National Institute for Health and Care Excellence

Kidney cancer: diagnosis and management

[I1] Evidence review for CT and MRI for diagnosing renal lesions in adults with suspected renal cell carcinoma

NICE guideline [number]
Evidence review underpinning recommendations 1.2.1 to 1.2.4 and 1.2.7 to 1.2.8 in the NICE guideline

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1.1 Review questions

1. What is the clinical and cost effectiveness of CT compared with MRI for diagnosing renal lesions in adults with suspected renal cell carcinoma?

2. In adults with suspected renal cell carcinoma, what is the diagnostic accuracy and cost effectiveness of CT or MRI for diagnosing renal lesions?

1.1.1 Introduction

Early diagnosis of renal cell carcinoma (RCC) allows for the best chance of curative treatment, thereby reducing morbidity and mortality. Most instances of RCC are diagnosed incidentally. Contrast enhanced CT (CECT) or contrast enhanced MRI (CEMRI) are thought to be the most accurate imaging modalities for detecting malignancy, including in incidentally detected lesions. Additional imaging (for example, contrast enhanced ultrasound or 99mTc-Sestamibi SPECT/CT - see evidence review I2) may be required if contrast enhanced CT / MRI results are equivocal.

This review aims to investigate the diagnostic test accuracy of contrast enhanced CT and contrast enhanced MRI scans for detecting malignancy in people presenting with suspected renal cell carcinoma, using biopsy or histopathology from surgery as a reference standard.

1.1.2 Summary of the protocol

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

Population	Adults with suspected renal cell carcinoma (RCC) based on signs and symptoms
Index test	Computed Tomography (CT) scan
Comparator	Magnetic resonance imaging (MRI)
Outcomes	• Need for further imaging • Need for biopsy • Progressing directly to surgery • Overall survival • Quality of life
Study type	• Test and treat RCTs and systematic reviews of test and treat RCTs

CT: computed tomography; MRI: magnetic resonance imaging; RCT: randomised controlled trial; RCC: renal cell carcinoma

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

Population	Adults with suspected renal cell carcinoma (RCC) based on signs and symptoms
Index tests	Magnetic resonance imaging (MRI) Computed Tomography (CT) scan
Reference standard	Pathology confirmation of RCC from surgery or biopsy
Outcome measures and clinical outcomes	Diagnostic accuracy outcome measures • 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 or cohort studies.

CT: computed tomography; MRI: magnetic resonance imaging; RCC: renal cell carcinoma

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, the methods document and below.

1. Where meta-analysis could not be conducted for statistical reasons, sensitivity and specificity forest plots were obtained from Cochrane RevMan (version 8.16.0) and likelihood ratio forest plots were obtained from R using the mada package (RStudio version 2024.12.0). The range for the point estimates were presented in the results table as 95% confidence intervals for a pooled effect estimate could not be obtained in these instances.

2. The QUADAS-2 tool was used to assess the risk of bias of individual studies. Where a meta-analysis could not be conducted, individual studies reporting LR+ and LR- had equal weighting. Where ≥50% of the studies had some concerns in the risk of bias, the evidence was downgraded by one level and where ≥50% of the studies had high risk of bias the evidence was downgraded by two levels.

3. 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 by discussion. 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). The same method was used when a meta-analysis could not be conducted.

4. Based on committee input, where studies reported results from the index test as ‘indeterminate’, these results were combined with malignant results. The committee agreed that in their experience indeterminate results would be more likely to follow the

same diagnostic and treatment pathway as malignant results, rather than benign results. This decision affects 2 studies (Dechet et al. 2003 and Takebayashi et al. 1999).

5. Some studies reported multiple observations per person, where the person had more than one lesion. Observations from the same person are more likely to be correlated whilst observations from different people can be considered as statistically independent. Therefore, each person with multiple observations was considered as a cluster and measurements within a cluster are more likely to respond in a similar way (Gönen et al. 2001). It is difficult to assess the extent of the correlation and therefore combining data from clusters and individual patients could lead to an over estimation of statistical significance. For this reason, data for individual lesions were analysed separately from data reported for individual people.

6. Subgroup analyses were not carried out because the included studies did not report data in a format that could be used to carry out these analyses.

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

1.1.3.1 Search methods

The searches for the clinical effectiveness and diagnostic accuracy evidence were run on 24/10/2024 and re-run on 15/04/2025. The following databases were searched: Cochrane CENTRAL (Wiley), Cochrane CDSR (Wiley), Embase (Ovid), Epistemonikos (Epistemonikos), Medline ALL (Ovid). Limits were applied to remove animal studies, conference abstracts, editorials, letters, news items and commentaries, as well as papers not published in the English language. Filters were used to limit to OECD countries, systematic reviews, randomised controlled trials, observational studies and diagnosis studies.

The searches for the cost effectiveness evidence were run on 30/10/2024 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.

One search was developed to cover both review I1 (this review) and I2 (on other types of imaging). 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

We used MetaDTA based on the R glmer package instead of the mada package due to NICE methods changing after the protocol was written.

1.1.4 Effectiveness and diagnostic evidence

1.1.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 6,688 references (see appendix B for the literature search strategy).

These 6,688 references were screened at title and abstract level against the review protocol, with 6,585 excluded at this level. 10% of references were screened separately by two reviewers with 99.7% agreement. Discrepancies were resolved by discussion.

The full texts of 103 references were ordered for closer inspection. Seven of these studies met the criteria specified in the review protocol (appendix A). All 7 studies were diagnostic studies (retrospective cohorts) and no effectiveness studies were identified. For a summary of the included studies see Table 3. The clinical evidence study selection is presented as a PRISMA diagram in appendix C.

See section 1.1.12 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	Location/ Funding	Population	Index test	Reference test	Target condition definition	Risk of bias
Baldari (2015) N= 29 people with 31 renal masses	Location: Italy Funding source: Not reported	People with histological or cytological diagnoses of renal masses, who underwent CT and MRI in the same week	• Contrast-enhanced CT • Contrast-enhanced MRI	Pathological confirmation after surgical intervention	Malignant: based on structural characteristics according to the following scores 2, 3b, 5 and 6, irregular margins (score 1) and/or of the presence of significant contrast enhancement (score 1), fat and/or vascular structures infiltration (score 1). Benign: based on structural characteristics according to the following scores 1, 3a, 4 and 7, as well as on the margin regularity (score 0), absence of significant contrast enhancement (score 0), fat and vascular structures infiltration (score 0).	Moderate
Dechet (2003) N= 100 people. Only 81 people analysed	Location: USA Funding source: Not reported	People diagnosed with a solid mass who were awaiting surgery	• CT	Pathological confirmation after surgical intervention	Lesions were categorised as malignant, benign or non-diagnostic based on results suspicious for, consistent with or indicative of malignancy or benign tumours Malignant included: RCC, transitional cell carcinoma, collecting duct tumour, neuroendocrine tumour, metastatic thyroid carcinoma Benign included: Oncocytoma, angiomyolipoma, cyst, pyelonephritis, solitary fibrous tumour	High

Study details	Location/ Funding	Population	Index test	Reference test	Target condition definition	Risk of bias
Kim (2023) N= 410 people	Location: Korea Funding source: Not reported	People who had undergone partial and radial nephrectomy and had both CT and MRI scans	• Contrast-enhanced CT • Contrast-enhanced MRI	Pathological confirmation after surgical intervention	Only the first report considered to assess malignancy if multiple results were found on scans. Malignant lesions included: clear cell RCC, chromophobe RCC, papillary RCC (type 1, type 2 and unclassified), MiT family translocation RCC, mixed epithelial and stromal tumour and unclassified RCC Benign lesions included: angiomyolipoma, oncocytoma, multilocular cystic renal neoplasm, simple cortical cyst, localised cystic disease, lymphoid tissue	High
Kutman (2013) N= 149 people	Location: Turkey Funding source: Not reported	People with a renal tumour	Contrast-enhanced CT	Pathological confirmation after surgical intervention	Degree of tumour enhancement was determined by measuring attenuation of 3 regions of interest and mean calculated. Cut off was 138HU.	High
Marschner (2020) N= 255 people Only 124 analysed (88 had CT and 36 had MRI)	Location: Germany Funding source: Not reported	People with an unclear cystic or solid renal mass in preliminary imaging	• Contrast-enhanced CT • Contrast-enhanced MRI	• Pathological confirmation after surgical intervention • Biopsy	Inconclusive findings from the first CT or MRI were adjusted to the findings of CEUS examination, which were evaluated as benign or malignant based on established qualitative image parameters. Malignant lesions included: clear cell RCC, papillary RCC, chromophobe RCC, combined clear cell and papillary RCC and other malignant lesions such as metastases	Moderate

Study details	Location/ Funding	Population	Index test	Reference test	Target condition definition	Risk of bias
					Benign lesions included: Angiomyolipoma, oncocytomas, benign renal cysts and other benign lesions such as renal adenomas	
Monn (2015) N= 120 people	Location: USA Funding source: Not reported	Adults undergoing nephrectomy who had had a preoperative multiphasic CT scan	Contrast-enhanced CT (multiphasic)	Pathological confirmation after surgical intervention	A standardised computer questionnaire was generated with questions focusing on whether the tumour was interpreted as benign or malignant and, if malignant, whether it was clear-cell RCC or an alternative histology. Reviewers had access to all sequences and standard radiographic tools including HU measurements. Malignant lesions included: Clear cell RCC, papillary RCC, chromophobe RCC and unclassified. Benign lesions were: Angiomyolipoma, oncocytoma and others	High
Takebayashi (1999) N= 23 people with 225 lesions	Location: Japan Funding source: Not reported	People undergoing haemodialysis, who underwent nephrectomy for suspected renal cell carcinoma	Contrast-enhanced CT	Pathological confirmation after surgical intervention	Not reported	High

CT: computed tomography; HU: Hounsfield unit; MiT: microphthalmia; MRI: magnetic resonance imaging; RCC: renal cell carcinoma

See appendix D for full evidence tables.

1.1.6 Summary of the diagnostic evidence

The interpretation of the diagnostic ability of each index test was based on the thresholds listed in the methods document. Where the positive likelihood ratio value is more than 1 it shows an increase in probability of a positive result in a person with the condition (a malignant tumour) compared to a person without. Where the negative likelihood ratio is any value less than 1 it shows a decrease in likelihood that a person with the condition (a malignant tumour) will have a negative result compared to someone without the condition.

See appendix F for full GRADE tables.

Table 4: Summary of findings for diagnostic accuracy of CT (person as unit of analysis) for suspected renal cell carcinoma

Number of studies	Outcome	Sample size	Effect estimate (95% CI)	Certainty	Interpretation of diagnostic ability
5 (Dechet 2003, Kim 2023, Kutman 2013, Marschner 2020, Monn 2015)	Diagnostic accuracy (malignant versus benign)	1289 (848 counting multiple interpretation studies only once)	LR + 1.58 (1.24, 2.00)	VERY LOW	Slight increase in probability of disease
			LR – 0.13 (0.06, 0.29)	VERY LOW	Large decrease in probability of disease

CI: confidence interval; LR: likelihood ratio

Reasons for downgrading can be found in the full GRADE tables in appendix F.

Table 5: Summary of findings for diagnostic accuracy of CT (lesion as unit of analysis) for suspected renal cell carcinoma

Number of studies	Outcome	Sample size	Effect estimate (95% CI)	Certainty	Interpretation of diagnostic ability
1 (Baldari 2015)	Diagnostic accuracy (malignant versus benign)	29 (31 lesions)	LR + 2.67 (1.09, 6.52)	VERY LOW	Moderate increase in probability of disease
			LR – 0.03 (0.00, 0.56)	VERY LOW	Very large decrease in probability of disease

CI: confidence interval; LR: likelihood ratio

Reasons for downgrading can be found in the full GRADE tables in appendix F.

Table 6: Summary of findings for diagnostic accuracy of CT – population of people on haemodialysis (lesion as unit of analysis) for suspected renal cell carcinoma

Number of studies	Outcome	Sample size	Effect estimate (95% CI)	Certainty	Interpretation of diagnostic ability
1 (Takebayashi 1999)	Diagnostic accuracy (malignant versus benign)	23 (225 lesions)	LR + 38.53 (16.15, 91.92)	VERY LOW	Very large increase in probability of disease
			LR – 0.04 (0.01, 0.29)	VERY LOW	Very large decrease in probability of disease

CI: confidence interval; LR: likelihood ratio

Reasons for downgrading can be found in the full GRADE tables in appendix F.

Table 7: Summary of findings for diagnostic accuracy of MRI (person as unit of analysis) for suspected renal cell carcinoma

Number of studies	Outcome	Sample size	Effect estimate range[1]	Certainty	Interpretation of diagnostic ability
2 (Kim 2023, Marschner 2020)	Diagnostic accuracy	446	LR+ 1.44 – 3.86	VERY LOW	Slight to moderate increase in probability of disease
			LR – 0.05 – 0.24	VERY LOW	Moderate to very large to decrease in probability of disease

CI: confidence interval; LR: likelihood ratio

Reasons for downgrading can be found in the full GRADE tables in appendix F.

1. A bivariate meta-analysis could not be conducted due to the low number of studies, so the range has been presented for the effect estimates.

Table 8: Summary of findings for diagnostic accuracy of MRI (lesion as unit of analysis) for suspected renal cell carcinoma

Number of studies	Outcome	Sample size	Effect estimate (95% CI)	Certainty	Interpretation of diagnostic ability
1 (Baldari 2015)	Diagnostic accuracy (malignant versus benign)	29 (31 lesions)	LR + 2.67 (1.08, 6.50)	VERY LOW	Moderate increase in probability of disease
			LR – 0.03 (0.00, 0.56)	VERY LOW	Very large decrease in probability of disease

CI: confidence interval; LR: likelihood ratio

Reasons for downgrading can be found in the full GRADE tables in appendix F.

1.1.7 Economic evidence

A single literature search was conducted to identify published economic evaluations of relevance to the review questions on imaging for diagnosis of renal lesions in this guideline, which included evidence review I1 for CT and MRI (this review) and evidence review I2 for additional imaging tests (see appendix B for the search strategy).

This search retrieved 182 studies, and based on title and abstract screening seven studies were identified as potentially relevant for either review I1 and I2 on imaging for diagnosis of renal lesions. On review of the full text, one study was included for evidence review I2, and six studies were excluded. For details on study selection, see economic study selection flow chart in appendix G.

1.1.7.1 Included studies

No economic studies were included for I1 for CT and MRI. One economic study was included for I2 for additional imaging tests (see evidence review I2 for details).

1.1.7.2 Excluded studies

Six studies were excluded at full text review (see appendix J for a list of excluded economic studies at full text with reasons for exclusion).

1.1.8 Economic model

No original economic modelling was conducted for this review.

1.1.9 Unit costs

Unit costs of imaging are provided in Table 9 to aid committee deliberations around cost-effectiveness

Table 9: Unit costs of imaging

Resource	Unit costs	Source
CT of one area, with contrast	£146	NHS Cost Collection (2024), HRG code RD22Z Computerised Tomography Scan of One Area, with Pre- and Post-Contrast, 19 years and over
CT-CAP, with contrast	£123	NHS Cost Collection (2024), HRG code RD26Z Computerised Tomography Scan of Three Areas, with Contrast
MRI of one area, without contrast	£165	NHS Cost Collection (2024), HRG code RD01A Magnetic Resonance Imaging Scan of One Area, without Contrast
MRI of one area, with contrast	£199	NHS Cost Collection (2024), HRG code RD03Z Magnetic Resonance Imaging Scan of One Area, with Pre- and Post-Contrast

Resource	Unit costs	Source
MRI of two or three areas, without contrast	£154	NHS Cost Collection (2024), HRG code RD04Z Magnetic Resonance Imaging Scan of Two or Three Areas, without Contrast
MRI of two or three areas, with contrast	£202	NHS Cost Collection (2024), HRG code RD05Z Magnetic Resonance Imaging Scan of Two or Three Areas, with Contrast

CT-CAP, CT of chest, abdomen and pelvis

1.1.10 The committee's discussion and interpretation of the evidence

1.1.10.1. The outcomes that matter most

The committee agreed that likelihood ratios were the critical diagnostic accuracy outcome measures of interest for this review. Likelihood ratios provide information on how much more or less likely a given test result (positive or negative) is in someone with renal cell carcinoma compared to someone without it. For more detail about what information likelihood ratios provide, see the methods document. They also considered sensitivity and specificity important, and so assessed these as secondary measures. Sensitivity and specificity provide information on how well the index test would accurately identify those with renal cell carcinoma and those without. Likelihood ratios were chosen as the primary measure of interest for decision making.

The committee discussed the consequences of false positive and false negative results with imaging using contrast enhanced CT (CECT) or contrast enhanced MRI (CEMRI). They noted that false positive results of the index test may lead to overtreatment via unnecessary surgery with potentially negative effects on a person's health from the side effects of the surgery and consequences of the surgery, in particular relating to a reduction in renal function. A false negative result of the index test may mean that a malignancy is overlooked with the risk of delayed diagnosis increasing the risk of the disease spreading, especially where surveillance is not conducted. But the committee noted that false negative results are rare in practice, as CT imaging tests are very sensitive in identifying RCCs.

The committee also briefly discussed the clinical outcomes from test and treat studies that would be particularly important for this review. These included the need for further imaging, the need for biopsy, progressing directly to surgery, overall survival and quality of life because these would provide information about the impact of receiving treatment following a positive index test. However, there were no test and treat studies identified in this review.

1.1.10.2 The certainty of the evidence

The evidence was rated as very low certainty for both CECT and CEMRI. The evidence was assessed for risk of bias using the QUADAS-2 tool. The reasons for downgrading for risk of bias were often due to insufficient information on how participants were selected into the study, and concerns around whether the interpreters of the reference standard test had knowledge of the index test results. Some of the evidence was downgraded for inconsistency as the point estimates for some studies lay outside the confidence interval of other studies. Downgrading for imprecision occurred when the confidence intervals crossed one or more

decision making thresholds, which were 1 and 2 for positive likelihood ratios and 0.5 and 1 for negative likelihood ratios.

Some of the evidence was downgraded for indirectness because the participants in the included study or studies did not fully represent the population in the protocol. The participants in 5 studies (Dechet et al. 2003, Kim et al. 2023, Kutman et al. 2013, Monn et al. 2015 and Takebayashi et al.1999) only included people who had surgery. While this meets the conditions of the protocol and the committee recognised that the studies would have been constrained by clinical practice, they acknowledged that the exclusion of people who had the index test but who did not proceed to surgery would likely have increased the prevalence of cancer in the sample of the included studies, compared with the population of interest. This could have affected the results of the studies.

The committee agreed that the population in one study (Takebayashi et al. 1999) was very different from the wider population covered by the review as it included people receiving haemodialysis. They noted that these people were likely to have a much higher incidence of renal cell carcinoma, so results from this study have been analysed separately.

The committee discussed the evidence in the review and noted that none of the included studies were from a UK population. However, they agreed that the evidence is still relevant as the studies included were from OECD countries. The committee also recognised that practice has changed over the past 20 years due to technical improvement in ultrasound, CT and MRI, such that lesion identification and characterisation is likely to be more accurate. However, they agreed that there was no clear cut off point for dates and the changes would not be significant enough to justify excluding older studies.

None of the planned subgroup analyses were carried out for this review because the included studies did not report data for the subgroups of interest in a format that could be used to carry out these analyses.

1.1.10.3 Benefits and harms

The committee noted that the evidence from this review complemented the findings from the review on the diagnostic accuracy of imaging using contrast-enhanced ultrasound (CEUS) and ^{99m}Tc-sestamibi SPECT/CT, reported in evidence review I2. The recommendations in the section on diagnosis in the guideline were based on the evidence from both reviews. The discussion below covers the recommendations that were made based on the evidence in this review, while the recommendations made for imaging using CEUS or ^{99m}Tc-sestamibi SPECT/CT are covered in review I2.

The committee examined the diagnostic accuracy outcome results for CT and noted that six out of the included seven studies looked at contrast enhanced CT (CECT), while the remaining one looked at CT and did not mention contrast enhancement (Dechet et al. 2003). The findings from this study were assessed in comparison with other studies looking at CECT and the results were not considered sufficiently different based on visual inspection of the forest plots (Figure 2 to Figure 5). Therefore, the committee judged that removing the CT only study was unlikely to meaningfully change results, and they focused on the CECT evidence for making recommendations.

For analysis by person, the likelihood ratios showed a slight increase in probability of having RCC given a positive test and a large decrease in the probability of having RCC given a

negative test, and the evidence was very low certainty (See appendix F for full GRADE tables.

Table 4). For the analysis by lesion, the likelihood ratios showed a moderate increase in the probability of having RCC given a positive test and a very large decrease in the probability of having RCC given a negative test, and the evidence was very low certainty (Table 13). Moreover, for analysis by lesion in a population on haemodialysis, there was a very large increase in the probability of having RCC given a positive test, and very large decrease in the probability of having RCC given a negative test, and the evidence was very low certainty (Table 14). Similarly, the sensitivity and specificity evidence were discussed and the committee agreed that CT is good at identifying those with RCC (high sensitivity) but may not be as good at identifying those without and may rule in a reasonable number of people without RCC (low specificity).

The evidence for MRI came from 3 studies that all looked at CEMRI. For analysis by person, the likelihood ratios showed a slight-to-moderate increase in probability of having RCC given a positive test and a moderate-to-very large decrease in probability of having RCC given a negative test result, and the evidence was very low certainty (Table 15). For analysis by lesion numbers, the likelihood ratios showed a moderate increase in probability of having RCC given a positive test and a very large decrease in the probability of having RCC given a negative test, and the evidence was very low certainty (Table 16). The sensitivity and specificity evidence were discussed and the committee agreed that MRI is good at identifying those with renal cell carcinoma (high sensitivity) but may not be as good at identifying those without and may rule in a reasonable number of people without RCC (low specificity). However, they noted the limitations associated with using an MRI in practice, which included limited availability of machines, cost and that the time taken to complete each MRI scan (up to 45 minutes) is longer than for a CT scan. They therefore agreed that although CECT and MRI have similar diagnostic accuracy for the detection of RCC, they would recommend CECT as the preferred option for diagnostic imaging for the reasons listed above.

The committee discussed the different types of CT imaging including CT without contrast, CECT and multiphasic CECT. Based on their knowledge and experience, they agreed that triple-phase (multiphasic) CECT provides a more detailed imaging result when compared with other types of CT by showing the enhancement at different timepoints. The enhancement on a triple-phase CT can be used to provide information about the type of lesion, for example a clear cell RCC will enhance avidly on the arterial phase and a papillary RCC will enhance more gradually and to a lesser degree. Therefore, based on the very low certainty evidence and their experience, they recommended that people referred for suspicion of RCC, which could either be via an incidental finding or clinical suspicion, should be offered a triple-phase CECT of the abdomen. The committee acknowledged that there may be people who are unable to have a CECT for reasons such as allergies to the contrast agent used or reduced renal function and discussed alternative options. The committee agreed that based on the evidence and their experience, MRI of the abdomen would be the best alternative option to offer to these people and that ideally it would be carried out with a contrast agent. They made a recommendation to reflect this. This decision was based on consensus among the committee members and an understanding of the availability of different imaging modalities in the UK.

The committee were aware of other related NICE guidance on point-of-care creatinine devices to assess kidney function before CT imaging with intravenous contrast media, and on assessing risk and avoiding acute kidney injury in adults having iodine-based contrast

media in NICE's guidance on acute kidney injury. They included cross references to this guidance.

The committee noted that in some cases, there may be uncertainty about whether a lesion is malignant or benign following triple phase CECT imaging. Based on the evidence and their experience, the committee recommended that in these situations MRI, ideally with contrast, should be offered. As CECT and MRI function differently and have different strengths in terms of the information they provide, this could supplement information from the CECT on the nature of the lesion and support decisions about further testing or treatment. Where a suspected RCC is detected on CECT or MRI, they recommended, based on their experience and expertise, that CECT of the chest and pelvis or, for people who are unable to have CECT, MRI of the pelvis and CT (without contrast) of the chest should be offered to complete staging. However, they agreed that by offering MRI after CECT or where CECT is not suitable this should mean that the population of people undergoing an MRI scan should remain relatively small as per current practice.

The committee discussed what happens when the result of the imaging from CECT or MRI (with or without contrast) indicate that a malignancy is likely to be present or where there is uncertainty around the nature of the lesion. They agreed that potential next steps include additional imaging (see evidence review I2 on contrast enhanced ultrasound or 99mTc-Sestamibi SPECT/CT), biopsy, a surgical or non- surgical intervention, or active surveillance. They agreed that the decision on what to do next will also depend on the nature of the tumour, patient's preference and health status, and clinician's judgement, and agreed that this decision will require input from various health practitioners including radiologists, urologists, oncologists and other clinicians as well as the patient themselves. Therefore, they agreed that a multidisciplinary team discussion will be required to ensure that the best possible courses of action and next steps are determined following a malignant or uncertain result and made a recommendation to reflect this.

The committee discussed the next steps in decision making that occur when the results of CECT, MRI or CEMRI suggest a benign lesion. They noted that it is often not possible to conclusively determine from imaging results whether a tumour is benign or malignant and from their experiences additional imaging or biopsy may be required to increase their levels of certainty. The exception to this is in cases where the result shows clearly that the lesion is not a solid mass or a Bosniak 2F, 3 or 4 cyst. They agreed that if the result of the CECT, MRI or CEMRI imaging clearly shows that the lesion is benign, such as a simple cyst (Bosniak 1 or 2) or angiomyolipoma, a multidisciplinary team discussion may not be necessary, and they recommended that the person should be discharged if they are not at high risk of complications. However, the committee noted that there may be reasons why people with benign lesions are referred for further monitoring instead of being discharged. For example, a person with a Bosniak 1 or 2 cyst which causes pain may be at risk of complications and may not be discharged but monitored for a period. In addition, women, trans men and non-binary people registered female at birth who are of childbearing age and have an angiomyolipoma may also be at higher risk of complications and need additional monitoring.

The committee discussed how diagnosis using imaging affects the psychological state of people with suspected RCC. They acknowledged that waiting for the results of a scan can be very stressful for people with suspected RCC and that uncertain scan results may increase their anxiety. The committee agreed that informing the person of the results as soon as possible may be beneficial to their psychological state. However, they noted that it may not be possible to tell people about the results of a scan before an MDT discussion because the time period between when the scan results are available and when the MDT discussion

happens is usually very tight in order to meet the 28 Day Faster Diagnosis Standard. In addition, the results of the imaging are only part of the MDT discussion about suitable treatment options. The committee agreed that it is more appropriate to wait until after the multidisciplinary team meeting to hold a discussion with the person with suspected RCC about their imaging results, whether further imaging or biopsy is needed and possible care options. They agreed that it is important that people with suspected RCC are able to make informed decisions and were aware of the recommendations in NICE's shared decision-making process guideline that support this goal.

No test and treat RCTs were identified to inform the effectiveness review question, indicating a gap in the evidence. However, the committee were confident that, at the early stages of disease detection, test accuracy would have an effect on clinical outcomes and therefore agreed that testing the link between test accuracy and clinical outcomes was not necessary. This, combined with the difficulty of running test and treat trials, and the sufficiency of DTA evidence available, meant the committee agreed not to make a research recommendation for test and treat studies for this topic.

1.1.10.4 Cost effectiveness and resource use

No economic evaluations were identified which addressed the cost-effectiveness of MRI or CT imaging for diagnosis of renal lesions.

The committee were presented with the unit costs of different imaging modalities and noted that MRI is more expensive than CT. The committee recommended triple phase CECT to detect lesions. The committee specified that CECT of the abdomen would usually be enough to detect whether or not a lesion was present. GIRFT recommends that this includes non-contrast, arterial and venous phases, and so a unit cost of pre- and post-contrast CECT was presented. If a lesion is present, CT of the chest and pelvis should then be offered in order to complete staging. There are no costs for CECT of three areas that are specific to triple phase imaging, and the unit cost of CT-CAP likely includes a proportion of imaging procedures that are not multi-phasic, and may therefore underrepresent the unit cost for triple phase CT-CAP to some extent.

The committee recommended CT over MRI, given CT is cheaper, more widely available and more time efficient than MRI. Both CT and MRI are good at identifying people with RCC and particularly are good for ruling out malignancy in people with a negative test result, which are costly due to managing disease at a more advanced stage and have highly negative impacts to the person's health. CT and MRI may rule in some people without RCC. Downstream consequences of false positive results are likely to be unnecessary treatments, which have a high cost to the NHS and to the patient, and also can have negative effects on a person's health from the side effects and consequences of the surgery, in particular relating to a reduction in renal function.

The committee expressed concerns about the availability of MRI machines across the UK and the cost of using MRI for diagnosis. They noted that CT machines are more widely available, less expensive to use and more time efficient as the time taken to carry out a CT scan is much shorter than for an MRI.

The recommendations made are unlikely to increase resource use as they are broadly aligned with current practice and are expected to encourage standardisation of practice.

1.1.10.5 Other factors the committee took into account

The committee discussed the definition of the term “indeterminate” which is used in some of the included studies. The committee agreed that using the term “indeterminate” could be confusing as for some healthcare professionals it could be used to refer to a lesion where it was unclear if the person had cancer or not whilst other healthcare professionals may use the term to refer to difficulty in establishing enhancement or if a lesion is solid or cystic. The committee agreed to not use the term “indeterminate” when referring to lesions that are unclear.

The committee discussed whether any specific equality issues applied to CT or MRI imaging for diagnosis of RCC and whether any specific population groups could be disadvantaged by the recommendations. Most of the issues identified in the equality and health inequalities assessment (EHIA) were societal in nature and focused on non-kidney cancer or imaging specific issues to do with access for populations such as older adults, disabled people and people with lower socio-economic status. However, the committee noted that CT and MRI scanners have an upper weight limit due to safety concerns and the design of the equipment, therefore people with very high weight may have reduced options available for imaging. In these cases, the committee agreed that the person with suspected RCC could be considered for an ultrasound scan instead (see review I2 on additional imaging for a recommendation that covers contrast enhanced ultrasound, CEUS, for people who cannot have CECT or CEMRI).

1.1.11 Recommendations supported by this evidence review

This evidence review supports recommendations 1.2.1 to 1.2.4, 1.2.7 to 1.2.8 and the research recommendations on imaging to differentiate between solid and cystic lesions, and imaging combinations and sequences of novel diagnostic approaches. Both these research recommendations are described in detail in review I2.

1.1.12 References – included studies

1.1.12.1 Diagnostic

Baldari, Diana, Capece, Sergio, Mainenti, Pier Paolo et al. (2015) Comparison between computed tomography multislice and high-field magnetic resonance in the diagnostic evaluation of patients with renal masses. Quantitative imaging in medicine and surgery 5(5): 691-9

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

Kim, Jinu, Lee, Jong Soo, Jo, Youngheun et al. (2023) Superiority of magnetic resonance imaging in small renal mass diagnosis where image reports mismatches between computed tomography and magnetic resonance imaging. Investigative and clinical urology 64(2): 148-153

Kutman, Kerem, Suer, Evren, Beduk, Yasar et al. (2013) Is there a role of the enhancement degree of the lesion on computerized tomography for the characterization of renal tumors?. The Journal of urology 189(2): 436-40

Marschner, Constantin Arndt, Ruebenthaler, Johannes, Schwarze, Vincent et al. (2020) Comparison of computed tomography (CT), magnetic resonance imaging (MRI) and contrast-enhanced ultrasound (CEUS) in the evaluation of unclear renal lesions. RoFo : Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin 192(11): 1053-1059

Monn, M Francesca, Gellhaus, Paul T, Patel, Aashish A et al. (2015) Can radiologists and urologists reliably determine renal mass histology using standard preoperative computed tomography imaging?. Journal of endourology 29(4): 391-6

Takebayashi, S, Hidai, H, Chiba, T et al. (1999) Using helical CT to evaluate renal cell carcinoma in patients undergoing hemodialysis: value of early enhanced images. AJR. American journal of roentgenology 172(2): 429-33

1.1.12.2 Economic

No economic evidence was included.

1.1.13 References – other

Gönen M, Panageas KS, Larson SM. (2001) Statistical issues in analysis of diagnostic imaging experiments with multiple observations per patient. Br J Radiol. 221(3): 763-7

MetaDTA tool is described in the below papers:

Patel A, Cooper NJ, Freeman SC, Sutton AJ. Graphical enhancements to summary receiver operating characteristic plots to facilitate the analysis and reporting of meta-analysis of diagnostic test accuracy data. Research Synthesis Methods 2020, https://doi.org/10.1002/jrsm.1439.

Freeman SC, Kerby CR, Patel A, Cooper NJ, Quinn T, Sutton AJ. Development of an interactive web-based tool to conduct and interrogate meta-analysis of diagnostic test accuracy studies: MetaDTA. BMC Medical Research Methodology 2019; 19: 81 which can be accessed at MetaDTA version 1.27.

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

Diagnostic test accuracy review protocol for CT and MRI for diagnosing renal lesions in adults with suspected renal cell carcinoma

Table 10: Review Protocol

ID	Field	Content
1.	Review title	Accuracy and cost effectiveness of CT and MRI for diagnosing renal lesions in adults with suspected renal cell carcinoma (RCC)
2.	Review questions	• What is the clinical and cost effectiveness of CT compared with MRI for diagnosing renal lesions in adults with suspected renal cell carcinoma? (test and treat review) • In adults with suspected renal cell carcinoma, what is the diagnostic accuracy and cost effectiveness of: o CT o MRI for diagnosing renal lesions? (diagnostic accuracy)
3.	Objective	To evaluate and compare the clinical effectiveness, accuracy and cost effectiveness of CT and MRI for diagnosing renal lesions in adults with 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 • Epistemonikos 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 suspected RCC based on signs and symptoms
7.	Index test	• Magnetic Resonance Imaging (MRI) • Computed Tomography (CT) scan
8.	Reference standard	• Pathological confirmation of RCC from surgery or biopsy
9.	Types of study to be included	• Diagnostic accuracy cross-sectional studies and cohort studies. • Systematic reviews of diagnostic accuracy cross-sectional or cohort studies. • Where there are no cross-sectional or cohort studies identified, case-control studies will be included. • Test and treat RCTs and SRs of test and treat RCTs
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. A timely and accurate diagnosis of RCC is important for guiding treatment and improving patient's outcomes. Imaging approaches such as MRI and CT, are commonly used to evaluate solid renal mass or complex cysts. This review aims to compare the clinical effectiveness, diagnostic accuracy and cost-effectiveness of CT and MRI in suspected RCC.
12.	Outcomes	Diagnostic accuracy outcomes:

		• Sensitivity and specificity
		• Positive and negative likelihood ratios
		
		Clinical outcomes (for test and treat studies):
		• Need for further imaging (dichotomous outcome)
		• Need for biopsy (dichotomous outcome)
		• Progressing directly to surgery (dichotomous outcome)
		• Overall survival (time to event data)
		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.
		• 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)
		
		Minimal important differences
		Any statistically significant difference will be used for the following outcomes:
		• Need for further imaging
		• Need for biopsy
		• Overall survival
		• Quality of life using EORTC QLQ-C30
		
		MIDs for the following quality of life measure was identified in the literature:
		EQ-5D: 0.08 for UK-based scores and 0.07 for VAS scores

13.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.2). Study investigators may be contacted for missing data where time and resources allow. This review may make use of the priority screening functionality within the EPPI-reviewer software. If priority screening is used, the following rules will be adopted to determine when to stop screening: • at least 50% of the identified abstracts (or 1,000 records, if that is a greater number) will be screened. • After this point, screening is only terminated if a threshold of 750 is met for a number of abstracts being screened without a single new include being identified.

		• if sifting is terminated before the full database has been looked at additional checks will be carried out to ensure that relevant studies have not been missed.
14.	Risk of bias (quality) assessment	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 fitted 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. GRADE will be carried out on the LR results, but the results for sensitivity and specificity will also be presented. 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: • age, • tumour/complex cyst size, • location and complexity of the tumours/complex cysts, • renal function at baseline, and • performance status of the person at baseline (e.g., ECOG and Karnofsky).
17.	Type and method of review	Intervention X Diagnostic Prognostic Qualitative Epidemiologic Service Delivery Other (please specify)
18.	Language	English

<table>
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<tr><td>21.</td><td>Anticipated completion date</td><td colspan="3">March 2026</td></tr>
<tr><td rowspan="7">22.</td><td rowspan="7">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>23.</td><td>Named contact</td><td colspan="3">5a. Named contact
Centre for Guidelines, NICE

5b Named contact e-mail
kidneycancerguideline@nice.org.uk

5e Organisational affiliation of the review
National Institute for Health and Care Excellence (NICE) and Guideline Development Team.</td></tr>
<tr><td>24.</td><td>Review team members</td><td colspan="3">From the Guideline Development Team:
Steve Sharp, Technical adviser
Marie Harrisingh, Technical adviser
Sarah Boyce, Senior technical analyst
Fernando Zanghelini, Technical analyst
Adefisayo Abba-Abba, Technical Analyst
Olivia Crane, Senior technical analyst
Lucy Beggs, Health economics adviser
Hannah Tebbs, Health economist
Yuanyuan Zhang, Health economist
Amy Finnegan, Senior Information specialist</td></tr>
<tr><td>25.</td><td>Funding sources/sponsor</td><td colspan="3">This systematic review is being completed by the Guideline Development Team which receives funding from NICE.</td></tr>
<tr><td>26.</td><td>Conflicts of interest</td><td colspan="3">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</td></tr>
</table>

		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 X 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

Economic review protocol

Table 11: Economic review protocol

ID	Field	Content
1.	Review titles	I1: Cost effectiveness of CT and MRI for diagnosing renal lesions in adults with suspected renal cell carcinoma I2: Cost effectiveness of additional imaging tests for diagnosing renal lesions in adults who have had CT or MRI for suspected renal cell carcinoma
2.	Objective	To identify economic studies for the review to evaluate the accuracy of CT and MRI for diagnosing renal lesions in adults with suspected RCC

3.	Inclusion criteria	• Populations, interventions and comparators as specified in the diagnostic accuracy 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.
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 RCC. • Studies only focussing on productivity losses or gains.
5.	Search strategy	An economic study search will be undertaken using question-specific terms and an 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

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:

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 searches documented in this appendix covered both review I1 and review I2.

In Medline and Embase, for the clinical searches, the strategy was split into two. The first set searched for population and intervention on title only, without applying study limits. This was

used to retrieve relevant diagnostic studies that were not identified by the search filters. The second part of the search limited the population and intervention (on title and abstract) by study filters (randomised controlled trials, diagnostic studies and the amended observational filter). Both sets were combined using OR at the end of the search. For databases where this approach was not used, the population terms were searched for on title and abstract. In Epistemonikos, the search was limited to retrieving systematic reviews.

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.

To manage the total number of results retrieved and improve the precision of the search, subject headings were focused. This approach was taken as the risk of missing a relevant paper was balanced by the searching for the population and intervention on title only.

The observational filter was amended to only identify studies that were in scope. The focus was on cohort and cross-sectional studies.

The population and intervention sets picked up all 10 of the test papers identified. 1 test paper was not retrieved by the study filters.

For rerun searches, no date limits were applied. Instead, the complete strategy was rerun again. Duplicate records were managed and removed within EPPI Reviewer 5 (reference management software). The discrepancy in CENTRAL records was reported to Cochrane and resolved. Cochrane had removed a batch of records during the year end processing carried out in January 2025. The records had been duplicates.

Clinical searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	24/10/2024	Wiley	Issue 10 of 12, October 2024	459
Cochrane Database of Systematic Reviews (CDSR)	24/10/2024	Wiley	Issue 10 of 12, October 2024	1
Embase	24/10/2024	Ovid	1974 to 2024 October 23	4856
Epistemonikos	24/10/2024	Epistemonikos	N/A	228

MEDLINE ALL	24/10/2024	Ovid	1946 to October 23, 2024	4343

Re-run search results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	15/04/2025	Wiley	Issue 3 of 12, March 2025	444
Cochrane Database of Systematic Reviews (CDSR)	15/04/2025	Wiley	Issue 3 of 12, March 2025	1
Embase	15/04/2025	Ovid	1974 to 2025 April 14	5149
Epistemonikos	15/04/2025	Epistemonikos	n/a	256
MEDLINE ALL	15/04/2025	Ovid	1946 to April 14, 2025	4629

CDSR – the 1 record found was not imported into EPPI as it was a duplicate of the record found in the original search.

Search strategy history

Database name: CDSR and CENTRAL

Searches:
#1 [mh "Kidney Neoplasms"] 1998
#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 3397
#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 4208
#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} 5641

Searches:
#7 [mh ^"tomography, emission-computed"] or [mh ^"tomography, emission-computed, single-photon"] or [mh ^"tomography, x-ray computed"] or [mh ^"single photon emission computed tomography computed tomography"] 8317
#8 (CAT NEXT (electron-beam* or examination* or imag* or scan* or x ray*)):ti,ab,kw 37
#9 ((comput* NEAR/3 tomogra*) or (CT not PET)):ti,ab,kw 98571
#10 [mh "Magnetic Resonance Imaging"] 13155
#11 (magnet* resonance or MRI):ti,ab,kw 53567
#12 ((magnet* or MR) NEXT (examination* or imag* or scan* or tomograph* or spectroscop* or multiparametric*)):ti,ab,kw 2439
#13 (contrast-enhanc* or contrastenhanc* or CEUS or SPECT or SPECTs or sestamibi* or mibi):ti,ab,kw 6209
#14 {OR #7-#13} 143378
#15 #6 and #14 in Cochrane Reviews 1
#16 #6 and #14 in Trials 781
#17 "conference":pt or (clinicaltrials or trialsearch):so 784063
#18 #16 not #17 459

1 **Database name: Embase**

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. (5957)
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. (316)
3 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti. (62148)
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. (321)
5 or/1-4 (68066)
6 (CAT adj (electron-beam* or examination* or imag* or scan* or x ray*)).ti. (257)
7 ((comput* adj3 tomogra*) or (CT not PET)).ti. (230658)
8 (magnet*-resonance or MRI).ti. (253806)
9 ((magnet* or MR) adj (examination* or imag* or scan* or tomograph* or spectroscop* or multiparametric*)).ti. (30700)
10 (contrast-enhanc* or contrastenhanc* or CEUS or SPECT or SPECTs or sestamibi* or mibi).ti. (52326)
11 5 and (or/6-10) (2465)
12 nonhuman/ not (human/ and nonhuman/) (5553494)
13 11 not 12 (2457)
14 limit 13 to english language (2201)
15 14 not (letter or editorial).pt. (2143)

Searches
16 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6047975)
17 15 not 16 (1696)
18 exp *kidney tumor/ (102833)
19 (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. (24619)
20 (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. (759)
21 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (110461)
22 (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. (1254)
23 or/18-22 (155233)
24 *computer assisted emission tomography/ or *computer assisted tomography/ or *emission tomography/ or *single photon emission computed tomography/ or *x-ray computed tomography/ or *single photon emission computed tomography-computed tomography/ (178240)
25 (CAT adj (electron-beam* or examination* or imag* or scan* or x ray*)).ti,ab. (2031)
26 ((comput* adj3 tomogra*) or (CT not PET)).ti,ab. (1007697)
27 *nuclear magnetic resonance imaging/ (224007)
28 (magnet*-resonance or MRI).ti,ab. (936241)
29 ((magnet* or MR) adj (examination* or imag* or scan* or tomograph* or spectroscop*)).ti,ab. (103836)
30 (contrast-enhanc* or contrastenhanc* or CEUS).ti,ab,kw. (100173)
31 (SPECT or SPECTs or sestamibi* or mibi).ti,ab,kw. (66201)
32 or/24-31 (1906701)
33 23 and 32 (20425)
34 nonhuman/ not (human/ and nonhuman/) (5553494)
35 33 not 34 (20097)
36 limit 35 to english language (17084)
37 36 not (letter or editorial).pt. (16982)
38 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6047975)
39 37 not 38 (10146)
40 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

Searches
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/ (1820274)
41 exp "organisation for economic co-operation and development"/ (3207)
42 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/ (3941952)
43 european union/ (32855)
44 developed country/ (36519)
45 or/41-44 (3977397)
46 40 not 45 (1658091)
47 39 not 46 (10073)
48 Clinical study/ (167953)
49 Case control study/ (225527)
50 Retrospective study/ (1702185)
51 comparative study/ (1085243)
52 Prospective study/ (946412)
53 Randomized controlled trials/ (283943)
54 52 not 53 (934752)
55 Cohort analysis/ (1235615)
56 cohort analy$.tw. (22274)
57 (Cohort adj (study or studies)).tw. (532832)
58 (Case control$ adj (study or studies)).tw. (184830)
59 (cross sectional adj (study or studies)).tw. (393316)
60 case series.tw. (163043)
61 prospective.tw. (1195904)
62 retrospective.tw. (1405044)
63 or/48-52,54-62 (5591422)

Searches	
64	sensitiv*.tw. (2227361)
65	diagnostic accuracy.sh. (328996)
66	diagnostic.tw. (1341646)
67	((likelihood adj ratio*) or lr or plr or nlr).ti,ab. (88625)
68	or/64-67 (3514049)
69	random:.tw. (2135134)
70	placebo:.mp. (547843)
71	double-blind:.tw. (257069)
72	or/69-71 (2421168)
73	63 or 68 or 72 (10129959)
74	47 and 73 (4337)
75	(17 not 46) or 74 (4856)

Database name: Epistemonikos

Searches
(title:((kidney* AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*)) OR (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 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-tumours" 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*))) OR abstract:((kidney* AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*)) OR (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 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-tumours" 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 (title:((cat AND ("electron-beam" OR "electron-beams" OR "electron beam" OR "electron beams" OR examination* OR imag* OR scan* OR x ray*)) OR ((comput* AND tomogra*) OR (ct NOT pet)) OR (magnet* resonance OR mri) OR ((magnet* OR mr) AND (examination* OR imag* OR scan* OR tomograph* OR spectroscop* OR multiparametric*)) OR ((contrast AND enhance*) OR contrastenhanc* OR ceus OR spect OR spects OR sestamibi* OR mibi)) OR abstract:((cat AND ("electron-beam" OR "electron-beams" OR "electron beam" OR "electron beams" OR examination* OR imag* OR scan* OR x ray*)) OR ((comput* AND tomogra*) OR (ct NOT pet)) OR (magnet* resonance OR mri) OR ((magnet* OR mr) AND

Searches
(examination* OR imag* OR scan* OR tomograph* OR spectroscop* OR multiparametric*)) OR ((contrast AND enhance*) OR contrastenhanc* OR ceus OR spect OR spects OR sestamibi* OR mibi)))
Limited to systematic reviews

Database name: Medline ALL

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. (4893)
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. (235)
3 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti. (43585)
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. (213)
5 or/1-4 (48484)
6 (CAT adj (electron-beam* or examination* or imag* or scan* or x ray*)).ti. (209)
7 ((comput* adj3 tomogra*) or (CT not PET)).ti. (173368)
8 (magnet*-resonance or MRI).ti. (189240)
9 ((magnet* or MR) adj (examination* or imag* or scan* or tomograph* or spectroscop* or multiparametric*)).ti. (25364)
10 (contrast-enhanc* or contrastenhanc* or CEUS or SPECT or SPECTs or sestamibi* or mibi).ti. (35846)
11 5 and (or/6-10) (1802)
12 animals/ not humans/ (5235447)
13 11 not 12 (1794)
14 limit 13 to english language (1670)
15 limit 14 to (letter or historical article or comment or editorial or news or case reports) (272)
16 14 not 15 (1398)
17 exp *Kidney Neoplasms/ (75451)
18 (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. (16705)
19 (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)
20 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (73582)
21 (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. (877)
22 or/17-21 (111768)

Searches
23 *tomography, emission-computed/ or *tomography, emission-computed, single-photon/ or *tomography, x-ray computed/ or *single photon emission computed tomography computed tomography/ (154481)
24 (CAT adj (electron-beam* or examination* or imag* or scan* or x ray*)).ti,ab. (1326)
25 ((comput* adj3 tomogra*) or (CT not PET)).ti,ab. (665236)
26 exp *Magnetic Resonance Imaging/ (212124)
27 (magnet*-resonance or MRI).ti,ab. (632082)
28 ((magnet* or MR) adj (examination* or imag* or scan* or tomograph* or spectroscop*)).ti,ab. (75776)
29 (contrast-enhanc* or contrastenhanc* or CEUS).ti,ab,kw. (69572)
30 (SPECT or SPECTs or sestamibi* or mibi).ti,ab,kw. (38746)
31 or/23-30 (1311928)
32 22 and 31 (12493)
33 animals/ not humans/ (5235447)
34 32 not 33 (12273)
35 limit 34 to english language (10095)
36 limit 35 to (letter or historical article or comment or editorial or news or case reports) (3793)
37 35 not 36 (6302)
38 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/ (1377466)
39 "organisation for economic co-operation and development"/ (633)
40 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

Searches
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/ (3603817)
41 european union/ (18233)
42 developed countries/ (21648)
43 or/39-42 (3620388)
44 38 not 43 (1285607)
45 37 not 44 (6246)
46 exp Case-Control Studies/ (1546412)
47 exp Cohort Studies/ (2664320)
48 Cross-Sectional Studies/ (518920)
49 Comparative Study.pt. (1930436)
50 case control$.tw. (170694)
51 (cohort adj (study or studies)).tw. (370112)
52 cohort analy$.tw. (13776)
53 prospective.tw. (778770)
54 longitudinal.tw. (357872)
55 retrospective.tw. (848949)
56 cross sectional.tw. (588897)
57 or/46-56 (5709379)
58 (sensitiv: or predictive value:).mp. or accurac:.tw. (2769213)
59 ((likelihood adj ratio*) or lr or plr or nlr).ti,ab. (60268)
60 diagnos*.ti. (728709)
61 or/58-60 (3379331)
62 exp Randomized Controlled Trial/ (625616)
63 randomi?ed.mp. (1148239)
64 placebo.mp. (261245)
65 or/62-64 (1216851)
66 57 or 61 or 65 (9049180)
67 45 and 66 (4059)
68 16 or 67 (4346)
69 (16 not 44) or 67 (4343)

Cost-effectiveness searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Econlit	30/10/2024	Ovid	1886 to October 24, 2024	1
Embase	30/10/2024	Ovid	1974 to 2024 October 29	141
International Health Technology Assessment Database from INAHTA	30/10/2024	https://database.inahta.org/	n/a	5
Medline ALL	30/10/2024	Ovid	1946 to October 29, 2024	110

Re-run search results

1

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	08/05/2025	Ovid	1886 to May 01, 2025	1
Embase	08/05/2025	Ovid	1974 to 2025 May 07	151
International Health Technology Assessment Database from INAHTA	08/05/2025	https://database.inahta.org/	n/a	130
MEDLINE	08/05/2025	Ovid	1946 to May 07, 2025	113

2 ### Search strategy history

3 ### 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)

Searches
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 (CAT adj (electron-beam* or examination* or imag* or scan* or x ray*)).ti,ab. (2)
7 ((comput* adj3 tomogra*) or (CT not PET)).ti,ab. (257)
8 (magnet*-resonance or MRI).ti,ab. (215)
9 ((magnet* or MR) adj (examination* or imag* or scan* or tomograph* or spectroscop*)).ti,ab. (3)
10 (contrast-enhanc* or contrastenhanc* or CEUS).ti,ab. (6)
11 (SPECT or SPECTs or sestamibi* or mibi).ti,ab. (5)
12 or/6-11 (469)
13 5 and 12 (1)

Database name: Embase

Searches
1 exp *kidney tumor/ (102891)
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. (24640)
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. (759)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (110502)
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. (1257)
6 or/1-5 (155311)
7 *computer assisted emission tomography/ or *computer assisted tomography/ or *emission tomography/ or *single photon emission computed tomography/ or *x-ray computed tomography/ or *single photon emission computed tomography-computed tomography/ (178422)
8 (CAT adj (electron-beam* or examination* or imag* or scan* or x ray*)).ti,ab. (2030)
9 ((comput* adj3 tomogra*) or (CT not PET)).ti,ab. (1008747)
10 *nuclear magnetic resonance imaging/ (224224)
11 (magnet*-resonance or MRI).ti,ab. (937217)
12 ((magnet* or MR) adj (examination* or imag* or scan* or tomograph* or spectroscop*)).ti,ab. (103890)
13 (contrast-enhanc* or contrastenhanc* or CEUS).ti,ab,kw. (100307)
14 (SPECT or SPECTs or sestamibi* or mibi).ti,ab,kw. (66228)

Searches
15 or/7-14 (1908638)
16 6 and 15 (20442)
17 nonhuman/ not (human/ and nonhuman/) (5557871)
18 16 not 17 (20115)
19 limit 18 to english language (17101)
20 19 not (letter or editorial).pt. (16999)
21 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6052334)
22 20 not 21 (10159)
23 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/ (1822220)
24 exp "organisation for economic co-operation and development"/ (3211)
25 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/ (3942805)
26 european union/ (32876)
27 developed country/ (36524)
28 or/24-27 (3978273)
29 23 not 28 (1659918)

Searches
30 22 not 29 (10085)
31 cost utility analysis/ (13284)
32 quality adjusted life year/ (38688)
33 cost*.ti. (205642)
34 (cost* adj2 utilit*).tw. (13710)
35 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (415968)
36 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (71764)
37 (qualit* adj2 adjust* adj2 life*).tw. (29556)
38 QALY*.tw. (28951)
39 (incremental* adj2 cost*).tw. (30868)
40 ICER.tw. (14273)
41 utilities.tw. (16149)
42 markov*.tw. (43081)
43 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (77461)
44 ((utility or effective*) adj2 analys*).tw. (40811)
45 (willing* adj2 pay*).tw. (16210)
46 (EQ5D* or EQ-5D*).tw. (28843)
47 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (5944)
48 (european* adj2 quality adj3 ("5" or five)).tw. (1118)
49 or/31-48 (681931)
50 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kf. (29673)
51 (illness state$1 or health state$1).ti,ab,kf. (15845)
52 (hui or hui1 or hui2 or hui3).ti,ab,kf. (3457)
53 (multiattribute$ or multi attribute$).ti,ab,kf. (1720)
54 (utility adj3 (score$1 or valu$ or health$ or cost$ or measur$ or disease$ or mean or gain or gains or index$)).ti,ab,kf. (35081)
55 (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or euroquol or euro quol5d or euroquol5d or eur qol or euroqol or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol).ti,ab,kf. (35022)
56 (euro$ adj3 (5 d or 5d or 5 dimension$ or 5dimension$ or 5 domain$ or 5domain$)).ti,ab,kf. (10052)
57 (sf36$ or sf 36$ or sf thirtysix or sf thirty six).ti,ab,kf. (48567)
58 (time trade off$1 or time tradeoff$1 or tto or timetradeoff$1).ti,ab,kf. (3824)
59 quality of life/ and ((quality of life or qol) adj (score$1 or measure$1)).ti,ab,kf. (36357)
60 quality of life/ and ec.fs. (69255)
61 quality of life/ and (health adj3 status).ti,ab,kf. (22882)
62 (quality of life or qol).ti,ab,kf. and Cost-Benefit Analysis/ (7315)
63 or/50-62 (252273)
64 Health economics/ (36874)

Searches	
65	exp health care cost/ (360061)
66	exp Fee/ (45826)
67	exp Budget/ (35304)
68	Funding/ (82648)
69	budget*.ti,ab. (50554)
70	(economic* or pharmaco?economic*).ti. (81597)
71	(price* or pricing*).ti,ab. (78919)
72	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab. (314627)
73	(financ* or fee or fees).ti,ab. (253399)
74	(value adj2 (money or monetary)).ti,ab. (4398)
75	or/64-74 (1069430)
76	49 or 63 or 75 (1500970)
77	30 and 76 (141)

1 **Database name: INAHTA**

Searches		
#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 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*	172

Searches		
	or malignan* or sarcoma* or parenchyma*)))) OR ("Kidney Neoplasms"[mhe])	
#7	"Tomography Emission-Computed"[mh]	116
#8	"Tomography Emission-Computed Single-Photon"[mh]	22
#9	"Tomography X-Ray Computed"[mh]	178
#10	"Single Photon Emission Computed Tomography Computed Tomography"[mh]	3
#11	cat AND ("electron beam" or "electron beams" or examination* or imag* or scan* or x ray*)	6
#12	(comput* AND tomogra*) or CT	292
#13	"Magnetic Resonance Imaging"[mh]	277
#14	(magnet* AND resonance) OR mri	417
#15	(magnet* or mr) AND (examination* or imag* or scan* or tomograph* or spectroscop* or multiparametric*)	277
#16	"contrast enhance" or "contrast enhanced" or "contrast enhancing" or contrastenhanc* or ceus or spect or spects or sestamibi* or mibi	53
#17	("contrast enhance" or "contrast enhanced" or "contrast enhancing" or contrastenhanc* or ceus or spect or spects or sestamibi* or mibi) OR ((magnet* or mr) AND (examination* or imag* or scan* or tomograph* or spectroscop* or multiparametric*)) OR ((magnet* AND resonance) OR mri) OR ("Magnetic Resonance Imaging"[mh]) OR ((comput* AND tomogra*) or CT) OR (cat AND ("electron beam" or "electron beams" or examination* or imag* or scan* or x ray*)) OR ("Single Photon Emission Computed Tomography Computed Tomography"[mh]) OR ("Tomography X-Ray Computed"[mh]) OR ("Tomography Emission-Computed Single-Photon"[mh]) OR ("Tomography Emission-Computed"[mh])	823
#18	(("contrast enhance" or "contrast enhanced" or "contrast enhancing" or contrastenhanc* or ceus or spect or spects or sestamibi* or mibi) OR ((magnet* or mr) AND (examination* or imag* or scan* or tomograph* or spectroscop* or multiparametric*)) OR ((magnet* AND resonance) OR mri) OR ("Magnetic Resonance Imaging"[mh]) OR ((comput* AND tomogra*) or CT) OR (cat AND ("electron beam" or "electron beams" or examination* or imag* or scan* or x ray*)) OR ("Single Photon Emission Computed Tomography Computed Tomography"[mh]) OR ("Tomography X-Ray Computed"[mh]) OR ("Tomography Emission-Computed Single-Photon"[mh]) OR ("Tomography Emission-Computed"[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	5

Searches
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]))

1 **Database name: Medline ALL**

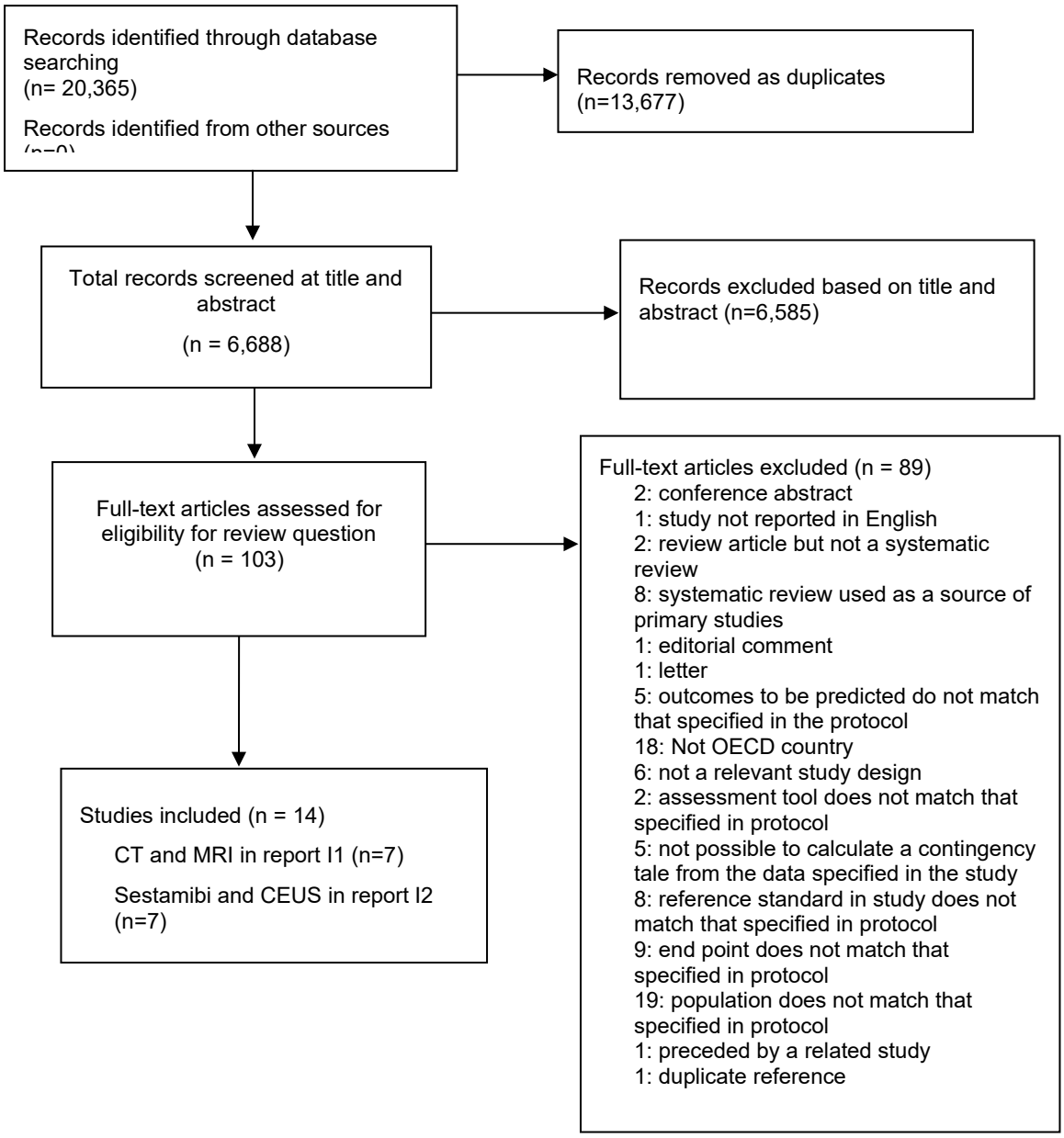
Searches
1 exp *Kidney Neoplasms/ (75501)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (16726)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* 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. (73655)
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. (877)
6 or/1-5 (111864)
7 *tomography, emission-computed/ or *tomography, emission-computed, single-photon/ or *tomography, x-ray computed/ or *single photon emission computed tomography computed tomography/ (154655)
8 (CAT adj (electron-beam* or examination* or imag* or scan* or x ray*)).ti,ab. (1327)
9 ((comput* adj3 tomogra*) or (CT not PET)).ti,ab. (665997)
10 exp *Magnetic Resonance Imaging/ (212458)
11 (magnet*-resonance or MRI).ti,ab. (632758)
12 ((magnet* or MR) adj (examination* or imag* or scan* or tomograph* or spectroscop*)).ti,ab. (75805)
13 (contrast-enhanc* or contrastenhanc* or CEUS).ti,ab,kw. (69660)
14 (SPECT or SPECTs or sestamibi* or mibi).ti,ab,kw. (38777)
15 or/7-14 (1313347)
16 6 and 15 (12501)
17 animals/ not humans/ (5237764)
18 16 not 17 (12281)
19 limit 18 to english language (10103)
20 limit 19 to (letter or historical article or comment or editorial or news or case reports) (3796)
21 19 not 20 (6307)
22 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

Searches
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/ (1379258)
23 "organisation for economic co-operation and development"/ (634)
24 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/ (3606459)
25 european union/ (18239)
26 developed countries/ (21655)
27 or/23-26 (3623041)
28 22 not 27 (1287342)
29 21 not 28 (6251)
30 Cost-Benefit Analysis/ (96031)
31 Quality-Adjusted Life Years/ (16997)
32 Markov Chains/ (16539)
33 exp Models, Economic/ (16561)
34 cost*.ti. (153289)
35 (cost* adj2 utilit*).tw. (8371)
36 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (303397)
37 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (51588)
38 (qualit* adj2 adjust* adj2 life*).tw. (19428)
39 QALY*.tw. (15767)
40 (incremental* adj2 cost*).tw. (18869)
41 ICER.tw. (6765)

Searches
42 utilities.tw. (10150)
43 markov*.tw. (34270)
44 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (57566)
45 ((utility or effective*) adj2 analys*).tw. (27241)
46 (willing* adj2 pay*).tw. (10970)
47 (EQ5D* or EQ-5D*).tw. (15137)
48 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (4434)
49 (european* adj2 quality adj3 ("5" or five)).tw. (805)
50 or/30-49 (541932)
51 (quality adjusted or adjusted life year$).ti,ab,kf. (26626)
52 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kf. (16206)
53 (illness state$1 or health state$1).ti,ab,kf. (9099)
54 (hui or hui1 or hui2 or hui3).ti,ab,kf. (2151)
55 (multiattribute$ or multi attribute$).ti,ab,kf. (1520)
56 (utility adj3 (score$1 or valu$ or health$ or cost$ or measur$ or disease$ or mean or gain or gains or index$)).ti,ab,kf. (22311)
57 (sf36$ or sf 36$ or sf thirtysix or sf thirty six).ti,ab,kf. (28377)
58 (time trade off$1 or time tradeoff$1 or tto or timetradeoff$1).ti,ab,kf. (2583)
59 quality of life/ and ((quality of life or qol) adj (score$1 or measure$1)).ti,ab,kf. (17100)
60 quality of life/ and ec.fs. (11109)
61 quality of life/ and (health adj3 status).ti,ab,kf. (12729)
62 (quality of life or qol).ti,ab,kf. and Cost-Benefit Analysis/ (18189)
63 or/51-62 (115281)
64 Economics/ (27540)
65 Value of life/ (5833)
66 exp "Costs and Cost Analysis"/ (274077)
67 exp Economics, Hospital/ (26015)
68 exp Economics, Medical/ (14450)
69 Economics, Nursing/ (4013)
70 Economics, Pharmaceutical/ (3150)
71 exp "Fees and Charges"/ (31551)
72 exp Budgets/ (14270)
73 budget*.ti,ab. (38428)
74 (economic* or pharmaco?economic*).ti. (65635)
75 (price* or pricing*).ti,ab. (58091)
76 (financ* or fee or fees).ti,ab. (176680)
77 (value adj2 (money or monetary)).ti,ab. (3302)
78 or/64-77 (589850)
79 50 or 63 or 78 (994639)
80 29 and 79 (110)

Appendix C – Diagnostic evidence study selection

Figure 1: PRISMA diagram for reviews I1 and I2



Appendix D – Diagnostic evidence

Baldari, 2015

Bibliographic Reference	Baldari, Diana; Capece, Sergio; Mainenti, Pier Paolo; Tucci, Anna Giacoma; Klain, Michele; Cozzolino, Immacolata; Salvatore, Marco; Maurea, Simone; Comparison between computed tomography multislice and high-field magnetic resonance in the diagnostic evaluation of patients with renal masses.; Quantitative imaging in medicine and surgery; 2015; vol. 5 (no. 5); 691-9

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location - Italy Study dates - Not reported. CT and MRI tests were completed in the same week. Sources of funding - Not reported
Inclusion criteria	Patients with histological or cytological diagnoses of renal masses, who underwent CT and MRI in the same week
Exclusion criteria	Not reported
Number of participants	N = 29 patients with 31 renal masses Unit of analysis: tumour
Length of follow-up	Not reported
Loss to follow-up	None
Target condition	Malignant diagnosis versus benign diagnosis
Index test(s)	Contrast-enhanced CT MRI
Index test detail	Imaging test: **Enhanced Computed Tomography (CT):**

	Type of test: Multi-detector/Multislice CT (MDCT), 64-slice scanner Use of contrast: Yes, after initial scan (non ionic water-soluble iodinated contrast) Scan coverage: at the level of the upper abdomen in cranio-caudal direction from the diaphragm to the iliac crests Test performed by: Not reported Test interpreted by: 2 radiologists with at least 5 years of experience in imaging of the abdomen Method of interpretation (single, consensus, quant/qual): Consensus. A third evaluator was consulted when there was disagreement in interpretation. Malignancy was interpreted based on structural characteristics according to the following scores 2, 3b, 5 and 6, irregular margins (score 1) and/or of the presence of significant contrast enhancement (score 1), fat and/or vascular structures infiltration (score 1). Benign tumours based on structural characteristics according to the following scores 1, 3a, 4 and 7, as well as on the margin regularity (score 0), absence of significant contrast enhancement (score 0), fat and vascular structures infiltration (score 0). Imaging test: **Magnetic resonance imaging (MRI)** Type of test: High-field (3 Tesla) scanner Use of contrast: Yes (paramagnetic contrast) Scan coverage: Not reported Test performed by: Not reported Test interpreted by: 2 radiologists with at least 5 years of experience in imaging of the abdomen Method of interpretation (single, consensus, quant/qual): Consensus. A third evaluator was consulted when there was disagreement in interpretation. Malignancy was interpreted based on structural characteristics according to the following scores 2, 3b, 5 and 6, irregular margins (score 1) and/or of the presence of significant contrast enhancement (score 1), fat and/or vascular structures infiltration (score 1). Benign tumours based on structural characteristics according to the following scores 1, 3a, 4 and 7, as well as on the margin regularity (score 0), absence of significant contrast enhancement (score 0), fat and vascular structures infiltration (score 0).

Reference standard (s)	Pathological confirmation after surgical intervention Histological data available for n=30 tumours and cytological data in 1.
Reference standard detail	No additional information provided

Population characteristics

Study-level characteristics

Characteristic	Study (N = 29)
% Female (Patients) Double lesion was observed in 2 male patients. All female patients had single lesions Sample size	n = 13 ; % = 44.8
Age (years) Mean (SD)	61 (17)
Tumour / complex cyst size - Measured by CT Range	15x11 to 190x140
Tumour / complex cyst size - Measured by MRI Range	14x11 to 191x137
Location of tumour / complex cyst - Left Kidney Sample size	n = 12 ; % = 38.7
Location of tumour / complex cyst - Right Kidney Sample size	n = 19 ; % = 61.3

Critical appraisal - GDT Crit App - QUADAS-2

Question	Answer
Risk of Bias	Moderate *(Moderate risk of bias in flow and timing and unclear risk of bias in the reference standard test.)*
Directness	Directly applicable

Dechet, 2003

Bibliographic Reference	Dechet, Christopher B; Zincke, Horst; Sebo, Thomas J; King, Bernard F; LeRoy, Andrew J; Farrow, George M; Blute, Michael L; 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; 2003; vol. 169 (no. 1); 71-4

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location - USA Study dates - Not reported Sources of funding - Not reported
Inclusion criteria	Patients diagnosed with a solid mass who were awaiting surgery
Exclusion criteria	Not reported
Number of participants	N = 100 patients Unit of analysis: patients n = 81 CT images reviewed by 2 independent radiologists. Only these 81 participants were included in the analysis
Length of follow-up	Not reported
Loss to follow-up	n = 19 (19%)
Target condition	Malignant diagnosis versus benign diagnosis
Index test(s)	CT
Index test detail	Imaging test: **Computed Tomography (CT):** Type of test: Pre-operative CT

	Use of contrast: Not reported Scan coverage: Not reported Test performed by: Not reported Test interpreted by: 2 independent radiologists blinded to each other Method of interpretation (single, consensus, quant/qual): Single (qualitative) for each radiologist. Lesions were categorised as malignant, benign or non-diagnostic based on results suspicious for, consistent with or indicative of malignancy or benign tumours
Reference standard (s)	Pathological confirmation after surgical intervention
Reference standard detail	Pathology from surgery (whole tissue specimen) The removed surgical specimen was biopsied through the tumour to produce 2 specimens (2 or more) with an 18 gauge Tru-Cut (Bard Maxcor, Covington, Georgia) biopsy gun. Tissue samples from the tumours were sent for permanent section. However, the results from whole tissue specimen was compared with the results from CT.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 100)
% Female Sample size	n = 36 ; % = 36
Age (years) Mean (range)	61 (21 to 85)

Critical appraisal - GDT Crit App - QUADAS-2

Question	Answer
Risk of Bias	High *(High risk of bias in patient selection and flow and timing domains, and unclear risk of bias in reference standard domain.)*

Question	Answer
Directness	Partially applicable *(Patients included do not fully represent the cohort of patients specified in the protocol because only patients undergoing surgery were included)*

1

2 **Kim, 2023**

Bibliographic Reference	Kim, Jinu; Lee, Jong Soo; Jo, Youngheun; Han, Woong Kyu; Superiority of magnetic resonance imaging in small renal mass diagnosis where image reports mismatches between computed tomography and magnetic resonance imaging.; Investigative and clinical urology; 2023; vol. 64 (no. 2); 148-153

3

4 **Study Characteristics**

Study type	Retrospective cohort study
Study details	Study location - Korea Study dates - January 2017 to December 2021 Sources of funding - Not reported
Inclusion criteria	Cases of partial or radial nephrectomy Undergone both CT and MRI scans
Exclusion criteria	Renal mass >4cm Presence of multiple renal masses Known genetic diseases for example Von Hippel-Lindau Previously confirmed histology by ultrasound-guided renal mass biopsy
Number of participants	N = 410 patients Unit of analysis: patients
Length of follow-up	Not reported

Loss to follow-up	None
Target condition	Malignant diagnosis versus benign diagnosis
Index test(s)	Contrast-enhanced CT MRI
Index test detail	Imaging test: **Contrast-enhanced CT** Type of test: Not reported Use of contrast: Yes Scan coverage: Not reported Test performed by: Not reported Test interpreted by: 2 experienced radiologists Method of interpretation (single, consensus, quant/qual): Single qualitative (only the first report considered to assess malignancy if multiple results were found on scans) Imaging test: **Contrast-enhanced MRI** Type of test: Not reported Use of contrast: Yes Scan coverage: Not reported Test performed by: Not reported Test interpreted by: 2 experienced radiologists Method of interpretation (single, consensus, quant/qual): Single qualitative (only the first report considered to assess malignancy if multiple results were found on scans)
Reference standard (s)	Pathological confirmation after surgical intervention
Reference standard detail	No additional information provided

Population characteristics

Study-level characteristics

Characteristic	Study (N = 410)
% Female Sample size	n = 154 ; % = 37.6
Age (years) Mean (SD)	54.61 (12.66)
Tumour / complex cyst size (cm) Mean (SD)	2.22 (0.84)

Critical appraisal - GDT Crit App - QUADAS-2

Question	Answer
Risk of Bias	High *(High risk of bias in patient selection, and unclear risk of bias in index test, reference standard test and flow and timing domains)*
Directness	Partially applicable *(Study population does not fully represent the cohort of patients required in the protocol because only patients undergoing surgery were included.)*

Kutman, 2013

Bibliographic Reference	Kutman, Kerem; Suer, Evren; Beduk, Yasar; Ozturk, Erdem; Gulpinar, Omer; Gokce, Ilker; Baltaci, Sumer; Is there a role of the enhancement degree of the lesion on computerized tomography for the characterization of renal tumors?.; The Journal of urology; 2013; vol. 189 (no. 2); 436-40

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location - Turkey

	Study dates - June 2007 to November 2011 Sources of funding - Not reported
Inclusion criteria	Patients with a renal tumour
Exclusion criteria	Patients with a solitary kidney, multiple or bilateral tumours, chronic kidney disease or advanced clinical stage (T3 to T4)
Number of participants	N = 149 patients Unit of analysis: patients
Length of follow-up	Not reported
Loss to follow-up	None
Target condition	Malignant diagnosis versus benign diagnosis
Index test(s)	Contrast-enhanced CT
Index test detail	Imaging test: **Computed tomography (CT)** Type of test: Dynamic Enhanced CT Use of contrast: Yes, 500ml Urografin contrast material orally 1 hour before scan and 100ml nonionic iohexol contrast material intravenously Scan coverage: Not reported Test performed by: Not reported Test interpreted by: Radiologist Method of interpretation (single, consensus, quantitative/qualitative): Single, quantitative using attenuation/enhancement difference - degree of tumour enhancement was determined by measuring attenuation of 3 regions of interest were measured and mean calculated. Cut off was 138HU.
Reference standard (s)	Pathological confirmation after surgical intervention
Reference standard detail	Pathological evaluation was completed after tumours were surgically removed The 2009 TNM staging system and Furham grade criteria were used.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 149)
% Female Sample size	n = 64 ; % = 43
Age (years) Mean (SD)	57 (13)
Tumour / complex cyst size (cm) Mean tumour diameter Mean (SD)	4.8 (2.7)
Complexity of tumour / complex cyst - Low grade RCC (grade 1-2) Sample size	n = 75 ; % = 50
Complexity of tumour / complex cyst - High grade RCC (grade 3-4) Sample size	n = 52 ; % = 34.9

Critical appraisal - GDT Crit App - QUADAS-2

Question	Answer
Risk of Bias	High *(Unclear risk of bias in the patient selection, index test, reference standard and flow and timing domains)*
Directness	Partially applicable *(Only patients who had undergone surgery were represented in the study, although this was not an inclusion criteria.)*

Marschner, 2020

Bibliographic Reference	Marschner, Constantin Arndt; Ruebenthaler, Johannes; Schwarze, Vincent; Negrao de Figueiredo, Giovanna; Zhang, Lan; Clevert, Dirk Andre; Comparison of computed tomography (CT), magnetic resonance imaging (MRI) and contrast-enhanced ultrasound (CEUS) in the evaluation of unclear renal lesions.; RoFo : Fortschritte auf dem Gebiete der

Rontgenstrahlen und der Nuklearmedizin; 2020; vol. 192 (no. 11); 1053-1059

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location - Germany Study dates - 2005 to 2015 Sources of funding - Not reported
Inclusion criteria	Patients with an unclear cystic or solid renal mass in preliminary imaging All patients had incidental findings Received histological clarification using Fine needle aspiration, biopsy or surgery
Exclusion criteria	Not reported
Number of participants	N = 255 patients Unit of analysis: patients n = 124 patients analysed Patients who had CT: n = 88 Patients who had MRI: n= 36
Length of follow-up	Not reported
Loss to follow-up	None
Target condition	Malignant diagnosis versus benign diagnosis
Index test(s)	Contrast-enhanced CT

	MRI
Index test detail	Imaging test: **Computed tomography (CT)** Type of test: Unenhanced CT and contrast enhanced CT Use of contrast: Yes, between 1.0ml and 4.8ml of a second-generation contrast agent (SonoVue®, Bracco, Milan, Italy) Scan coverage: Not reported Test performed by: Not reported Test interpreted by: Not reported Method of interpretation (single, consensus, quantitative/qualitative): Qualitative (if the findings of the first CT or MRI were inconclusive, the findings were adjusted to the findings of CEUS examination, which were evaluated as benign or malignant based on established qualitative image parameters.) Imaging test: **Magnetic resonance imaging (MRI)** Type of test: Unenhanced MRI and contrast enhanced MRI Use of contrast: Yes, between 1.0ml and 4.8ml of a second-generation contrast agent (SonoVue®, Bracco, Milan, Italy) Scan coverage: Not reported Test performed by: Not reported Test interpreted by: Not reported Method of interpretation (single, consensus, quantitative/qualitative): Qualitative (if the findings of the first CT or MRI were inconclusive, the findings were adjusted to the findings of CEUS examination, which were evaluated as benign or malignant based on established qualitative image parameters.)
Reference standard (s)	Pathological confirmation from biopsy / surgery
Reference standard detail	Histopathological material was obtained after lesion was surgically removed, after biopsy or after fine needle aspiration. 10 patients underwent FNA/biopsy and 245 patients had surgery.

Additional comments	Patient characteristics for the subset of patients who had CT/MRI was not reported.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 255)
Age (years) Mean (SD)	62 (13)
Tumour / complex cyst size - Benign lesions Mean (range)	1.8 (0.8 to 6.3)
Tumour / complex cyst size - Malignant lesions Mean (range)	2.3 (0.7 to 7.8)

Critical appraisal - GDT Crit App - QUADAS-2

Question	Answer
Risk of Bias	Moderate *(Unclear risk of bias in the patient selection and reference standard domains)*
Directness	Directly applicable

Monn, 2015

Bibliographic Reference	Monn, M Francesca; Gellhaus, Paul T; Patel, Aashish A; Masterson, Timothy A; Tann, Mark; Boris, Ronald S; Can radiologists and urologists reliably determine renal mass histology using standard preoperative computed tomography imaging?.; Journal of endourology; 2015; vol. 29 (no. 4); 391-6

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location

	- USA Study dates - 2003 to 2013 Sources of funding - Not reported
Inclusion criteria	Adult patients Patients undergoing nephrectomy Have had a preoperative multiphasic CT scan
Exclusion criteria	Preoperative multiphasic CT not available Known metastatic or locally advanced disease Tumour diameter >10cm With polycystic kidney disease Patients receiving care from study reviewers
Number of participants	N = 120 patients Unit of analysis: patients
Length of follow-up	Not reported
Loss to follow-up	None
Target condition	Malignant diagnosis versus benign diagnosis
Index test(s)	CT
Index test detail	Imaging test: **Computed Tomography** Type of test: Preoperative multiphasic CT (dual phasic, triphasic, or CT angiogram) Use of contrast: Not reported Scan coverage: Not reported Test performed by: Not reported

	Test interpreted by: 2 urologic oncologists and 2 abdominal radiologists Method of interpretation (single, consensus, quantitative/qualitative): Single qualitative. A standardised computer questionnaire was generated with questions focusing on whether the tumour was interpreted as benign or malignant and, if malignant, whether it was clear-cell RCC or an alternative histology. Reviewers had access to all sequences and standard radiographic tools including HU measurements.
Reference standard (s)	Pathological confirmation after surgical intervention
Reference standard detail	No additional information provided
Additional comments	Results were reported separately for all 4 reviewers, and all results were extracted and analysed.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 120)
% Female Sample size	n = 51 ; % = 42.5
Age (years) Mean (SD)	59.5 (13.2)
Tumour / complex cyst size (cm) Mean (SD)	3.3 (1.9)
Location of tumour / complex cyst - Left-side tumour Sample size	n = 63 ; % = 52.5
Nephrectomy score Median (IQR)	7 (5 to 9)

Critical appraisal - GDT Crit App - QUADAS-2

Question	Answer
Risk of Bias	High *(High risk of bias in the selection of patients and unclear risk of bias in the reference standard test and flow and timing domains)*
Directness	Partially applicable *(Patients only included those undergoing surgery and so does not fully represent the cohort of patients required in the protocol)*

Takebayashi, 1999

Bibliographic Reference	Takebayashi, S; Hidai, H; Chiba, T; Takagi, H; Koike, S; Matsubara, S; Using helical CT to evaluate renal cell carcinoma in patients undergoing hemodialysis: value of early enhanced images.; AJR. American journal of roentgenology; 1999; vol. 172 (no. 2); 429-33

Study Characteristics

Study type	Retrospective cohort study
Study details	Study location - Japan Study dates - November 1994 to March 1998 Sources of funding - Not reported
Inclusion criteria	Patients undergoing haemodialysis Patients who underwent nephrectomy for suspected renal cell carcinoma
Exclusion criteria	Not reported
Number of participants	N = 23 patients with 225 lesions Unit of analysis: tumour

Length of follow-up	Not reported
Loss to follow-up	None
Target condition	Malignant diagnosis versus benign diagnosis
Index test(s)	Contrast-enhanced CT
Index test detail	Imaging test: **Computed tomography (CT)** Type of test: Unenhanced and contrast-enhanced Helical CT using Lemage SX scanner Use of contrast: Yes, 100ml iohexol contrast agent Scan coverage: Not reported Test performed by: Not reported Test interpreted by: 2 radiologists experienced in body CT blinded to other imaging, clinical histories and laboratory data. Method of interpretation (single, consensus, quantitative/qualitative): Consensus, quantitative (criterion for RCC was renal masses >10HU without fat density, however 10 to 20 HU of increased attenuation was not considered enhancement when the SD was >4 or if streaky artefact was present)
Reference standard (s)	Pathological confirmation after surgical intervention
Reference standard detail	Pathologic examinations of all masses shown on the cut surfaces through suspected renal neoplasms were performed
Additional comments	Study reported on early and delayed enhanced helical CT images. Images were obtained during a single 18 to 25 seconds breath-hold. For the early scan results, there was a 40 seconds delay from injecting the contrast material to initiating scan or a delay of 50 seconds if the patients had cardiac failure. Delayed scans were obtained using similar parameters to the early scan but with a delay of 120 seconds from the injection of contrast. Only early CT results were used for analysis as they correspond more closely with current practice.

1

Population characteristics

Study-level characteristics

Characteristic	Study (N = 23)
% Female Sample size	n = 6 ; % = 26
Age (years) Mean (range)	46 (27 to 78)
Tumour / complex cyst size - Renal cell carcinomas associated with acquired cystic kidney disease (ACKD) Mean (SD)	2.8 (1.5)
Tumour / complex cyst size - Renal cell carcinoma not associated with acquired cystic kidney disease (ACKD) Mean (SD)	1.5 (0.3)
Location of tumour / complex cyst - Exophytic RCC tumours Of the 24 RCCs present Sample size	n = 6 ; % = 25
Location of tumour / complex cyst - Small intracystic RCC tumours Of the 24 RCCs present Sample size	n = 3 ; % = 13
Renal function - Duration of haemodialysis in ACKD patients with RCC Mean (range)	5.58 (3.83 to 7.17)
Renal function - Renal function - Duration of haemodialysis in non-ACKD patients with RCC Mean (range)	1.83 (1.17 to 2.5)

Critical appraisal - GDT Crit App - QUADAS-2

Question	Answer
Risk of Bias	High *(High risk of bias in the patient selection and unclear risk of bias in reference standard test and flow and timing domains)*

Question	Answer
Directness	Partially applicable *(Patients included do not fully represent the cohort of patients specified in the protocol because only patients undergoing surgery were included.)*

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2

Appendix E – Forest plots

Forest plots for CT tests

Figure 2: Forest plot for positive likelihood ratio of CT (person as unit of analysis)

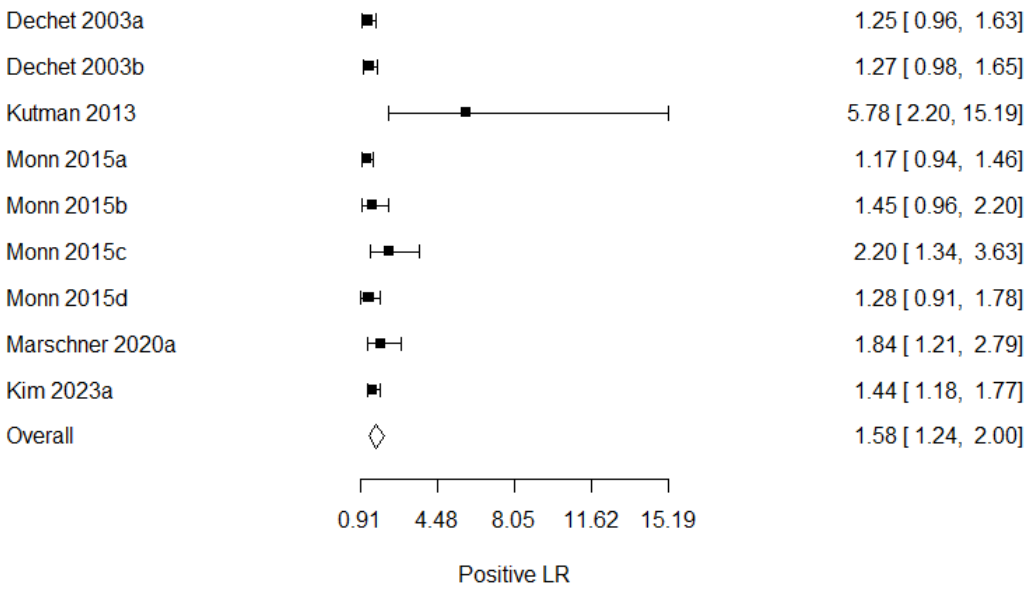


Figure 3: Forest plot for negative likelihood ratio of CT (person as unit of analysis)

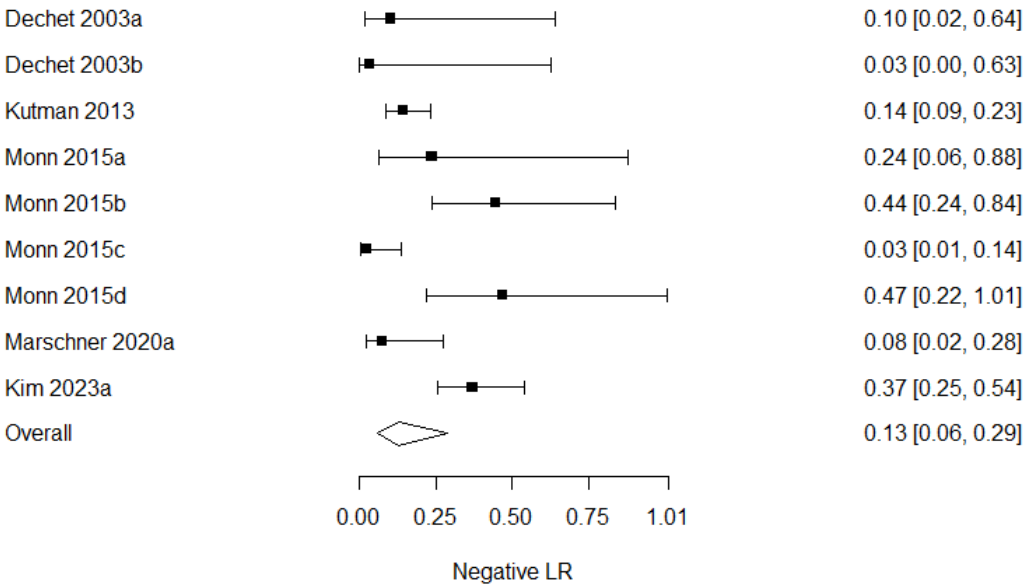


Figure 4: Forest plot for sensitivity of CT (person as unit of analysis)

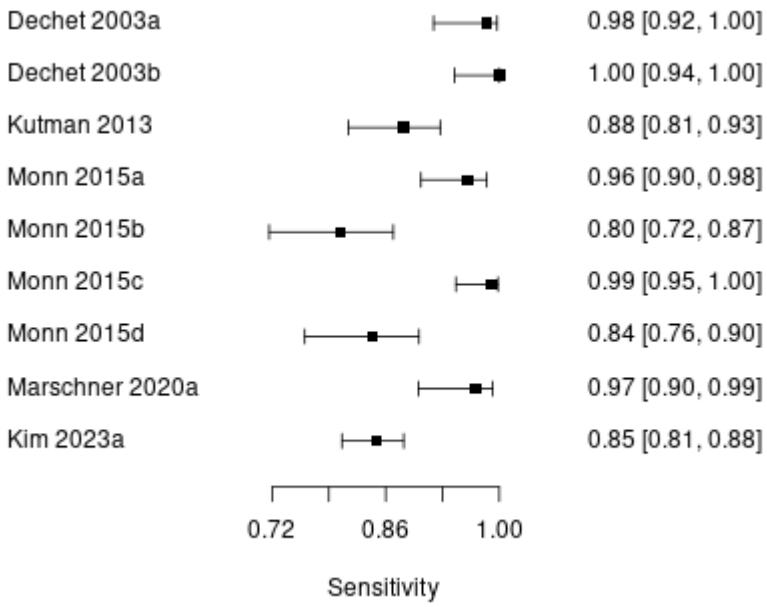
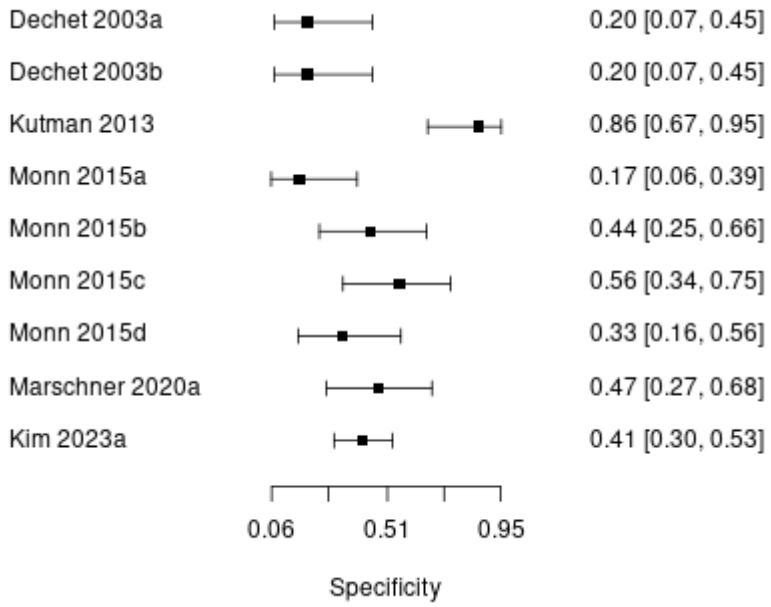


Figure 5: Forest plot for specificity of CT (person as unit of analysis)



Forest plots for MRI tests

Figure 6: Forest plot for positive likelihood ratio of MRI (person as unit of analysis)

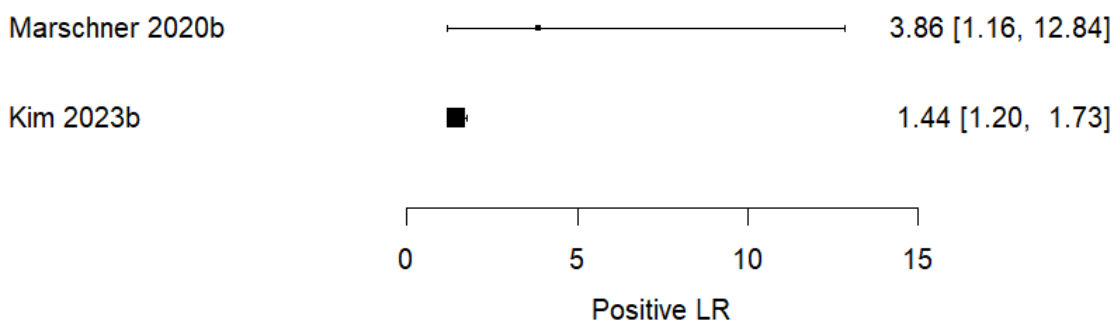


Figure 7: Forest plot for negative likelihood ratio of MRI (person as unit of analysis)

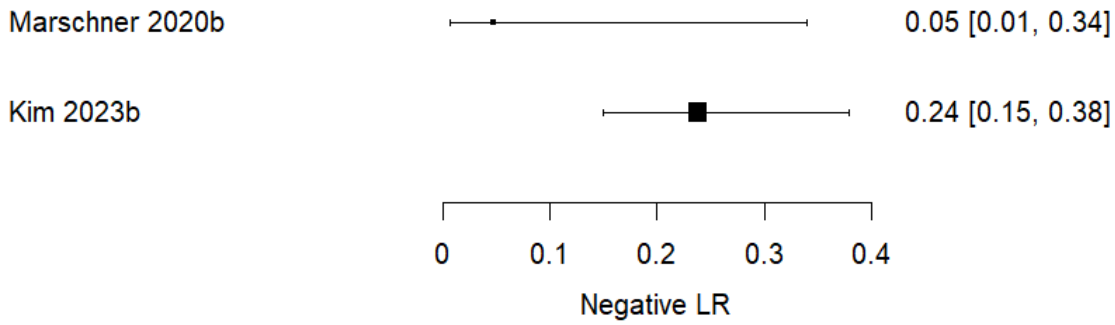
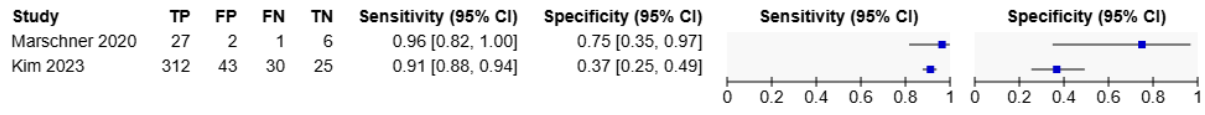


Figure 8: Forest plot for sensitivity and specificity of MRI (person as unit of analysis)



Appendix F – GRADE

GRADE tables for CT tests

Table 12: Clinical evidence profile (diagnostic accuracy) for CT (persons as unit of analysis)

No of studies	Study design	Sample size	Sensitivity (95% CI)	Specificity (95% CI)	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
5 (Dechet 2003, Kim 2023, Kutman 2013, Marschner 2020, Monn 2015)[1]	Retrospective cohort	1289	0.95 (0.88, 0.98)	0.40 (0.26, 0.55)	LR + 1.58 (1.24, 2.00)	Very serious[2]	Not serious	Serious[4]	Serious[5]	VERY LOW
					LR – 0.13 (0.06, 0.29)	Very serious[2]	Serious[3]	Serious[4]	Not serious	VERY LOW

CI: confidence interval; LR: likelihood ratio

1. 5 studies total, including 1 study with 2 interpretations and 1 study with 4 interpretations (see Methods and processes section 1.1.3 for an explanation)
2. Downgraded twice as ≥50% of the weighting of studies in a meta-analysis at high risk of bias as assessed by QUADAS-2
3. Downgraded once for serious inconsistency on visual inspection of point estimates and confidence intervals
4. Downgraded once as ≥50% of the weighting of studies in the meta-analysis had samples which did not fully represent the population specified in the protocol
5. Downgraded once as 95% CI crosses 1 decision making thresholds (for LR+, thresholds are 1 and 2)

Table 13: Clinical evidence profile (diagnostic accuracy) for CT (lesions as unit of analysis)

No of studies	Study design	Sample size	Sensitivity (95% CI)	Specificity (95% CI)	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
1 (Baldari 2015)	Retrospective cohort	29 (31 lesions)	1.00 (0.85, 1.00)	0.63 (0.24, 0.91)	LR + 2.67 (1.09, 6.52)	Very serious[1]	Not serious	Not serious	Serious[2]	VERY LOW
					LR – 0.03 (0.00, 0.56)	Very serious[1]	Not serious	Not serious	Serious[2]	VERY LOW

CI: confidence interval; LR: likelihood ratio
1. Downgraded twice as study at high risk of bias as assessed by QUADAS-2
2. Downgraded once as 95% CI crosses 1 decision making thresholds (for LR+, thresholds are 1 and 2; for LR-, thresholds are 0.5 and 1)

Table 14: Clinical evidence profile (diagnostic accuracy) for CT – population of people on haemodialysis (lesions as unit of analysis)

No of studies	Study design	Sample size	Sensitivity (95% CI)	Specificity (95% CI)	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
1 (Takebayashi 1999)	Retrospective cohort	23 (225 lesions)	0.96 (0.80, 0.99)	0.98 (0.94, 0.99)	LR + 38.53 (16.15, 91.92)	Very serious[1]	Not serious	Serious[2]	Not serious	VERY LOW
					LR – 0.04 (0.01, 0.29)	Very serious[1]	Not serious	Serious[2]	Not serious	VERY LOW

CI: confidence interval; LR: likelihood ratio

1. Downgraded twice as study at high risk of bias as assessed by QUADAS-2
2. Downgraded once as study had samples which did not fully represent the population specified in the protocol

GRADE tables for MRI tests

Table 15: Clinical evidence profile (diagnostic accuracy) for MRI (persons as unit of analysis)

No of studies	Study design	Sample size	Sensitivity (95% CI)	Specificity (95% CI)	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
1 (Marschner 2020)	Retrospective cohort	36	0.96 (0.82, 1.00)	0.75 (0.35, 0.97)	LR + 3.86 (1.16, 12.84)	Very serious[1]	Not serious	Serious[2]	Serious[3] for LR+ Not serious for LR-	VERY LOW for LR+ VERY LOW for LR –
					LR – 0.05 (0.01, 0.34)					
1 (Kim 2023)	Retrospective cohort	410	0.91 (0.88, 0.94)	0.37 (0.25, 0.49)	LR+ 1.44 (1.20, 1.73)					
					LR- 0.24 (0.15, 0.38)					

CI: confidence interval; LR: likelihood ratio
Meta-analysis was not possible as a minimum of 3 studies are needed for bivariate meta-analysis
1. Downgraded twice 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 once as ≥50% of the weighting of the meta-analysis had samples which did not fully represent the population specified in the protocol
3. Downgraded once as 95% CI crosses 1 decision making thresholds (for LR+, thresholds are 1 and 2)

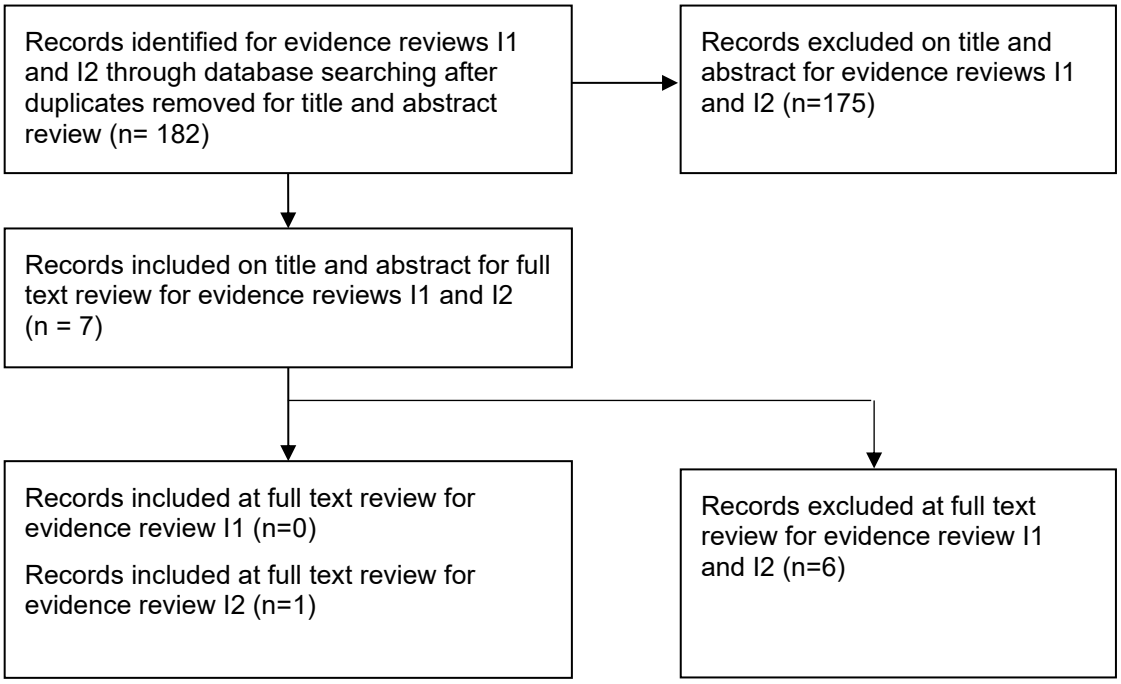
Table 16: Clinical evidence profile (diagnostic accuracy) for MRI (lesions as unit of analysis)

No of studies	Study design	Sample size	Sensitivity (95% CI)	Specificity (95% CI)	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
1 (Baldari 2015)	Retrospective cohort	29 (31 lesions)	1.00 (0.85, 1.00)	0.63 (0.31, 0.86)	LR + 2.67 (1.08, 6.50)	Very serious[1]	Not serious	Not serious	Serious[2]	VERY LOW
					LR – 0.03 (0.00, 0.56)	Very serious[1]	Not serious	Not serious	Serious[2]	VERY LOW

CI: confidence interval; LR: likelihood ratio
1. Downgraded twice as study at high risk of bias as assessed by QUADAS-2
2. Downgraded once as 95% CI crosses 1 decision making thresholds (for LR+, thresholds are 1 and 2; for LR-, thresholds are 0.5 and 1)

Appendix G – Economic evidence study selection

Figure 9: Economic evidence study selection



Appendix H – Economic evidence tables

No published economic evidence was identified for this review question.

Appendix I – Health economic model

No original economic modelling was conducted for this review question.

Appendix J – Excluded studies

Diagnostic test accuracy references excluded at full text (n = 89)

Table 17: Excluded diagnostic test accuracy studies

Study	Reason
Almalki, Yassir Edrees, Basha, Mohammad Abd Alkhalik, Refaat, Rania et al. (2023) Bosniak classification version 2019: a prospective comparison of CT and MRI. European radiology 33(2): 1286-1296	- Not OECD country *Egypt*
Almeida Dores, J., Kronenberg, P., Bargao Santos, P. et al. (2016) Renal oncocytoma: Is URO-CT useful in histological diagnosis?. Acta Urologica Portuguesa 33(3): 98-103	- Study not reported in English
Atri, Mostafa, Tabatabaeifar, Leila, Jang, Hyun-Jung et al. (2015) Accuracy of Contrast-enhanced US for Differentiating Benign from Malignant Solid Small Renal Masses. Radiology 276(3): 900-8	- Population *Different target condition to protocol criteria - this study is looking to investigate people with malignant mass versus benign mass*
Balyemez, Fikret, Aslan, Ahmet, Inan, Ibrahim et al. (2017) Diffusion-weighted magnetic resonance imaging in cystic renal masses. Canadian Urological Association journal = Journal de l'Association des urologues du Canada 11(12): e8-e14	- End point does not match that specified in the protocol *Study outcome was on ADC values and sensitivity and specificity were reported for a cut off ADC value. The study aim was to characterise complex renal cystic masses, therefore only cystic masses were included. Also, the reference test was not consistent for all participants and include histopathological results and follow-up*
Barr, Richard G (2022) Use of lumason/sonovue in contrast-enhanced ultrasound of the kidney for characterization of renal masses-a meta-analysis. Abdominal radiology (New York) 47(1): 272-287	- Systematic review used as source of primary studies
Barr, Richard G; Peterson, Cynthia; Hindi, Ammar (2014) Evaluation of indeterminate renal masses with contrast-enhanced US: a diagnostic performance study. Radiology 271(1): 133-42	- Population *Not investigating a population with condition of interest - looking at CEUS to identify benign/malignant rather than solid renal mass versus cystic mass.*
Bertolotto, Michele, Cicero, Calogero, Perrone, Rosaria et al. (2015) Renal Masses With Equivocal Enhancement at CT: Characterization With Contrast-	- Population *Mainly used to differentiate between malignant and benign*

Study	Reason
Enhanced Ultrasound. AJR. American journal of roentgenology 204(5): w557-65	
Catalano, C, Fraioli, F, Laghi, A et al. (2003) High-resolution multidetector CT in the preoperative evaluation of patients with renal cell carcinoma. AJR. American journal of roentgenology 180(5): 1271-7	- Not possible to calculate a contingency table from the data specified in the protocol *End point was level of agreement between image assessment and pathologic findings but sensitivity and specificity were only reported for a subgroup of the population (evaluating stage 1 of RCC for fat infiltration). No other data for contingency table reported.*
Chen, Lin, Wang, Ling, Diao, Xuehong et al. (2015) The diagnostic value of contrast-enhanced ultrasound in differentiating small renal carcinoma and angiomyolipoma. Bioscience trends 9(4): 252-8	- Population *Aims to look at diagnostic value of differentiating between small renal carcinoma and angiomyolipoma only.*
Das, Chandan J, Agarwal, Keshav, Sharma, Sanjay et al. (2023) Role of Contrast-Enhanced Ultrasound in Evaluation of Cystic Renal Mass. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine 42(12): 2873-2881	- Not a relevant study design *Long follow-up (3 years) and pathological confirmation not available for all patients. Study comparing CEUS to CECT. CEUS used to differentiate between benign and malignant.*
de Silva, Suresh, Lockhart, Kathleen Rebecca, Aslan, Peter et al. (2021) The diagnostic utility of diffusion weighted MRI imaging and ADC ratio to distinguish benign from malignant renal masses: sorting the kittens from the tigers. BMC urology 21(1): 67	- Outcome to be predicted do not match that specified in the protocol *Study reported on ADC values of various types of renal masses*
Deb, Abdalla Ali, Agag, Ayman, Naushad, Naufal et al. (2022) The value of sestamibi single-photon emission computed tomography/computed tomography in differentiating and staging renal cell carcinomas: A systematic review. Current urology 16(1): 32-37	- Systematic review used as source of primary studies
Eisenbrey, John R, Shaw, Colette M, Lyshchik, Andrej et al. (2015) Contrast-Enhanced Subharmonic and Harmonic Ultrasound of Renal Masses Undergoing Percutaneous Cryoablation. Academic radiology 22(7): 820-6	- Population *Looking at population receiving cryoablation only and CEUS used to differentiate between benign and malignant*
Elbanna, Khaled Y, Jang, Hyun-Jung, Kim, Tae Kyoung et al. (2021) The added value of contrast-enhanced ultrasound in	- Population *A significant proportion of patients did not have CT/MRI prior to CEUS.*

Study	Reason
evaluation of indeterminate small solid renal masses and risk stratification of cystic renal lesions. European radiology 31(11): 8468-8477	
Fang, Liang, Bai, Kun, Chen, Yue et al. (2021) A comparative study of contrast-enhanced ultrasound and contrast-enhanced CT for the detection and characterization of renal masses. Bioscience trends 15(1): 24-32	- Not OECD country
Ferda, Jiri, Hora, Milan, Hes, Ondrej et al. (2007) Computed tomography of renal cell carcinoma in patients with terminal renal impairment. European journal of radiology 63(2): 295-301	- Outcome to be predicted do not match that specified in the protocol *Study does not report on any diagnostic accuracy outcomes (sensitivity, specificity, PPV, NPV or likelihood ratios) or clinical outcomes specified in the protocol.*
Furrer, Marc A, Spycher, Samuel C J, Buttiker, Sophia M et al. (2020) Comparison of the Diagnostic Performance of Contrast-enhanced Ultrasound with That of Contrast-enhanced Computed Tomography and Contrast-enhanced Magnetic Resonance Imaging in the Evaluation of Renal Masses: A Systematic Review and Meta-analysis. European urology oncology 3(4): 464-473	- Systematic review used as source of primary studies
Gobara, Aiko, Yoshizako, Takeshi, Yoshida, Rika et al. (2019) T1a renal cell carcinoma on unenhanced CT: analysis of detectability and imaging features. Acta radiologica open 8(5): 2058460119849706	- Reference standard in study does not match that specified in protocol *Refence standard include pathology and contrast-enhanced CT and unable to tell if both were used or either*
Goyal, Ankur, Sharma, Raju, Bhalla, Ashu S et al. (2018) Comparison of MDCT, MRI and MRI with diffusion-weighted imaging in evaluation of focal renal lesions: The defender, challenger, and winner!. The Indian journal of radiology & imaging 28(1): 27-36	- Not OECD country *India*
Grajo, Joseph R, Terry, Russell S, Ruoss, Justin et al. (2019) Using Aorta-Lesion-Attenuation Difference on Preoperative Contrast-enhanced Computed Tomography Scan to Differentiate Between Malignant and Benign Renal Tumors. Urology 125: 123-130	- Assessment tool does not match that specified in the protocol *Study used quantitative method of assessing CT - aorta-lesion-attenuation difference (ALAD)*
Hashimoto, Masahiro, Ohkuma, Kiyoshi, Akita, Hirotaka et al. (2019) Usefulness of	- End point does not match that specified in the protocol

Study	Reason
contrast-enhanced ultrasonography for diagnosis of renal cell carcinoma in dialysis patients: Comparison with computed tomography. Medicine 98(47): e18053	*Only includes participants with solid renal masses - target condition is not solid versus cystic.*
Ho, V.B. and Choyke, P.L. (2004) MR evaluation of solid renal masses. Magnetic Resonance Imaging Clinics of North America 12(3): 413-427	- Review article but not a systematic review
Homayounieh, Fatemeh, Gopal, Nikhil, Firouzabadi, Fatemeh Dehghani et al. (2024) A Prospective Study of the Diagnostic Performance of Photon-Counting CT Compared With MRI in the Characterization of Renal Masses. Investigative radiology	- Not possible to calculate a contingency table from the data specified in the protocol *Study did not report sensitivity, specificity, PPV or NPV. Study focused on comparing the findings on proton-counting CT with those on MRI by 2 radiologists.*
Hovsepian, D M, Levy, H, Amis, E S Jr et al. (1990) MR evaluation of renal space-occupying lesions: diagnostic criteria. Urologic radiology 12(2): 74-9	- End point does not match that specified in the protocol *Study identified and defined MRI criteria that can be used in diagnosis/classification of renal lesions. Sensitivity and specificity not reported. Also, reference test included pathology and well-established US and/or CT criteria*
Jin, Dong-Dong, Zhuang, Bo-Wen, Lin, Ke et al. (2024) Contrast-enhanced US Bosniak Classification: intra- and inter-rater agreement, confounding features, and diagnostic performance. Insights into imaging 15(1): 285	- Not OECD country
Jin, Li and Xie, Feng (2020) Untargeted Contrast-Enhanced Ultrasound Versus Contrast-Enhanced Computed Tomography: A Differential Diagnostic Performance (DDP) Study for Kidney Lesions. Clinics (Sao Paulo, Brazil) 75: e1489	- Not OECD country *China*
Kambadakone, Avinash, Arasu, Vignesh A, Samir, Anthony E et al. (2012) Qualitative assessment of enhancement in a renal mass: contribution of subtraction CT. Journal of computer assisted tomography 36(4): 381-7	- Reference standard in study does not match that specified in protocol *Reference standard included biopsy, surgery and follow-up, with the majority receiving follow-up. Number of patients that had biopsy and or surgery were specified but were not separated in the final analysis for diagnostic outcomes.*
Kang, Stella K, Zhang, Angela, Pandharipande, Pari V et al. (2015) DWI for	- Systematic review used as source of primary studies

Study	Reason
Renal Mass Characterization: Systematic Review and Meta-Analysis of Diagnostic Test Performance. AJR. American journal of roentgenology 205(2): 317-24	
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	- Population *Some participants were excluded for refusing surgery. Also, scanners used on index test used a 5-point scale rated from 1- definitely not cancer to 5- definitely cancer, but the analysis only included categories 3 to 5. Unable to obtain 2x2 table for whole population*
Kim, Sooah, Jain, Monica, Harris, Andrew B et al. (2009) T1 hyperintense renal lesions: characterization with diffusion-weighted MR imaging versus contrast-enhanced MR imaging. Radiology 251(3): 796-807	- Conference abstract
Kreft, B P, Muller-Miny, H, Sommer, T et al. (1997) Diagnostic value of MR imaging in comparison to CT in the detection and differential diagnosis of renal masses: ROC analysis. European radiology 7(4): 542-7	- Reference standard in study does not match that specified in protocol *Reference standard included histology, and follow-up or angiography*
Kwon, Taekmin, Jeong, In Gab, Yoo, Sangjun et al. (2015) Role of MRI in indeterminate renal mass: diagnostic accuracy and impact on clinical decision making. International urology and nephrology 47(4): 585-93	- Reference standard in study does not match that specified in protocol *Reference standard included pathology for 74.2% of population and 18-month follow-up for 25.8%*
Laguna, M.P. (2016) Re: Prospective Evaluation of 99mTc-Sestamibi SPECT/CT for the Diagnosis of Renal Oncocytomas and Hybrid Oncocytic/Chromophobe Tumors. Journal of Urology 195(6): 1718-1719	- Editorial comment
Lal, N.R., Boruah, D.K., Raj, G. et al. (2024) Role of Advanced Magnetic Resonance Imaging (MRI) in the Evaluation of Renal Masses: A Prospective Cross-Sectional Study. International Journal of Pharmaceutical and Clinical Research 16(6): 2230-2236	- Not OECD country *India*
Li, Guorong, Cuilleron, Muriel, Gentil-Perret, Anne et al. (2004) Characteristics of image-detected solid renal masses: implication for optimal treatment. International journal of	- Population *Population excludes people with cystic masses. Also, diagnostic outcomes as per protocol were not reported. Study focused*

Study	Reason
urology : official journal of the Japanese Urological Association 11(2): 63-7	*on assessing tumours based on set CT criteria*
Li, Jing, Huang, Xiao, Wang, Lan et al. (2024) Role of Contrast-Enhanced Ultrasound With the Enhancement Pattern and Qualitative Analysis for Differentiating Hypovascular Solid Renal Lesions. Ultrasound in medicine & biology 50(2): 295-303	- Population *Population only with solid renal masses underwent CEUS*
Li, Xin, Liang, Ping, Guo, Mingzhou et al. (2013) Real-time contrast-enhanced ultrasound in diagnosis of solid renal lesions. Discovery medicine 16(86): 15-25	- Not OECD country
Liang, Xia, Zeng, Xian-Tao, Hong, Zhi-Liang et al. (2024) Determinants of conventional and contrast-enhanced ultrasound diagnosis of fat-poor angiomyolipoma <5 cm. Frontiers in oncology 14: 1446801	- Not OECD country
Ludwig, D R, Thacker, Y, Luo, C et al. (2023) CT-derived textural analysis parameters discriminate high-attenuation renal cysts from solid renal neoplasms. Clinical radiology 78(10): e782-e790	- Assessment tool does not match that specified in the protocol *no SPECT/CT or CEUS*
Mauro, M A, Balfe, D M, Stanley, R J et al. (1982) Computed tomography in the diagnosis and management of the renal mass. JAMA 248(21): 2894-6	- Review article but not a systematic review
Mazzei, Francesco Giuseppe, Mazzei, Maria Antonietta, Cioffi Squitieri, Nevada et al. (2014) CT perfusion in the characterisation of renal lesions: an added value to multiphasic CT. BioMed research international 2014: 135013	- End point does not match that specified in the protocol *Study reported on specific paraments of CT perfusion that could be used in diagnosing benign or malignant lesions such as permeability surface (PS), blood volume and blood flow. The sensitivity and specificity of PS was reported but unable to obtain contingency table values from data reported*
Millet, Ingrid, Doyon, Fernanda Curros, Hoa, Denis et al. (2011) Characterization of small solid renal lesions: can benign and malignant tumors be differentiated with CT?. AJR. American journal of roentgenology 197(4): 887-96	- Conference abstract
Miron Mombiela, Rebeca, Balschmidt, Trine, Birch, Carsten et al. (2025)	- Systematic review used as source of primary studies

Study	Reason
Diagnostic performance of contrast enhancement to differentiate benign and malignant renal lesions in CT and MRI: a systematic review and meta-analysis of diagnostic test accuracy (DTA) studies. Abdominal radiology (New York) 50(1): 360-378	*All relevant primary studies already reviewed in initial search. No additional new studies to include from this systematic review.*
Mlambo, Nompumelelo E; Dlamini, Nondumiso N M; Urry, Ronald J (2018) Correlation between radiological and histopathological findings in patients undergoing nephrectomy for presumed renal cell carcinoma on computed tomography scan at Grey's Hospital. SA journal of radiology 22(1): 1339	- Not OECD country *South Africa*
Mueller-Peltzer, K, Negrao de Figueiredo, G, Graf, T et al. (2019) Papillary renal cell carcinoma in contrast-enhanced ultrasound (CEUS) - A diagnostic performance study. Clinical hemorheology and microcirculation 71(2): 159-164	- Not a relevant study design *Aim of study to evaluate the observed enhancement features of histopathological confirmed papillary RCC*
Nazir, Z.; Maqsood, A.; Asgher, M.A. (2019) Detection of renal malignancy on multi-detector computed tomography in patients presented with hematuria. Pakistan Journal of Medical and Health Sciences 13(3): 845-847	- Not OECD country *Pakistan*
O'Connor, Stacy D, Pickhardt, Perry J, Kim, David H et al. (2011) Incidental finding of renal masses at unenhanced CT: prevalence and analysis of features for guiding management. AJR. American journal of roentgenology 197(1): 139-45	- End point does not match that specified in the protocol *Study focused on analysing renal masses incidentally detected during CT colonography, not on assessing the diagnostic accuracy of CT imaging*
Oh, Tae Hoon; Lee, Young Hwan; Seo, Ill Young (2014) Diagnostic efficacy of contrast-enhanced ultrasound for small renal masses. Korean journal of urology 55(9): 587-92	- Population *Population did not have CT/MRI prior. US was used prior as a baseline to detect renal masses.*
Patel, Neesha S, Poder, Liina, Wang, Zhen J et al. (2009) The characterization of small hypoattenuating renal masses on contrast-enhanced CT. Clinical imaging 33(4): 295-300	- Not a relevant study design *Case-control study (two-gate) involving patients with a small simple renal cyst and patients with renal cell carcinoma*
Rajan Harihar Prasad, P.K.A.; Toppo, S.K.; Ranjan, R. (2023) Study of Computed Tomography (CT) in Assessment in	- Not OECD country *India*

Study	Reason
Characterization of Renal Masses at a Tertiary Hospital. Journal of Cardiovascular Disease Research 14(9): 2273-2278	
Repeckaite, Gerta, Zviniene, Kristina, Jankauskiene, Justina et al. (2022) Small Renal Masses without Gross Fat: What Is the Role of Contrast-Enhanced MDCT?. Diagnostics (Basel, Switzerland) 12(2)	- End point does not match that specified in the protocol *Diagnostic outcomes (sensitivity, specificity, PPV and NPV) were reported for individual parameters of CT predictive of malignancy such as central scar, middle third and diameter of the tumour. Diagnostic outcomes for CT as a whole in diagnosis of renal masses was not reported*
Riccabona, M, Szolar, D, Preidler, K et al. (1999) Renal masses--evaluation by amplitude coded colour Doppler sonography and multiphasic contrast-enhanced CT. Acta radiologica (Stockholm, Sweden : 1987) 40(4): 457-61	- Reference standard in study does not match that specified in protocol *Reference standard includes histopathology and follow-up*
Rowe, Steven P, Gorin, Michael A, Gordetsky, Jennifer et al. (2015) Initial experience using 99mTc-MIBI SPECT/CT for the differentiation of oncocytoma from renal cell carcinoma. Clinical nuclear medicine 40(4): 309-13	- Not possible to calculate a contingency table from the data specified in the protocol
Rubenthaler, J, Paprottka, K, Marcon, J et al. (2016) Comparison of magnetic resonance imaging (MRI) and contrast-enhanced ultrasound (CEUS) in the evaluation of unclear solid renal lesions. Clinical hemorheology and microcirculation 64(4): 757-763	- Duplicate reference *Population and data reported is the same as in a study already included in the review*
Sanz, Enrique, Hevia, Vital, Gomez, Victoria et al. (2016) Renal Complex Cystic Masses: Usefulness of Contrast-Enhanced Ultrasound (CEUS) in Their Assessment and Its Agreement with Computed Tomography. Current urology reports 17(12): 89	- Population *CEUS used to differentiate between benign and malignant lesions and reference standard not pathological for all participants and CT is also used*
Sevcenco, S, Heinz-Peer, G, Ponhold, L et al. (2014) Utility and limitations of 3-Tesla diffusion-weighted magnetic resonance imaging for differentiation of renal tumors. European journal of radiology 83(6): 909-913	- Outcome to be predicted do not match that specified in the protocol *Sensitivity and specificity were only reported for the differentiation of papillary RCC from non-papillary RCC*
Shang, Wenwen; Hong, Guohui; Li, Wei (2023) MRI for the detection of small	- Systematic review used as source of primary studies

Study	Reason
malignant renal masses: a systematic review and meta-analysis. Frontiers in oncology 13: 1194128	
Shen, Lin, Li, Yanyan, Li, Na et al. (2019) Clinical utility of contrast-enhanced ultrasonography in the diagnosis of benign and malignant small renal masses among Asian population. Cancer medicine 8(18): 7532-7541	- Not OECD country
Siddiqui, M.A., Ali, A., Khalid, K. et al. (2022) Diagnostic Accuracy of Multi-Detector CT for Evaluation of Renal Masses. Pakistan Journal of Medical and Health Sciences 16(3): 253-254	- Not OECD country *Pakistan*
Siddiqui, Tariq Saeed, Tariq, Asima, Rehman, Bushra et al. (2010) Accuracy of multiphase helical tomography in detection and characterisation of suspected renal masses using histopathological findings as gold standard. Journal of Ayub Medical College, Abbottabad : JAMC 22(3): 170-3	- Not OECD country *Pakistan*
Silverman, S G, Lee, B Y, Seltzer, S E et al. (1994) Small (< or = 3 cm) renal masses: correlation of spiral CT features and pathologic findings. AJR. American journal of roentgenology 163(3): 597-605	- Not possible to calculate a contingency table from the data specified in the protocol
Smith, F.W.; Hutchison, J.M.S.; Mallard, J.R. (1981) Renal cyst or tumour? Differentiation by whole-body nuclear magnetic resonance imaging. Diagnostic Imaging 50(2): 61-65	- Not a relevant study design *Case report*
Song, Cheryn, Min, Gyeong Eun, Song, Kanghyon et al. (2009) Differential diagnosis of complex cystic renal mass using multiphase computerized tomography. The Journal of urology 181(6): 2446-50	- Population *Population includes only cystic renal masses managed surgically which does not meet protocol criteria. Also, data is presented for each Bosniak category separately*
Songib, Nor-Azalina, Nazri, Mohammad, Yaakup, Nur Adura et al. (2013) Multiphase renal CT in the evaluation of renal masses: is the nephrographic phase necessary?. Clinical imaging 37(6): 1037-42	- Not OECD country *Malaysia*
Spahn, M, Portillo, F J, Michel, M S et al. (2001) Color Duplex sonography vs. computed tomography: accuracy in the	- End point does not match that specified in the protocol

Study	Reason
preoperative evaluation of renal cell carcinoma. European urology 40(3): 337-42	*Study assessed extent of tumour thrombosis of renal masses, as well as the localisation, size and lymph node metastasis*
Tamai, Hideyuki, Takiguchi, Yoshie, Oka, Masashi et al. (2005) Contrast-enhanced ultrasonography in the diagnosis of solid renal tumors. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine 24(12): 1635-40	- Population *Not using CEUS in a population to differentiate solid renal masses from complex cysts*
Tello, R, Davison, B D, O'Malley, M et al. (2000) MR imaging of renal masses interpreted on CT to be suspicious. AJR. American journal of roentgenology 174(4): 1017-22	- Outcome to be predicted do not match that specified in the protocol *Study reported on the degree of enhancement and other characteristics of renal masses on MRI*
Thaiss, Wolfgang M, Bedke, Jens, Kruck, Stephan et al. (2019) Can contrast-enhanced ultrasound and acoustic radiation force impulse imaging characterize CT-indeterminate renal masses? A prospective evaluation with histological confirmation. World journal of urology 37(7): 1339-1346	- Not possible to calculate a contingency table from the data specified in the protocol
Tufano, Antonio, Antonelli, Luca, Di Pierro, Giovanni Battista et al. (2022) Diagnostic Performance of Contrast-Enhanced Ultrasound in the Evaluation of Small Renal Masses: A Systematic Review and Meta-Analysis. Diagnostics (Basel, Switzerland) 12(10)	- Population *Inclusion criteria for mode of initial diagnosis of small renal masses was ultrasound and not CT/MRI*
Tzortzakakis, Antonios, Gustafsson, Ove, Karlsson, Mattias et al. (2017) Visual evaluation and differentiation of renal oncocytomas from renal cell carcinomas by means of 99mTc-sestamibi SPECT/CT. EJNMMI research 7(1): 29	- Preceded by a related study *Tzortzakakis 2017 study only includes a sample of total study population included in Tzortzakakis 2022.*
Urraro, Fabrizio, Piscopo, Marco, Giordano, Nicoletta et al. (2024) Diagnostic Value of Contrast-Enhanced Ultrasound in Differentiating Malignant from Benign Small Renal Masses After CT/MRI. Journal of clinical medicine 13(21)	- End point does not match that specified in the protocol *Looking at differentiating between benign/malignant renal lesions rather than complex cysts/solid renal mass*
Voci, S L, Gottlieb, R H, Fultz, P J et al. (2000) Delayed computed tomographic characterization of renal masses:	- Reference standard in study does not match that specified in protocol

Study	Reason
preliminary experience. Abdominal imaging 25(3): 317-21	*Included pathologic confirmation in 25% of lesions and conventional CT showing no enhancement for the remaining lesions*
Wang, JingLing, Shi, JiaYu, Gao, Long et al. (2024) High-frame-rate contrast-enhanced ultrasound to differentiate between clear cell renal cell carcinoma and angiomyolipoma. BMC cancer 24(1): 659	- Population *CEUS used to differentiate between clear cell renal cell carcinoma and angiomyolipoma*
Warren, Hannah, Boydell, Anna-Rita, Reza, Abbas et al. (2022) Use of 99m Tc-sestamibi SPECT/CT for indeterminate renal tumours: a pilot diagnostic accuracy study. BJU international 130(6): 748-750	- Letter
Warren, Hannah, Fanshawe, Jack B, Mok, Valerie et al. (2024) Imaging modalities for characterising T1 renal tumours: A systematic review and meta-analysis of diagnostic accuracy. BJUI compass 5(7): 636-650	- Systematic review used as source of primary studies
Wei, Shu-Ping, Xu, Chao-Li, Zhang, Qing et al. (2017) Contrast-enhanced ultrasound for differentiating benign from malignant solid small renal masses: comparison with contrast-enhanced CT. Abdominal radiology (New York) 42(8): 2135-2145	- Not a relevant study design *Not a DTA study design of interest - comparing CEUS to contrast enhanced CT. CEUS used to differentiate benign from malignant.*
Wilson, Mitchell P, Katlariwala, Prayash, Murad, Mohammad H et al. (2020) Diagnostic accuracy of 99mTc-sestamibi SPECT/CT for detecting renal oncocytomas and other benign renal lesions: a systematic review and meta-analysis. Abdominal radiology (New York) 45(8): 2532-2541	- Reference standard in study does not match that specified in protocol *Pathology confirmation or contrast enhanced CEUS or two sonographers with expertise*
Wu, Hailan, Shi, Jiayu, Gao, Long et al. (2024) Qualitative and quantitative analysis of solid renal tumors by high-frame-rate contrast-enhanced ultrasound. Cancer imaging : the official publication of the International Cancer Imaging Society 24(1): 139	- Population *Ultrasound was used initially to identify renal mass rather than CT/MRI.*
Xia, Qingqing, Yuan, Xinchun, Huang, Meifeng et al. (2022) Contrast-enhanced Ultrasound for Diagnosis of Renal Cystic Mass. Current medical imaging 18(3): 292-298	- Not OECD country

Study	Reason
Xu, Zuo-Feng, Xu, Hui-Xiong, Xie, Xiao-Yan et al. (2010) Renal cell carcinoma and renal angiomyolipoma: differential diagnosis with real-time contrast-enhanced ultrasonography. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine 29(5): 709-17	- Population *Patients had undergone baseline ultrasonography to identify suspicious renal masses rather than CT/MRI*
Yamashita, Y, Miyazaki, T, Hatanaka, Y et al. (1995) Dynamic MRI of small renal cell carcinoma. Journal of computer assisted tomography 19(5): 759-65	- Outcome to be predicted do not match that specified in the protocol *Diagnostic and clinical outcomes as per protocol were not reported. Study describes characteristic of tumours on MRI*
Yanagi, Masato, Kiriyama, Tomonari, Akatsuka, Jun et al. (2022) Differential diagnosis and prognosis of small renal masses: association with collateral vessels detected using contrast-enhanced computed tomography. BMC cancer 22(1): 856	- End point does not match that specified in the protocol *Study focused on the diagnostic accuracy of predictive biomarkers of CT such as overflowing beer sign (OBS), angular interface (AI) and collateral vessels.*
Yin, Qihua, Xu, Huiting, Zhong, Yanqi et al. (2022) Diagnostic performance of MRI, SPECT, and PET in detecting renal cell carcinoma: a systematic review and meta-analysis. BMC cancer 22(1): 163	- Systematic review used as source of primary studies
Yong, C; Teo, Y M; Jeevesh, K (2016) Diagnostic performance of contrast-enhanced ultrasound in the evaluation of renal masses in patients with renal impairment. The Medical journal of Malaysia 71(4): 193-198	- Not a relevant study design *Not a DTA design - patients selected were non-consecutive patients with indeterminant lesions picked up incidentally.*
Zarzour, Jessica G, Lockhart, Mark E, West, Janelle et al. (2017) Contrast-Enhanced Ultrasound Classification of Previously Indeterminate Renal Lesions. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine 36(9): 1819-1827	- Population *Population group initially had CT/MRI/US to identify indeterminate lesions rather than CT/MRI alone.*
Zhang, Fan, Li, Rui, Li, Gang et al. (2019) Value of Contrast-Enhanced Ultrasound in the Diagnosis of Renal Cancer and in Comparison With Contrast-Enhanced Computed Tomography: A Meta-analysis. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine 38(4): 903-914	- Population *Target condition is malignant versus benign rather than solid renal mass versus cystic*

Study	Reason
Zhou, Xiang, Yan, Feng, Luo, Yan et al. (2011) Characterization and diagnostic confidence of contrast-enhanced ultrasound for solid renal tumors. Ultrasound in medicine & biology 37(6): 845-53	- Reference standard in study does not match that specified in protocol *Reference standard was surgical specimens or MRI*
Zhu, Hongjing, Yang, Bo, Dong, Aisheng et al. (2020) Dual-Phase 99mTc-MIBI SPECT/CT in the Characterization of Enhancing Solid Renal Tumors: A Single-Institution Study of 147 Cases. Clinical nuclear medicine 45(10): 765-770	- Not OECD country
Zokalj, Ivan, Marotti, Miljenko, Saghir, Hussein et al. (2012) Multiphase computed tomography of malignant kidney tumors: radiologic-pathologic comparison. Acta clinica Croatica 51(4): 563-71	- Not OECD country *Croatia*

ADC: apparent diffusion coefficient; AI: angular interface; ALAD: aorta-lesion-attenuation difference; CECT: contrast enhanced computed tomography; CEUS: contrast enhanced ultrasound; CT: computed tomography; DTA: diagnostic accuracy study; MRI: magnetic resonance imaging; NPV: negative predictive value; OBS: overflowing beer sign; OECD: Organisation for economic cooperation and development; PPV: positive predictive value; PS: permeability surface; RCC: renal cell carcinoma; RN: radial nephrectomy; SPECT: single-photon emission computed tomography; US: ultrasound

Economic references excluded at full text (n = 6)

Table 18: Excluded economic studies

Study	Reason
Gassert, Felix, Schnitzer, Moritz, Kim, Su Hwan et al. (2021) Comparison of Magnetic Resonance Imaging and Contrast-Enhanced Ultrasound as Diagnostic Options for Unclear Cystic Renal Lesions: A Cost-Effectiveness Analysis. Ultraschall in der Medizin (Stuttgart, Germany : 1980) 42(4): 411-417	- Non-protocol country setting (US healthcare perspective)
Oh, Aaron, Bhardwaj, Lokesh, Cacciamani, Giovanni et al. (2023) Cost-effectiveness of Contrast-Enhanced Ultrasound for Diagnosis and Active Surveillance of Complex Cystic Renal Lesions. Urology practice 10(1): 11-19	- Non-protocol country setting (US healthcare perspective) - Non-protocol cost perspective (third party payer perspective) - Non-protocol intervention/comparator (active surveillance instead of diagnosis)

Study	Reason
Patel, Bhavik N, Boltyenkov, Artem T, Martinez, Maria G et al. (2020) Cost-effectiveness of dual-energy CT versus multiphasic single-energy CT and MRI for characterization of incidental indeterminate renal lesions. Abdominal radiology (New York) 45(6): 1896-1906	- Non-protocol country setting (US healthcare perspective)
Runtemund, Jasmin, Rubenthaler, Johannes, von Munchhausen, Niklas et al. (2022) Diagnostic Workup for Patients with Solid Renal Masses: A Cost-Effectiveness Analysis. Cancers 14(9)	- Non-protocol country setting (US healthcare perspective) - Non-protocol intervention/comparator (compares CEUS to CT and MRI)
Su, Zhuo T, Patel, Hiten D, Huang, Mitchell M et al. (2021) Cost-effectiveness Analysis of 99mTc-sestamibi SPECT/CT to Guide Management of Small Renal Masses. European urology focus 7(4): 827-834	- Non-protocol country setting (US healthcare perspective)
Zbroja, Monika, Kuczynska, Maryla, Drelich, Katarzyna et al. (2024) Contrast-Enhanced Ultrasound in the Diagnosis of Solid Renal Lesions. Journal of clinical medicine 13(13)	- Not economic evaluation

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