP definition and supported by minimal FP rates): 0 FN (benign histopathology and renal mass progression (increase size or metastatic spread) on MRI 12 follow-up; OR non-diagnostic sample with malignant histology on repeat biopsy): 3 Total N=43

Population characteristics

Study-level characteristics

Characteristic	Study (N = 101)
% Female Sample size	n = 32 ; % = 32
Age Median (IQR)	68 (60 to 76)
Tumour size - <2.3 cm Sample size	n = 39 ; % = 39
Tumour size - 2.3 cm or greater Sample size	n = 62 ; % = 61
Median RENAL score - 4 to 6 Sample size	n = 64 ; % = 63
Median RENAL score - 7 to 12 Sample size	n = 37 ; % = 37

Characteristic	Study (N = 101)
Ethnicity	NR

Critical appraisal - Critical Appraisal - QUADAS-2

Question	Answer
Risk of Bias	Low
Directness	Directly applicable

Chyhrai, 2010

Bibliographic Reference	Chyhrai, Aliaksei; Sanjmyatav, Jimsgene; Gajda, Mieczyslaw; Reichelt, Olaf; Wunderlich, Heiko; Steiner, Thomas; Tanovic, Enis; Junker, Kerstin; Multi-colour FISH on preoperative renal tumour biopsies to confirm the diagnosis of uncertain renal masses; World journal of urology; 2010; vol. 28 (no. 3); 269-74

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location Germany Setting Not reported Study dates July 2004 to February 2006 Sources of funding Not reported
Inclusion criteria	Those who underwent fine-needle biopsy under the following indications: • small homogenous and non-cystic renal masses <=4cm • old and multimorbid patients

	Threshold for 'old' not reported. Fine-needle biopsy described in index-test and assumed to be core-biopsy and not fine-needle aspiration
Exclusion criteria	None specified
Number of participants	N=25 N=21 who underwent surgery Those who did not have surgery: 1 leiomyoma, 1 died before surgery 1 denied surgery, 1 unaccounted for
Length of follow-up	Mean 24 months. Surveillance in 3 participants, surgery in 2 of them 1 and 2 years after biopsy.
Loss to follow-up	Not reported
Index test(s)	3 ultrasound-guided percutaneous biopsies of the tumour, which were homogenous and non-cystic on ultrasound. 2 biopsies were evaluated histopathologically. Operator performing biopsy not reported.
Reference standard (s)	Surgical therapy or follow-up
Additional comments	TP: 13 TN: 6 FN: 2 FP: 0

Population characteristics

Study-level characteristics

Characteristic	Study (N = 25)
Age Mean (SD)	63 (7.7)
Tumour size, mm Mean (SD)	25 (10.3)

Characteristic	Study (N = 25)
Ethnicity	NR

1
2

3 **Critical appraisal - Critical Appraisal - QUADAS-2**

Question	Answer
Risk of Bias	High *(Participants were selected. Follow-up time unclear between biopsy and surgery, and 24 months for benign surveillance.)*
Directness	Directly applicable

4

5 **Doganca, 2019**

Bibliographic Reference	Doganca, Tunkut; Obek, Can; Evaluation of Diagnostic Accuracy of Percutaneous Biopsy for Small Renal Masses and First Report of Post-Biopsy Adhesions: A Prospective Study; Urology journal; 2019; vol. 16 (no. 4); 357-360

6

7 **Study Characteristics**

Study type	Prospective cohort study
Study details	Study location Turkey Study dates Not reported Sources of funding Not reported
Inclusion criteria	• Renal mass <5 cm • candidate for extirpative surgery.
Exclusion criteria	• Cysts with heterogeneity and masses suspected for collecting system malignancies
Number of participants	N= 19 total sample core biopsy and fine-needle aspiration

	N=13 core biopsy only for 2x2 table
Length of follow-up	Mean time between biopsy and operation was 26.4 (± 7.2) days
Loss to follow-up	None
Index test(s)	Tru-cut biopsy performed under local anaesthesia with the guidance of ultrasonography. Operator performing biopsy not reported.
Reference standard (s)	Extirpative surgery
Additional comments	TP: 11 TN: 2 FP: 0 FN: 0

Population characteristics

Study-level characteristics

Characteristic	Study (N = 19)
% Female Sample size	n = 8
Age Mean (SD)	56 (10.5)
Tumour size, mm Mean (SD)	36 (10.6)
Ethnicity	NR

Critical appraisal - Critical Appraisal - QUADAS-2

Question	Answer
Risk of Bias	Moderate *(Unclear whether patient selection was consecutive or random)*
Directness	Directly applicable

Eshed, 2004

Bibliographic Reference	Eshed, I.; Elias, S.; Sidi, A. A.; Diagnostic value of CT-guided biopsy of indeterminate renal masses; Clinical radiology; 2004; vol. 59 (no. 3); 262-7

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location Israel Study dates January 1996 to August 2001 Sources of funding Not reported
Inclusion criteria	• Indeterminate renal masses • referred for CT-guided core biopsy • indications for core biopsy: imaging findings suggestive of either metastatic renal disease or another primary malignant origin, a history of previous malignancy, minimally enhancing renal masses and small (< 3 cm) renal masses.
Exclusion criteria	Not reported
Number of participants	N=22 biopsies, but 18 had surgery or follow-up.
Length of follow-up	Not reported
Index test(s)	CT-guide core biopsy, performed percutaneously with a biopsy gun and an 18-gauge needle. Performed by radiologist.

Reference standard (s)	Open resection or open biopsy or surgery
Additional comments	TP: 14 FP: 0 FN: 1 TN: 3

Population characteristics

Study-level characteristics

Characteristic	Study (N = 22)
Sample size Sample size	n = 22
% Female Sample size	n = 8
Age Custom value	Mean 61, range 36 to 89
Ethnicity	NR

Critical appraisal - Critical Appraisal - QUADAS-2

Question	Answer
Risk of Bias	High *(Unclear whether patient selection was consecutive or random. Time between biopsy and surgery unclear.)*
Directness	Directly applicable

Gao, 2023

Bibliographic Reference	Gao, Haijuan; Nowroozizadeh, Behdokht; Zepeda, Joaquin Ponce; Landman, Jaime; Farzaneh, Ted; Johnson, Cary; Hosseini, Hirad; Han, Min; The success rate of small renal mass core needle biopsy and its

impact on lowering benign resection rate; BMC urology; 2023; vol. 23 (no. 1); 189

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location USA Study dates January 2015 to December 2019 Sources of funding No funding
Inclusion criteria	• Renal mass 4 cm or less
Exclusion criteria	• Sample acquired by fine-needle aspiration
Number of participants	N=168 N=63 surgery only participants
Length of follow-up	The time period from biopsy to resection was 3.4 months (range 0.5 to 21 months)
Index test(s)	• Core needle biopsy using 18 to 20 gauge biopsy needle. CT or US guided • Performed by experienced urologist or interventional radiologist.
Reference standard (s)	Resection
Additional comments	TP: 58 FP: 0 FN: 3 TN: 2

Population characteristics

Study-level characteristics

Characteristic	Study (N = 168)
Sample size Sample size	n = 63
% Female Sample size	n = 65
Age Custom value	Mean 63.4 (range 28 to 87)
Ethnicity	NR

Critical appraisal - Critical Appraisal - QUADAS-2

Question	Answer
Risk of Bias	Moderate *(Potential for benign on biopsy to have been excluded)*
Directness	Directly applicable

Lee, 2013

Bibliographic Reference	Lee, Seung Woo; Lee, Min Ho; Yang, Hee Jo; Yang, Won Jae; Kim, Doo Sang; Lee, Nam Kyu; Jeon, Youn Soo; Experience of ultrasonography-guided percutaneous core biopsy for renal masses; Korean journal of urology; 2013; vol. 54 (no. 10); 660-5

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location Korea Setting Hospital

Inclusion criteria	• Predominantly solid lesion • suspicious for malignancy on abdominal CT.
Exclusion criteria	Not reported
Number of participants	N=30 N=17 who underwent surgery Some participants underwent follow-up but results not available for 2x2 table
Length of follow-up	Not reported
Index test(s)	• Ultrasound guided biopsy using an 18-gauge core biopsy needle gun • performed by two radiologists.
Reference standard (s)	Surgery
Additional comments	Only results for those that had surgery, as full follow-up results not available for 2x2 TP: 14 FP: 0 FN: 0 TN: 3

Population characteristics

Study-level characteristics

Characteristic	Study (N = 30)
% Female Sample size	n = 14
Age Custom value	Mean (range): 57.7 (41-79)
Tumour size (cm) Custom value	Mean (range): 3.39 (1.10-8.70)

Characteristic	Study (N = 30)
Ethnicity	NR

1
2

3 **Critical appraisal - Critical Appraisal - QUADAS-2**

Question	Answer
Risk of Bias	Moderate *(Time between biopsy and surgery unclear.)*
Directness	Directly applicable

4

5 **Maturen, 2007**

Bibliographic Reference	Maturen, Katherine E.; Nghiem, Hanh V.; Caoili, Elaine M.; Higgins, Ellen G.; Wolf, J. Stuart, Jr.; Wood, David P., Jr.; Renal mass core biopsy: accuracy and impact on clinical management; AJR. American journal of roentgenology; 2007; vol. 188 (no. 2); 563-70

6

7 **Study Characteristics**

Study type	Retrospective cohort study
Study details	Study location USA Setting Hospital Study dates February 1999 to July 2005 Sources of funding Not reported
Inclusion criteria	• Renal mass biopsies formed by the radiology cross-sectional interventional service
Exclusion criteria	• Biopsy to assess rejection in transplant kidney • biopsy to determine the cause of renal failure in native kidneys

	• FNA.
Number of participants	N=152 biopsies (6 non-diagnostic biopsy 2 went onto surgery, 20 had ablation N=128)
Length of follow-up	Time between biopsy and surgery not reported. Follow-up time if biopsy was definitely benign was over 2 years, and probably benign between 6 months and 2 years. The average imaging follow-up was 9.7 months (range, 0-60 months).
Loss to follow-up	Not reported
Index test(s)	CT or US guided biopsy using 18-gauge spring loaded biopsy gun. Operator performing biopsy not reported.
Reference standard (s)	Surgery, or follow-up if benign
Additional comments	TP: 85 FP: 0 FN: 2 (non-diagnostic on biopsy) TN: 41

Population characteristics

Study-level characteristics

Characteristic	**Study (N = 125)**
Sample size Sample size	n = 125
% Female Sample size	n = 55
Age Custom value	Mean (range): 60 (28-90)
Maximum tumour diameter (cm)	Mean (range): 4.1 (1-13)
Ethnicity	NR

Critical appraisal - Critical Appraisal - QUADAS-2

Question	Answer
Risk of Bias	High *(Unclear whether patient selection was consecutive or random. Time between biopsy and surgery unclear.)*
Directness	Directly applicable

Schmidbauer, 2008

Bibliographic Reference	Schmidbauer, Joerg; Remzi, Mesut; Memarsadeghi, Mazda; Haitel, Andrea; Klingler, Hans Christoph; Katzenbeisser, Daniela; Wiener, Helene; Marberger, Michael; Diagnostic accuracy of computed tomography-guided percutaneous biopsy of renal masses; European urology; 2008; vol. 53 (no. 5); 1003-11

Study Characteristics

Study type	Prospective cohort study
Study details	Study location Austria Setting Hospital Study dates December 2005 to May 2007 Sources of funding Not reported
Inclusion criteria	• Patients who had a pretherapeutic percutaneous biopsy of renal mass guided by CT • subsequent removal of the mass.
Exclusion criteria	• Cystic lesions • transitional cell carcinoma • tumour treated with energy ablative techniques.

Number of participants	N=118 includes fine-needle aspiration and core biopsy N=78 core biopsies 2 insufficient samples for diagnosis final N=76 Fine-needle aspiration included in the study but not extracted for this review. Study characteristics are based on total sample of fine-needle and core biopsy.
Length of follow-up	Not reported
Index test(s)	CT-guided core biopsy using an 18-guage core biopsy needle. 2 or 3 cores were obtained. Operator performing biopsy not reported.
Reference standard (s)	Surgical removal of the mass
Additional comments	TP: 60 TN:13 FN:3 FP:0

Population characteristics

Study-level characteristics

Characteristic	Study (N = 118)
% Female Sample size	n = 15 ; % = 20
Age Mean (SD)	63 (13.5)
Tumour size (cm) Mean (SD)	4 (1.8)
Ethnicity	NR

Critical appraisal - Critical Appraisal - QUADAS-2

Question	Answer
Risk of Bias	High *(Potential for exclusion of participants with a negative biopsy who went onto follow-up only. Time between biopsy and surgery unclear.)*
Directness	Directly applicable

Shannon, 2008

Bibliographic Reference	Shannon, Beverley A.; Cohen, Ronald J.; de Bruto, Hildemarie; Davies, Robert J.; The value of preoperative needle core biopsy for diagnosing benign lesions among small, incidentally detected renal masses; The Journal of urology; 2008; vol. 180 (no. 4); 1257-1261

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location Australia Setting Hospital Study dates February 2000 to December 2007 Sources of funding Not reported
Inclusion criteria	• Renal core biopsies from incidentally discovered asymptomatic solid masses less than 5 cm • suspicious for malignancy on imaging.
Exclusion criteria	Not reported
Number of participants	N=235 biopsies in total from 221 patients

	N=184 diagnostic biopsies. 10 ended up being repeat biopsies 38 malignant on biopsy did not undergo surgery but were not included in the analysis as there is no final diagnosis available for these participants. so total analysed N=136
Length of follow-up	Time from biopsy to surgery not reported. Follow-up time for benign biopsies who were followed-up with regular sonography as they did not undergo surgery: Median 18 months, range 1 to 91
Loss to follow-up	None
Index test(s)	• Renal core biopsy taken under ultrasound or CT guidance by interventional radiologist familiar with renal core biopsy • 18-guage core biopsy gun used to take 1 to 4 cores per lesion • biopsy reviewed by 1 specialist pathologist with a particular interest in renal tumours.
Reference standard (s)	Surgery, partial or radical nephrectomy. Benign biopsies underwent follow-up with ultrasound.
Additional comments	TP: 94 TN: 42 FP: 0 FN: 0

Population characteristics

Study-level characteristics

Characteristic	Study (N = 221)
Age Custom value	Median (range): 64 (22 to 92)
Tumour size (cm) Custom value	Median (range): 2.9 (1 to 4.9)

Characteristic	Study (N = 221)
Ethnicity	NR

1
2

3 **Critical appraisal - Critical Appraisal - QUADAS-2**

Question	Answer
Risk of Bias	Moderate *(Time between biopsy and surgery unclear. Time between surgery and biopsy unclear.)*
Directness	Directly applicable

4

5 **Sofikerim, 2010**

Bibliographic Reference	Sofikerim, Mustafa; Tatlisen, Atila; Canoz, Ozlem; Tokat, Fatma; Demirtas, Abdullah; Mavili, Ertugrul; What is the role of percutaneous needle core biopsy in diagnosis of renal masses?; Urology; 2010; vol. 76 (no. 3); 614-8

6

7 **Study Characteristics**

Study type	Prospective cohort study
Study details	Study location Turkey Study dates January 2001 to April 2008 Sources of funding Not reported
Inclusion criteria	• Suspicious masses not clearly diagnosed by imaging: when one or more criteria were not present and when the size of the tumour was less than 4 cm.
Exclusion criteria	Not reported
Number of participants	N=42

Length of follow-up	Mean 44.8 months (range, 10-85 months)
Loss to follow-up	Not reported
Index test(s)	Percutaneous needle biopsy performed under ultrasonographic guidance with an 18-gauge automatic core biopsy needle system by the same interventional radiologist.
Reference standard (s)	Radical or partial nephrectomies
Additional comments	TP: 33 FP: 1 FN: 5 TN: 3

Population characteristics

Study-level characteristics

Characteristic	Study (N = 42)
Sample size Sample size	n = 42
% Female Sample size	n = 21
Age Custom value	Mean 56.1 (range 21-77)
Ethnicity	NR

Critical appraisal - Critical Appraisal - QUADAS-2

Question	Answer
Risk of Bias	High *(Unclear whether patient selection was consecutive or random. Time between biopsy and surgery unclear.)*

Question	Answer
Directness	Directly applicable

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2

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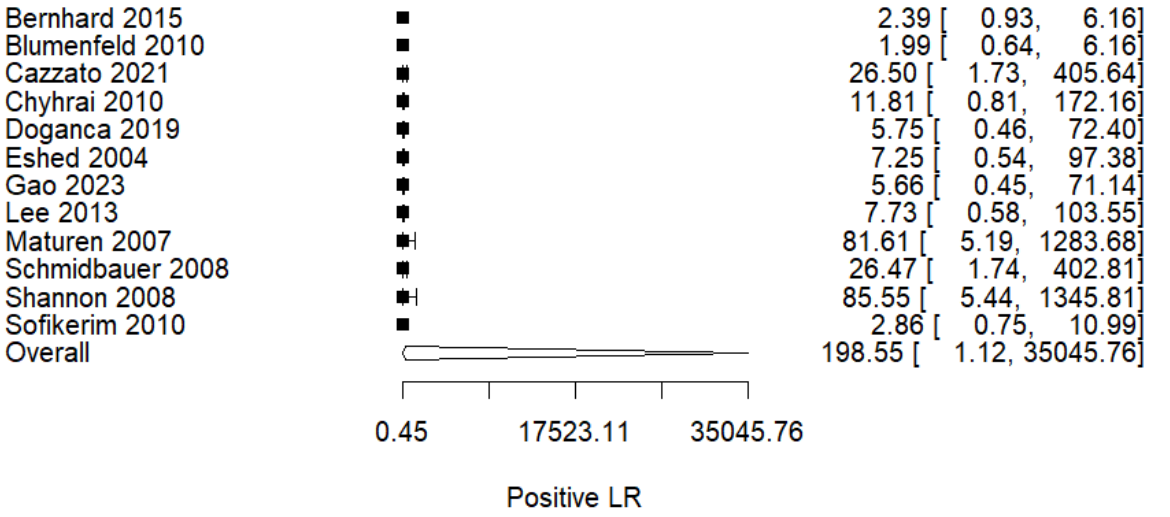
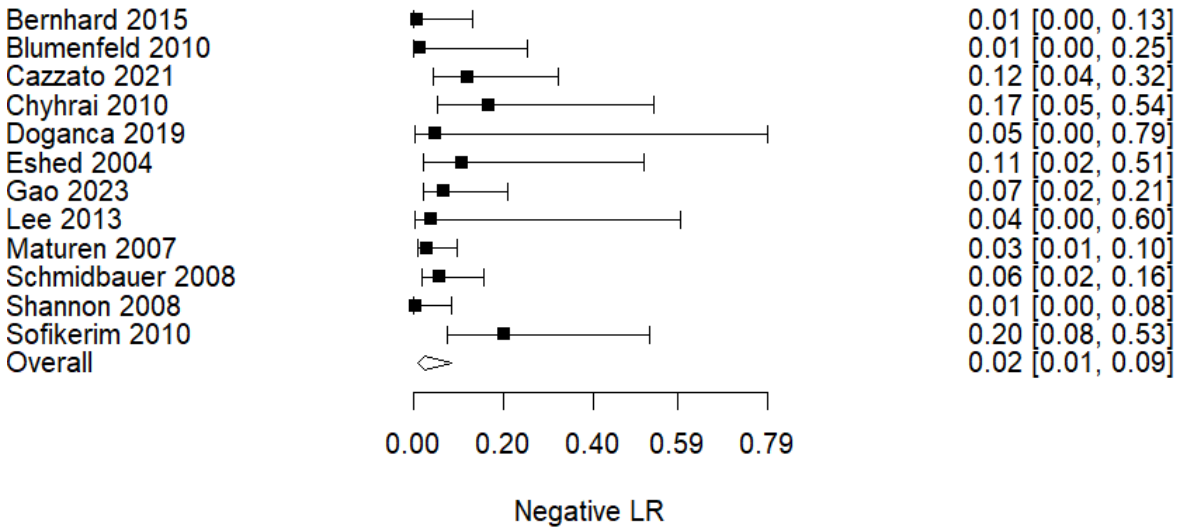
Appendix E – Forest plots

Figure 2: Forest plot for positive likelihood ratio: renal biopsy (reference standard: Pathology diagnosis after surgical intervention or follow-up) (reference standard: Pathology diagnosis after surgical intervention or follow-up)



LR: likelihood ratio

Figure 3: Forest plot for negative likelihood ratio: renal biopsy (reference standard: Pathology diagnosis after surgical intervention or follow-up)



LR: likelihood ratio

Figure 4: Forest plot for sensitivity: renal biopsy (reference standard: Pathology diagnosis after surgical intervention or follow-up)

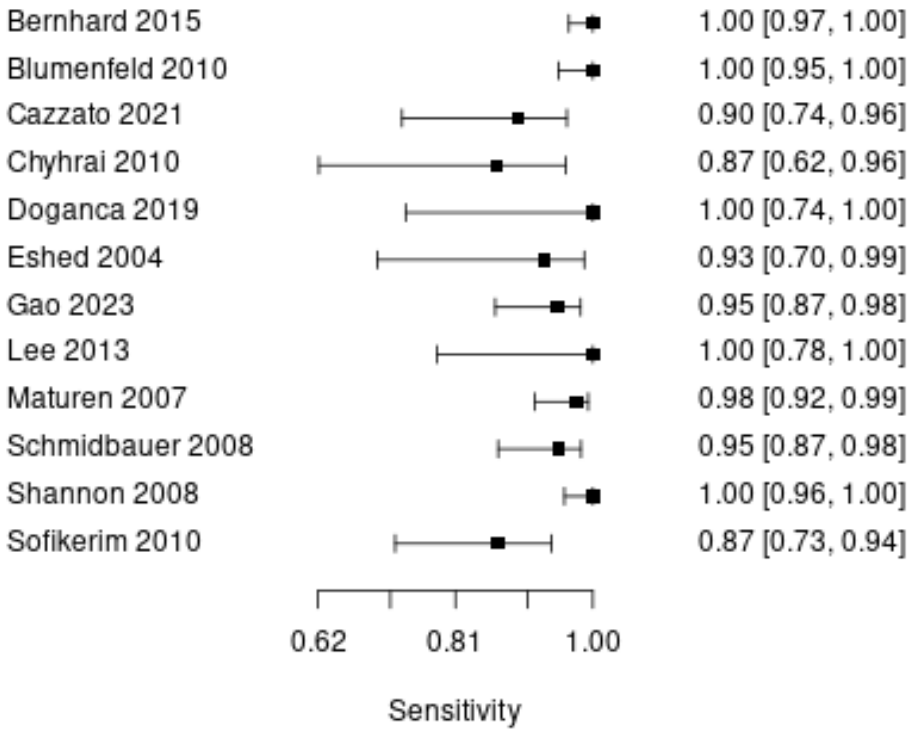
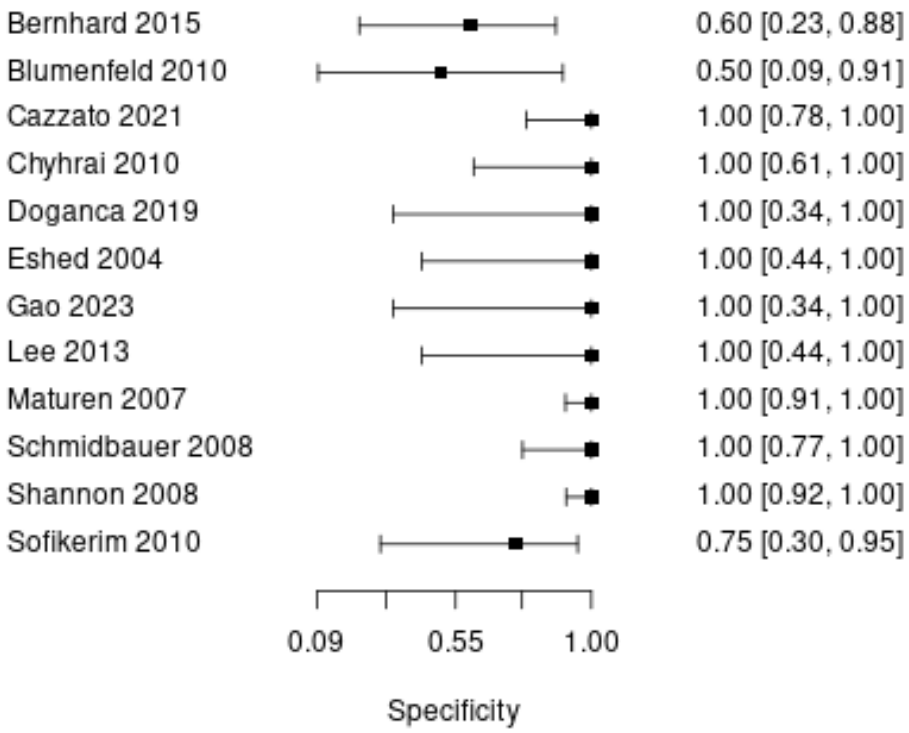


Figure 5: Forest plot for specificity: renal biopsy (reference standard: Pathology diagnosis after surgical intervention or follow-up)



Appendix F – GRADE

Table 9: Clinical evidence profile (diagnostic accuracy)

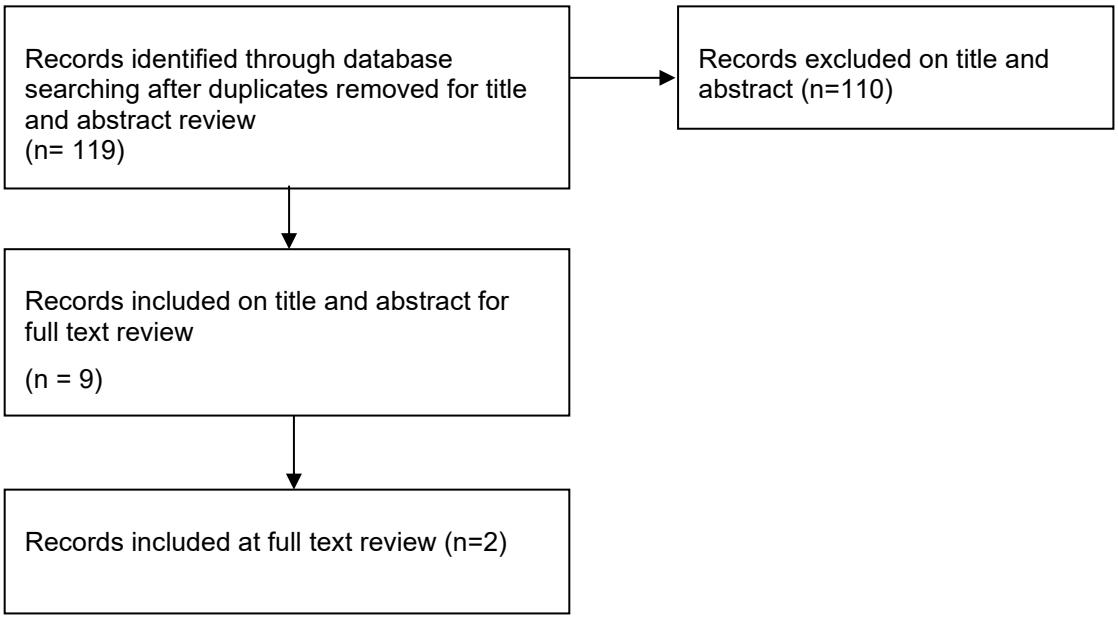
No of studies	Study design	Sample size	Sensitivity (95% CI)	Specificity (95% CI)	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
12 (Bernhard 2015; Blumenfeld 2010; Cazzato 2021; Chyhrai 2010; Doganca 2019; Eshed 2004; Gao 2023; Lee 2013; Maturen 2007; Schmidbauer 2008; Shannon 2008; Sofikerim 2010	Prospective and retrospective cohort	753	0.976 (0.936, 0.991)	0.995 (0.527, 1.000)	LR + 198.55 (1.16, 35045.76)	Serious[1]	Very serious[2]	Not serious	Serious[4]	VERY LOW
					LR- 0.024 (0.009, 0.065)	Serious[1]	Serious[3]	Not serious	Not serious	LOW

CI: confidence interval; LR: likelihood ratio

1. Downgraded once for risk of bias as >50% of the weighting of studies in a meta-analysis at some concerns or high risk of bias as assessed by QUADAS-2
2. Downgraded twice for inconsistency based on visual inspection of point estimates and confidence intervals
3. Downgraded once for inconsistency based on visual inspection of point estimates and confidence intervals
4. Downgraded once for imprecision as 95% CI crosses 1 decision making thresholds (for LR+: 1 ≤ LR <2)

Appendix G – Economic evidence study selection

Figure 6: Economic evidence study selection



Appendix H – Economic evidence tables

Table 10: Economic evidence table

Study	Study type	Setting	Interventions	Population	Methods of analysis	Base-case results	Sensitivity analyses	Additional details
Bhan (2013)	Economic analysis: Cost-utility analysis Study design: Decision analytic model (Markov) Time horizon: lifetime	Setting: Canada Perspective: Payer	1) Biopsy + RFA if required, 2) Biopsy + cryoablation if required, 3) Active surveillance and RFA if required, 4) Active surveillance and cryoablation if required, 5) Immediate RFA, 6) Immediate cryoablation.	Men aged 67 with small renal mass (≤4cm) not suitable for surgery. Women explored in sensitivity analysis.	Discount rate: 5% **Efficacy data**: Diagnostic accuracy data was estimated from 6 studies identified from a systematic review. The probability of first ablation, recurrence and metastatic disease for each strategy were estimated from published studies or estimated by the authors due to a lack of data. **Cost data**: Costs were estimated from the Ontario Ministry of Health and two Canadian health care centres. Included costs for monitoring include CT scans, bloodwork, clinic visits and ultrasound, and costs for management of metastatic disease included bisphosphonate therapy and sunitinib. Cost year: 2010. **Utility data:** Population QoL values were used to model baseline QoL. Treatment-based decrements were assumed by the author, and metastatic RCC was	Costs: 4) £6,813 6) £8,525 2) £8,775 3) £8,650 5) £10,123 1) £10,451 QALYs: 4) 8.463 6) 8.454 2) 8.447 3) 8.239 5) 8.234 1) 8.225 ICER: 4) Dominant 6) Dominated 2) Dominated 3) Dominated 5) Dominated 1) Dominated	Probabilistic sensitivity analysis was not conducted. Deterministic sensitivity analysis found that active surveillance plus cryoablation was dominant for both men and women, and across the age ranges considered. Immediate cryoablation would become the favoured strategy at higher rates of progression to early and late metastatic disease under an active surveillance strategy.	Immediate RFA and immediate cryoablation (with no biopsy) are not current practice in the UK and are considered inappropriate interventions. Monthly costs of managing metastases are very low and pre-date the introduction of many of the newer SACT options. The cost of biopsy is almost double the cost in the UK reported by NHS Reference Costs. The model is driven by a low rate of progression to metastatic disease, but there is uncertainty in the true rates due to a

Study	Study type	Setting	Interventions	Population	Methods of analysis	Base-case results	Sensitivity analyses	Additional details
					sourced from a published US cost-utility study.			lack of good quality, long-term data.
Florea (2024)	Economic analysis: Cost-utility analysis. Study design: Decision analytic model (decision tree and Markov) Time horizon: lifetime.	Setting: Canada Perspective: Payer	1) Biopsy in advance of ablation, 2) Concurrent biopsy and ablation.	Men aged 65 with small renal mass (1-3cm) amenable to ablation. Women explored in sensitivity analysis.	Discount rate: 1.5% **Efficacy data**: Diagnostic accuracy data was estimated from published literature, including a systematic review for the sensitivity and specificity of biopsy. The probability of recurrence and metastatic disease in untreated and in treated disease was obtained from published literature. **Cost data:** Baseline total health costs by age and sex and in the last year of life were estimated from the Canadian Institute for Health Information. Other costs included were management of adverse events, treatment of metastatic disease (SACT, hospitalisation, home care) and surveillance. Cost year: 2022. **Utility data:** Population QoL values were used to model baseline QoL. Treatment-based decrements were taken from Bhan (2013), which were assumed by the authors. Values for local recurrence and metastatic RCC were estimated from published literature.	Costs: 1) £160,583 2) £160,805 QALYs: 1) 13.009 2) 13.054 ICER: £4,891	Deterministic scenario analyses found that the concurrent strategy was the dominant strategy for a prevalence of benign mass of <5%. Sequential biopsy and ablation was only cost-effective when LYs were not quality-adjusted and ablation cost was >£6,795 or benign mass prevalence was >28%. Probabilistic sensitivity analysis found that almost all analyses demonstrated cost effectiveness (72%) or dominance (25%) for the concurrent strategy, at a threshold of £28,790 per QALY.	The sequential strategy avoided some associated negative side effects from RFA, but it was unclear on why the concurrent strategy had greater QALYs; this was possibly due to the model predicting fewer false negatives who would not receive treatment and would experience disease progression. Concurrent biopsy and RFA was not considered appropriate practice and was not a relevant comparison. The cost of biopsy in the analysis was half of the cost in the UK reported by NHS Reference Costs.

Table 11: Applicability and quality checklist for economic evaluations

Study identification Bhan et al. (2013) Active Surveillance, Radiofrequency Ablation, or Cryoablation for the Nonsurgical Management of a Small Renal Mass: A Cost-Utility Analysis.		
Category	**Rating**	**Comments**
Applicability		
1.1 Is the study population appropriate for the review question?	Yes	The study population is in line with a subgroup of the population in the review question (amenable for ablation, not suitable for surgery)
1.2 Are the interventions appropriate for the review question?	Partially	Interventions are generally appropriate for the subgroup included in the study, although some do not reflect practice in the UK
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	Study was conducted from a Canadian payer perspective
1.4 Is the perspective for costs appropriate for the review question?	Yes	Payer perspective
1.5 Is the perspective for outcomes appropriate for the review question?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Partially	Uses discount rate of 5%
1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.5 above).	Yes	
1.8 OVERALL JUDGEMENT	**PARTIALLY APPLICABLE**	Canadian setting and reflects only a subgroup of the people who may get biopsy in practice.
Limitations		
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	

Study identification Bhan et al. (2013) Active Surveillance, Radiofrequency Ablation, or Cryoablation for the Nonsurgical Management of a Small Renal Mass: A Cost-Utility Analysis.		
Category	**Rating**	**Comments**
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Partly	Many transition probabilities and treatment-related utility decrements were assumed by the author due to a lack of data
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	From a systematic review
2.6 Are all important and relevant costs included?	Yes	
2.7 Are the estimates of resource use from the best available source?	Yes	Costs are outdated and do not reflect current treatment options
2.8 Are the unit costs of resources from the best available source?	Partly	Costs are outdated and do not reflect current treatment options
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11 Has no potential financial conflict of interest been declared?	N/A	
2.12 OVERALL ASSESSMENT	**POTENTIALLY SERIOUS LIMITATIONS**	

1

2

Study identification Florea et al. (2022) Cost-Effectiveness Analysis Comparing Biopsy in Advance of Ablation with Concurrent Biopsy and Ablation for Small Renal Masses Measuring 1–3 cm.		
Category	**Rating**	**Comments**
Applicability		
1.1 Is the study population appropriate for the review question?	Yes	The study population is in line with a subgroup of the population in the review question (amenable for ablation, not suitable for surgery)
1.2 Are the interventions appropriate for the review question?	Partially	Interventions are generally appropriate for the subgroup included in the study, although some do not reflect practice in the UK
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	Study was conducted from a Canadian payer perspective
1.4 Is the perspective for costs appropriate for the review question?	Yes	Payer perspective
1.5 Is the perspective for outcomes appropriate for the review question?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Partially	Uses discount rate of 1.5%
1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.5 above).	Yes	
1.8 OVERALL JUDGEMENT	**PARTIALLY APPLICABLE**	Canadian setting and reflects only a subgroup of the people who may get biopsy in practice.
Limitations		
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	

Study identification Florea et al. (2022) Cost-Effectiveness Analysis Comparing Biopsy in Advance of Ablation with Concurrent Biopsy and Ablation for Small Renal Masses Measuring 1–3 cm.		
Category	**Rating**	**Comments**
2. Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	From a systematic review
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	From a systematic review
2.6 Are all important and relevant costs included?	Yes	
2.7 Are the estimates of resource use from the best available source?	Yes	
2.8 Are the unit costs of resources from the best available source?	Yes	
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11 Has no potential financial conflict of interest been declared?	N/A	
2.12 OVERALL ASSESSMENT	**POTENTIALLY SERIOUS LIMITATIONS**	Interpretation of the results lacked transparency and was unclear on why the concurrent strategy had greater QALYs

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Appendix I – Health economic model

No original economic modelling was undertaken for this review question.

Appendix J – Excluded studies

Effectiveness or diagnostic accuracy studies

Study	Reason
Abdelsalam, Mohamed E., Lu, Thomas, Baiomy, Ali et al. (2024) Magnetic resonance imaging-guided renal biopsy shows high safety and diagnostic yield: a tertiary cancer center experience. European radiology 34(9): 5551-5560	- Study does not contain any relevant index tests *Some participants had fine-needle aspiration. Results do not separate from core biopsy*
Abel, E. Jason, Carrasco, Alonso, Culp, Stephen H. et al. (2012) Limitations of preoperative biopsy in patients with metastatic renal cell carcinoma: comparison to surgical pathology in 405 cases. BJU international 110(11): 1742-6	- Study does not contain any relevant index tests *Fine-needle aspiration in some participants and results do not separate from core biopsy*
Abel, E. Jason, Culp, Stephen H., Matin, Surena F. et al. (2010) Percutaneous biopsy of primary tumor in metastatic renal cell carcinoma to predict high risk pathological features: comparison with nephrectomy assessment. The Journal of urology 184(5): 1877-81	- Study does not contain any relevant index tests *Index test included fine needle aspiration and core biopsy, however, results not separate for core biopsy only*
Alle, N., Tan, N., Huss, J. et al. (2018). Percutaneous image-guided core biopsy of solid renal masses: analysis of safety, efficacy, pathologic interpretation, and clinical significance. Abdom Radiol 43, 1813–1819	- Not possible to calculate a contingency table from the data specified in the protocol
Altay, Ali Yilmaz, Karatay, Huseyin, Bakir, Baris et al. (2021) Diagnostic accuracy of core biopsies of renal masses: Experience in a real-life setting from a tertiary center. Annals of diagnostic pathology 55: 151830	- Not possible to calculate a contingency table from the data specified in the protocol
Azawi, N.H., Tolouee, S.A., Madsen, M. et al. (2018). Core needle biopsy clarify the histology of the small renal masses and may prevent overtreatment. Int Urol Nephrol 50, 1205–1209	- Not possible to calculate a contingency table from the data specified in the protocol
Bada, Maida, Rapisarda, Sebastiano, Cicero, Calogero et al. (2021) The role of renal biopsy to improve small renal mass diagnosis and management: are there predictive factors for a higher detection rate?. The first Italian study of 100 cases.	- Study does not contain any relevant index tests *some had fine-needle aspiration, and results not separate from core biopsy*

Study	Reason
Minerva urology and nephrology 73(1): 78-83	
Barocas DA, Rohan SM, Kao J, Gurevich RD, Del Pizzo JJ, Vaughan ED, et al.(2006). Diagnosis of Renal Tumors on Needle Biopsy Specimens by Histological and Molecular Analysis. The Journal of urology 176(5): 1957-62	- Biopsy taken from tissue post-nephrectomy
Beisland, Christian, Johannesen, Tom B., Reisaeter, Lars Anders R. et al. (2018) Real-life use of diagnostic biopsies before treatment of kidney cancer: results from a Norwegian population-based study. Scandinavian journal of urology 52(1): 38-44	- Reference standard in study does not match that specified in protocol
Beland, Michael D., Mayo-Smith, William W., Dupuy, Damian E. et al. (2007) Diagnostic yield of 58 consecutive imaging-guided biopsies of solid renal masses: should we biopsy all that are indeterminate?. AJR. American journal of roentgenology 188(3): 792-7	- Not possible to calculate a contingency table from the data specified in the protocol
Bigot, P, Barthelemy, P, Boissier, R et al. (2022) French AFU Cancer Committee Guidelines - Update 2022-2024: management of kidney cancer. Progres en urologie : journal de l'Association francaise d'urologie et de la Societe francaise d'urologie 32(15): 1195-1274	- Review article but not a systematic review
Buijs, Mara et al. (2017) An In-vivo Prospective Study of the Diagnostic Yield and Accuracy of Optical Biopsy Compared with Conventional Renal Mass Biopsy for the Diagnosis of Renal Cell Carcinoma: The Interim Analysis. European urology focus 4(6): 978-985	- Reference standard in study does not match that specified in protocol *Some had ablation and results do not separate from surgery participants*
Cate, Frances, Kapp, Meghan E., Arnold, Shanna A. et al. (2017) Core Needle Biopsy and Fine Needle Aspiration Alone or in Combination: Diagnostic Accuracy and Impact on Management of Renal Masses. The Journal of urology 197(6): 1396-1402	- Reference standard in study does not match that specified in protocol *Some had ablation and results do not separate from surgery participants*
Crispen, P. L. and Blute, M. L. (2009) The value of preoperative needle core biopsy for diagnosing benign lesions among small, incidentally detected renal masses.	- Systematic review used as a source of primary studies, but not included as criteria did not match that specified in protocol

Study	Reason
Shannon BA, Cohen RJ, de Bruto H, Davies RJ, Tissugen Pty. Ltd., Perth, Western Australia, Australia. Urologic Oncology: Seminars and Original Investigations 27(1): 106	
Curry, N. S., Reinig, J., Schabel, S. I. et al. (1984) An evaluation of the effectiveness of CT vs. other imaging modalities in the diagnosis of atypical renal masses. Investigative radiology 19(5): 447-54	- Study does not contain any relevant index tests
Dave, Chirag N., Seifman, Brian, Chennamsetty, Avinash et al. (2017) Office-based Ultrasound-guided Renal Core Biopsy Is Safe and Efficacious in the Management of Small Renal Masses. Urology 102: 26-30	- Study does not contain any relevant index tests *Some participants had cryoablation and results do not separate from surgery participants*
Dechet, Christopher B., Zincke, Horst, Sebo, Thomas J. et al. (2003) Prospective analysis of computerized tomography and needle biopsy with permanent sectioning to determine the nature of solid renal masses in adults. The Journal of urology 169(1): 71-4	- Study does not contain any relevant index tests
Dominguez-Esteban, M., Villacampa-Auba, F., Garcia-Munoz, H. et al. (2014) Lessons learned from the comparative study between renal mass biopsy and the analysis of the surgical specimen. Actas urologicas espanolas 38(10): 655-61	- Study not reported in English
Faraj, Kassem, Dave, Chirag N., Patel, Kunal et al. (2018) A Retrospective Comparative Outcomes and Cost Analysis of Office Based, Ultrasound Guided Renal Mass Biopsy Performed by Urologists and Standard Hospital Biopsies for Small Renal Masses. Urology practice 5(4): 260-265	- Reference standard in study does not match that specified in protocol *Some participants had cryoablation and results do not separate from surgery participants*
Galosi, Andrea Bendetto, Macchini, Marco, Candelari, Roberto et al. (2023) The use of renal biopsy in the kidney tumor management: A retrospective analysis of consecutive cases in a referral center. Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica 95(2): 11115	- Not possible to calculate a contingency table from the data specified in the protocol

Study	Reason
Garnon, J., Schlier, A., Buy, X. et al. (2015) Evaluation of percutaneous biopsies of renal masses under MRI-guidance: a retrospective study about 26 cases. European radiology 25(3): 617-23	- Reference standard in study does not match that specified in protocol *Some participants had cryoablation and results do not separate from surgery participants*
Gellert, Lan L., Mehra, Rohit, Chen, Ying-Bei et al. (2014) The diagnostic accuracy of percutaneous renal needle core biopsy and its potential impact on the clinical management of renal cortical neoplasms. Archives of pathology & laboratory medicine 138(12): 1673-9	- Reference standard in study does not match that specified in protocol
Halverson, Schuyler J., Kunju, Lakshmi P., Bhalla, Ritu et al. (2013) Accuracy of determining small renal mass management with risk stratified biopsies: confirmation by final pathology. The Journal of urology 189(2): 441-6	- Not possible to calculate a contingency table from the data specified in the protocol
Hara, I., Miyake, H., Hara, S. et al. (2001) Role of percutaneous image-guided biopsy in the evaluation of renal masses. Urologia internationalis 67(3): 199-202	- Reference standard in study does not match that specified in protocol *Not all participants received reference test*
Harisinghani, Mukesh G., Maher, Michael M., Gervais, Debra A. et al. (2003) Incidence of malignancy in complex cystic renal masses (Bosniak category III): should imaging-guided biopsy precede surgery?. AJR. American journal of roentgenology 180(3): 755-8	- Study does not contain any relevant index tests *Some participants had fine-needle aspiration and results are not separate from core biopsy*
He, Qiqi, Wang, Hanzhang, Kenyon, Jonathan et al. (2015) Accuracy of Percutaneous Core Biopsy in the Diagnosis of Small Renal Masses (<= 4.0 cm): A Meta-analysis. International braz j urol : official journal of the Brazilian Society of Urology 41(1): 15-25	- Systematic review used as a source of primary studies, but not included as criteria did not match that specified in protocol
Hoare, Dylan, Evans, Howard, Richards, Heidi et al. (2018) Evaluating the role for renal biopsy in T1 and T2 renal masses: A single-centre study. Canadian Urological Association journal = Journal de l'Association des urologues du Canada 12(5): E226-E230	- Not possible to calculate a contingency table from the data specified in the protocol
Hu, Rong; Montemayor-Garcia, Celina; Das, Kasturi (2015) Role of percutaneous needle core biopsy in diagnosis and clinical	- Reference standard in study does not match that specified in protocol

Study	Reason
management of renal masses. Human pathology 46(4): 570-6	
Iguchi, T., Hiraki, T., Matsui, Y. et al. (2020) Image-guided core biopsy of 2-cm or smaller renal tumors. Diagnostic and interventional imaging 101(11): 715-720	- Reference standard in study does not match that specified in protocol
Iguchi, Toshihiro, Hiraki, Takao, Matsui, Yusuke et al. (2018) CT fluoroscopy-guided renal tumour cutting needle biopsy: retrospective evaluation of diagnostic yield, safety, and risk factors for diagnostic failure. European radiology 28(1): 283-290	- Reference standard in study does not match that specified in protocol
Ingels, Alexandre, Barret, Eric, Sanchez-Salas, Rafael et al. (2016) Percutaneous Renal Biopsies for Small Renal Masses: Complex Tumors on Nephrometry Should Be the First Targets. Clinical genitourinary cancer 14(5): e457-e462	- Not possible to calculate a contingency table from the data specified in the protocol
Izumi, Kouji, Narimoto, Kazutaka, Sugimoto, Kazuhiro et al. (2010) The role of percutaneous needle biopsy in differentiation of renal tumors. Japanese journal of clinical oncology 40(11): 1081-6	- Reference standard in study does not match that specified in protocol
Jaeger, H. J., MacFie, J., Mitchell, C. J. et al. (1990) Diagnosis of abdominal masses with percutaneous biopsy guided by ultrasound. BMJ (Clinical research ed.) 301(6762): 1188-91	- Reference standard in study does not match that specified in protocol
Jaff, Ameer, Molinie, Vincent, Mellot, Francois et al. (2005) Evaluation of imaging-guided fine-needle percutaneous biopsy of renal masses. European radiology 15(8): 1721-6	- Population not suspected renal cell carcinoma
Jeon, Hwang Gyun, Seo, Seong Il, Jeong, Byong Chang et al. (2016) Percutaneous Kidney Biopsy for a Small Renal Mass: A Critical Appraisal of Results. The Journal of urology 195(3): 568-73	- Reference standard in study does not match that specified in protocol
Johnson, P. T., Nazarian, L. N., Feld, R. I. et al. (2001) Sonographically guided renal mass biopsy: indications and efficacy. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine 20(7): 749-755	- Reference standard in study does not match that specified in protocol

Study	Reason
Kim, Jae Heon, Sun, Hwa Yeon, Hwang, Jiyoung et al. (2016) Diagnostic accuracy of contrast-enhanced computed tomography and contrast-enhanced magnetic resonance imaging of small renal masses in real practice: sensitivity and specificity according to subjective radiologic interpretation. World journal of surgical oncology 14(1): 260	- Study does not contain any relevant index tests
Kim, Mi-Hyun (2017) CT-Guided Biopsy of Entirely Endophytic Small Renal Masses: Diagnostic Rates and Complications Using Standard-Dose and Reduced-Dose CT Protocols. AJR. American journal of roentgenology 208(5): 1030-1036	- Reference standard in study does not match that specified in protocol
Kroeze, Stephanie G. C., Huisman, Merel, Verkooijen, Helena M. et al. (2012) Real-time 3D fluoroscopy-guided large core needle biopsy of renal masses: a critical early evaluation according to the IDEAL recommendations. Cardiovascular and interventional radiology 35(3): 680-5	- Not possible to calculate a contingency table from the data specified in the protocol
Kummerlin, Intan, ten Kate, Fiebo, Smedts, Frank et al. (2008) Core biopsies of renal tumors: a study on diagnostic accuracy, interobserver, and intraobserver variability. European urology 53(6): 1219-25	- Biopsy taken from tissue post-nephrectomy
Lang, Erich K., Macchia, Richard J., Gayle, Brian et al. (2002) CT-guided biopsy of indeterminate renal cystic masses (Bosniak 3 and 2F): accuracy and impact on clinical management. European radiology 12(10): 2518-24	- Study does not contain any relevant index tests
Lebret, Thierry, Poulain, Jean Eudes, Molinie, Vincent et al. (2007) Percutaneous core biopsy for renal masses: indications, accuracy and results. The Journal of urology 178(4pt1): 1184-1188	- Not possible to calculate a contingency table from the data specified in the protocol
Lechevallier, E., Andre, M., Barriol, D. et al. (2000) Fine-needle percutaneous biopsy of renal masses with helical CT guidance. Radiology 216(2): 506-10	- Reference standard in study does not match that specified in protocol
Leveridge, Michael J., Finelli, Antonio, Kachura, John R. et al. (2011) Outcomes of small renal mass needle core biopsy, nondiagnostic percutaneous biopsy, and the	- Not possible to calculate a contingency table from the data specified in the protocol

Study	Reason
role of repeat biopsy. European urology 60(3): 578-84	
Li, Guorong, Cuilleron, Muriel, Zhao, An et al. (2012) Combination of core biopsy and fine-needle aspiration increases diagnostic rate for small solid renal tumors. Anticancer research 32(8): 3463-6	- Not possible to calculate a contingency table from the data specified in the protocol
Londono, Diana C., Wuerstle, Melanie C., Thomas, Anil A. et al. (2013) Accuracy and implications of percutaneous renal biopsy in the management of renal masses. The Permanente journal 17(3): 4-7	- Reference standard in study does not match that specified in protocol *Not all underwent surgery, but follow-up data not available*
Marconi, Lorenzo, Dabestani, Saeed, Lam, Thomas B. et al. (2016) Systematic Review and Meta-analysis of Diagnostic Accuracy of Percutaneous Renal Tumour Biopsy. European urology 69(4): 660-673	- Systematic review used as a source of primary studies, but not included as criteria did not match that specified in protocol
Mazin Hashim, Bassam, Chabok, Abbas, Ljungberg, Borje et al. (2024) Diagnostic accuracy and safety of renal tumour biopsy in patients with small renal masses and its impact on treatment decisions. Scandinavian journal of urology 59: 141-146	- Reference standard in study does not match that specified in protocol *Some had ablation and results do not separate from surgery participants*
Menhadji, A. D., Nguyen, V., Okhunov, Z. et al. (2016) Technique for office-based, ultrasonography-guided percutaneous biopsy of renal cortical neoplasms using a novel transducer for facilitated ultrasound targeting. BJU International 117(6): 948	- Reference standard in study does not match that specified in protocol *Not all underwent surgery, follow-up results not available for those that did not*
Menogue, Stuart R., O'Brien, Beverley A., Brown, Alexandra L. et al. (2013) Percutaneous core biopsy of small renal mass lesions: a diagnostic tool to better stratify patients for surgical intervention. BJU international 111(4ptb): E146-51	- Reference standard in study does not match that specified in protocol *Some had ablation and results do not separate from surgery participants*
Millet, Ingrid, Curros, Fernanda, Serre, Isabelle et al. (2012) Can renal biopsy accurately predict histological subtype and Fuhrman grade of renal cell carcinoma?. The Journal of urology 188(5): 1690-4	- Not possible to calculate a contingency table from the data specified in the protocol
Nadel, L.; Baumgartner, B. R.; Bernardino, M. E. (1986) Percutaneous renal biopsies: accuracy, safety, and indications. Urologic radiology 8(2): 67-71	- Reference standard in study does not match that specified in protocol

Study	Reason
Neuzillet, Yann, Lechevallier, Eric, Andre, Marc et al. (2004) Accuracy and clinical role of fine needle percutaneous biopsy with computerized tomography guidance of small (less than 4.0 cm) renal masses. The Journal of urology 171(5): 1802-5	- Reference standard in study does not match that specified in protocol *Not all underwent surgery, but full follow-up information not available for those that did not.*
Palko, A., Kuhn, E., Grexa, E. et al. (1990) Renal cell carcinoma: value of imaging examinations in diagnosis and staging. RoFo : Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin 153(5): 585-90	- Study does not contain any relevant index tests
Pandharipande, Pari V., Gervais, Debra A., Hartman, Rebecca I. et al. (2010) Renal mass biopsy to guide treatment decisions for small incidental renal tumors: a cost-effectiveness analysis. Radiology 256(3): 836-46	- Not possible to calculate a contingency table from the data specified in the protocol
Park, Sung Yoon, Park, Byung Kwan, Kim, Chan Kyo et al. (2013) Ultrasound-guided core biopsy of small renal masses: diagnostic rate and limitations. Journal of vascular and interventional radiology : JVIR 24(1): 90-6	- Reference standard in study does not match that specified in protocol
Patel, Hiten D., Druskin, Sasha C., Rowe, Steven P. et al. (2017) Surgical histopathology for suspected oncocytoma on renal mass biopsy: a systematic review and meta-analysis. BJU international 119(5): 661-666	- Systematic review used as a source of primary studies, but not included as criteria did not match that specified in protocol
Patel, Hiten D., Johnson, Michael H., Pierorazio, Phillip M. et al. (2016) Diagnostic Accuracy and Risks of Biopsy in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma: Systematic Review of the Literature. The Journal of urology 195(5): 1340-1347	- Systematic review used as a source of primary studies, but not included as criteria did not match that specified in protocol
Paterson, Catherine, Ghaemi, Joseph, Alashkham, Abduelmenem et al. (2018) Diagnostic accuracy of image-guided biopsies in small (<4 cm) renal masses with implications for active surveillance: a systematic review of the evidence. The British journal of radiology 91(1090): 20170761	- Systematic review used as a source of primary studies, but not included as criteria did not match that specified in protocol

Study	Reason
Prince, J., Bultman, E., Hinshaw, L. et al. (2015) Patient and tumor characteristics can predict nondiagnostic renal mass biopsy findings. Journal of Urology 193(6): 1899	- Reference standard in study does not match that specified in protocol
Reichelt, Olaf, Gajda, Mieczyslaw, Chyhrai, Aliaksei et al. (2007) Ultrasound-guided biopsy of homogenous solid renal masses. European urology 52(5): 1421-6	- Reference standard in study does not match that specified in protocol
Richard, Patrick O., Jewett, Michael A. S., Bhatt, Jaimin R. et al. (2015) Renal Tumor Biopsy for Small Renal Masses: A Single-center 13-year Experience. European urology 68(6): 1007-13	- Reference standard in study does not match that specified in protocol *Not all underwent surgery. Follow-up data not available for all those that did not have surgery.*
Richter, F., Kasabian, N. G., Irwin, R. J., Jr. et al. (2000) Accuracy of diagnosis by guided biopsy of renal mass lesions classified indeterminate by imaging studies. Urology 55(3): 348-52	- Not possible to calculate a contingency table from the data specified in the protocol
Rybicki, Frank J., Shu, Kirstin M., Cibas, Edmund S. et al. (2003) Percutaneous biopsy of renal masses: sensitivity and negative predictive value stratified by clinical setting and size of masses. AJR. American journal of roentgenology 180(5): 1281-7	- Reference standard in study does not match that specified in protocol *Positive biopsy did not undergo surgery but were considered true positive*
Salem, Sepehr, Ponsky, Lee E., Abouassaly, Robert et al. (2013) Image-guided biopsy of small renal masses in the era of ablative therapies. International journal of urology : official journal of the Japanese Urological Association 20(6): 580-4	- Reference standard in study does not match that specified in protocol
Seager, Matthew J., Patel, Uday, Anderson, Christopher J. et al. (2018) Image-guided biopsy of small (<=4 cm) renal masses: the effect of size and anatomical location on biopsy success rate and complications. The British journal of radiology 91(1085): 20170666	- Reference standard in study does not match that specified in protocol *Some had thermal ablation and results do not separate from surgery participants*
Shah, Rajal B., Bakshi, Nasir, Hafez, Khaled S. et al. (2005) Image-guided biopsy in the evaluation of renal mass lesions in contemporary urological practice: indications, adequacy, clinical impact, and	- Reference standard in study does not match that specified in protocol

Study	Reason
limitations of the pathological diagnosis. Human pathology 36(12): 1309-15	
Siegel, C. (2012) Re: Outcomes of small renal mass needle core biopsy, nondiagnostic percutaneous biopsy, and the role of repeat biopsy. Journal of Urology 188(1): 66	- Editorial comment
Somani, Bhaskar Kumar, Nabi, Ghulam, Thorpe, Peter et al. (2007) Image-guided biopsy-diagnosed renal cell carcinoma: critical appraisal of technique and long-term follow-up. European urology 51(5): 1289-7	- Not possible to calculate a contingency table from the data specified in the protocol
Steil, S., Zerwas, S., Moos, G. et al. (2009) CT-guided percutaneous core needle biopsy in oncology outpatients: Sensitivity, specificity, complications. Onkologie 32(5): 254	- Reference standard in study does not match that specified in protocol
Sutherland, Edward L., Choromanska, Agnieszka, Al-Katib, Sayf et al. (2018) Outcomes of ultrasound guided renal mass biopsies. Journal of ultrasound 21(2): 99-104	- Reference standard in study does not match that specified in protocol
Ushijima, Yasuhiro, Nishie, Akihiro, Fujita, Nobuhiro et al. (2023) Diagnostic accuracy of percutaneous core biopsy before cryoablation for small-sized renal cell carcinoma. Diagnostic and interventional radiology (Ankara, Turkey) 29(6): 800-804	- Reference standard in study does not match that specified in protocol
Vasudevan, Arvind, Davies, Robert J., Shannon, Beverley A. et al. (2006) Incidental renal tumours: the frequency of benign lesions and the role of preoperative core biopsy. BJU international 97(5): 946-9	- Not possible to calculate a contingency table from the data specified in the protocol
Veltri, Andrea, Garetto, Irene, Tosetti, Irene et al. (2011) Diagnostic accuracy and clinical impact of imaging-guided needle biopsy of renal masses. Retrospective analysis on 150 cases. European radiology 21(2): 393-401	- Reference standard in study does not match that specified in protocol *Some participants received ablation and results do not separate from surgery participants*
Volpe, Alessandro, Mattar, Kamal, Finelli, Antonio et al. (2008) Contemporary results of percutaneous biopsy of 100 small renal masses: a single center experience. The Journal of urology 180(6): 2333-7	- Study does not contain any relevant index tests *Some participants had fine-needle aspiration and results not separated from core biopsies*

Study	Reason
Vu, Tuan, Shin, Benjamin, Mittal, Anisha et al. (2022) Ultrasound Versus Computed Tomography-Guided Native Parenchymal Kidney Biopsies for Hospitalized Patients: Comparison of Clinical Outcomes and Complications. Ultrasound quarterly 38(4): 328-333	- Reference standard in study does not match that specified in protocol
Walton, T. J., Amery, C., Moore, D. et al. (2012) Utility of renal mass biopsy in a UK tertiary referral centre. British Journal of Medical and Surgical Urology 5(5): 216	- Not possible to calculate a contingency table from the data specified in the protocol
Wang, Rou, Wolf, J. Stuart, Jr., Wood, David P., Jr. et al. (2009) Accuracy of percutaneous core biopsy in management of small renal masses. Urology 73(3): 586-1	- Reference standard in study does not match that specified in protocol *Some participants had ablation and results do not separate from surgery participants*
Wood, B. J., Khan, M. A., McGovern, F. et al. (1999) Imaging guided biopsy of renal masses: indications, accuracy and impact on clinical management. The Journal of urology 161(5): 1470-4	- Reference standard in study does not match that specified in protocol
Xu, Hongzhi, Taylor-Cho, Ian A., Sara Jiang, Xiaoyin et al. (2024) Diagnostic accuracy and clinical impact of renal biopsy cytology. Diagnostic cytopathology 52(9): 505-510	- Study does not contain any relevant index tests *Some participants had fine needle aspiration and results do not separate from core biopsy*
Yang, Chi-Shun, Choi, Euna, Idrees, Muhammad T. et al. (2017) Percutaneous biopsy of the renal mass: FNA or core needle biopsy?. Cancer cytopathology 125(6): 407-415	- Study does not contain any relevant index tests

Health economics studies

Economic references excluded at full text (n = 7)

Study	Reason
Dutta Rahul, Okhuvov Zhamshid, Vernez Simone L, et al. (2016) Cost Comparisons Between Different Techniques of Percutaneous Renal Biopsy for Small Renal Masses. J Endourol. 30 Suppl 1(Suppl 1):S28-33.	Inappropriate perspective (single centre in USA)
McAlpine Kristen, Sud Maneesh, Finelli Antonio, et al. (2022) Optimizing the	Not a cost utility study

Study	Reason
management of patients with small renal masses in a Canadian context: A Markov decision-analysis model. Can Urol Assoc J. 16(1):E32-E38.	
Pandharipandi Pari V, Gervis Debra A, Hartmann Rebecca I, et al. (2010) Renal mass biopsy to guide treatment decisions for small incidental renal tumors: a cost-effectiveness analysis. Radiology. 256(3):836-46.	Inappropriate perspective (USA)
Heilbrun Marta E, Yu Junhua, Smith Kenneth J, et al. (2012) The cost-effectiveness of immediate treatment, percutaneous biopsy and active surveillance for the diagnosis of the small solid renal mass: evidence from a Markov model. J Urol. 187(1):39-43.	Inappropriate perspective (USA)
Su Zhuo T, Patel Hiten D, Huang Mitchell M, et al (2021) Cost-effectiveness Analysis of ^{99m}Tc-sestamibi SPECT/CT to Guide Management of Small Renal Masses. Eur Urol Focus. 7(4):827-834.	Wrong intervention
Srivastava Abhishek, Uzzo Robert N, Lee Jennifer, et al. (2021) Renal mass biopsy: A strategy to reduce associated costs and morbidity when managing localized renal masses. Urol Oncol. 39(11):790.e9-790.e15.	Inappropriate perspective (USA), not a cost utility study
Wang Ye, Chen Yu-Wei, Leow Jeffery J, et al. (2016) Cost-effectiveness of Management Options for Small Renal Mass: A Systematic Review. Am J Clin Oncol. 39(5):484-90.	Systematic review of cost-effectiveness of management of small renal mass, no additional included studies were relevant

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Appendix K– Research recommendations – full details

The committee did not make any research recommendations for this topic.

Appendix L – Expert testimony

Section A:	
Name:	Professor Elena Pizzo
Role:	Academic
Institution:	Department of Primary Care and Population Health, UCL. 1-19 Torrington Place, London WC1E 7HB.
Guideline title:	Kidney cancer: diagnosis and management
Guideline Committee:	Guideline committee meeting 11 Day 2 (May 2025)
Subject of expert testimony:	Cost effectiveness of MIBI, biopsy or surgery in diagnosing T1 kidney cancer
Evidence gaps or uncertainties:	What is the clinical and cost effectiveness of core biopsy (compared with no biopsy) for suspected renal cell carcinoma?

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.

There are uncertainties regarding the accuracy, safety, and cost effectiveness of biopsy compared with no biopsy in adults with suspected RCC. Some solid renal masses are difficult to diagnose on imaging, which can lead to overtreatment of a benign tumour if they are removed surgically. A minimally invasive procedure such as a core biopsy of the tumour may be able to distinguish between malignant and benign tumours, and prevent unnecessary surgery. The likelihood of malignancy

increases with size of tumour. 30% of early-stage renal tumours are found to be benign on surgical histopathology, with overtreatment driven by a lack of pre-operative diagnostic tools.

Progression and recurrence of disease, and overall survival were important outcomes to look at as they would give an indication of the implications in practice of continuing with treatment following a positive index test. There were no test and treat studies identified for inclusion in the review.

Biopsy has not been routinely adopted everywhere and the committee reported great variation in practice across the country.

The committee reached a consensus that this review question should be prioritised for HE analysis to support a change in practice. There is potentially a high resource impact given the cost of biopsy and likely large population size who may benefit. Supportive evidence from economic modelling would optimise the use of biopsy and associated patient benefits, preventing misdiagnosis or delayed treatment, and can support business cases for its uptake.

The review of existing economic evidence found two non-UK studies which compared strategies containing biopsy and ablation in people with tumours of size less than 4cm who are not candidates for surgery. The committee considered the greatest economic and patient benefit of biopsy would be for the purpose of avoiding unnecessary surgery, which is associated with complications and decreased renal function over the lifetime; however, there was no relevant economic evidence comparing strategies containing biopsy and surgical options for treatment. The committee identified an ongoing study that modelled the cost-effectiveness of renal biopsy compared with empiric surgery to diagnose T1 tumours of size 2-7cm. The expert testimony is in relation to this economic study.

Section B:

Summary testimony:

The testimony related to a cost effectiveness analysis developed as part of a wider piece of work regarding the feasibility of 99m Tc-sestamibi CT/SPECT for diagnosing T1 kidney tumours in the UK. This was a multicentre trial run in 6 UK sites including 50 adult patients with a solid cT1 renal tumour 2-7cm. This comparator is out of scope of this review, but the cost effectiveness analysis conducted as part of the project was still considered relevant as it contained a comparison between two comparators under consideration, biopsy and no biopsy (empiric surgery).

A decision analytic model was developed to simulate a cohort of patients being diagnosed with T1 tumours. The model evaluated outcomes over the patient lifetime, from a UK NHS and PSS perspective. The model and assumptions were validated by clinicians and other clinical academics. The short-term part of the model consisted of a decision tree which evaluated immediate outcomes after diagnosis (true positive, false positive, true negative, false negative). Patients on empiric surgery by definition received treatment regardless of whether the tumour was benign or malignant; patients receiving biopsy would receive surgery if the result was positive and active surveillance if the result was negative, and indeterminate biopsy would require a second confirmatory biopsy. The long-term part of the model was a Markov model which predicted the rate at which patients experience local tumour recurrence, development of metastatic RCC or death, and differentiated outcomes depending on whether patients had an unoperated tumour or an operated tumour in the decision tree part of the model.

Modelled sensitivity and specificity for percutaneous core biopsy was estimated from a published systematic review and meta-analysis, Marconi et al. (2016), which estimated a 99.1% (95% CI 96.4–99.8%) sensitivity and 99.7% (95% CI 93.7–100%) specificity from 17 studies. The analysis included studies that had a range of median tumour sizes: 6 studies did not report tumour size, 3 of the studies had a median tumour diameter of more than 4cm and the remaining 8 studies had a median tumour diameter between 2 and 4cm.

The prevalence of cancer in T1 tumours was estimated as 82% from Fernando et al. (2016), an audit of 148 surgeons in 86 centres in the UK on 6,042

nephrectomies undertaken in 2012. Included costs were complications due to biopsy, the cost of biopsy and repeat biopsy, surgery, management of local recurrence and of metastasis. Costs were estimated in 2024 GBP using a micro-costing approach using NHS tariffs, BNF and PSSRU. QoL for model health states was estimated from published studies. Future costs and QALYs were discounted at 3.5%.

The model predicted that, in the first year, empiric surgery was associated with 180 unnecessary surgeries and 820 surgeries of malignant tumours per 1,000 patients, while biopsy only resulted in 2 unnecessary surgeries per 1,000 patients but slightly fewer surgeries of malignant tumours (813 per 1,000 patients). The predicted number of quality-adjusted life-years (QALY) gained by biopsy compared to empiric surgery was 0.497 per patient. The biopsy strategy was also associated with cost savings over the lifetime of £189 per patient compared to empiric surgery, due to fewer surgeries. Biopsy was also cost saving and improved survival and quality of life in the short-term. Therefore, biopsy was considered cost effective as it was the dominant strategy. Sensitivity analysis on sensitivity and specificity of the test did not change the cost-saving result and confirmed the robustness of the analysis.

References to other work or publications to support your testimony' (if applicable):

- Source of effectiveness evidence for MIBI: Warren et al. 2025 {99mTc}Tc-sestamibi SPECT/CT for the diagnosis of kidney tumours: A multi-centre feasibility study (under revision, Radiology)

- Source of effectiveness evidence for biopsy: Marconi L, Dabestani S, Lam T B, et al. (2016) Systematic Review and Meta-analysis of Diagnostic Accuracy of Percutaneous Renal Tumour Biopsy. Eur Urol Apr;69(4):660-673.

- Source of evidence for incidence rates: Fernando A. Fowler S., Brien TO. Nephron-sparing surgery across a nation-outcomes from the British

Association of Urological Surgeons 2012 national partial nephrectomy audit. BJU int. 2016;117:874-82
• **Disclosure:**
None

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