

# **National Institute for Health and Care Excellence**

## **Kidney cancer: diagnosis and management**

**[H] Management of advanced renal cell  
carcinoma using non-pharmacological  
interventions**

**NICE guideline [number]**

**Evidence review underpinning recommendations 1.11.1  
to 1.11.2, 1.14.1 to 1.14.7, and a research  
recommendation in the NICE guideline**

**September 2025**

**Draft for consultation**

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# 1 Management of advanced renal cell carcinoma using non-pharmacological interventions before systemic anti-cancer therapy

## 1.1 Review question

What is the clinical and cost-effectiveness of non-pharmacological interventions used before systemic anti-cancer therapy for adults with advanced renal cell carcinoma?

### 1.1.1 Introduction

There are number of treatment options available for advanced renal cell carcinoma. These usually include pharmacological (systemic anti-cancer therapy, SACT) and non-pharmacological interventions. It is important to understand where non-pharmacological treatment modalities could be considered alongside SACT for reducing disease burden and improving survival benefits in the most effective manner.

Therefore, this review aims to evaluate the clinical and cost-effectiveness of non-pharmacological interventions before initial treatment with SACT in managing advanced renal cell carcinoma. [Review H2](#) assesses the clinical and cost-effectiveness of non-pharmacological interventions after SACT.

### 1.1.2 Summary of the protocol

**Table 1: PICOS inclusion criteria**

<b>Population</b>	Adults (18 years or over) with advanced RCC* who have not previously received systemic anti-cancer treatment (SACT). *defined as metastatic/ advanced RCC or locally advanced inoperable RCC (histologically confirmed or suspected on imaging).  Advanced RCC diagnosis confirmed according to the clinical or pathological TNM classification  Exclusion: <ul style="list-style-type: none"><li>• Adults with localised or locally advanced disease that is considered to be operable.</li><li>• Adults with advanced disease who are having palliative care only.</li></ul>
<b>Interventions</b>	<ul style="list-style-type: none"><li>• Non-pharmacological procedures carried out before SACT to manage primary mass:<ul style="list-style-type: none"><li>○ Cytoreductive nephrectomy</li><li>○ Stereotactic ablative radiotherapy (SABR)</li></ul></li><li>• Managing metastases:</li></ul>

	<ul style="list-style-type: none"> <li>○ Surgical removal</li> <li>○ Thermal ablation: <ul style="list-style-type: none"> <li>▪ Radiofrequency ablation</li> <li>▪ Cryotherapy</li> <li>▪ Microwave ablation</li> </ul> </li> <li>○ Radiotherapy: <ul style="list-style-type: none"> <li>▪ External beam radiotherapy (EBRT)</li> <li>▪ Stereotactic ablative radiotherapy (SABR)</li> </ul> </li> </ul>
<b>Comparator</b>	No non-pharmacological intervention before SACT (no delayed SACT): <ul style="list-style-type: none"> <li>• SACT without a non-pharmacological intervention</li> <li>• SACT followed by an included non-pharmacological intervention</li> </ul>
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>• Progression-free survival</li> <li>• Overall survival or if not reported: <ul style="list-style-type: none"> <li>○ Mortality</li> </ul> </li> <li>• Cancer-specific survival or if not reported: <ul style="list-style-type: none"> <li>○ Cancer-specific mortality</li> </ul> </li> <li>• Severe adverse events reported as: <ul style="list-style-type: none"> <li>○ observed in the intraoperative period</li> <li>○ observed in postoperative period</li> </ul> </li> <li>• Duration of hospital stay</li> <li>• Quality of life</li> </ul>
<b>Study type</b>	<ul style="list-style-type: none"> <li>• Randomised controlled trials (RCTs)</li> <li>• Any controlled, non-randomised studies</li> <li>• Cohort studies (prospective and retrospective observational studies)</li> <li>• Systematic reviews of the above studies</li> </ul>

1 For the full protocol see [appendix A](#).

### 2 **1.1.3 Methods and process**

3 This evidence review was developed using the methods and process described in  
4 [Developing NICE guidelines: the manual](#). Methods specific to this review question are  
5 described in the review protocol in [appendix A](#).

6 Methods and technical decisions specific to this review are summarised below:

- 7 1. Mortality at timepoints of 90 days or less was not included in this review. This was  
8 considered to be within the postoperative period and therefore covered by the outcome of  
9 postoperative severe adverse events (PSAE). PSAE was required to be reported using  
10 the acceptable classifications - Clavien-Dindo classification or Common Terminology  
11 Criteria for Adverse Events (CTCAE) in order to be included.
- 12 2. Where more than 1 timepoint was reported we reported data at up to 5 years and 5 to 10  
13 years. Where several time points were reported that could fit in the same category, the  
14 latest time point was used.

3. For outcomes where the line of no effect was defined as the minimal important difference (MID), a power calculation from a robust RCT (Mejean et al. 2018, included in this review) was used to determine the minimum sample size needed for consideration for the second downgrade criteria for the imprecision domain in GRADE. For all outcomes in this review, a sample size of less than 576 was used for downgrading.
4. Important confounders considered for assessing the quality of the included studies under this review were discussed and agreed with the committee. These confounders were:
  - Age
  - TNM classification
  - Primary RCC type e.g. clear cell, papillary and chromophobe
  - Tumour grade
  - Renal function at baseline
  - Performance status of participants at baseline
  - Location and number of metastases

### 1.1.3.1 Search methods

The searches for the effectiveness evidence were run on 18/01/2024 and re-run on 14/02/2025. The following databases were searched: Central Register of Controlled Trials (Wiley), Cochrane Database of Systematic Reviews (Wiley), Embase (Ovid), Epistemonikos (Epistemonikos) and 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 and observational studies.

The searches for the cost effectiveness evidence were run between 05/01/2024 and 07/01/2024 and re-run on 06/05/2025. The following databases were searched: EconLit (Ovid), Embase (Ovid), HTA (CRD), International HTA database (INAHTA), MEDLINE ALL (Ovid) and NHS Economic Evaluations Database (CRD). 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 and cost utility studies.

A NICE senior information specialist (SIS) conducted the searches. The MEDLINE strategy was quality assured by another NICE SIS. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the [2015 PRESS Guideline Statement](#). Further details and full search strategies for each database are provided in [appendix B](#).

### 1.1.3.2 Protocol deviations

1. Severe adverse event classifications were further specified:

- The Intraoperative Adverse Incident Classification (EAUiaiC) and Clavien-Dindo Classification, both of which were already specified in the protocol, were used for thermal ablation and surgery interventions only.

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- 1       • The Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 or 4 was  
2       added to the protocol to be used for SABR and EBRT interventions, or for  
3       comparisons where one arm was SACT only. This addition aligns this protocol with  
4       others in this guideline (reviews A, B and C) and reflects the fact that Clavien-Dindo is  
5       usually used for surgery.
- 6       2. The quality of life outcomes were extracted when measured using EORTC Core Quality  
7       of Life Questionnaire and EuroQol-5 dimensions (EQ-5D). Later in the process it was  
8       agreed to include two additional scales assessing the quality of life outcomes as these  
9       are specific to advanced RCC. These two additional scales were:
  - 10       • Functional Assessment of Cancer Therapy Kidney Cancer Symptom Index (FKSI:  
11       both the FKSI-15 and the FKSI-DRS)
  - 12       • Renal Cell Carcinoma Symptom Index (RCC-SI)

#### 13       **1.1.4 Effectiveness evidence**

##### 14       **1.1.4.1 Included studies**

15       A single systematic search was carried out to identify potentially relevant studies for the  
16       current review (parts H1 and H2) and reviews A, B and C (review A: surgical interventions for  
17       localised RCC, review B: non-surgical interventions for localised RCC, review C:  
18       nephrectomy or stereotactic ablative radiotherapy for locally advanced RCC). This search  
19       found 19,882 references (see [appendix B](#) for the literature search strategy).

20       These 19,882 references were screened at title and abstract level against the review  
21       protocols, with 19,208 excluded at this level. 176 articles were assessed at full text for review  
22       H (H1 and H2 combined) (the remainder of those not excluded at title and abstract were  
23       assessed at full text stage for review A, B or C). 10% of references were screened separately  
24       by two reviewers with 99.9% agreement. Discrepancies were resolved by discussion.

25       The full texts of 176 references were ordered for closer inspection. A total of 27 articles – five  
26       RCTs and 22 retrospective cohort studies – met the criteria specified in the review protocol  
27       for review H1 ([appendix A](#)). Eighteen studies compared upfront cytoreductive nephrectomy  
28       (cytoreductive nephrectomy before systemic anti-cancer therapy [SACT]) with SACT alone,  
29       and 15 studies compared upfront cytoreductive nephrectomy with deferred cytoreductive  
30       nephrectomy (cytoreductive nephrectomy after SACT).

31       For a summary of the 27 articles included in this review see [Table 2](#).

32       The clinical evidence study selection is presented as a PRISMA diagram in [appendix C](#).

##### 33       **1.1.4.2 Excluded studies**

34       Details of studies excluded at full text, along with reasons for exclusion are given in [appendix](#)  
35       [J](#).



### 1.1.5 Summary of studies included in the effectiveness evidence

**Table 2: Summary of characteristics of the included randomised controlled trials**

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
<p>Bex (2019)</p> <p>SURTIME (NCT01099423)</p> <p>Multicentre study with 19 institutions in the Netherlands, Belgium, the United Kingdom, and Canada</p> <p>Study dates: This randomised clinical trial began on July 14, 2010, and continued until March 24, 2016, with a median follow-up of 3.3 years (range, 0-6.2 years) and a clinical cutoff date for this report of May 5, 2017</p>	<p>N = 99</p> <p>People aged 18 years or older, histologically confirmed, previously untreated clear cell metastatic renal cell carcinoma, resectable asymptomatic primary tumour in situ, required therapy with sunitinib, a life expectancy greater than 3 months, adequate bone marrow, liver, cardiac, and renal function, and 3 or fewer surgical risk factors</p> <p>Key exclusion criteria: not reported</p>	<p>Immediate cytoreductive nephrectomy + sunitinib (n = 50)</p>	<p>Deferred cytoreductive nephrectomy + sunitinib (n = 49)</p>	<ul style="list-style-type: none"> <li>Overall survival</li> <li>Progression-free survival</li> </ul>	Moderate
<p>De Bruijn (2019)</p> <p>SURTIME (NCT01099423)</p> <p>Multicentre study with 19 institutions in the Netherlands,</p>	<p>N = 99</p> <p>People aged 18 years or older, histologically confirmed, previously untreated clear cell metastatic renal cell carcinoma,</p>	<p>Immediate cytoreductive nephrectomy + sunitinib (n = 50)</p>	<p>Deferred cytoreductive nephrectomy + sunitinib (n = 49)</p>	<ul style="list-style-type: none"> <li>Duration of hospital stay</li> </ul>	Moderate

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Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Belgium, the United Kingdom, and Canada  Study dates: Began on July 14, 2010, and continued until March 24, 2016	resectable asymptomatic primary tumour in situ, required therapy with sunitinib, a life expectancy greater than 3 months, adequate bone marrow, liver, cardiac, and renal function, and 3 or fewer surgical risk factors  Key exclusion criteria: not reported				
Mejean (2021)  CARMENA trial - NCT00930033  Multicentre - Not reported where the centres were based  Study dates: 2009 to October 2018	N = 450  Patients with clear cell renal cell carcinoma confirmed on mandatory biopsy and documented metastatic disease, Eastern Cooperative Oncology Group (ECOG) status score of 0 to 1, absence of brain metastases or treated brain metastases without recurrence 3 weeks after treatment, acceptable organ function  Key exclusion criteria: Patients who received previous systemic treatment for kidney cancer (including VEGF-targeted	Cytoreductive nephrectomy + sunitinib (n = 226)	Sunitinib alone (n = 224)	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
	therapy) or anticoagulants, patients with any medical condition, including cardiovascular disease, that ruled them out as candidates for treatment				
<p>Mejean (2018)</p> <p>CARMENA trial - NCT00930033</p> <p>Multicentre - Not reported where the centres were based</p> <p>Study dates: 2009 to October 2017</p>	<p>N = 450</p> <p>Patients with clear cell renal cell carcinoma confirmed on mandatory biopsy and documented metastatic disease, Eastern Cooperative Oncology Group (ECOG) status score of 0 to 1, absence of brain metastases or treated brain metastases without recurrence 3 weeks after treatment, acceptable organ function</p> <p>Key exclusion criteria: Patients who received previous systemic treatment for kidney cancer (including VEGF-targeted therapy) or anticoagulants, patients with any medical condition, including cardiovascular disease, that ruled</p>	Cytoreductive nephrectomy + sunitinib (n = 226)	Sunitinib alone (n = 224)	<ul style="list-style-type: none"> <li>Progression-free survival</li> <li>Adverse event grade <math>\geq 3</math> (Clavien Dindo)</li> </ul>	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
	them out as candidates for treatment				
Shen (2023)  China  Study dates: 2018 – 2020	<p>N = 84</p> <p>Histologically or cytologically confirmed clear cell renal cell carcinoma, measurable disease according to RECIST 1.1 criteria, including primary and metastatic lesions, Eastern Cooperative Oncology Group (ECOG) status score of 0 to 1, life expectancy &gt; 24 weeks, primary resectable tumour at first diagnosis</p> <p>Key exclusion criteria: Brain or liver metastases, poor prognosis as defined by Memorial Sloan-Kettering Cancer Center (MSKCC) or Heng criteria, severe hepatic or renal insufficiency or uncontrolled hypertension or diabetes mellitus, active infection, primary tumours from other sites, previous surgical or systemic treatment for metastatic renal cell carcinoma</p>	Immediate cytoreductive nephrectomy (n = 42) before PD1 inhibitor SACT (nivolumab)	Delayed cytoreductive nephrectomy (n = 42) after PD1 inhibitor SACT (nivolumab)	<ul style="list-style-type: none"> <li>Overall survival</li> <li>Progression-free survival</li> </ul>	Moderate

See [appendix D](#) for full evidence tables.

**Table 3: Summary of characteristics of the included non-randomised controlled trials**

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Bakouny (2023)  United States - uses the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) database  Study dates: January 2020	N = 437  Initiated first-line systemic therapy on or after January 1, 2009  Diagnosed with de novo metastatic renal cell carcinoma or had not received a nephrectomy for localised renal cell carcinoma  Key exclusion criteria: Missing dates of diagnosis or dates of metastatic disease  Missing information on whether they had a nephrectomy or the date of nephrectomy	Immune checkpoint inhibitors with upfront cytoreductive nephrectomy (n = 234)	Immune checkpoint inhibitors no upfront cytoreductive nephrectomy (n = 203)	<ul style="list-style-type: none"><li>• Cytoreductive nephrectomy versus no cytoreductive nephrectomy</li><li>• age (&lt;65, 65–74, or &gt;75 yr)</li><li>• presence of bone, brain, or liver metastases (yes or no)</li><li>• non– clear cell or sarcomatoid histology (yes or no)</li><li>• Karnofsky Performance Scale (KPS: ≥80 or &lt;80)</li><li>• the number of IMDC risk factors (≤1, 2, 3, or ≥4)</li></ul>	<ul style="list-style-type: none"><li>• Overall survival</li></ul>	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
	Missing dates of death or last follow-up					
Bhindi (2018)  United States – utilises NCDB database  Study dates: 2006 - 2013	N = 15,068  People with metastatic kidney cancer. Key exclusion criteria: any other carcinoma, missing data, not receiving treatment within 3 months of diagnosis.	Initial cytoreductive nephrectomy then targeted therapy (n = 6,731)	Initial targeted therapy followed by cytoreductive nephrectomy (n = 8,337)	<ul style="list-style-type: none"> <li>• Age</li> <li>• Sex</li> <li>• Race</li> <li>• Charlson co-morbidity index</li> <li>• Income</li> <li>• Educational status</li> <li>• Country</li> <li>• Facility location</li> <li>• Facility type</li> <li>• Primary tumour histology</li> <li>• TNM classification</li> </ul>	<ul style="list-style-type: none"> <li>• Overall survival</li> </ul>	Serious
Bhindi (2020)  IMDC database (33 centres globally) Study dates: 2006 to 2018	N = 1,541  People receiving sunitinib as first line systemic anti-cancer therapy. Key exclusion criteria: unknown timings of	Upfront cytoreductive nephrectomy then sunitinib (n = 805)	Sunitinib followed by deferred cytoreductive nephrectomy (n = 85)	<ul style="list-style-type: none"> <li>• Age</li> <li>• Sex</li> <li>• Year of diagnosis</li> <li>• IMDC risk,</li> <li>• Clear cell histology</li> </ul>	<ul style="list-style-type: none"> <li>• Overall survival</li> </ul>	Serious

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Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
	surgery, missing data, SACT after 12 months of diagnosis.		Sunitinib alone (n = 651)	<ul style="list-style-type: none"> <li>Number of metastatic sites</li> <li>Location of metastases</li> </ul>		
Chakiryan (2022)  United States – utilises NCDB database  Study dates: 2006 to 2016	N = 12,154  People with metastatic renal cancer with complete data.	Up-front cytoreductive nephrectomy (n = 4393) before SACT (described only as targeted therapy)	No cytoreductive nephrectomy, only systemic anti-cancer therapy alone (n = 7761) after SACT (described only as targeted therapy)	<ul style="list-style-type: none"> <li>Age</li> <li>Sex</li> <li>Race</li> <li>Charlson-Deyo score</li> <li>Year of diagnosis</li> <li>Clinical staging</li> <li>Cytoreductive nephrectomy status</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious
Choueiri (2011)  United States and Canada  Study dates: August 2004 and July 2008	N = 314  Patients diagnosed with metastatic renal cell carcinoma of any pathological subtype and treated with sunitinib, sorafenib or bevacizumab	Cytoreductive nephrectomy, before systemic anti-cancer therapy (sunitinib, sorafenib or bevacizumab) (n = 201)	No cytoreductive nephrectomy, only systemic anti-cancer therapy (sunitinib, sorafenib or bevacizumab) (n = 113)	<ul style="list-style-type: none"> <li>Patients with or without brain metastases</li> <li>with Karnofsky performance status 80% or greater vs less than 80%</li> <li>with more than 1 site of metastasis</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
				vs 1 site of metastasis <ul style="list-style-type: none"> <li>on different types of vascular endothelial growth factor targeted therapy</li> </ul>		
de Groot (2016)  Netherlands - Patients from the Dutch Cancer Registry  Study dates: January 2008 and December 2010	N = 146  Patients diagnosed with metastatic renal cell carcinoma (i.e., metastases at initial presentation) of any histologic subtype and treated with first-line sunitinib  Key exclusion criteria: Not reported	Cytoreductive nephrectomy then sunitinib (n = 73)	No cytoreductive nephrectomy, only sunitinib (n = 73)	<ul style="list-style-type: none"> <li>Baseline demographics (age at diagnosis and gender)</li> <li>3 additional clinical factors (histology, clinical tumour stage, and regional lymph node involvement)</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious
Dragomir (2022)  Canada – utilises Canadian Kidney Cancer information system	N = 708  People with histologically diagnosed renal cell carcinoma.	Cytoreductive nephrectomy before systemic therapy (n = 383)  Type of SACT – sunitinib (n=230), pazopanib (n=72), ipilimumab/nivolumab (n=	Cytoreductive nephrectomy after systemic therapy (n = 73)	<ul style="list-style-type: none"> <li>Age</li> <li>Sex</li> <li>Sites and number of organs for metastasis</li> <li>Cell histology</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious

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Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Study dates: 2011 to 2020	Key exclusion criteria: People with indolent metastatic disease	3), nivolumab, everolimus / pembrolizumab / temsirolimus / atezolizumab / axitinib / lenvatinib (n= 37)	Systemic therapy only (n = 252)  Type of SACT – sunitinib (n=52), pazopanib (n=8), ipilimumab / nivolumab (n= 3), nivolumab, everolimus / pembrolizumab / temsirolimus / atezolizumab / axitinib / lenvatinib (n= 10)	<ul style="list-style-type: none"> <li>IMDC risk</li> <li>Charlson comorbidity index</li> </ul>		
Ghatalia (2022)  United States - uses the nationwide US Flatiron Health (FH) electronic health record (EHR)-derived deidentified database  Study dates:2011 - 2020	N = 1,719  Patients with clear cell histology and synchronous metastases  Key exclusion criteria: Not reported	Upfront cytoreductive nephrectomy (n = 605)  Type of SACT- ipilimumab / nivolumab (n=59), Pembrolizumab / axitinib (n= 18), avelumab / axitinib (n=2), nivolumab/ pazopanib (n= 1), bevacizumab / INFa2b (n= 3), immunotherapy alone (n=33), VEGFR inhibitors	Deferred cytoreductive nephrectomy (n = 142)  Systemic therapy alone (n = 972)  Type of SACT - ipilimumab / nivolumab (n=17), pembrolizumab /	<ul style="list-style-type: none"> <li>Age</li> <li>Gender</li> <li>Race</li> <li>insurance at diagnosis</li> <li>IMDC risk group</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious

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Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
		(n= 388), mTOR inhibitors (n= 101)	axitinib (n= 11), immunotherapy alone (n= 4), VEGFR inhibitors (n= 89), mTOR inhibitors (n= 13)			
<p>Gunenc (2024)</p> <p>United States</p> <p>Study dates: April 2016 – October 2022</p>	<p>N = 51</p> <p>Patients with metastatic renal cell carcinoma receiving immunotherapy-based therapies and undergoing cytoreductive nephrectomy</p> <p>Key exclusion: patients who did not receive immunotherapy-based therapies</p>	<p>Upfront cytoreductive nephrectomy (n=13): patients who were receiving immunotherapy-based therapies after surgery</p> <p>Type of SACT – immune checkpoint inhibitors, tyrosine kinase inhibitors (in combination or as monotherapies).</p>	<p>Deferred cytoreductive nephrectomy (n=38): patients who were receiving immunotherapy-based therapies in the preoperative setting</p> <p>Type of SACT – immune checkpoint inhibitors, tyrosine kinase inhibitors (in combination or as monotherapies).</p>	<ul style="list-style-type: none"> <li>Not reported</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> <li>Progression free survival</li> </ul>	Serious
<p>Hara (2023)</p> <p>Japan - used the institutional medical</p>	<p>N = 54</p>	<p>Cytoreductive nephrectomy before ipilimumab plus nivolumab (n = 21)</p>	<p>Without cytoreductive nephrectomy (n = 33)</p>	<ul style="list-style-type: none"> <li>Age</li> <li>Body mass index</li> <li>Sex</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> <li>Progression-free survival</li> </ul>	Serious

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
<p>record database at Kobe University Hospital and five affiliated hospitals</p> <p>Study dates: October 2018 and December 2021</p>	<p>Patients with synchronous metastatic renal cell carcinoma</p> <p>Key exclusion criteria: Patients who received deferred cytoreductive nephrectomy</p>			<ul style="list-style-type: none"> <li>• International Metastatic RCC Database Consortium risk classification</li> <li>• Histology</li> <li>• Presence of liver, brain, or bone metastasis</li> <li>• Clinical T stage</li> <li>• Neutrophil lymphocyte ratio</li> <li>• Number of metastasis</li> <li>• Presence of tumour associated symptoms</li> </ul>		
<p>Hatakeyama (2021)</p> <p>Japan - Michinoku Japan Urological Cancer Study Group database</p>	<p>N = 278</p> <p>Patients with primary metastatic renal cell carcinoma</p> <p>Key exclusion criteria: Treatment with first-line</p>	<p>Immediate cytoreductive nephrectomy followed by first-line tyrosine kinase inhibitors (n = 107)</p>	<p>Deferred cytoreductive nephrectomy - after receiving tyrosine kinase inhibitors (n = 39)</p>	<ul style="list-style-type: none"> <li>• Age</li> <li>• Sex</li> <li>• Performance status</li> <li>• Number of IMDC risk factors</li> </ul>	<ul style="list-style-type: none"> <li>• Overall survival</li> </ul>	<p>Serious</p>

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Study dates: January 2008 - November 2019	interferon, mammalian target of rapamycin inhibitors, immunotherapy, or chemotherapy; a period from diagnosis to first treatment of more than 3 months; a period of surveillance after immediate cytoreductive nephrectomy of more than 3 months; a follow-up period from the first treatment of less than 3 months		Systemic anti-cancer therapy alone - tyrosine kinase inhibitors (n = 132)	<ul style="list-style-type: none"> <li>Clinical stage (cT3b–4)</li> <li>Number of metastatic organs</li> </ul>		
Macleod (2018)  United States - data use agreement set forth by The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program data linked with Medicare claims	N = 537 Patients with metastatic renal cell carcinoma  Key exclusion criteria: Incomplete treatment claims data, under 66 years of age, patients receiving cytoreductive nephrectomy but no additional therapy, competing non-metastatic	Initial cytoreductive nephrectomy followed by targeted therapy (n = 190)	No cytoreductive nephrectomy, only initial systemic therapy (n = 347)	<ul style="list-style-type: none"> <li>Demographic factors (age, race, ethnicity, rural status)</li> <li>Treatment era (first half and latter half of study period)</li> <li>Cancer severity (tumour stage, nodal status, histology)</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Study dates: 2006 – 2011	renal cell carcinoma stage IV cancer			<ul style="list-style-type: none"> <li>Comorbidity (Charlson-Klabunde index)</li> <li>SEER registry</li> </ul>		
Manley (2017)  United States  Study dates: 2005 - 2013	N = 123  Patients with metastatic renal cell carcinoma  Key exclusion criteria: Patients with missing survival data, with incomplete clinical data and patients who received prior immunotherapy	Cytoreductive nephrectomy then targeted therapy (n = 88)	No cytoreductive nephrectomy, only targeted therapy (n = 35)	<ul style="list-style-type: none"> <li>Age</li> <li>Comorbidity</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious
Meagher (2024)  Italy and Spain – used data from the REMARCC database which collected data from 14 North American and European institutions	N = 189  Patients diagnosed with metastatic renal cell carcinoma who underwent cytoreductive nephrectomy	Upfront cytoreductive nephrectomy followed by systemic therapy  Type of SACT – tyrosine kinase inhibitor or immunotherapy	Systemic therapy followed by deferred cytoreductive nephrectomy  Type of SACT – tyrosine kinase inhibitor or immunotherapy	Not reported	<ul style="list-style-type: none"> <li>Overall survival</li> <li>Cancer-specific survival</li> </ul>	Serious

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Study dates: January 2006 to October 2019						
Patel (2016)	N = 48	Cytoreductive nephrectomy then sunitinib (n = 27)	Sunitinib followed by cytoreductive nephrectomy (n = 21)	<ul style="list-style-type: none"> <li>• Age</li> <li>• Race</li> <li>• BMI</li> <li>• ECOG</li> <li>• Type of procedure performed</li> <li>• Surgical approach</li> <li>• RENAL nephrometry score</li> <li>• Tumour grade</li> <li>• Presence of thrombus</li> </ul>	<ul style="list-style-type: none"> <li>• Duration of hospital stay</li> <li>• Surgical complications – Grade 3a/b (Clavien-Dindo)</li> </ul>	Serious
United States	Patients diagnosed with metastatic renal cell carcinoma, primary systemic therapy was offered to all patients					
Study dates: July 2007 to January 2014	Key exclusion criteria: Patients with overwhelming burden of metastatic disease, with poor performance status, who proceeded to systemic therapy after the initial evaluation without a plan to offer cytoreductive nephrectomy, tumour histology was not clear cell renal cell carcinoma, patients who undergone prior chemotherapy or immunotherapy					

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
<p>Poprach (2020)</p> <p>Czech Republic - RenIS Registry database</p> <p>Study dates: 2007 to 2018</p>	<p>N = 730</p> <p>Patients with synchronous metastatic disease or</p> <p>Key exclusion criteria: Not reported</p>	<p>Cytoreductive nephrectomy within 3 months of diagnosis then targeted therapies (pazopanib or sunitinib) (n = 458)</p>	<p>No cytoreductive nephrectomy, only targeted therapies (pazopanib or sunitinib) (n = 272)</p>	<ul style="list-style-type: none"> <li>Not reported</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> <li>Progression-free survival</li> </ul>	Serious
<p>Singla (2020)</p> <p>United States - uses the National Cancer Database (NCDB)</p> <p>Study dates: 2015 - 2016</p>	<p>N = 221</p> <p>Patients diagnosed with metastatic renal clear cell carcinoma</p> <p>Key exclusion criteria: Patients who received any non-immunotherapy systemic therapies</p>	<p>Cytoreductive nephrectomy then immunotherapy (n = 197)</p>	<p>Immunotherapy followed by cytoreductive nephrectomy (n = 24)</p>	<ul style="list-style-type: none"> <li>Patient demographics</li> <li>Performance of cytoreductive nephrectomy</li> <li>Presence of sarcomatoid features</li> <li>Primary tumour size</li> <li>cT stage</li> <li>cN stage</li> <li>Presence of bone, brain, liver, or lung metastases</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
				<ul style="list-style-type: none"> <li>Number of known metastatic sites</li> <li>Time to receipt of immunotherapy from diagnosis</li> </ul>		
<p>Stroup (2013)</p> <p>United States - multi-institutional (University of California San Diego Medical Centre; San Diego Veterans Administration Medical Centre; University of Tennessee Health Sciences Centre Memphis)</p> <p>Study dates: May 2005 to August 2009</p>	<p>N = 35</p> <p>Patients diagnosed with metastatic renal cell carcinoma</p> <p>Key exclusion criteria: Patients with an overwhelming burden of metastatic disease, with poor performance status, who proceeded to systemic therapy after the initial evaluation without a plan to offer cytoreductive nephrectomy, tumour histology was not clear cell renal cell carcinoma, patients who had undergone prior chemotherapy or immunotherapy</p>	Cytoreductive nephrectomy then sunitinib (n = 17)	<p>Sunitinib followed by cytoreductive nephrectomy (n = 11)</p> <p>Sunitinib alone (n = 7)</p>	<ul style="list-style-type: none"> <li>Age</li> <li>Race</li> <li>BMI</li> <li>ECOG score (0 or 1 vs &gt;1)</li> <li>Tumour size (&lt;7 vs ≥7 cm)</li> <li>Tumour grade</li> <li>Inferior vena cava thrombus</li> <li>Number of metastatic lesions (&lt;5 vs ≥5)</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> <li>Cancer specific survival</li> </ul>	Serious

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)



Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
<p>Takemura (2023)</p> <p>Multicentre collaboration involving participants from more than 40 institutions worldwide: Australia, Belgium, Canada, Denmark, Germany, Greece, Italy, Japan, Mexico, Netherlands, New Zealand, Singapore, South Korea, Spain, UK, and the United States</p> <p>Study dates: Not reported</p>	<p>N = 807</p> <p>Patients received frontline immuno-oncology based combinations, including immuno-oncology/immuno-oncology doublet therapy and immuno-oncology/tyrosine kinase inhibitor combination therapy, patients diagnosed with either synchronous metastatic renal cell carcinoma or metachronous metastatic renal cell carcinoma without previous nephrectomy for localized renal cell carcinoma, patient did not die nor were censored within a fixed landmark time, with different landmark time periods (6, 9, 12, and 18 months) examined</p> <p>Key exclusion criteria: Patients with missing data</p>	<p>Upfront cytoreductive nephrectomy (n = 327)</p> <p>Immuno-oncology alone (n = 440)</p>	<p>Deferred cytoreductive nephrectomy (n = 40)</p> <p>Type of SACT – Immuno-oncology based combination</p>	<ul style="list-style-type: none"> <li>Not reported</li> </ul>	<ul style="list-style-type: none"> <li>Mortality</li> </ul>	Serious

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Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
	for the date of diagnosis or metastasis, patients with missing data for whether they underwent nephrectomy, or the date of nephrectomy, patients with missing data for whether they are dead or alive, or the date of death or last follow-up					
Xu (2019)  China - Department of Urology, Fudan University Shanghai Cancer Centre (FUSCC) Shanghai  Study dates: May 2009 and June 2018	N = 118  Patients who had metastases on initial diagnosis and who were treated by urologists according to the standard treatment at the institution  Key exclusion criteria: Not reported	Cytoreductive nephrectomy then sunitinib (n = 70)	Sunitinib alone (n = 48)	<ul style="list-style-type: none"> <li>Not reported</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> <li>Progression-free survival</li> </ul>	Serious
Yoshino (2022)  Japan - five affiliated institutions	N = 41  Patients with synchronous metastatic renal cell carcinoma	Upfront cytoreductive nephrectomy then nivolumab plus ipilimumab initiation (n = 21)	No cytoreductive nephrectomy (n = 13)  Nivolumab plus ipilimumab +	<ul style="list-style-type: none"> <li>Not reported</li> </ul>	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Study dates: September 2016 and July 2021	Key exclusion criteria: Patients whose duration of post-treatment follow-up was short (i.e. <1 month) or whose clinical data were missing		deferred cytoreductive nephrectomy (n = 7)			
You (2021)  Republic of Korea  Study dates: November 2006 to December 2009	N = 78  Patients diagnosed with metastatic renal clear cell carcinoma  Key exclusion criteria: Non-clear cell type renal cell carcinoma, no evidence of residual disease due to complete nephrectomy and metastasectomy	Cytoreductive nephrectomy + targeted therapy (n = 45)	Targeted therapy alone (n = 33)	<ul style="list-style-type: none"><li>Memorial Sloan-Kettering Cancer Centre prognostic factors</li></ul>	<ul style="list-style-type: none"><li>Overall survival</li><li>Progression-free survival</li></ul>	Serious

1 See [appendix D](#) for full evidence tables.  
2

1     **1.1.6 Summary of the effectiveness evidence**

2     Clinical decision thresholds for minimally important differences (MIDs) were used to interpret  
3     the evidence. The line of no effect (in this case represented by 1.0) was used as a clinical  
4     decision threshold for the outcomes of overall survival, mortality, progression-free survival,  
5     cancer specific survival, duration of hospital stay, and complications grade  $\geq 3$  (Clavien  
6     Dindo). No data was identified for need for further systemic therapy, and quality of life.

7     The following criteria were used to interpret the effect (column of 'Interpretation of effect'  
8     below) in the summary GRADE tables:

- 9     • For outcomes without a defined MID or where the MID is set as the line of no effect,  
10     evidence statements are divided into 2 groups as follows:
- 11         ○ We state that the evidence showed that there is an effect if the 95% CI does not  
12         cross the line of no effect.
  - 13         ○ It is not possible from the evidence to differentiate between comparators if the  
14         95% CI crosses the line of no effect.

15     Further details on GRADE assessment are described in [appendix F](#).

16     Cytoreductive nephrectomy (CN) followed by systemic anti-cancer therapy (SACT) is  
17     summarised as "upfront CN". CN delivered after SACT is summarised as "deferred CN".

1 **Upfront cytoreductive nephrectomy (CN) vs. deferred CN**

2 **Survival outcomes**

3 **Table 4: Survival outcomes comparing upfront cytoreductive nephrectomy and then systemic anti-cancer therapy versus**  
4 **systemic anti-cancer therapy followed by cytoreductive nephrectomy**

Number of studies	Study design	Outcome	Histological type	Sample size	Effect estimate	Certainty	Interpretation of effect
2 (Bex 2018, Shen 2023)	Randomised controlled trial	Progression-free survival, ≤5 years	Clear cell	183	HR 1.35 (0.94 to 1.95)	Very low	Could not differentiate
1 (Gunenc 2024)	non-randomised study	Progression-free survival, ≤5 years	Mixed	51	HR 0.40 (0.12 to 1.39)	Very low	Could not differentiate
2 (Bex 2018, Shen 2023)	Randomised controlled trial	Overall survival, ≤5 years	Clear cell	183	HR 1.54 (1.02 to 2.32)	Low	Effect favours deferred cytoreductive nephrectomy
2 (Meagher 2024, Stroup 2013)	Non-randomised controlled trial	Cancer-specific survival, ≤5 years	Clear cell	217	HR 2.15 (1.43 to 3.25)	Very low	Effect favours deferred cytoreductive nephrectomy
8 (Bhindi 2018, Bhindi 2020, Ghatalia 2022, Gunenc 2024, Macleod 2018, Meagher 2024, Singla 2020, Stroup 2013 )	Non-randomised controlled trial	Overall survival, ≤5 years	Mixed	17,731	HR 0.94 (0.70 to 1.28)	Very low	Could not differentiate

Number of studies	Study design	Outcome	Histological type	Sample size	Effect estimate	Certainty	Interpretation of effect
2 (Takemura 2024, Yoshino 2022*)	Non-randomised controlled trial	Mortality, ≤5 years	Mixed	395	RR 5.08 (1.03 to 25.03)	Very low	Effect favours deferred cytoreductive nephrectomy
1 (Hatakeyama 2021)	Non-randomised controlled trial	Overall survival, >5 years	Mixed	146	HR 1.64 (0.87 to 3.09)	Very low	Could not differentiate

\* Converted from 'overall survival' reported as events  
Reasons for downgrading can be found in the full GRADE tables in [appendix F](#).

1   **All other outcomes**

2   **Table 5: All other outcomes comparing upfront cytoreductive nephrectomy and then systemic anti-cancer therapy versus**  
3   **systemic anti-cancer therapy followed by cytoreductive nephrectomy**

Number of studies	Study design	Outcome	Histological type	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Bex 2018)	Randomised controlled trial	Adverse events grade ≥3 (Clavien Dindo)	Clear cell	80	RR 0.45 (0.05 to 4.15)	Very low	Could not differentiate
1 (De Bruijn 2019)	Randomised controlled trial	Duration of hospital stay - Days	Clear cell	80	MD 1.00 (-1.35 to 3.35)	Very low	Could not differentiate
1 (Patel 2016)	Non-randomised controlled trial	Adverse events grade ≥3 (Clavien Dindo)	Clear cell	48	RR 0.06 (0.00 to 1.02)	Very low	Could not differentiate
1 (Patel 2016)	Non-randomised controlled trial	Duration of hospital stay - Days	Clear cell	48	MD -2.50 (-6.19 to 1.19)	Very low	Could not differentiate

4   Reasons for downgrading can be found in the full GRADE tables in [appendix F](#).

1 **Upfront cytoreductive nephrectomy (CN) vs. no CN (systemic anti-cancer therapy, SACT, alone)**

2 **Survival outcomes**

3 **Table 6: Survival outcomes comparing upfront cytoreductive nephrectomy and then systemic anti-cancer therapy versus**  
4 **systemic anti-cancer therapy alone**

Number of studies	Study design	Outcome	Histological type	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Méjean 2018)	Randomised controlled trial	Progression-free survival, ≤5 years	Clear cell	399	HR 0.82 (0.67 to 1.00)	Very low	Could not differentiate
1 (Méjean 2021)	Randomised controlled trial	Overall survival, ≤5 years	Clear cell	450	HR 0.97 (0.79 to 1.19)	Very low	Could not differentiate
3 (Hara 2023, Xu 2019, You 2011)	Non-randomised controlled trial	Progression-free survival, ≤5 years	Clear cell	350	HR 0.73 (0.39 to 1.37)	Very low	Could not differentiate
1 (Stroup 2013)	Non-randomised controlled trial	Cancer specific survival, ≤5 years	Clear cell	35	HR 0.10 (0.02 to 0.42)	Very low	Effect favours upfront cytoreductive nephrectomy
11 (Bakouny 2023, Bhindi 2020, Chakiryan 2022, Choueiri 2011, Dragomir 2022, de Groot 2016, Ghatalia 2022, Hara 2023, Manley 2017, Xu 2019, You 2011)	Non-randomised controlled trial	Overall survival, ≤5 years	Mixed	20,957	HR 0.67 (0.54 to 0.82)	Very low	Effect favours upfront cytoreductive nephrectomy



Number of studies	Study design	Outcome	Histological type	Sample size	Effect estimate	Certainty	Interpretation of effect
2 (Takemura 2024, Yoshino 2022*)	Non-randomised controlled trial	Mortality, ≤5 years	Mixed	801	RR 0.56 (0.41 to 0.76)	Low	Effect favours upfront cytoreductive nephrectomy
2 (Hatakeyama 2021, Poprach 2020)	Non-randomised controlled trial	Overall survival, >5 years	Mixed	969	HR 0.57 (0.47 to 0.68)	Low	Effect favours upfront cytoreductive nephrectomy

Reasons for downgrading can be found in the full GRADE tables in [appendix F](#).

**All other outcomes**

**Table 7: All other outcomes comparing upfront cytoreductive nephrectomy and then systemic anti-cancer therapy versus systemic anti-cancer therapy alone**

Number of studies	Study design	Outcome	Histological type	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Méjean 2018)	Randomised controlled trial	Adverse events grade ≥3	Mixed	399	RR 0.77 (0.59 to 0.99)	Very low	Effect favours upfront cytoreductive nephrectomy
1 (Hara 2023)	Non-randomised controlled trial	Adverse events grade ≥3 (Clavien Dindo)	Mixed	54	RR 1.75 (0.85 to 3.57)	Very low	Could not differentiate

Reasons for downgrading can be found in the full GRADE tables in [appendix F](#).

See [appendix F](#) for full GRADE tables.

### 1.1.7 Economic evidence

Evidence review H contains two parts (H1 and H2). A single literature search was conducted to identify published economic evaluations of relevance to the review questions on the management of RCC in this guideline (see [appendix B](#)), which includes both H1 and H2 for the management of advanced RCC, as well as reviews for the management of localised RCC (evidence reviews A and B) and locally advanced RCC (evidence review C).

This search retrieved 326 studies and based on title and abstract screening four studies were identified as potentially relevant for any of the evidence reviews covered by the search. On review of the full text, two studies were included for evidence review B, and two 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 evidence was identified for the present review questions H1 and H2 on the non-pharmacological management of advanced RCC. Two economic studies were included in evidence review B on non-surgical interventions or active surveillance in adults with localised RCC (see evidence review B for details).

#### 1.1.7.2 Excluded studies

Two studies were excluded at full text review (see [appendix J](#) for a list of studies and 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 interventions are listed in [Table 8](#).

**Table 8: Unit costs of interventions**

Resource	Unit cost	Source
Open nephrectomy	£10,142.10	NHS Cost Collection (2024). Weighted average of codes LB61C-G, Major, Open or Percutaneous, Kidney or Ureter Procedures, 19 years and over
Laparoscopic nephrectomy	£9,970.10	NHS Cost Collection (2024). Weighted average of codes LB62C-D, Major Laparoscopic, Kidney or Ureter Procedures, 19 years and over
Robot-assisted nephrectomy	£10,172.87	Ratio of robotic to laparoscopic partial nephrectomy cost estimated from Camp et al. (2018), calculated as £4,444 / £4,356 = 1.02. Ratio applied to the laparoscopic nephrectomy unit cost to estimate the robotic nephrectomy unit cost.

Resource	Unit cost	Source
CT preparation for SABR therapy	£1,770.46	NHS Cost Collection (2024). SC41Z preparation for intensity modulated radiation therapy with technical support
One fraction of SABR	£239.83	NHS Cost Collection (2024). SC22Z deliver a fraction of treatment on a megavoltage machine
Radiofrequency ablation	£1,960.46	NHS Cost Collection (2024). YL02Z Standard Percutaneous Ablation of Lesion of Kidney
Cryoablation	£3,474.14	NHS Cost Collection (2024). YL01Z Complex Percutaneous Ablation of Lesion of Kidney
Microwave ablation	£1,960.46	NHS Cost Collection (2024). YL02Z Standard Percutaneous Ablation of Lesion of Kidney
Metastasectomy	£4,160.46 - £6,774.33	NHS Cost Collection (2024). LB06J-M Kidney urinary tract or prostate neoplasms with interventions and DZ17P-R Respiratory neoplasms with single intervention

SABR: stereotactic ablative radiotherapy, CT: computed tomography

### 1 1.1.10 The committee's discussion and interpretation of the evidence

- 2 Evidence review H contains two parts (H1 and H2). The committee discussed both parts of  
3 the evidence review together, and there is a single discussion section to record this. See  
4 [section 2.1.8](#) for the full discussion.

**1.1.11 References – included studies**

**1.1.12.1 Effectiveness – randomised controlled trials**

[Bex A, Mulders P, Jewett M et al. \(2019\) Comparison of Immediate vs Deferred Cytoreductive Nephrectomy in Patients With Synchronous Metastatic Renal Cell Carcinoma Receiving Sunitinib: The SURTIME Randomized Clinical Trial. JAMA oncology 5\(2\): 164-170](#)

[De Bruijn R.E, Mulders P, Jewett M. A et al. \(2019\) Surgical Safety of Cytoreductive Nephrectomy Following Sunitinib: Results from the Multicentre, Randomised Controlled Trial of Immediate Versus Deferred Nephrectomy \(SURTIME\). European urology 76\(4\): 437-440](#)

[Mejean A, Ravaud A, Thezenas S et al. \(2021\) Sunitinib Alone or After Nephrectomy for Patients with Metastatic Renal Cell Carcinoma: Is There Still a Role for Cytoreductive Nephrectomy?. European urology 80\(4\): 417-424](#)

[Mejean A, Ravaud A, Thezenas S et al. \(2018\) Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma. The New England journal of medicine 379\(5\): 417-427](#)

[Shen X-P, Xie M, Wang J-S et al. \(2023\) Efficacy of immunotherapy-based immediate cytoreductive nephrectomy vs. deferred cytoreductive nephrectomy in metastatic renal cell carcinoma. European review for medical and pharmacological sciences 27\(12\): 5684-5691](#)

**1.1.12.2 Effectiveness – non-randomised controlled trials**

[Bakouny Z, El Zarif T, Dudani S et al. \(2023\) Upfront Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma Treated with Immune Checkpoint Inhibitors or Targeted Therapy: An Observational Study from the International Metastatic Renal Cell Carcinoma Database Consortium. European urology 83\(2\): 145-151](#)

[Bhindi B, Habermann E.B., Mason R.J. et al. \(2018\) Comparative Survival following Initial Cytoreductive Nephrectomy versus Initial Targeted Therapy for Metastatic Renal Cell Carcinoma. Journal of Urology 200\(3\): 528-534](#)

[Bhindi B, Graham J, Wells JC et al. \(2020\) Deferred Cytoreductive Nephrectomy in Patients with Newly Diagnosed Metastatic Renal Cell Carcinoma. European urology 78\(4\): 615-623](#)

[Chakiryan N.H, Gore L.R, Reich R.R et al. \(2022\) Survival Outcomes Associated With Cytoreductive Nephrectomy in Patients With Metastatic Clear Cell Renal Cell Carcinoma. JAMA network open 5\(5\): e2212347](#)

[Choueiri T.K, Xie W, Kollmannsberger C et al. \(2011\) The impact of cytoreductive nephrectomy on survival of patients with metastatic renal cell carcinoma receiving vascular endothelial growth factor targeted therapy. The Journal of urology 185\(1\): 60-6](#)

[de Groot S, Redekop W.K, Sleijfer S et al. \(2016\) Survival in Patients With Primary Metastatic Renal Cell Carcinoma Treated With Sunitinib With or Without Previous Cytoreductive Nephrectomy: Results From a Population-based Registry. Urology 95: 121-7](#)

[Dragomir A, Nazha S, Tanguay S et al. \(2022\) Outcomes of Cytoreductive Nephrectomy for Patients with Metastatic Renal Cell Carcinoma: Real World Data from Canadian Centers. European Urology Focus 8\(6\): 1703-1710](#)

- 1 [Ghatalia P, Handorf E.A, Geynisman D M et al. \(2022\) The Role of Cytoreductive](#)
- 2 [Nephrectomy in Metastatic Renal Cell Carcinoma: A Real-World Multi-Institutional Analysis.](#)
- 3 [The Journal of urology 208\(1\): 71-79](#)
- 4 [Gunenc D, Issa W, Gerald T, Zhou Q, Zhang S et al. Pathological Response and Outcomes](#)
- 5 [in Patients With Metastatic Renal Cell Carcinoma \(mRCC\) Receiving Immunotherapy-Based](#)
- 6 [Therapies and Undergoing Deferred Cytoreductive Nephrectomy \(CN\). Clin Genitourin](#)
- 7 [Cancer 22\(5\): 102177.](#)
- 8 [Hara T, Furukawa J, Shiraishi Y et al. \(2023\) Impact of cytoreductive nephrectomy prior to](#)
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# 2 Management of advanced renal cell carcinoma using non-pharmacological interventions after systemic anti-cancer therapy

## 2.1 Review question

What is the clinical and cost-effectiveness of non-pharmacological interventions used after systemic anti-cancer therapy for adults with advanced renal cell carcinoma?

### 2.1.1 Introduction

There are number of treatment options available for advanced renal cell carcinoma. These usually include pharmacological (systemic anti-cancer therapy, SACT) and non-pharmacological interventions. It is important to understand the sequence of these treatment modalities for reducing disease burden and improving survival benefits in the most effective manner.

Therefore, this review aims to evaluate the clinical and cost-effectiveness of non-pharmacological interventions after initial treatment with SACT in managing advanced renal cell carcinoma. [Review H1](#) assesses the clinical and cost-effectiveness of non-pharmacological interventions before SACT.

### 2.1.2 Summary of the protocol

**Table 9: PICO inclusion criteria**

<b>Population</b>	Adults (18 years or over) with advanced RCC* who have previously received systemic anti-cancer treatment (SACT). *defined as metastatic/ advanced RCC or locally advanced inoperable RCC (histologically confirmed or suspected on imaging).  Advanced RCC diagnosis confirmed according to the clinical or pathological TNM classification  Exclusion: <ul style="list-style-type: none"><li>• Adults with localised or locally advanced disease that is considered to be operable.</li><li>• Adults with advanced disease who are having palliative care only.</li></ul>
<b>Interventions</b>	<ul style="list-style-type: none"><li>• Non-pharmacological procedures carried out after SACT to manage primary mass:<ul style="list-style-type: none"><li>○ Cytoreductive nephrectomy</li><li>○ Stereotactic ablative radiotherapy (SABR)</li></ul></li><li>• Managing metastases:<ul style="list-style-type: none"><li>○ Surgical removal</li><li>○ Thermal ablation:</li></ul></li></ul>

	<ul style="list-style-type: none"> <li>▪ Radiofrequency ablation</li> <li>▪ Cryotherapy</li> <li>▪ Microwave ablation</li> <li>○ Radiotherapy: <ul style="list-style-type: none"> <li>▪ External beam radiotherapy (EBRT)</li> <li>▪ Stereotactic ablative radiotherapy (SABR)</li> </ul> </li> </ul>
<b>Comparator</b>	<p>When both arms have previously had SACT for advanced RCC:</p> <ul style="list-style-type: none"> <li>• No intervention (compared with non-pharma intervention)</li> </ul> <p>When neither arm has previously had SACT for advanced RCC:</p> <ul style="list-style-type: none"> <li>• SACT (compared with SACT then non-pharma intervention)</li> </ul>
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>• Progression-free survival</li> <li>• Overall survival or if not reported: <ul style="list-style-type: none"> <li>○ Mortality</li> </ul> </li> <li>• Cancer-specific survival or if not reported: <ul style="list-style-type: none"> <li>○ Cancer-specific mortality</li> </ul> </li> <li>• Severe adverse events reported as: <ul style="list-style-type: none"> <li>○ observed in the intraoperative period</li> <li>○ observed in postoperative period</li> </ul> </li> <li>• Need for further systemic therapy</li> <li>• Number of hospital admissions</li> <li>• Duration of hospital stay</li> <li>• Quality of life</li> </ul>
<b>Study type</b>	<ul style="list-style-type: none"> <li>• Randomised controlled trials (RCTs)</li> <li>• Any controlled, non-randomised studies</li> <li>• Cohort studies (prospective and retrospective observational studies)</li> <li>• Systematic reviews of the above studies</li> </ul>

1 For the full protocol see [appendix A](#). Note: this PICO reflects the protocol deviations (see  
2 [section 2.1.3.2](#) for details).

### 3 **2.1.3 Methods and process**

4 This evidence review was developed using the methods and process described in  
5 [Developing NICE guidelines: the manual](#). Methods specific to this review question are  
6 described in the review protocol in [appendix A](#), the text below and the methods document.

7 Methods and technical decisions specific to this review are summarised below:

- 8 1. Mortality at timepoints of 90 days or less was not included in this review. This was  
9 considered to be within the postoperative period and therefore covered by the outcome of  
10 postoperative severe adverse events (PSAE). PSAE was required to be reported using  
11 the acceptable classifications - Clavien-Dindo classification or Common Terminology  
12 Criteria for Adverse Events (CTCAE) in order to be included.
- 13 2. Where more than 1 timepoint was reported we reported data at up to 5 years and 5 to 10  
14 years. Where several time points were reported that could fit in the same category, the  
15 latest time point was used.

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3. For outcomes where the line of no effect was defined as the minimal important difference (MID), a power calculation from a robust RCT (Mejean 2018, included in this review) was used to determine the minimum sample size needed for consideration for the second downgrade criteria for the imprecision domain in GRADE. One RCT was identified which compared upfront cytoreductive nephrectomy with sunitinib alone (Mégean 2018). This trial does not meet the inclusion criteria for this review, but is related. It was used as a source to inform the minimum sample size needed. For all outcomes sample size of less than 576 was used for downgrading.
4. Important confounders considered for assessing the quality of the included studies under this review were discussed and agreed with the committee. These confounders were:
  - Age
  - TNM classification
  - Primary RCC type e.g. clear cell, papillary and chromophobe
  - Tumour grade
  - Renal function at baseline
  - Performance status of participants at baseline
  - Location and number of metastases
  - Type of SACT previously received.

### 2.1.3.1 Search methods

The searches for the effectiveness evidence were run on 18/01/2024 and re-run on 14/02/2025. The following databases were searched: Central Register of Controlled Trials (Wiley), Cochrane Database of Systematic Reviews (Wiley), Embase (Ovid), Epistemonikos (Epistemonikos) and 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 and observational studies.

The searches for the cost effectiveness evidence were run between 05/01/2024 and 07/01/2024 and re-run on 06/05/2025. The following databases were searched: EconLit (Ovid), Embase (Ovid), HTA (CRD), International HTA database (INAHTA), MEDLINE ALL (Ovid) and NHS Economic Evaluations Database (CRD). 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 and cost utility studies.

A NICE senior information specialist (SIS) conducted the searches. The MEDLINE strategy was quality assured by another NICE SIS. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the [2015 PRESS Guideline Statement](#). Further details and full search strategies for each database are provided in [appendix B](#).

### 2.1.3.2 Protocol deviations

1. Severe adverse event classifications were further specified:  
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- 1       • The Intraoperative Adverse Incident Classification (EAUIaiC) and Clavien-Dindo  
2       Classification, both of which were already specified in the protocol, were used for  
3       thermal ablation and surgery interventions only.
- 4       • The Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 or 4  
5       was added to the protocol to be used for SABR and EBRT interventions only, or  
6       for comparisons where one arm was SACT only. This addition aligns this protocol  
7       with others in this guideline (reviews A, B and C) and reflects the fact that  
8       Clavien-Dindo is usually used for surgery.
- 9       2. The quality of life outcomes were extracted when measured using EORTC Core  
10      Quality of Life Questionnaire and EuroQol-5 dimensions (EQ-5D). Later in the  
11      process it was agreed to include two additional scales assessing the quality of life  
12      outcomes. These two additional scales were:
  - 13      • Functional Assessment of Cancer Therapy Kidney Cancer Symptom Index (FKSI:  
14      both the FKSI-15 and the FKSI-DRS)
  - 15      • Renal Cell Carcinoma Symptom Index (RCC-SI)
- 16      3. Initially it was decided that the population to be included in this review will be people  
17      who have previously received systemic anti-cancer treatment (SACT). This decision  
18      had the possibility of potentially missing out the population who only received SACT  
19      during the study. A protocol deviation was made to include people who had not  
20      previously received SACT for advanced RCC but who received SACT in the course of  
21      the study. This meant that there were two possible comparisons for this review:
  - 22      • In people who have all previously had SACT for advanced RCC: Non-pharma  
23      intervention vs no intervention.
  - 24      • In people who have never had SACT for advanced RCC: SACT then non-pharma  
25      intervention vs SACT alone.

## 26       **2.1.4 Effectiveness evidence**

### 27       **2.1.4.1 Included studies**

28       A single systematic search was carried out to identify potentially relevant studies for the  
29       current review (review H2) and reviews A, B, C and H1 combined (review A: surgical  
30       interventions for localised RCC, review B: non-surgical interventions for localised RCC,  
31       review C: nephrectomy or stereotactic ablative radiotherapy for locally advanced RCC,  
32       reviews H1: non-pharmacological management of advanced RCC). This search found  
33       19,882 references (see [appendix B](#) for the literature search strategy).

34       These 19,882 references were screened at title and abstract level against the review  
35       protocols, with 19,208 excluded at this level. 176 articles were assessed at full text for review  
36       H (H1 and H2 combined) (the remainder of those not excluded at title and abstract were  
37       assessed at full text stage for review A, B or C). 10% of references were screened separately  
38       by two reviewers with 99.9% agreement. Discrepancies were resolved by discussion.

39       The full texts of 176 references were ordered for closer inspection. A total of 7 articles, all  
40       retrospective cohort studies, met the criteria specified in the review protocol for review H2  
41       ([appendix A](#)). All studies compared deferred cytoreductive nephrectomy (cytoreductive  
42       nephrectomy after systemic anti-cancer therapy) with systemic anti-cancer therapy alone. Six

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1 out of 7 included cohort studies reported similar outcomes (overall survival) and one study  
2 reported cancer specific survival data.

3 For a summary of the 7 articles included in this review see [Table 10](#).

4 The clinical evidence study selection is presented as a PRISMA diagram in [appendix C](#) .

#### 5 **2.1.4.2 Excluded studies**

6 Details of studies excluded at full text, along with reasons for exclusion are given in [appendix](#)  
7 [J](#).

1 **2.1.5 Summary of studies included in the effectiveness evidence**2 **Table 10: Summary of characteristics of the included non-randomised studies**

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Bhindi (2018)  United States – utilises NCDB database Study dates: 2006 - 2013	N= NR  People with metastatic kidney cancer. Key exclusion criteria: any other carcinoma, missing data, not receiving treatment within 3 months of diagnosis.	Deferred cytoreductive nephrectomy (n=7520) Type of SACT – not reported	SACT alone (n=NR)  Type of SACT – not reported	Age, sex, race, Charlson co-morbidity index, income, educational status, country, facility location, facility type, primary tumour histology, TNM classification	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious
Bhindi (2020)  IMDC database (33 centres globally) Study dates: 2006 to 2018	N=736  People receiving sunitinib as first line systemic anti-cancer therapy. Key exclusion criteria: unknown timings of surgery, missing data, SACT after 12 months of diagnosis.	Deferred cytoreductive nephrectomy (n=85) Type of SACT – first-line therapy with sunitinib	SACT alone (n=651)  Type of SACT – sunitinib	Age, sex, year of diagnosis, IMDC risk, clear cell histology, number of metastatic sites, location of metastases	<ul style="list-style-type: none"> <li>Overall survival</li> </ul>	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Chakiryan (2022)  United States – utilises NCDB database  Study dates: 2006 to 2016	N=8328  People with metastatic renal cancer with complete data.	Deferred cytoreductive nephrectomy (n=612)  Type of SACT – targeted therapy as first-line treatment	SACT alone (n=7716)  Type of SACT – targeted therapy as first-line treatment	Age, sex, race, Charlson-Deyo score, year of diagnosis, clinical staging, cytoreductive nephrectomy status.	• Overall survival	Serious
Day (2016)  Australia  Study dates: 2006 to 2012	N=76  People with metastatic renal cancer and complete data. Key exclusion criteria: received SACT before January 2006.	Deferred cytoreductive nephrectomy (n=42)  Type of SACT – first-line treatment with sunitinib (n= 33), Pazopanib (n= 4), Bevacizumab (n= 2), Interferon (n= 2), temsirolimus (n= 1)	SACT alone (n=34)  Type of SACT – first-line treatment with sunitinib (n= 34), everolimus (n= 4)	Cytoreductive nephrectomy (CN), MSKCC risk classification, neutrophil-to-lymphocyte ratio, histology and systemic treatment	• Overall survival	Serious
Dragomir (2022)  Canada – utilises Canadian Kidney Cancer information system  Study dates: 2011 to 2020	N=325  People with histologically diagnosed renal cell carcinoma.  Key exclusion criteria: People with indolent metastatic disease	Deferred cytoreductive nephrectomy (n=73)  Type of SACT – sunitinib (n=52), pazopanib (n=8), ipilimumab / nivolumab (n=3), nivolumab / everolimus / pembrolizumab / temsirolimus /	SACT alone (n=252)  Type of SACT – sunitinib (n=121), pazopanib (n=52), ipilimumab / nivolumab (n=57), nivolumab / everolimus / pembrolizumab /	Age, sex, sites and number of organs for metastasis, cell histology, IMDC risk and Charlson comorbidity index	• Overall survival	Serious

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Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
		atezolizumab / axitinib / lenvatinib (n= 10)	temsirolimus / atezolizumab / axitinib / lenvatinib (n= 22)			
Fransen (2023)	N=26	Deferred cytoreductive nephrectomy (n=19)	SACT alone (n=7)	Not stated	• Cancer-specific mortality	Serious
Netherlands and England	People with histologically diagnosed renal cell carcinoma.	Type of SACT – first-line therapy with ipilimumab-nivolumab	Type of SACT – first-line therapy with ipilimumab-nivolumab			
Study dates: 2019 to 2022	Key exclusion criteria: NR					
Hatakeyama (2021)	N=171	Deferred cytoreductive nephrectomy (n=39)	SACT alone (n=132)	Age, sex, performance status, IMDC risk factors, clinical staging, number of metastatic organs	• Overall survival	Moderate
Japan	People with primary metastatic renal cell carcinoma.	Type of SACT – first-line therapy with TKI – sunitinib (n= 17), sorafenib (n=2), axitinib (n= 19), Pazopanib (n=1)	Type of SACT – first-line therapy with TKI – sunitinib (n= 65), sorafenib (n=16), axitinib (n= 47), Pazopanib (n=4)			
Study dates: 2008 to 2019	Key exclusion criteria: missing data, fist-line treatment other than kinase inhibitors, follow-up less than 3 months.					

1 SACT: systemic anti-cancer therapy; NR: not reported. Risk of bias: risk of bias of reported outcomes

2 See [appendix D](#) for full evidence tables

3

**2.1.6 Summary of the effectiveness evidence**

Clinical decision thresholds for minimally important differences (MIDs) were used to interpret the evidence. The line of no effect (in this case represented by 1.0) was used as a clinical decision threshold for the outcomes of overall survival and cancer specific survival. No data was identified for progression-free survival, intraoperative or postoperative severe adverse events, need for further systemic therapy, number of hospital admissions, duration of hospital stay and quality of life.

- The following criteria were used to interpret the effect (column of ‘Interpretation of effect’ below) in the summary GRADE tables:
- For outcomes without a defined MID or where the MID is set as the line of no effect, evidence statements are divided into 2 groups as follows:
    - We state that the evidence showed that there is an effect if the 95% CI does not cross the line of no effect.
    - The evidence could not differentiate between comparators if the 95% CI crosses the line of no effect.

Cytoreductive nephrectomy (CN) delivered after systemic anti-cancer therapy (SACT) is summarised as “deferred CN”. SACT alone refers to participants who did not receive CN either before or after SACT.

**Table 11: Deferred cytoreductive nephrectomy (CN) vs systemic anti-cancer therapy (SACT) alone**

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
6 (Bhindi 2018, Bhindi 2020, Chakiryan 2022, Day 2016, Dragomir 2022, Hatakeyama 2021)	Overall survival ≤5 years	17,080 <sup>a</sup>	HR 0.43 (0.37 to 0.51)	Low	Effect favours deferred CN
1 (Fransen 2023)	Cancer-specific mortality ≤5 years	26	RR 0.83 (0.61 to 1.11)	Very low	Could not differentiate

a. Bhindi 2018 does not report the number of participants for SACT alone arm.

Included studies only reported overall survival and cancer-specific mortality outcomes.

See [appendix F](#) for full GRADE tables and further details on GRADE assessment.

1     **2.1.7 Economic evidence**

2     Evidence review H contains two parts (H1 and H2). One review was conducted for all  
3     questions relating to the management options for RCC, which includes both H1 and H2 for  
4     the management of advanced RCC, as well as reviews for the management of localised  
5     RCC (evidence review C) and locally advanced RCC (evidence reviews A and B).

6     The review is described in section [1.1.7 Economic evidence](#). Unit costs relevant for this  
7     review are described in section [1.1.9 Unit costs](#).

8     **2.1.8 The committee's discussion and interpretation of the evidence**

9     Evidence review H contains two parts (H1 and H2). The committee discussed both parts of  
10    the evidence review together, and there is therefore a single discussion section to record  
11    this.

12    Note about the terminology used in this review: Cytoreductive nephrectomy (CN) followed by  
13    systemic anti-cancer therapy (SACT) is summarised as “upfront CN”. CN delivered after  
14    SACT is summarised as “deferred CN”. The committee noted whilst these terms have been  
15    used throughout the review and discussion sections, they preferred to use “CN before SACT”  
16    and “CN after SACT has been started” for the recommendations as they are more easily  
17    understood.

18    **2.1.8.1. The outcomes that matter most**

19    The committee agreed that survival outcomes (overall survival, progression free survival and  
20    cancer specific survival) and quality of life outcomes were of most importance as they are the  
21    best indicators to evaluate the effectiveness of each treatment pathway and they indicate the  
22    impact of surgical and non-surgical interventions on the lives of people diagnosed with  
23    metastatic renal cell carcinoma (mRCC), respectively. However, no evidence was identified  
24    for quality of life outcomes.

25    Of importance, but less so than the outcomes above, were severe adverse events, need for  
26    systemic therapy, number of hospital admissions and duration of hospital stay. These  
27    outcomes impact people's quality of life and health status in the short and long term and may  
28    also play an important role in deciding which treatment pathway is best for individuals as well  
29    as being indicative of the relative resource impact of the treatment. However, no evidence  
30    was identified for the outcomes of need for further systemic therapy and number of hospital  
31    admissions.

32    **2.1.8.2 The certainty of the evidence**

33    This review was conducted in two parts. The first part of the review explored the impact of  
34    non-pharmacological interventions before systemic anti-cancer therapy (SACT) (H1) whilst  
35    the second part looked at the effectiveness of non-pharmacological intervention after SACT  
36    (H2). The majority of the evidence for both reviews came from non-randomised studies,  
37    however, some randomised trials were included for H1.

38    Overall, the evidence from both parts of the review was graded as low or very low certainty,  
39    with the majority being very low certainty when assessed using GRADE. Much of the  
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evidence was downgraded for the risk of bias domain due to more than 50% of the weight of the meta-analysis coming from outcomes at serious or moderate risk of bias:

- The outcomes from RCTs were rated as at moderate risk of bias due to a lack of clarity about the randomisation process, and some deviation from the intended interventions. The committee interpreted the results from two of the included RCTs – Bex et al. (2019) (SURTIME trial) and Méjean et al. (2021) (CARMENA trial) with caution. They noted that the SURTIME trial reported overall survival as a secondary outcome and the CARMENA trial failed to accrue sufficient participants, resulting in low power to detect a treatment effect.
- The evidence from non-randomised studies was downgraded mostly due to the bias arising from insufficient adjustment of confounding variables in the analysis, limited reporting or missing data. The committee agreed it was likely that participants were selected based on treatment suitability. This would mean that arms including a non-pharmacological intervention would be likely to include people with a better performance status or lower metastatic burden at baseline. They agreed that even where all confounders specified in the protocol were adjusted for, there would always be a chance of residual confounders. This would be likely to bias results towards arms containing a non-pharmacological intervention (when compared with SACT alone), or towards upfront non-pharmacological intervention (when compared with deferred non-pharmacological intervention). Therefore, the committee was very cautious about putting too much weight on the evidence from the non-randomised studies.

The certainty of the evidence from both RCTs and non-RCTs was also downgraded due to imprecision (where the effect estimate crossed the line of no effect, and the sample size was smaller than 576) and inconsistency (where the  $I^2$  value was high, or the outcome was contributed to by a single study).

This review looked at interventions to treat the primary renal mass and the metastases. There was only evidence of cytoreductive nephrectomy (CN) as an intervention to treat the primary renal mass before or after SACT. No evidence was identified for other interventions specified in the protocol (for treating the primary mass: stereotactic ablative radiotherapy [SABR]; for treating the metastases: metastasectomy, thermal ablation, external beam radiotherapy [EBRT] or SABR). The committee were aware of ongoing trials that will be of relevance for this review in the future. See the section on '[other factors the committee took into account](#)' for more details and for information about the 2 of the research recommendations they drafted.

The population of interest for these reviews was people with advanced renal cell carcinoma (RCC) – that is, RCC which is metastatic or locally advanced and inoperable. Because the only interventions identified in the studies were surgical, there was no evidence to support specific management recommendations for people with locally advanced inoperable disease. The committee noted this gap in the evidence base and made a [research recommendation](#) for SABR in this population. As factors that would make the disease inoperable, such as proximity to or invasion of a critical organ such as the bowel, would also prevent SABR being delivered in this group, the research recommendation specifies SABR after SACT has been started. SACT may cause changes to the primary mass which make SABR a suitable treatment option. The committee noted that people with locally advanced inoperable RCC are covered by recommendations about SACT also included in this guideline. (The Technology Appraisals (TAs) in the SACT section of the guideline apply to people with

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advanced RCC – that is, people with metastatic, or locally advanced and inoperable, RCC unless otherwise specified.)

The committee noted that there were other gaps in the evidence base:

- No randomised trials for SACT then CN compared with SACT alone were identified.
- No evidence was identified for the following outcomes: need for systemic therapy; number of hospital admissions; duration of hospital stay; and quality-of-life.

The committee highlighted that the therapeutic landscape for advanced (metastatic and locally advanced inoperable) RCC treatment has changed in recent years. There has been a shift away from tyrosine kinase inhibitors (TKIs), also known as the TKI era, and towards immunotherapies and combination therapy regimes. Sunitinib (a TKI) was the most common type of SACT used across the studies, while other studies failed to provide sufficient information on the type of SACT used. Therefore, the included evidence does not evaluate the role of non-pharmacological interventions in the setting of combination therapy which is currently practiced. The committee could not judge what impact the type of SACT had on the results, or how the results would differ if the studies had been conducted using combination therapy. They accepted this as a limitation of the evidence.

It was not possible to carry out most of the planned subgroup analyses due to too few studies in the meta-analysis or insufficient detail in the level of reporting to categorise participants. However, there were no subgroup differences when subgroup analysis based on histological subtype of renal cell carcinoma was carried out for overall survival  $\leq 5$  years for either the comparison of upfront CN compared with deferred CN ([Figure 3](#)), or upfront CN compared with SACT alone ([Figure 14](#)).

### **2.1.8.3 Benefits and harms**

#### **Referring people with advanced RCC**

The committee highlighted that in current practice the decision about whether to use non-pharmacological interventions in addition to pharmacological treatment is a complex one that relies on assessment of the person's individual clinical characteristics (such as number and location of metastases, general health and comorbidities) as well as the their risk of progression, the risks and benefits of potential treatments, and the timing of any non-pharmacological interventions. They agreed that people with metastatic renal cell carcinoma should be referred to a multi-disciplinary team (MDT) with relevant expertise in managing kidney cancer to facilitate this decision-making process. They also recognised that depending on their location (for example, in the brain, spine or lung), other treatments may be suitable to manage the metastases and that additional expertise from MDTs that specialise in those areas may be required. The committee made recommendations to reflect these points.

The committee were aware of other NICE guidelines could be relevant for people with RCC who have metastases and they included cross references to the following: the [section on recognising spinal metastases or MSCC in NICE's guideline on spinal metastases and metastatic spinal cord compression](#) and the [section on investigation of suspected brain metastases in NICE's guideline on brain tumours \(primary\) and brain metastases in over 16s](#).

## 1     **Non-pharmacological treatments**

2     The committee noted that the aim of SACT is to treat the metastases, as opposed to  
 3     localised treatment which targets a specific lesion or small group of lesions. The committee  
 4     noted that the evidence comparing upfront with deferred CN was low to very low certainty  
 5     and therefore they could not draw any firm conclusions from it. However, the RCT evidence  
 6     showed a statistically significant improvement in overall survival favouring deferred CN when  
 7     compared to upfront CN (low certainty). The committee noted that this was consistent with  
 8     current clinical practice of preferring deferred CN over upfront CN in most cases. They noted  
 9     that lack of an observed effect in most of the non-randomised data could be due to bias  
 10    towards the upfront CN arms (see [“the certainty of the evidence”](#) section).

11    The committee agreed that for people with high-volume metastatic RCC immediate SACT  
 12    would be indicated to target the spread of the cancer. Initial treatment with SACT (before any  
 13    non-pharmacological interventions) could potentially also reduce the size of the renal mass  
 14    at the primary site. Reduced mass burden at metastatic and primary sites could also make  
 15    people with metastatic RCC more likely to be eligible for a non-pharmacological intervention  
 16    after SACT. Therefore, the committee agreed that offering any potential non-pharmacological  
 17    interventions *after* treatment with SACT has been started was the best course of action for  
 18    most people with high volume metastatic RCC (defined as 3 or more metastatic deposits in  
 19    different organs). The committee acknowledged that there are exceptions, where it may be  
 20    appropriate to offer a non-pharmacological intervention before SACT (see below under  
 21    treating the primary mass for further information about this).

22    The committee agreed that in their experience people with low-volume (1 or 2 metastatic  
 23    deposits that can be treated directly), slow-growing metastases are unlikely to need SACT  
 24    immediately. In these cases, regular imaging using CT could be used to monitor disease  
 25    progression and to determine when SACT is needed. Although evidence for surveillance was  
 26    not considered as part of this review, the committee highlighted the importance of monitoring  
 27    low-volume, slow-growing metastases until they needed treatment and agreed that not  
 28    including a recommendation on this would leave a clear gap in the guidance that could cause  
 29    confusion. They therefore used their expertise and experience to make a recommendation to  
 30    reflect this scenario. In addition, the committee highlighted that some people may not want to  
 31    receive SACT immediately, due to the impact of side effects on their family life and ability to  
 32    work.

## 33    **Treating the primary renal lesion**

34    The committee noted that although some low and very low certainty evidence showed  
 35    improved outcomes for upfront nephrectomy compared with SACT alone, whether surgery at  
 36    this stage is appropriate would depend on the person’s individual clinical characteristics,  
 37    including the mass burden, site of the mass, extent of metastasis and overall health of a  
 38    person, as well as clinical judgement of risks and benefits. They agreed that upfront CN  
 39    would not be suitable for most people.

40    The committee discussed 2 scenarios where it might be appropriate to delay SACT in favour  
 41    of surgery. In the first scenario, if SACT is not needed immediately and if surgery is suitable  
 42    then CN could be used for oncological control (i.e. to reduce disease burden, prevent the  
 43    cancer from growing or causing symptoms). The committee was of the opinion that this could  
 44    apply to people with a good performance status and low metastatic burden where upfront  
 45    removal of the primary mass could potentially improve survival outcomes ([Figure 2](#)).

1 In the second scenario, the committee discussed situations where people with metastatic  
2 RCC have severe symptoms related to their primary mass such as pain, bleeding and  
3 obstructive uropathy. In the committee's experience, surgically removing the primary mass  
4 can help alleviate these symptoms. The committee acknowledged that this review did not  
5 focus on using non-pharmacological interventions to relieve cancer symptoms, but it did  
6 include quality of life outcomes. Although no evidence was found relating to effects on quality  
7 of life, the committee used their clinical expertise to recommend that in cases where the  
8 person with metastatic RCC has symptoms that could be controlled by surgery, CN could be  
9 considered before or after SACT has been started for this purpose.

10 The committee agreed that in current practice CN is more likely to be performed when there  
11 has been at least a durable partial response to SACT in the metastatic sites and most of the  
12 disease that is left after SACT is in the primary site and used their expertise and experience  
13 to make a consider recommendation to reflect this. They also included in the  
14 recommendation that surgery would have to be suitable based on the clinical characteristics  
15 of the person and their renal lesion. They noted that deferred CN allows an assessment of  
16 how metastatic disease responds to initial systemic treatment. Where people have a good  
17 initial response to SACT, the primary mass may shrink, potentially making the surgery safer  
18 and easier, and leading to fewer surgical complications. The committee agreed that any  
19 SACT-induced reduction or control of metastases could lead to a reduced overall disease  
20 burden and better survival outcomes.

21 The committee discussed the definition of a durable partial response and advised that this  
22 referred to a decrease in renal lesion size of at least 30% of the sum of diameters of target  
23 measurable lesions compared with pre-treatment, that is observed at least 6 months after the  
24 start of treatment with systemic anticancer therapy and after at least 1 follow-up imaging  
25 scan.) They noted that this is consistent with the definition in the RECIST guidelines  
26 ([RECIST 1.1 – RECIST](#)).

27 The committee also highlighted the importance of taking into account people's wishes when  
28 offering non-pharmacological interventions i.e. if they want to have their primary mass  
29 removed. They noted that having cancer present in the body can be psychologically difficult  
30 for some people, and they may want to have CN to remove it, even if it is not clinically  
31 indicated. However, the committee agreed that there would be situations where this would  
32 not be possible, for example, if the individual is not able to have surgery based on their  
33 individual clinical characteristics. In other cases, CN to remove the primary mass may not be  
34 advisable before SACT is initiated, for example, if the person has fast growing metastases. In  
35 this scenario CN could be considered after SACT has been started if the person wants to  
36 have the primary tumour removed, surgery is suitable based on the individual's clinical  
37 characteristics, the person has had at least a durable partial response to SACT in the  
38 metastatic sites and most of the disease that is left after SACT is in the primary site.  
39 Incorporating the person's wishes into decision making about treatments should be standard  
40 practice, and so the committee did not include this in their recommendation.

## 41 **Treating metastases**

42 The committee acknowledged that there was no evidence identified for treatment of  
43 metastases using thermal ablation, SABR, external beam radiotherapy (EBRT) or  
44 metastasectomy. The committee noted that the decision to offer SABR, EBRT or thermal  
45 ablation for metastases varies on a case by case basis and depends on metastatic site,  
46 number of metastases and response to SACT (where SACT has already been received).

The committee discussed the use of EBRT to treat metastases. They were aware that SABR, a type of EBRT, is currently commissioned as a treatment option for people with a controlled primary cancer with up to three extracranial metachronous oligometastases which manifest after a disease-free interval of at least 6 months from primary treatment as outlined in the [SABR commission policy](#). They agreed that SABR might give good local control of the disease and noted that it is usually used in controlling metastases where surgical resection is not an option or metastases are in areas that are difficult to treat surgically. SABR may be particularly effective for oligometastatic disease and can be used in the brain, liver, bones or other distant metastases. The committee also noted that thermal ablation may offer good control of metastases in brain, bone or liver.

In the committee's experience, metastasectomy can be an effective treatment option for localised metastatic deposits where no new lesions have occurred in the past 6 months and complete excision is achievable. The committee characterised this as 'no visible evidence of disease'. Taking these factors into account, the committee used their experience and expertise to make a consensus recommendation to consider the use of EBRT including SABR, thermal ablation or metastasectomy to treat metastases. They also made a separate recommendation to detail the specifics about when to consider metastasectomy reflecting the information above.

The committee were aware that NICE guidelines to treat spinal and brain metastases already exist and should be referred to for management of these metastases (for example, the sections on [radiotherapy](#) and [invasive interventions](#) in the NICE guideline on [Spinal metastases and metastatic spinal cord compression](#), and the section on [management of confirmed brain metastases](#) in the NICE guideline [Brain tumours \(primary\) and brain metastases in over 16s](#)). In addition, as part of this review they had already made a recommendation about referral to MDTs that specialise in the area where the metastases are located where additional input or skills are needed to manage treatment of these patients (see above under the heading 'referring people with advanced RCC').

#### **2.1.8.4 Cost effectiveness and resource use**

No published economic evidence was identified and original economic modelling was not conducted for this evidence review. The committee were presented with unit costs of the relevant interventions and used their expertise to discuss potential resource use implications and changes to current clinical practice.

The committee recommended that cases of previously untreated metastatic RCC should be referred to specialist MDTs with the relevant expertise and indicated that in practice this is usually done but can be inconsistent in some areas. The recommendations made are expected to encourage standardisation of practice.

The committee recommended that treatment with SACT should be considered first for most people with metastatic RCC as this may be necessary to gain some control over the spread of cancer and can potentially eradicate low burden RCC or shrink mass sizes. This type of control could improve outcomes for the patient and potentially reduce the risk of disease progression which in turn is beneficial from a cost-effectiveness perspective as progressed disease tends to have costly management and poor quality of life outcomes.

For non-pharmacological interventions in people with advanced RCC, the committee discussed all interventions currently used in practice and noted that practice is varied and is highly dependent on the individual case. The committee made 'consider' recommendations

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1 and stated the specific factors that should be thought about for each intervention, which  
2 should limit the use of interventions to those cases where it is most effective and therefore  
3 more likely to be cost-effective, while still ensuring individuals have the choice of options. It is  
4 not expected that these recommendations will substantially affect resource use given  
5 practice is already individualised according to the person's needs and preferences, and  
6 these recommendations should provide some standardisation of care across services.

#### 7 **2.1.8.5 Other factors the committee took into account**

8 The committee highlighted that shared decision making is crucial in decisions about  
9 managing metastatic RCC. They stressed the importance of involving individuals in their own  
10 care to make a shared decision in choosing treatment options that align with people's values,  
11 goals and preferences. This collaborative approach empowers people with RCC, improves  
12 their satisfaction, and enhances clinical outcomes. It allows people to play an active role in  
13 their care, ensuring they are informed about their prognosis and the benefits and risks of  
14 available treatment options. By understanding these options, people with metastatic RCC are  
15 better equipped to make decisions that reflect their personal health goals and lifestyles.  
16 Shared decision making also helps clinicians to understand and tailor treatment options to  
17 the individual's priorities, such as avoiding side effects or opting for more aggressive  
18 therapies. The committee noted that each person will place a different weight on the benefits  
19 and harms of the available treatments to reach a decision. The committee was aware of the  
20 recommendations in [NICE's shared decision-making process guideline](#) that support the goals  
21 discussed above.

22 The committee was aware of and contributed to the Equality and Health Inequalities Impact  
23 Assessment (EHIA) for this guideline. They noted that health inequalities impact on the  
24 prevalence and incidence of kidney cancer, and also on people's access to and choice of  
25 treatment for RCC. In particular, they noted that for some people, the costs of attending  
26 treatment – especially where multiple or specialist treatments are required or where the  
27 treatment is not provided locally – could be prohibitive. This may be especially relevant for  
28 non-pharmacological interventions for metastatic RCC, which are usually offered at high-  
29 volume specialist centres. This problem may also be exacerbated if the person has less  
30 secure employment. The committee noted that this barrier to treatment also affects a wider  
31 population of people especially carers who accompany the people receiving the treatment.

32 The committee acknowledged the large gaps in the current evidence (see above under the  
33 certainty of the evidence for more details), including no evidence for non-pharmacological  
34 interventions other than CN and no RCT evidence for deferred CN compared to SACT alone.  
35 They noted that there was also no evidence around the use of SABR to treat the primary  
36 mass. However, the committee were aware of ongoing randomised trials in these areas.  
37 Some of these trials evaluate the survival benefits of deferred CN compared with a no  
38 surgery group while others explore the role of SABR for treating primary mass:

- 39 • [NORDIC-SUN](#) and [PROBE](#) trial – both trials aim to evaluate the effectiveness and  
40 overall survival benefits of CN after SACT has been started when compared with no  
41 surgery group in treating primary metastatic RCC. Both arms will receive  
42 immunotherapy-based treatment. One of the main objectives of the trials is to  
43 demonstrate the need to personalise the most effective treatment pathway to avoid  
44 unnecessary overtreatment.

- [CYTOSHRINK](#) and [SAMURAI](#) trials – these trials aim to evaluate the effectiveness of adding SABR to standard combination therapy compared with SACT alone for treating metastatic primary RCC. Survival benefits are one of the primary outcomes of these trials.

Taking the gaps in the evidence base and the ongoing trials into account, the committee drafted the 3 research recommendations. The first [research recommendation](#) was aimed at providing information about whether metastasectomy was beneficial before systemic anticancer therapy (SACT) or after SACT has been started in people with metastatic RCC who have had their kidney and primary mass removed. The second [research recommendation](#) was aimed at determining the effectiveness of thermal ablation and EBRT (other than SABR due to ongoing trials) for treating metastases after SACT has been started in people with metastatic RCC. The third [research recommendation](#) was aimed at determining the effectiveness of SABR to treat the primary mass after SACT has been started in people with locally advanced inoperable RCC.

## **2.1.9 Recommendations supported by this evidence review**

Evidence review H contains two parts (H1 and H2). Evidence review H supports recommendations 1.11.1 to 1.11.2, and 1.14.1 to 1.14.7 and the research recommendations on (1) metastasectomy for metastatic RCC, (2) thermal ablation and EBRT after SACT has been started for metastatic RCC and (3) SABR for treating the primary mass after SACT has been started in people with locally advanced inoperable renal cell carcinoma.

## **2.1.10 References – included studies**

### **2.1.10.1 Effectiveness**

- [Bhindi B, Habermann E.B., Mason R.J. et al. \(2018\) Comparative Survival following Initial Cytoreductive Nephrectomy versus Initial Targeted Therapy for Metastatic Renal Cell Carcinoma. Journal of Urology 200\(3\): 528-534](#)
- [Bhindi B, Graham J, Wells J.C. et al. \(2020\) Deferred Cytoreductive Nephrectomy in Patients with Newly Diagnosed Metastatic Renal Cell Carcinoma. European urology 78\(4\): 615-623](#)
- [Chakiryan N.H, Gore L.R., Reich R.R. et al. \(2022\) Survival Outcomes Associated With Cytoreductive Nephrectomy in Patients With Metastatic Clear Cell Renal Cell Carcinoma. JAMA network open 5\(5\): e2212347](#)
- [Day D, Kanjanapan Y, Kwan E et al. \(2016\) Benefit from cytoreductive nephrectomy and the prognostic role of neutrophil-to-lymphocyte ratio in patients with metastatic renal cell carcinoma. Internal medicine journal 46\(11\): 1291-1297](#)
- [Dragomir A, Nazha S, Tanguay S. et al. \(2022\) Outcomes of Cytoreductive Nephrectomy for Patients with Metastatic Renal Cell Carcinoma: Real World Data from Canadian Centers. European Urology Focus 8\(6\): 1703-1710](#)
- [Fransen van de Putte. E.E, van den Brink L, Mansour M A et al. \(2023\) Indications and Outcomes for Deferred Cytoreductive Nephrectomy Following Immune Checkpoint Inhibitor Combination Therapy: Can Systemic Therapy be Withdrawn in Patients with No Evidence of Disease?. European urology open science 55: 15-22](#)

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1 [Hatakeyama S, Naito S, Numakura K et al. \(2021\) Impact of cytoreductive nephrectomy in](#)  
2 [patients with primary metastatic renal cell carcinoma receiving systemic tyrosine kinase](#)  
3 [inhibitor therapy: A multicenter retrospective study](#). International journal of urology : official  
4 journal of the Japanese Urological Association 28(4): 369-375

5 **2.1.10.2 Economic**

6 No economic evidence was included.

7 **2.1.11 References – other references**

8 [Mejean A, Ravaud A, Thezenas S et al. \(2018\) Sunitinib Alone or after Nephrectomy in](#)  
9 [Metastatic Renal-Cell Carcinoma](#). The New England journal of medicine 379(5): 417-427

10 NHS England. National Cost Collection for the NHS 2023/24. Available from:  
11 <https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/>. [online, accessed: 2  
12 July 2025].



# 1 Appendices

## 2 Appendix A – Review protocols

### 3 Effectiveness review protocol H1 for management of advanced renal cell 4 carcinoma using non-pharmacological interventions before systemic anti- 5 cancer therapy

6

ID	Field	Content
1.	Review title	Clinical and cost-effectiveness analysis of non-pharmacological interventions, used before systemic anti-cancer therapy for adults with advanced renal cell carcinoma.
2.	Review question	What is the clinical and cost-effectiveness of non-pharmacological interventions used before systemic anti-cancer therapy for adults with advanced renal cell carcinoma?
3.	Objective	<p>To evaluate the clinical and cost effectiveness of non-surgical interventions used before previous systemic anti-cancer treatments (SACT) for adults with advanced renal cell carcinoma (RCC).</p> <p>The aim of this review is to identify where there may be clinical benefit in carrying out a surgical or non-surgical procedure after SACT.</p>
4.	Searches	<p>The following databases will be searched:</p> <ul style="list-style-type: none"> <li>• Cochrane Central Register of Controlled Trials (CENTRAL)</li> <li>• Cochrane Database of Systematic Reviews (CDSR)</li> <li>• Embase</li> <li>• MEDLINE</li> <li>• Epistemonikos</li> <li>• INAHTA</li> </ul> <p>For the economics review the following databases will be searched:</p> <ul style="list-style-type: none"> <li>• Embase</li> <li>• MEDLINE</li> <li>• Medline in Process</li> <li>• Medline EPub Ahead of Print</li> <li>• Econlit</li> <li>• HTA (legacy records)</li> <li>• NHS EED (legacy records)</li> <li>• INAHTA</li> </ul> <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> <li>• Date limitations: None</li> <li>• English language</li> <li>• Human studies</li> </ul>

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		<ul style="list-style-type: none"> <li>Abstracts, conference presentations and theses will be excluded</li> </ul> <p>The full search strategies will be published in the final review.</p>
5.	Condition or domain being studied	Advanced renal cell carcinoma
6.	Population	<p>Adults (18 years or over) with advanced RCC* who have previously received cytoreductive nephrectomy (CN). *defined as metastatic/ advanced RCC or locally advanced inoperable RCC (histologically confirmed or suspected on imaging).</p> <p>Advanced RCC diagnosis confirmed according to the clinical or pathological TNM classification</p> <p>Exclusion:</p> <ul style="list-style-type: none"> <li>Adults who have not received SACT.</li> <li>Adults with localised or locally advanced disease that is considered to be operable.</li> <li>Adults with advanced disease who are having palliative care only.</li> </ul>
7.	Intervention	<p><b>Non-pharmacological procedures carried out before SACT to:</b></p> <p><b>Manage primary mass:</b></p> <ol style="list-style-type: none"> <li>Surgical interventions (where metastatic RCC is considered operable) <ul style="list-style-type: none"> <li>Cytoreductive nephrectomy in people without prior nephrectomy with or without surgical removal of lymph nodes (lymphadenectomy).</li> </ul> </li> <li>Non-surgical interventions <ul style="list-style-type: none"> <li>Stereotactic ablative radiotherapy (SABR)</li> </ul> </li> </ol> <p><b>Manage metastases:</b></p> <ol style="list-style-type: none"> <li>Surgical interventions <ul style="list-style-type: none"> <li>Surgical removal of metastases also known as metastasectomy (distinguish between complete and incomplete metastasectomy)</li> </ul> </li> <li>Non-surgical interventions <ul style="list-style-type: none"> <li>Thermal ablation including: <ul style="list-style-type: none"> <li>Radiofrequency ablation</li> <li>Cryotherapy</li> <li>Microwave ablation</li> </ul> </li> <li>Radiotherapy: <ul style="list-style-type: none"> <li>External beam radiotherapy (EBRT)</li> <li>Stereotactic ablative radiotherapy (SABR)</li> </ul> </li> </ul> </li> </ol>
8.	Comparator	No non-pharmacological intervention after second or further-line SACT and SACT alone.
9.	Types of study to be included	<ul style="list-style-type: none"> <li>Systematic reviews of RCTs and RCTs are preferred where available for a comparison.</li> </ul>

		<ul style="list-style-type: none"> <li>Where RCTs are not available for a comparison, systematic reviews of prospective and retrospective cohort studies and prospective and retrospective cohort studies will be considered.</li> <li>Where good quality systematic reviews are identified, these may be used completely or as a source of references, depending on applicability. Alternatively, they may be updated by the addition of studies published after the review was completed.</li> </ul>
10.	Other exclusion criteria	<ul style="list-style-type: none"> <li>Abstracts, conference presentations and theses</li> <li>Non-human studies</li> <li>Non-English language studies</li> </ul>
11.	Context	<p>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.</p> <p>There are various non-pharmacological (surgical and non-surgical) interventions for treating advanced RCC but their clinical benefit following SACT is uncertain. Therefore an evidence review is needed to evaluate the clinical and cost-effectiveness of these interventions in people with advanced RCC who have had previous treatment with SACT.</p>
12.	Outcomes	<ul style="list-style-type: none"> <li>Progression-free survival (time to event data)</li> <li>Overall survival (time to event data)</li> </ul> <p>Some studies may report overall survival as death or mortality. These will be extracted as an alternative related outcomes if overall survival is not reported (dichotomous data).</p> <ul style="list-style-type: none"> <li>Cancer-specific survival (time to event data)</li> </ul> <p>If cancer specific survival is not reported, then cancer specific mortality (dichotomous data) will be extracted instead where available.</p> <ul style="list-style-type: none"> <li>Severe adverse events reported as: <ul style="list-style-type: none"> <li>observed in the intraoperative period (measured according to Intraoperative Adverse Incident Classification – EAUiaIC; dichotomous data)</li> <li>observed in the postoperative period (according to Clavien-Dindo Classification of Surgical Classifications at 30-days and 90-day period after surgery; dichotomous data)</li> </ul> </li> <li>Need for further systemic therapy, often expressed as the time-to-second line or further line of therapy (dichotomous or time to event data)</li> <li>Number of hospital admissions (continuous data)</li> <li>Duration of hospital stay (continuous data)</li> <li>Quality of life using: <ul style="list-style-type: none"> <li>EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30; dichotomous or continuous data))</li> </ul> </li> </ul>

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		<p>EuroQol-5 dimensions (EQ-5D; dichotomous or continuous data)</p> <p><b>Minimal important differences</b> Any statistically significant difference will be used for the following outcomes:</p> <ul style="list-style-type: none"> <li>○ Survival outcomes</li> <li>○ Severe adverse events</li> <li>○ Quality of life using EORTC QLQ-C30</li> </ul> <p>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</p>
13.	Data extraction (selection and coding)	<p>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.</p> <p>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 section 6.2). Study investigators may be contacted for missing data where time and resources allow.</p> <p>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:</p> <ul style="list-style-type: none"> <li>• at least 50% of the identified abstracts (or 1,000 records, if that is a greater number) will be screened</li> <li>• After this point, screening is only terminated if a pre-specified threshold of 750 is met for a number of abstracts being screened without a single new include being identified.</li> </ul>
14.	Risk of bias (quality) assessment	<p>Risk of bias will be carried out using the preferred checklists as described in Appendix H of <a href="#">Developing NICE guidelines: the manual</a>.</p> <p>The risk of bias for RCTs will be assessed using the Cochrane Risk of Bias v.2.0 checklist and for systematic reviews, the Risk of Bias in Systematic Reviews (ROBIS) tool will be used</p> <p>The risk of bias for non-RCT studies will be assessed using the Cochrane Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tool.</p>
15.	Strategy for data synthesis	<p>Where possible, meta-analyses will be conducted to combine the results of quantitative studies for each outcome.</p> <p>Where data can be disambiguated it will be separated into the subgroups identified in section 17 (below).</p> <p>Pairwise meta-analyses will be performed in Cochrane Review Manager V5.3. Continuous outcomes will be</p>

		<p>analysed as pooled mean differences (using the inverse variance method) unless multiple scales are used to measure the same factor. In these cases, standardised mean differences will be used instead. Where different studies present continuous data measuring the same outcome but using different numerical scales (e.g. a 0-10 and a 0-100 visual analogue scale), these outcomes will all be converted to the same scale before meta-analysis is conducted on the mean differences.</p> <p>Pooled relative risks will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event. Absolute risks will be presented where possible.</p> <p>Hazard ratios will be pooled using the generic inverse-variance method. Adjusted, unadjusted and partially adjusted hazard ratios will be pooled. Sensitivity analysis will be carried out to look at the effect of removing partially and unadjusted studies</p> <p>For survival outcomes, time-to-event data is preferred. Where this data is not available, relative risks will be calculated for proxy outcomes as described in section 12.</p> <p>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:</p> <ul style="list-style-type: none"> <li>• Significant between-study heterogeneity in methodology, population, intervention, or comparator was identified by the reviewer in advance of data analysis.</li> <li>• The presence of significant statistical heterogeneity in the meta-analysis, defined as <math>I^2 \geq 50\%</math>.</li> </ul> <p>GRADE will be used to assess the certainty of the outcomes. Data from randomised controlled trials and non-randomised comparative trials will be initially rated as high certainty where they come from:</p> <ul style="list-style-type: none"> <li>• RCTs and systematic reviews of RCTs (where individual studies have been quality assessed using Cochrane risk of bias)</li> <li>• non-randomised comparative trials and systematic reviews of non-randomised studies (where individual studies have been quality assessed using the ROBINS-I assessment tool)</li> </ul> <p>The quality of the evidence for each outcome will then be downgraded or not from this starting point based on the other GRADE domains.</p>
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		<p>To assess imprecision, where there are no defined MIDs we will set the MID as the line of no effect for all outcomes except for (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.</p> <p>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.</p>
16.	Analysis of sub-groups	<p>Where the data allows, subgroup analyses may be conducted to explore heterogeneity considering the following:</p> <ul style="list-style-type: none"> <li>• according to interventions received</li> <li>• according to line of SACT received previously</li> <li>• age</li> <li>• by primary RCC type e.g. clear cell, papillary, chromophobe</li> <li>• location of metastases</li> <li>• performance status of the person at baseline (e.g. ECOG and Karnofsky).</li> </ul>
17.	Type and method of review	<p>X Intervention Diagnostic Prognostic Qualitative Epidemiologic Service Delivery Other (please specify)</p>
18.	Language	English
19.	Country	England
20.	Anticipated or actual start date	January 2025
21.	Anticipated completion date	December 2025
22.	Named contact	<p><b>5a. Named contact</b> Centre for Guidelines, NICE</p> <p><b>5b Named contact e-mail</b> kidneycancerguideline@nice.org.uk</p> <p><b>5e Organisational affiliation of the review</b> National Institute for Health and Care Excellence (NICE) and Guideline Development Team.</p>
23.	Review team members	<p>From the Guideline Development Team:</p> <ul style="list-style-type: none"> <li>• Steve Sharp, Technical adviser</li> <li>• Marie Harrisingh, Technical adviser</li> <li>• Sarah Boyce, Senior technical analyst</li> <li>• Fernando Zanghelini, Technical analyst</li> <li>• Olivia Crane, Technical analyst</li> </ul>

		<ul style="list-style-type: none"> <li>• Lindsay Claxton, Health economics adviser</li> <li>• Hannah Tebbs, Senior Health economist</li> <li>• Yuanyuan Zhang, Senior Health economist</li> <li>• Amy Finnegan, Senior Information specialist</li> </ul>
24.	Funding sources/sponsor	This systematic review is being completed by the Guideline Development Team which receives funding from NICE.
25.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
26.	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 <a href="#">Developing NICE guidelines: the manual</a> . Members of the guideline committee are available on the NICE website: <a href="#">Kidney Cancer (GID-NG10398)</a> .
27.	Other registration details	None
28.	Reference/URL for published protocol	None
29.	Dissemination plans	<p>NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:</p> <ul style="list-style-type: none"> <li>• notifying registered stakeholders of publication</li> <li>• publicising the guideline through NICE's newsletter and alerts</li> <li>• 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.</li> </ul>
30.	Keywords	Localised renal cell carcinoma, thermal ablation, stereotactic ablative radiotherapy, active surveillance
31.	Details of existing review of same topic by same authors	Not applicable
32.	Current review status	<div>X</div> <div>Ongoing</div> <div>Completed but not published</div> <div>Completed and published</div>

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		Completed, published and being updated
		Discontinued
33.	Additional information	None
34.	Details of final publication	<a href="http://www.nice.org.uk">www.nice.org.uk</a>

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## Effectiveness review protocol H2 for management of advanced renal cell carcinoma using non-pharmacological interventions after systemic anti-cancer therapy

ID	Field	Content
1.	Review title	Clinical and cost-effectiveness analysis of non-pharmacological interventions, used after systemic anti-cancer therapy for adults with advanced renal cell carcinoma.
2.	Review question	What is the clinical and cost-effectiveness of non-pharmacological interventions used after systemic anti-cancer therapy for adults with advanced renal cell carcinoma?
3.	Objective	<p>To evaluate the clinical and cost effectiveness of non-surgical interventions used after previous systemic anti-cancer treatments (SACT) for adults with advanced renal cell carcinoma (RCC).</p> <p>The aim of this review is to identify where there may be clinical benefit in carrying out a surgical or non-surgical procedure after SACT.</p>
4.	Searches	<p>The following databases will be searched:</p> <ul style="list-style-type: none"> <li>• Cochrane Central Register of Controlled Trials (CENTRAL)</li> <li>• Cochrane Database of Systematic Reviews (CDSR)</li> <li>• Embase</li> <li>• MEDLINE</li> <li>• Epistemonikos</li> <li>• INAHTA</li> </ul> <p>For the economics review the following databases will be searched:</p> <ul style="list-style-type: none"> <li>• Embase</li> <li>• MEDLINE</li> <li>• Medline in Process</li> <li>• Medline EPub Ahead of Print</li> <li>• Econlit</li> <li>• HTA (legacy records)</li> <li>• NHS EED (legacy records)</li> <li>• INAHTA</li> </ul> <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> <li>• Date limitations: None</li> <li>• English language</li> <li>• Human studies</li> <li>• Abstracts, conference presentations and theses will be excluded</li> </ul> <p>The full search strategies will be published in the final review.</p>

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5.	Condition or domain being studied	Advanced renal cell carcinoma
6.	Population	<p>Adults (18 years or over) with advanced RCC* who have previously received systemic anti-cancer treatment (SACT). *defined as metastatic/ advanced RCC or locally advanced inoperable RCC (histologically confirmed or suspected on imaging).</p> <p>Advanced RCC diagnosis confirmed according to the clinical or pathological TNM classification</p> <p>Exclusion:</p> <ul style="list-style-type: none"> <li>• Adults who have not received SACT previously.</li> <li>• Adults with localised or locally advanced disease that is considered to be operable.</li> <li>• Adults with advanced disease who are having palliative care only.</li> </ul>
7.	Intervention	<p><b>Non-pharmacological procedures carried out after SACT to:</b></p> <p><b>Manage primary mass:</b></p> <ol style="list-style-type: none"> <li>1. Surgical interventions (where metastatic RCC is considered operable) <ul style="list-style-type: none"> <li>• Cytoreductive nephrectomy in people without prior nephrectomy with or without surgical removal of lymph nodes (lymphadenectomy).</li> </ul> </li> <li>2. Non-surgical interventions <ul style="list-style-type: none"> <li>• Stereotactic ablative radiotherapy (SABR)</li> </ul> </li> </ol> <p><b>Manage metastases:</b></p> <ol style="list-style-type: none"> <li>3. Surgical interventions <ul style="list-style-type: none"> <li>• Surgical removal of metastases also known as metastasectomy (distinguish between complete and incomplete metastasectomy)</li> </ul> </li> <li>4. Non-surgical interventions <ul style="list-style-type: none"> <li>• Thermal ablation including: <ul style="list-style-type: none"> <li>▪ Radiofrequency ablation</li> <li>▪ Cryotherapy</li> <li>▪ Microwave ablation</li> </ul> </li> <li>• Radiotherapy: <ul style="list-style-type: none"> <li>• External beam radiotherapy (EBRT)</li> <li>• Stereotactic ablative radiotherapy (SABR)</li> </ul> </li> </ul> </li> </ol>
8.	Comparator	No non-pharmacological intervention before second or further-line SACT.
9.	Types of study to be included	<ul style="list-style-type: none"> <li>• Systematic reviews of RCTs and RCTs are preferred where available for a comparison.</li> <li>• Where RCTs are not available for a comparison, systematic reviews of prospective and retrospective cohort studies and prospective and retrospective cohort studies will be considered.</li> </ul>

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		<ul style="list-style-type: none"> <li>Where good quality systematic reviews are identified, these may be used completely or as a source of references, depending on applicability. Alternatively, they may be updated by the addition of studies published after the review was completed.</li> </ul>
10.	Other exclusion criteria	<ul style="list-style-type: none"> <li>Abstracts, conference presentations and theses</li> <li>Non-human studies</li> <li>Non-English language studies</li> </ul>
11.	Context	<p>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.</p> <p>There are various non-pharmacological (surgical and non-surgical) interventions for treating advanced RCC but their clinical benefit following SACT is uncertain. Therefore an evidence review is needed to evaluate the clinical and cost-effectiveness of these interventions in people with advanced RCC who have had previous treatment with SACT.</p>
12.	Outcomes	<ul style="list-style-type: none"> <li>Progression-free survival (time to event data)</li> <li>Overall survival (time to event data)</li> </ul> <p>Some studies may report overall survival as death or mortality. These will be extracted as an alternative related outcomes if overall survival is not reported (dichotomous data).</p> <ul style="list-style-type: none"> <li>Cancer-specific survival (time to event data)</li> </ul> <p>If cancer specific survival is not reported, then cancer specific mortality (dichotomous data) will be extracted instead where available.</p> <ul style="list-style-type: none"> <li>Severe adverse events reported as: <ul style="list-style-type: none"> <li>observed in the intraoperative period (measured according to Intraoperative Adverse Incident Classification – EAUiaiC; dichotomous data)</li> <li>observed in the postoperative period (according to Clavien-Dindo Classification of Surgical Classifications at 30-days and 90-day period after surgery; dichotomous data)</li> </ul> </li> <li>Need for further systemic therapy, often expressed as the time-to-second line or further line of therapy (dichotomous or time to event data)</li> <li>Number of hospital admissions (continuous data)</li> <li>Duration of hospital stay (continuous data)</li> <li>Quality of life using: <ul style="list-style-type: none"> <li>EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30; dichotomous or continuous data))</li> <li>EuroQol-5 dimensions (EQ-5D; dichotomous or continuous data)</li> </ul> </li> </ul> <p><b>Minimal important differences</b> Any statistically significant difference will be used for the following outcomes:</p>

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		<ul style="list-style-type: none"> <li>○ Survival outcomes</li> <li>○ Severe adverse events</li> <li>○ Quality of life using EORTC QLQ-C30</li> </ul> <p>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</p>
13.	Data extraction (selection and coding)	<p>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.</p> <p>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 section 6.2). Study investigators may be contacted for missing data where time and resources allow.</p> <p>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:</p> <ul style="list-style-type: none"> <li>• at least 50% of the identified abstracts (or 1,000 records, if that is a greater number) will be screened</li> <li>• After this point, screening is only terminated if a pre-specified threshold of 750 is met for a number of abstracts being screened without a single new include being identified.</li> </ul>
14.	Risk of bias (quality) assessment	<p>Risk of bias will be carried out using the preferred checklists as described in Appendix H of <a href="#">Developing NICE guidelines: the manual</a>.</p> <p>The risk of bias for RCTs will be assessed using the Cochrane Risk of Bias v.2.0 checklist and for systematic reviews, the Risk of Bias in Systematic Reviews (ROBIS) tool will be used</p> <p>The risk of bias for non-RCT studies will be assessed using the Cochrane Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tool.</p>
15.	Strategy for data synthesis	<p>Where possible, meta-analyses will be conducted to combine the results of quantitative studies for each outcome.</p> <p>Where data can be disambiguated it will be separated into the subgroups identified in section 17 (below).</p> <p>Pairwise meta-analyses will be performed in Cochrane Review Manager V5.3. Continuous outcomes will be analysed as pooled mean differences (using the inverse variance method) unless multiple scales are used to measure the same factor. In these cases, standardised mean differences will be used instead. Where different studies present continuous data measuring the same outcome but using different numerical scales (e.g. a 0-10</p>

		<p>and a 0-100 visual analogue scale), these outcomes will all converted to the same scale before meta-analysis is conducted on the mean differences.</p> <p>Pooled relative risks will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event. Absolute risks will be presented where possible.</p> <p>Hazard ratios will be pooled using the generic inverse-variance method. Adjusted, unadjusted and partially adjusted hazard ratios will be pooled. Sensitivity analysis will be carried out to look at the effect of removing partially and unadjusted studies</p> <p>For survival outcomes, time-to-event data is preferred. Where this data is not available, relative risks will be calculated for proxy outcomes as described in section 12.</p> <p>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:</p> <ul style="list-style-type: none"> <li>• Significant between-study heterogeneity in methodology, population, intervention, or comparator was identified by the reviewer in advance of data analysis.</li> <li>• The presence of significant statistical heterogeneity in the meta-analysis, defined as <math>I^2 \geq 50\%</math>.</li> </ul> <p>GRADE will be used to assess the certainty of the outcomes. Data from randomised controlled trials and non-randomised comparative trials will be initially rated as certainty where they come from:</p> <ul style="list-style-type: none"> <li>• RCTs and systematic reviews of RCTs (where individual studies have been quality assessed using Cochrane risk of bias)</li> <li>• non-randomised comparative trials and systematic reviews of non-randomised studies (where individual studies have been quality assessed using the ROBINS-I assessment tool)</li> </ul> <p>The quality of the evidence for each outcome will then be downgraded or not from this starting point based on the other GRADE domains.</p> <p>To assess imprecision, where there are no defined MIDs we will set the MID as the line of no effect for all outcomes except for (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.</p>
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		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: <ul style="list-style-type: none"> <li>• according to interventions received</li> <li>• according to line of SACT received previously</li> <li>• age</li> <li>• by primary RCC type e.g. clear cell, papillary, chromophobe</li> <li>• location of metastases</li> <li>• performance status of the person at baseline (e.g. ECOG and Karnofsky).</li> </ul>
17.	Type and method of review	X Intervention Diagnostic Prognostic Qualitative Epidemiologic Service Delivery Other (please specify)
18.	Language	English
19.	Country	England
20.	Anticipated or actual start date	January 2025
21.	Anticipated completion date	December 2025
22.	Named contact	<p><b>5a. Named contact</b> Centre for Guidelines, NICE</p> <p><b>5b Named contact e-mail</b> kidneycancerguideline@nice.org.uk</p> <p><b>5e Organisational affiliation of the review</b> National Institute for Health and Care Excellence (NICE) and Guideline Development Team.</p>
23.	Review team members	<p>From the Guideline Development Team:</p> <ul style="list-style-type: none"> <li>• Steve Sharp, Technical adviser</li> <li>• Marie Harrisingh, Technical adviser</li> <li>• Sarah Boyce, Senior technical analyst</li> <li>• Fernando Zanghelini, Technical analyst</li> <li>• Olivia Crane, Technical analyst</li> <li>• Lindsay Claxton, Health economics adviser</li> <li>• Hannah Tebbs, Health economist</li> <li>• Yuanyuan Zhang, Health economist</li> <li>• Amy Finnegan, Senior Information specialist</li> </ul>
24.	Funding sources/sponsor	This systematic review is being completed by the Guideline Development Team which receives funding from NICE.

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25.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
26.	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 <a href="#">Developing NICE guidelines: the manual</a> . Members of the guideline committee are available on the NICE website: <a href="#">Kidney Cancer (GID-NG10398)</a> .
27.	Other registration details	None
28.	Reference/URL for published protocol	None
29.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: <ul style="list-style-type: none"> <li>• notifying registered stakeholders of publication</li> <li>• publicising the guideline through NICE's newsletter and alerts</li> <li>• 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.</li> </ul>
30.	Keywords	Localised renal cell carcinoma, thermal ablation, stereotactic ablative radiotherapy, active surveillance
31.	Details of existing review of same topic by same authors	Not applicable
32.	Current review status	<div>X</div> <div>Ongoing</div> <div>Completed but not published</div> <div>Completed and published</div> <div>Completed, published and being updated</div> <div>Discontinued</div>
33.	Additional information	None
34.	Details of final publication	<a href="http://www.nice.org.uk">www.nice.org.uk</a>

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2 **Economic review protocol for management of renal cell carcinoma**3 **Table 12: Economic review protocol**

ID	Field	Content
1.	Review questions	<p>A: Cost-effectiveness of partial versus radical nephrectomy in adults with localised renal cell carcinoma</p> <p>B: Cost-effectiveness of non-surgical interventions or active surveillance in adults with localised renal cell carcinoma</p> <p>C: Cost-effectiveness of nephrectomy or stereotactic ablative radiotherapy for treating locally advanced renal cell carcinoma in adults</p> <p>H1: Cost-effectiveness of non-pharmacological interventions, used before systemic anti-cancer therapy for adults with advanced renal cell carcinoma</p> <p>H2: Cost-effectiveness of non-pharmacological interventions, used after systemic anti-cancer therapy for adults with advanced renal cell carcinoma</p>
2.	Objective	To identify economic studies for all relevant guideline review questions on the management of renal cell carcinoma
3.	Inclusion criteria	<ul style="list-style-type: none"> <li>• Populations, interventions and comparators as specified in the effectiveness review protocol.</li> <li>• Relevant comparative economic study design: cost–utility analysis</li> <li>• Decision analytic model-based or within-trial economic analyses</li> <li>• OECD countries (except USA)</li> <li>• Healthcare and personal social services cost perspective</li> <li>• 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</li> </ul> <p>High-quality studies in line with the NICE reference case (recent UK NHS/PSS cost-utility analyses using the QALY as the measure of outcome) are the most applicable to NICE decision making. Not all studies meeting the inclusion criteria will therefore necessarily be used in decision-making - see Review strategy below for details.</p>
4.	Exclusion criteria	<ul style="list-style-type: none"> <li>• Conference posters or abstract only studies – these do not provide sufficient information for quality assessment.</li> <li>• 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</li> <li>• 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.</li> <li>• Non-comparative economic analyses including cost-of-illness studies.</li> <li>• Letters, editorials or commentaries, study protocols or reviews of economic evaluations (recent reviews will be ordered and the</li> </ul>

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		<p>bibliographies will be checked for relevant individual economic studies, which will then be ordered and checked for eligibility).</p> <ul style="list-style-type: none"> <li>• Non-English language papers.</li> <li>• Studies considering exclusively intervention costs, e.g. medicine acquisition costs, without considering wider healthcare costs associated with the management of renal cell carcinoma.</li> <li>• Studies comparing costs of branded vs generic forms of the same medicine.</li> <li>• Studies only focussing on productivity losses or gains.</li> </ul>
5.	Search strategy	<p>An economic study search will be undertaken covering all review questions relating to the management of renal cell carcinoma using guideline population-specific terms and a health economic study filter. For search details see <a href="#">appendix B</a> below.</p> <p>The following databases will be searched:</p> <ul style="list-style-type: none"> <li>• MEDLINE All, Ovid</li> <li>• Embase, Ovid</li> <li>• International HTA database, International Network of Agencies for Health Technology Assessment (INAHTA)</li> <li>• Econlit</li> <li>• NHS EED and HTA (legacy records)</li> </ul>
6.	Review strategy	<ul style="list-style-type: none"> <li>• 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 <a href="#">Developing NICE guidelines: the manual</a>.</li> <li>• The NICE economic evaluation checklist assesses: <ul style="list-style-type: none"> <li>○ Applicability to the NICE guideline decision making context with consideration of the <a href="#">NICE reference case relevant to the guideline</a>. Recent UK studies that use the NICE reference case methods are the most applicable when considering cost effectiveness.</li> <li>○ Methodological limitations.</li> </ul> </li> <li>• 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: <ul style="list-style-type: none"> <li>○ If multiple versions of a model are available for the UK and other countries it is usually reasonable to only present the UK version.</li> <li>○ If multiple versions of the same UK model are available, it is usually reasonable to present only the most recent.</li> <li>○ If there has been a NICE MTA or guideline model that informs current NHS practice it is usually reasonable not to present older</li> </ul> </li> </ul>

		<p>studies, unless they address a different subpopulation or other specific issue.</p> <ul style="list-style-type: none"> <li>○ 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.</li> <li>• 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.</li> <li>• Hierarchy of economic evaluation evidence based on quality assessment <ul style="list-style-type: none"> <li>○ 'Directly applicable' and 'Minor limitations' (only recent UK CUAs can get this rating). Usually presented and used in decision-making.</li> <li>○ 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.</li> <li>○ 'Not applicable' or 'Very serious limitations'. Typically not presented and not used in decision-making.</li> </ul> </li> </ul> <p>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.</p>
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## 1 **Appendix B – Literature search strategies**

### 2 **Background and development**

### 3 **Search design and peer review**

4 A NICE Senior Information Specialist (SIS) conducted the literature searches. The MEDLINE  
5 strategies below were quality assured (QA) by another NICE SIS. All translated search  
6 strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from  
7 the Peer Review of Electronic Search Strategies Guideline Statement (for further details see:  
8 McGowan J et al. [PRESS 2015 Guideline Statement](#). *Journal of Clinical Epidemiology*, 75,  
9 40-46).

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

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

### 16 **Review management**

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

### 21 **Prior work**

22 A test set of 8 systematic reviews were supplied by the technical analysts, this test set  
23 covered the current review (review H1 and H2) and reviews A, B, C (review A: surgical  
24 interventions for localised RCC, review B: non-surgical interventions for localised RCC and  
25 review C: nephrectomy or stereotactic ablative radiotherapy for locally advanced RCC).

### 26 **Search limits and other restrictions**

#### 27 **Formats**

28 Limits were applied in adherence to standard NICE practice and the review protocol to  
29 exclude:

- 30 • Animal studies
- 31 • Editorials, letters, news items and commentaries
- 32 • Conference abstracts and posters

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- 1 • Registry entries for ongoing clinical trials or those that contain no results
- 2 • Theses and dissertations
- 3 • Papers not published in the English language.

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

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

## 8 **Date limits**

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

## 10 **Search filters and classifiers**

### 11 **Effectiveness searches**

12 OECD:

13 The OECD countries filters were used without modification:

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

17  
18 Observational filter:

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

21  
22 Systematic reviews filters:

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

25 In MEDLINE, the standard NICE modifications were used: pubmed.tw added; systematic  
26 review.pt added from MeSH update 2019.

27 In Embase, the standard NICE modifications were used: pubmed.tw added to line  
28 medline.tw.

29  
30 Randomised controlled trials filters:

31 McMaster Therapy – Medline – "best balance of sensitivity and specificity" version:

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

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

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.

### Cost effectiveness searches

The precise version of the validated NICE cost utility filter was used in the MEDLINE and Embase strategies without amendment.

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

### Key decisions

A single systematic search was carried out to identify potentially relevant studies for the current review (review H1 and H2) and reviews A, B, C (review A: surgical interventions for localised RCC, review B: non-surgical interventions for localised RCC and review C: nephrectomy or stereotactic ablative radiotherapy for locally advanced RCC).

1 **Clinical searches**2 **Database results**

3

<b>Database</b>	<b>Date searched</b>	<b>Database Platform</b>	<b>Database segment or version</b>	<b>No. of results downloaded</b>
Cochrane Central Register of Controlled Trials (CENTRAL)	18/01/2024	Wiley	Issue 1 of 12, January 2024	767
Cochrane Database of Systematic Reviews (CDSR)	18/01/2024	Wiley	Issue 1 of 12, January 2024	8
Embase	18/01/2024	Ovid	1974 to 2024 January 18	13394
Epistemonikos	18/01/2024	Epistemonikos	n/a	1993
INAHTA	18/01/2024	INAHTA	n/a	97
MEDLINE ALL	18/01/2024	Ovid	1946 to January 17, 2024	9991

4 **Rerun search database results**

5

<b>Databases</b>	<b>Date searched</b>	<b>Database platform</b>	<b>Database segment or version</b>	<b>No. of results downloaded</b>
Cochrane Central Register of Controlled Trials (CENTRAL)	14/02/2025	Wiley	Issue 2 of 12, February 2025	845
Cochrane Database of Systematic Reviews (CDSR)	14/02/2025	Wiley	Issue 2 of 12, February 2025	8
Embase	14/02/2025	Ovid	1974 to 2025 February 13	14588
Epistemonikos	14/02/2025	Epistemonikos	n/a	2350
INAHTA	14/02/2025	INAHTA	n/a	177
MEDLINE ALL	14/02/2025	Ovid	1946 to February 13, 2025	10686

- 1 *No date limits were applied to the rerun searches due to technical issues in OVID.*
- 2 *Duplication of records was managed in EPPI Reviewer 5.*

### 3 Search strategy history

#### 4 Database name: Medline ALL

Searches
1 exp Kidney Neoplasms/ (85773)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (17162)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (490)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or grawitz-tumor* or hypernephroma* or nephrocarcinoma*).ti,ab. (70604)
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (808)
6 or/1-5 (118618)
7 exp nephrectomy/ (37938)
8 (nephrectom* or lymphadenectom*).ti,ab,kw. (62205)
9 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) adj3 (remov* or surg* or extract* or extirpat* or operat*)).ti,ab. (204663)
10 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) and (remov* or surg* or extract* or extirpat* or operat*)).kf. (59909)
11 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (918105)
12 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kf. (21870)
13 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (2661)
14 (nephron* and (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).kf. (446)
15 radiotherapy/ or lymphatic irradiation/ or radiosurgery/ or radiotherapy, adjuvant/ or radiotherapy dosage/ or radiotherapy, high-energy/ or re-irradiation/ or Cytoreduction Surgical Procedures/ or Ablation Techniques/ or Radiofrequency Ablation/ or Robotic Surgical Procedures/ or Minimally Invasive Surgical Procedures/ or Metastasectomy/ or Lymph Node Excision/ or Watchful Waiting/ (239644)
16 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (933898)
17 ((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (2177)
18 ((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kw. (11)
19 (minimal* adj2 invas* adj2 (surg* or procedur* or treat*)).ti,ab. (38472)
20 (minimal* and invas* and (surg* or procedur* or treat*)).kw. (5)
21 ((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (279)

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Searches	
22	((inferior-vena-cava or IVC) and thrombectom*).kw. (26)
23	((activ* or tumor* or delay*) adj2 (surveil* or monitor*)).ti,ab. (38392)
24	((activ* or tumor* or delay*) and (surveil* or monitor*)).kw. (266)
25	(delay* adj2 treat*).ti,ab. (20889)
26	(delay* and treat*).kw. (162)
27	(watchful* adj1 wait*).ti,ab. (3238)
28	(watchful* and wait*).kw. (4)
29	or/7-28 (2201330)
30	6 and 29 (38582)
31	animals/ not humans/ (5153512)
32	30 not 31 (36911)
33	limit 32 to english language (30806)
34	limit 33 to (letter or historical article or comment or editorial or news or case reports)
35	(9081)
36	33 not 34 (21725)
37	exp Randomized Controlled Trial/ (608436)
38	randomi?ed.mp. (1099661)
39	placebo.mp. (252799)
40	or/36-38 (1166623)
41	(MEDLINE or pubmed).tw. (344612)
42	systematic review.tw. (287748)
43	systematic review.pt. (249879)
44	meta-analysis.pt. (193317)
45	intervention\$.ti. (208375)
46	or/40-44 (719849)
47	Epidemiologic studies/ (9465)
48	exp case control studies/ (1474038)
49	exp cohort studies/ (2562056)
50	Case control.tw. (159034)
51	(cohort adj (study or studies)).tw. (337093)
52	Cohort analy\$.tw. (12565)
53	(Follow up adj (study or studies)).tw. (57443)
54	(observational adj (study or studies)).tw. (171478)
55	Longitudinal.tw. (336148)
56	Retrospective.tw. (784597)
57	Cross sectional.tw. (542555)
58	Cross-sectional studies/ (489693)
59	or/46-57 (3917614)
60	39 or 45 or 58 (5240090)
61	35 and 59 (10204)
61	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/

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**Searches**

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 russia/ 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/ (1322150)

62 "organisation for economic co-operation and development"/ (581)

63 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/ (3526314)

64 european union/ (17879)

65 developed countries/ (21470)

66 or/62-65 (3542495)

67 61 not 66 (1231834)

68 60 not 67 (9991)

1

2

**Database name: Embase****Searches**

1 exp kidney tumor/ (169289)

2 (Kidney\* adj2 (cancer\* or carcinoma\* or carcinosarcoma\* or adenocarcino\* or neoplas\* or tumor\* or mass or metastat\* or malignan\* or sarcoma\* or parenchyma\* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (25843)

3 (collecting-duct\* adj2 (cancer\* or carcinoma\* or carcinosarcoma\* or adenocarcino\* or neoplas\* or tumor\* or mass or metastat\* or malignan\* or sarcoma\* or parenchyma\* or stage-4)).ti,ab. (738)

4 (renal-cell\* or RCC or ccRCC or Renal-mass\* or renal-tumor\* or grawitz-tumor\* or hypernephroma\* or nephrocarcinoma\*).ti,ab. (105763)

5 (Kidney\* adj2 (Transitional-cell\* or cell or urothelial\* or duct or advanc\*) adj2 (cancer\* or carcinoma\* or carcinosarcoma\* or adenocarcino\* or neoplas\* or tumor\* or mass or metastat\* or malignan\* or sarcoma\* or parenchyma\*)).ti,ab. (1179)

6 or/1-5 (199212)

7 exp nephrectomy/ (79135)

8 (nephrectom\* or lymphadenectom\*).ti,ab,kw. (95869)

9 ((kidney\* or renal\* or RCC or ccRCC or lymph\* or adrenal\* or cancer\* or carcinoma\* or carcinosarcoma\* or adenocarcino\* or neoplas\* or tumor\* or mass or metastat\* or malignan\* or sarcoma\* or hypernephroma\* or nephrocarcinoma\*) adj3 (remov\* or surg\* or extract\* or extirpat\* or operat\*)).ti,ab. (296316)

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Searches
<p>10 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) and (remov* or surg* or extract* or extirpat* or operat*)).kf. (84073)</p> <p>11 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (1172497)</p> <p>12 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kf. (39682)</p> <p>13 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (4849)</p> <p>14 (nephron* and (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).kf. (923)</p> <p>15 radiotherapy/ or cancer radiotherapy/ or adjuvant radiotherapy/ or exp radiosurgery/ or radiotherapy dosage/ or megavoltage radiotherapy/ or re-irradiation/ or cytoreductive surgery/ or ablation therapy/ or radiofrequency ablation/ or robot assisted surgery/ or minimally invasive surgery/ or metastasis resection/ or lymph node dissection/ or cryotherapy/ or stereotactic body radiation therapy/ or active surveillance/ or watchful waiting/ (700411)</p> <p>16 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (1245790)</p> <p>17 ((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (3847)</p> <p>18 ((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kw. (21)</p> <p>19 (minimal* adj2 invas* adj2 (surg* or procedur* or treat*)).ti,ab. (58741)</p> <p>20 (minimal* and invas* and (surg* or procedur* or treat*)).kw. (8)</p> <p>21 ((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (642)</p> <p>22 ((inferior-vena-cava or IVC) and thrombectom*).kw. (36)</p> <p>23 ((activ* or tumor* or delay*) adj2 (surveil* or monitor*)).ti,ab. (56960)</p> <p>24 ((activ* or tumor* or delay*) and (surveil* or monitor*)).kw. (432)</p> <p>25 (delay* adj2 treat*).ti,ab. (32640)</p> <p>26 (delay* and treat*).kw. (278)</p> <p>27 (watchful* adj1 wait*).ti,ab. (4967)</p> <p>28 (watchful* and wait*).kw. (8)</p> <p>29 or/7-28 (3008790)</p> <p>30 6 and 29 (72417)</p> <p>31 nonhuman/ not human/ (5369703)</p> <p>32 30 not 31 (70586)</p> <p>33 limit 32 to english language (63135)</p> <p>34 33 not (letter or editorial).pt. (61048)</p> <p>35 34 not (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (41463)</p> <p>36 random:.tw. (2023923)</p> <p>37 placebo:.mp. (532136)</p> <p>38 double-blind:.tw. (248720)</p> <p>39 or/36-38 (2304835)</p> <p>40 (MEDLINE or pubmed).tw. (428718)</p> <p>41 exp systematic review/ or systematic review.tw. (533296)</p> <p>42 meta-analysis/ (304008)</p> <p>43 intervention\$.ti. (274290)</p> <p>44 or/40-43 (1007209)</p> <p>45 Clinical study/ (165319)</p> <p>46 Case control study/ (212430)</p>

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Searches	
47	Family study/ (25771)
48	Longitudinal study/ (205110)
49	Retrospective study/ (1556506)
50	comparative study/ (1042643)
51	Prospective study/ (902470)
52	Randomized controlled trials/ (268035)
53	51 not 52 (891477)
54	Cohort analysis/ (1106561)
55	cohort analy\$.tw. (20347)
56	(Cohort adj (study or studies)).tw. (487394)
57	(Case control\$ adj (study or studies)).tw. (176315)
58	(follow up adj (study or studies)).tw. (75066)
59	(observational adj (study or studies)).tw. (266587)
60	(epidemiologic\$ adj (study or studies)).tw. (124259)
61	(cross sectional adj (study or studies)).tw. (359262)
62	case series.tw. (152596)
63	prospective.tw. (1133006)
64	retrospective.tw. (1304827)
65	or/45-50,53-64 (5603678)
66	39 or 44 or 65 (7885322)
67	35 and 66 (13670)
68	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/ (1736652)
69	exp "organisation for economic co-operation and development"/ (2827)
70	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

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Searches	
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/ (3832351)	
71 european union/ (31891)	
72 developed country/ (35945)	
73 or/69-72 (3866518)	
74 68 not 73 (1580645)	
75 67 not 74 (13394)	

# 1 Database name: Cochrane CDSR & CENTRAL

Searches	
#1	MeSH descriptor: [Kidney Neoplasms] explode all trees 1694
#2	(Kidney* NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)):ti,ab 1332
#3	(collecting-duct* NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)):ti,ab 14
#4	(renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*):ti,ab 3747
#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 tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*)):ti,ab 69
#6	{or #1-#5} 5140
#7	MeSH descriptor: [Nephrectomy] explode all trees 594
#8	(nephrectom* or lymphadenectom*):ti,ab 3676
#9	MeSH descriptor: [Radiotherapy] this term only 2824
#10	MeSH descriptor: [Lymphatic Irradiation] this term only 76
#11	MeSH descriptor: [Radiosurgery] this term only 485
#12	MeSH descriptor: [Radiotherapy, Adjuvant] this term only 1427
#13	MeSH descriptor: [Radiotherapy Dosage] this term only 2429
#14	MeSH descriptor: [Radiotherapy, High-Energy] this term only 320
#15	MeSH descriptor: [Re-Irradiation] this term only 37
#16	MeSH descriptor: [Cyto reduction Surgical Procedures] this term only 232
#17	MeSH descriptor: [Ablation Techniques] this term only 127
#18	MeSH descriptor: [Radiofrequency Ablation] this term only 342
#19	MeSH descriptor: [Robotic Surgical Procedures] this term only 716
#20	MeSH descriptor: [Minimally Invasive Surgical Procedures] this term only 1280
#21	MeSH descriptor: [Metastasectomy] this term only 43
#22	MeSH descriptor: [Lymph Node Excision] this term only 1540
#23	MeSH descriptor: [Watchful Waiting] this term only 469
#24	((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) NEAR/3 (remov* or surg* or extract* or extirpat* or operat*)):ti,ab 18334
#25	((laproscop* or open or partial* or radical or transperiton* or retroperiton*) NEAR/3 (surg* or remov* or partial* or procedur* or treat* or operat*)):ti,ab 63782
#26	(nephron* NEAR/2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)):ti,ab 123
#27	(radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cyto reduct* or cyroablat* or stereostat* or SABR):ti,ab 63947

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Searches		
#28	((RAS or (robotic* NEAR/1 assist*)) NEAR/1 (surg* or remov* or partial* or procedur* or treat* or operat*)):ti,ab	256
#29	(minimal* NEAR/2 invas* NEAR/2 (surg* or procedur* or treat*)):ti,ab	3606
#30	((inferior-vena-cava or IVC) NEAR/2 thrombectom*):ti,ab	2
#31	((activ* or tumor* or tumour* or delay*) NEAR/2 (surveil* or monitor*)):ti,ab	4050
#32	(delay* NEAR/2 treat*):ti,ab	2913
#33	(watchful* NEAR/1 wait*):ti,ab	668
#34	{or #7-#33}	150254
#35	#6 AND #34	1693
#36	"conference":pt or (clinicaltrials or trialsearch):so	725938
#37	#35 NOT #36	776

## 1 Database name: Epistemonikos

Searches		
(kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4 or (stage 1) or (stage 2) or (stage 3) or (stage 4))) OR (collecting-duct* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4 or (stage 1) or (stage 2) or (stage 3) or (stage 4))) OR ((collecting duct*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4 or (stage 1) or (stage 2) or (stage 3) or (stage 4))) OR (renal-cell* or (renal cell*) or rcc or ccrcc or renal-mass* or (renal mass*) or renal-tumor* or (renal tumor*) or renal-tumour* or (renal tumour*) or grawitz-tumor* or (grawitz tumor*) or grawitz-tumour* or (grawitz tumour*) or hypernephroma* or nephrocarcinoma*) OR (kidney* AND (transitional-cell* or (transitional cell*) or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))		
AND		
(nephrectom* or lymphadenectom*) OR ((kidney* or renal* or rcc or ccrcc or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) AND (remov* or surg* or extract* or extirpat* or operat*)) OR ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) AND (surg* or remov* or partial* or procedur* or treat* or operat*)) OR (nephron* AND (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)) OR (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or sabr) OR ((ras or (robotic* AND assist*)) AND (surg* or remov* or partial* or procedur* or treat* or operat*)) OR (minimal* AND invas* AND (surg* or procedur* or treat*)) OR ((inferior-vena-cava or ivc or (inferior vena cava)) AND thrombectom*) OR ((activ* or tumor* or tumour* or delay*) AND (surveil* or monitor*)) OR (delay* AND treat*) OR (watchful* AND wait*)		

## 2 Database name: INAHTA

Searches		
#1	"Kidney Neoplasms"[mhe]	111

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Searches		
#2	((Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4))) OR ((collecting-duct* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*)) OR ((Kidney* AND (Transitional-cell* or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))) )	105
#3	((((Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4))) OR ((collecting-duct* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*)) OR ((Kidney* AND (Transitional-cell* or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))) )) OR ("Kidney Neoplasms"[mhe])	155
#4	"Nephrectomy"[mhe]	12
#5	((nephrectom* or lymphadenectom*))	31
#6	"Radiotherapy"[mh]	220
#7	"Lymphatic Irradiation"[mh]	0
#8	"Radiosurgery"[mh]	71
#9	"Radiotherapy Adjuvant"[mh]	27
#10	"Radiotherapy Dosage"[mh]	27
#11	"Radiotherapy High-Energy"[mh]	9
#12	"Re-Irradiation"[mh]	2
#13	"Cytoreduction Surgical Procedures"[mh]	2
#14	"Ablation Techniques"[mh]	35
#15	"Radiofrequency Ablation"[mh]	29
#16	"Robotic Surgical Procedures"[mh]	22
#17	"Minimally Invasive Surgical Procedures"[mh]	109
#18	"Metastasectomy"[mh]	1
#19	"Lymph Node Excision"[mh]	9
#20	((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) AND (remov* or surg* or extract* or extirpat* or operat*))	878
#21	((laproscop* or open or partial* or radical or transperiton* or retroperiton*) AND (surg* or remov* or partial* or procedur* or treat* or operat*))	756
#22	(nephron* AND (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*))	2
#23	radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR)	1000

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Searches		
#24	((RAS or (robotic* AND assist*)) AND (surg* or remov* or partial* or procedur* or treat* or operat*))	73
#25	(minimal* AND invas* AND (surg* or procedur* or treat*))	246
#26	((inferior-vena-cava or IVC) AND thrombectom*)	0
#27	((activ* or tumor* or tumour* or delay*) AND (surveil* or monitor*))	318
#28	(delay* AND treat*)	201
#29	(watchful* AND wait*)	45
#29	#28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4	2796
#30	#29 AND #3	155
Limit	English language	97

1

1 **Cost-effectiveness searches**2 **Database results**

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	05/02/2024	OVID	1886 to January 25, 2024	1
EED	07/02/2024	CRD	n/a	23
Embase	05/02/2024	Ovid	1974 to 2024 February 02	65
HTA	07/02/2024	CRD	n/a	27
INAHTA	05/02/2024	INAHTA	n/a	155
MEDLINE ALL	05/02/2024	Ovid	1946 to February 02, 2024	62

3 **Rerun search database results**

4

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	06/05/2025	OVID	1886 to May 01, 2025	1
Embase	06/05/2025	Ovid	1974 to 2025 May 05	73
INAHTA	06/05/2025	INAHTA	n/a	177
MEDLINE ALL	06/05/2025	Ovid	1946 to May 05, 2025	68

5 **Search strategy history**6 **Database name: Econlit**

Searches
1 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (8)
2 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (0)
3 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or grawitz-tumor* or hypernephroma* or nephrocarcinoma*).ti,ab. (22)
4 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (0)
5 or/1-4 (30)
6 (nephrectom* or lymphadenectom*).ti,ab,kw. (0)

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Searches
7 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) adj3 (remov* or surg* or extract* or extirpat* or operat*)).ti,ab. (80)
8 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (25798)
9 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (0)
10 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (599)
11 ((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (10)
12 ((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kw. (0)
13 (minimal* adj2 invas* adj2 (surg* or procedur* or treat*)).ti,ab. (7)
14 (minimal* and invas* and (surg* or procedur* or treat*)).kw. (0)
15 ((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (0)
16 ((inferior-vena-cava or IVC) and thrombectom*).kw. (0)
17 ((activ* or tumo?r* or delay*) adj2 (surveil* or monitor*)).ti,ab. (388)
18 ((activ* or tumo?r* or delay*) and (surveil* or monitor*)).kw. (4)
19 (delay* adj2 treat*).ti,ab. (48)
20 (delay* and treat*).kw. (0)
21 (watchful* adj1 wait*).ti,ab. (10)
22 (watchful* and wait*).kw. (0)
23 or/6-22 (26909)
24 5 and 23 (1)

## 1 Database name: CRD EED &amp; HTA

Searches		
Line	Search	Hits
1	MESH DESCRIPTOR Kidney Neoplasms EXPLODE ALL TREES	201
2	((Kidney* NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4))	194
3	((collecting-duct* NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4))	1
4	((renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*)	204
5	((Kidney* NEAR2 (Transitional-cell* or cell or urothelial* or duct or advanc*) NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))	3
6	#1 OR #2 OR #3 OR #4 OR #5	262
7	MESH DESCRIPTOR Nephrectomy EXPLODE ALL TREES	95
8	((nephrectom* or lymphadenectom*)	235
9	MESH DESCRIPTOR Radiotherapy	247
10	MESH DESCRIPTOR Lymphatic Irradiation	1
11	MESH DESCRIPTOR Radiosurgery	125
12	MESH DESCRIPTOR Radiotherapy, Adjuvant	176
13	MESH DESCRIPTOR Radiotherapy Dosage	112
14	MESH DESCRIPTOR Radiotherapy, High-Energy	15
15	MESH DESCRIPTOR Re-Irradiation	0
16	MESH DESCRIPTOR Cytoreduction Surgical Procedures	4
17	MESH DESCRIPTOR Ablation Techniques	29
18	MESH DESCRIPTOR Radiofrequency Ablation	0
19	MESH DESCRIPTOR Robotic Surgical Procedures	23
20	MESH DESCRIPTOR Minimally Invasive Surgical Procedures	260
21	MESH DESCRIPTOR Metastasectomy	5
22	MESH DESCRIPTOR Lymph Node Excision	171
23	((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) NEAR3 (remov* or surg* or extract* or extirpat* or operat*))	2281
24	((laproscop* or open or partial* or radical or transperiton* or retroperiton*) NEAR3 (surg* or remov* or partial* or procedur* or treat* or operat*))	1045
25	((nephron* NEAR2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*))	9
26	((radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytotoreduct* or cyroablat* or stereostat* or SABR)	3151
27	((RAS or (robotic* NEAR1 assist*)) NEAR1 (surg* or remov* or partial* or procedur* or treat* or operat*))	28
28	((minimal* NEAR2 invas* NEAR2 (surg* or procedur* or treat*))	425
29	((inferior-vena-cava or IVC) NEAR2 thrombectom*)	0
30	((activ* or tumor* or tumour* or delay*) NEAR2 (surveil* or monitor*))	119
31	((delay* NEAR2 treat*)	119
32	MESH DESCRIPTOR Watchful Waiting	38
33	((watchful* NEAR1 wait*)	137
34	#7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33	6388
35	#6 AND #34	97
36	(#35) IN NHSEED	23
37	(#35) IN HTA	27

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3

**Database name: Embase**

Searches
<p>1 exp kidney tumor/ (169657)</p> <p>2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (25905)</p> <p>3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (739)</p> <p>4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor?r* or grawitz-tumor?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (105980)</p> <p>5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (1182)</p> <p>6 or/1-5 (199645)</p> <p>7 exp nephrectomy/ (79289)</p> <p>8 (nephrectom* or lymphadenectom*).ti,ab,kw. (96024)</p> <p>9 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) adj3 (remov* or surg* or extract* or extirpat* or operat*)).ti,ab. (296981)</p> <p>10 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) and (remov* or surg* or extract* or extirpat* or operat*)).kf. (84341)</p> <p>11 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (1174471)</p> <p>12 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kf. (39794)</p> <p>13 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (4849)</p> <p>14 (nephron* and (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).kf. (927)</p> <p>15 radiotherapy/ or cancer radiotherapy/ or adjuvant radiotherapy/ or exp radiosurgery/ or radiotherapy dosage/ or megavoltage radiotherapy/ or re-irradiation/ or cytoreductive surgery/ or ablation therapy/ or radiofrequency ablation/ or robot assisted surgery/ or minimally invasive surgery/ or metastasis resection/ or lymph node dissection/ or cryotherapy/ or stereotactic body radiation therapy/ or active surveillance/ or watchful waiting/ (702412)</p> <p>16 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoeduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (1248256)</p> <p>17 ((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (3873)</p> <p>18 ((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kw. (21)</p> <p>19 (minimal* adj2 invas* adj2 (surg* or procedur* or treat*)).ti,ab. (58898)</p> <p>20 (minimal* and invas* and (surg* or procedur* or treat*)).kw. (8)</p> <p>21 ((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (647)</p> <p>22 ((inferior-vena-cava or IVC) and thrombectom*).kw. (36)</p>

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Searches	
23	((activ* or tumo?r* or delay*) adj2 (surveil* or monitor*)).ti,ab. (57069)
24	((activ* or tumo?r* or delay*) and (surveil* or monitor*)).kw. (432)
25	(delay* adj2 treat*).ti,ab. (32723)
26	(delay* and treat*).kw. (281)
27	(watchful* adj1 wait*).ti,ab. (4971)
28	(watchful* and wait*).kw. (8)
29	or/7-28 (3014855)
30	6 and 29 (72543)
31	nonhuman/ not human/ (5377221)
32	30 not 31 (70709)
33	limit 32 to english language (63258)
34	33 not (letter or editorial).pt. (61164)
35	34 not (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (41542)
36	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/ (1740991)
37	exp "organisation for economic co-operation and development"/ (2851)
38	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/ (3835523)
39	european union/ (31807)
40	developed country/ (35992)
41	or/37-40 (3869712)

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Searches	
42	36 not 41 (1584824)
43	35 not 42 (41050)
44	cost utility analysis/ (12696)
45	(cost* and ((qualit* adj2 adjust* adj2 life*) or qaly*)).tw. (30947)
46	((incremental* adj2 cost*) or ICER).tw. (31650)
47	(cost adj2 utilit*).tw. (11338)
48	(cost* and ((net adj benefit*) or (net adj monetary adj benefit*) or (net adj health adj benefit*))).tw. (3393)
49	((cost adj2 (effect* or utilit*)) and (quality adj of adj life)).tw. (37671)
50	(cost and (effect* or utilit*)).ti. (58589)
51	or/44-50 (92726)
52	43 and 51 (65)

## 1 Database name: Medline ALL

Searches	
1	exp Kidney Neoplasms/ (85968)
2	(Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (17223)
3	(collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (491)
4	(renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or grawitz-tumor* or hypernephroma* or nephrocarcinoma*).ti,ab. (70816)
5	(Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (817)
6	or/1-5 (118910)
7	exp nephrectomy/ (37965)
8	(nephrectom* or lymphadenectom*).ti,ab,kw. (62344)
9	((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) adj3 (remov* or surg* or extract* or extirpat* or operat*)).ti,ab. (205263)
10	((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) and (remov* or surg* or extract* or extirpat* or operat*)).kf. (60200)
11	((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (920508)
12	((laproscop* or open or partial* or radical or transperiton* or retroperiton*) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kf. (22001)
13	(nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (2662)
14	(nephron* and (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).kf. (447)
15	radiotherapy/ or lymphatic irradiation/ or radiosurgery/ or radiotherapy, adjuvant/ or radiotherapy dosage/ or radiotherapy, high-energy/ or re-irradiation/ or Cytoreduction Surgical Procedures/ or Ablation Techniques/ or Radiofrequency Ablation/ or Robotic Surgical Procedures/ or Minimally Invasive Surgical Procedures/ or Metastasectomy/ or Lymph Node Excision/ or Watchful Waiting/ (240052)

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Searches	
16	(radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or
17	ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (936452)
18	((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat*
19	or operat*).ti,ab. (2212)
20	((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat*
21	or operat*).kw. (11)
22	(minimal* adj2 invas* adj2 (surg* or procedur* or treat*).ti,ab. (38673)
23	(minimal* and invas* and (surg* or procedur* or treat*).kw. (5)
24	((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (279)
25	((inferior-vena-cava or IVC) and thrombectom*).kw. (26)
26	((activ* or tumor* or delay*) adj2 (surveil* or monitor*).ti,ab. (38554)
27	((activ* or tumor* or delay*) and (surveil* or monitor*).kw. (268)
28	(delay* adj2 treat*).ti,ab. (20957)
29	(delay* and treat*).kw. (163)
30	(watchful* adj1 wait*).ti,ab. (3243)
31	(watchful* and wait*).kw. (4)
32	or/7-28 (2207356)
33	6 and 29 (38664)
34	animals/ not humans/ (5159676)
35	30 not 31 (36990)
36	limit 32 to english language (30881)
37	limit 33 to (letter or historical article or comment or editorial or news or case reports)
38	(9092)
39	33 not 34 (21789)
40	afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa
41	south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or
42	andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or
43	bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/
44	or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or
45	burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african
46	republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or
47	"democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican
48	republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or
49	ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or
50	guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent
51	state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or
52	iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or
53	laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/
54	or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or
55	micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or
56	myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or
57	palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/
58	or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or
59	rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or
60	"sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or
61	seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/
62	or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/
63	or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or
64	united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or
65	west indies/ or yemen/ or zambia/ or zimbabwe/ (1325188)
66	37 "organisation for economic co-operation and development"/ (587)
67	38 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or
68	chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or
69	finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or

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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/ (3530229)
39	european union/ (17894)
40	developed countries/ (21491)
41	or/37-40 (3546443)
42	36 not 41 (1234802)
43	35 not 42 (21490)
44	Cost-Benefit Analysis/ (93959)
45	(cost* and ((qualit* adj2 adjust* adj2 life*) or qaly*)).tw. (18159)
46	((incremental* adj2 cost*) or ICER).tw. (18654)
47	(cost adj2 utilit*).tw. (7142)
48	(cost* and ((net adj benefit*) or (net adj monetary adj benefit*) or (net adj health adj benefit*))).tw. (2429)
49	((cost adj2 (effect* or utilit*)) and (quality adj of adj life)).tw. (24749)
50	(cost and (effect* or utilit*).ti. (39941)
51	or/44-50 (116479)
52	43 and 51 (62)

## 1 Database name: INAHTA

Searches	
#1	"Kidney Neoplasms"[mhe] 111
#2	((Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4))) OR ((collecting-duct* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*)) OR ((Kidney* AND (Transitional-cell* or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))) ) 105
#3	#1 or #2 155
#4	"Nephrectomy"[mhe] 12
#5	((nephrectom* or lymphadenectom*)) 31
#6	"Radiotherapy"[mh] 220
#7	"Lymphatic Irradiation"[mh] 0
#8	"Radiosurgery"[mh] 71
#9	"Radiotherapy Adjuvant"[mh] 27
#10	"Radiotherapy Dosage"[mh] 27
#11	"Radiotherapy High-Energy"[mh] 9
#12	"Re-Irradiation"[mh] 2
#13	"Cytoreduction Surgical Procedures"[mh] 2
#14	"Ablation Techniques"[mh] 35
#15	"Radiofrequency Ablation"[mh] 29
#16	"Robotic Surgical Procedures"[mh] 22

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

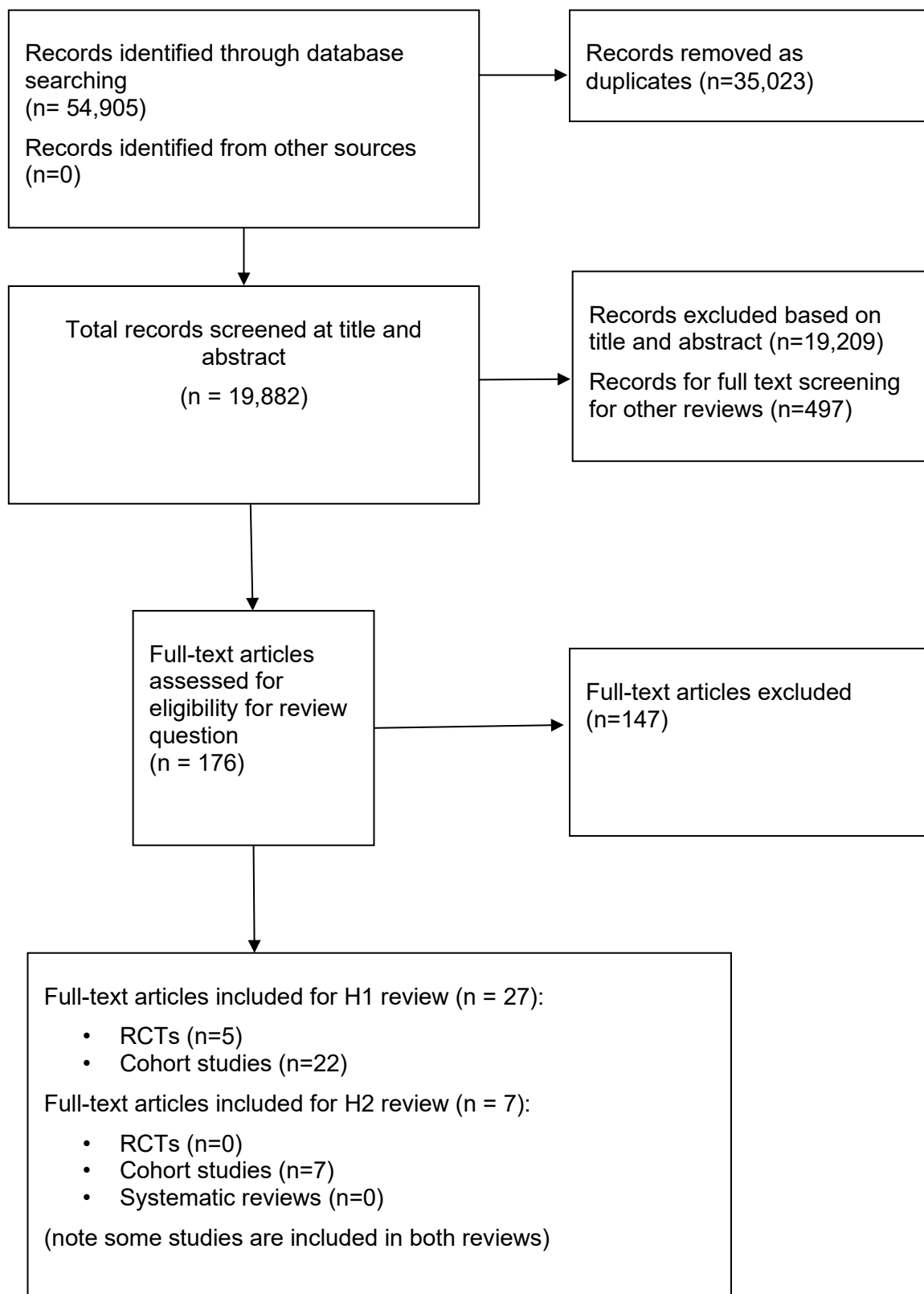
Searches		
#17	"Minimally Invasive Surgical Procedures"[mh]	109
#18	"Metastasectomy"[mh]	1
#19	"Lymph Node Excision"[mh]	9
#20	((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) AND (remov* or surg* or extract* or extirpat* or operat*))	878
#21	((laproscop* or open or partial* or radical or transperiton* or retroperiton*) AND (surg* or remov* or partial* or procedur* or treat* or operat*))	756
#22	(nephron* AND (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*))	2
#23	radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR)	1000
#24	((RAS or (robotic* AND assist*)) AND (surg* or remov* or partial* or procedur* or treat* or operat*))	73
#25	(minimal* AND invas* AND (surg* or procedur* or treat*))	246
#26	((inferior-vena-cava or IVC) AND thrombectom*)	0
#27	((activ* or tumor* or tumour* or delay*) AND (surveil* or monitor*))	318
#28	(delay* AND treat*)	201
#29	(watchful* AND wait*)	45
#30	"Watchful Waiting"[mh]	17
#31	#30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4	2803
#32	#31 AND #3	155

1

2



## 1 Appendix C – Effectiveness evidence study selection



# 1 **Appendix D – Effectiveness evidence**

## 2 **Review 1 Cytoreductive nephrectomy then systemic anti-cancer therapy**

### 3 **Randomised controlled trials evidence**

#### 4 **Bex, 2019**

**Bibliographic Reference** Bex, Axel; Mulders, Peter; Jewett, Michael; Wagstaff, John; van Thienen, Johannes V; Blank, Christian U; van Velthoven, Roland; Del Pilar Laguna, Maria; Wood, Lori; van Melick, Harm H E; Aarts, Maureen J; Lattouf, J B; Powles, Thomas; de Jong Md PhD, Igle Jan; Rottey, Sylvie; Tombal, Bertrand; Marreaud, Sandrine; Collette, Sandra; Collette, Laurence; Haanen, John; Comparison of Immediate vs Deferred Cytoreductive Nephrectomy in Patients With Synchronous Metastatic Renal Cell Carcinoma Receiving Sunitinib: The SURTIME Randomized Clinical Trial.; JAMA oncology; 2019; vol. 5 (no. 2); 164-170

5

#### 6 **Study details**

<b>Other publications associated with this study included in review</b>	Paper published by De Bruijn 2019 reported the duration of hospital stay from SURTIME trial
<b>Trial registration number and/or trial name</b>	SURTIME (NCT01099423)
<b>Study type</b>	Randomised Controlled Trial
<b>Study location</b>	Multicentre study with 19 institutions in the Netherlands, Belgium, the United Kingdom, and Canada
<b>Study dates</b>	This randomised clinical trial began on July 14, 2010, and continued until March 24, 2016, with a median follow-up of 3.3 years (range, 0-6.2 years) and a clinical cutoff date for this report of May 5, 2017.
<b>Sources of funding</b>	This study was supported by Pfizer and Kankerbestrijding/KWF from the Netherlands through the Cancer Research Fund of the European Organisation for Research and Treatment of Cancer
<b>Inclusion criteria</b>	People aged 18 years or older  Histologically confirmed, previously untreated clear cell metastatic RCC

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	<p>Resectable asymptomatic primary tumour in situ</p> <p>Required therapy with sunitinib</p> <p>World Health Organization (WHO) performance status of 0 or 1</p> <p>No clinical signs of central nervous system involvement</p> <p>A life expectancy greater than 3 months</p> <p>Adequate bone marrow, liver, cardiac, and renal function</p> <p>3 or fewer surgical risk factors</p> <p>Measurable disease according to Response Evaluation Criteria in Solid Tumours (RECIST), version 1.1</p>
<b>Intervention(s)</b>	Immediate cytoreductive nephrectomy followed by sunitinib therapy
<b>Comparator</b>	Treatment with 3 cycles of sunitinib followed by cytoreductive nephrectomy
<b>Outcome measures</b>	<p>Progression-free survival</p> <p>Overall survival</p> <p>Severe adverse events</p>
<b>Number of participants</b>	<p>N = 99</p> <p>Immediate cytoreductive nephrectomy + sunitinib = 50</p> <p>Deferred cytoreductive nephrectomy + sunitinib = 49</p>
<b>Duration of follow-up</b>	Median follow-up was 3.3 years (range, 0-6.2 years)
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	<p>The trial originally aimed to test for a hazard ratio (HR) of 0.75 on PFS with a 2-sided, 5%-level log-rank test with 80% power. After 3 years of recruitment, accrual indicated that the study would not reach its planned objective.</p> <p>The secondary end points of PFS and OS were estimated by Kaplan-Meier analysis and compared in the ITT population using a Cox proportional hazards regression model stratified by WHO performance status.</p>

1 **Study arms**2 **Immediate cytoreductive nephrectomy + sunitinib (N = 50)**3 **Deferred cytoreductive nephrectomy+ sunitinib (N = 49)**

4

5 **Characteristics**6 **Arm-level characteristics**

<b>Characteristic</b>	<b>Immediate cytoreductive nephrectomy + sunitinib (N = 50)</b>	<b>Deferred cytoreductive nephrectomy+ sunitinib (N = 49)</b>
<b>% Female</b>	n = 9 ; % = 18	n = 10 ; % = 20.4
No of events		
<b>Age</b>	60 (39 to 78)	58 (43 to 74)
Median (IQR)		
<b>Location of metastases - lung</b>	n = 43 ; % = 86	n = 42 ; % = 85.7
No of events		
<b>Location of metastases - bone</b>	n = 16 ; % = 32	n = 16 ; % = 32.6
No of events		
<b>Location of metastases - Adrenal gland</b>	n = 10 ; % = 20	n = 14 ; % = 28.6
No of events		
<b>Location of metastases - Liver</b>	n = 8 ; % = 16	n = 7 ; % = 14.3
No of events		
<b>Location of metastases - Other soft tissue</b>	n = 8 ; % = 16	n = 3 ; % = 6.1
No of events		
<b>Location of metastases - Malignant pleural effusion</b>	n = 5 ; % = 10	n = 0 ; % = 0
No of events		
<b>Location of metastases - Other site</b>	n = 6 ; % = 12	n = 1 ; % = 2
No of events		

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Characteristic	Immediate cytoreductive nephrectomy + sunitinib (N = 50)	Deferred cytoreductive nephrectomy+ sunitinib (N = 49)
No of events		
<b>Baseline performance status - WHO = 0</b>	n = 36 ; % = 72	n = 31 ; % = 63.3
No of events		
<b>Baseline performance status - WHO = 1</b>	n = 14 ; % = 38	n = 18 ; % = 36.7
No of events		
<b>MSKCC risk score - Intermediate risk (0-2 factors)</b>	n = 43 ; % = 86	n = 44 ; % = 89.8
No of events		
<b>MSKCC risk score - Poor risk (3 factors)</b>	n = 7 ; % = 14	n = 5 ; % = 10.2
No of events		
<b>Clinical T stage - T1</b>	n = 9 ; % = 18	n = 8 ; % = 16.3
No of events		
<b>Clinical T stage - T2</b>	n = 15 ; % = 30	n = 23 ; % = 46.9
No of events		
<b>Clinical T stage - T3</b>	n = 22 ; % = 44	n = 15 ; % = 30.6
No of events		
<b>Clinical T stage - T4</b>	n = 4 ; % = 8	n = 3 ; % = 6.1
No of events		
<b>Clinical N stage - N0</b>	n = 17 ; % = 34	n = 20 ; % = 40.8
No of events		
<b>Clinical N stage - N1</b>	n = 15 ; % = 30	n = 10 ; % = 20.4
No of events		
<b>Clinical N stage - N2</b>	n = 10 ; % = 20	n = 8 ; % = 16.3
No of events		

Characteristic	Immediate cytoreductive nephrectomy + sunitinib (N = 50)	Deferred cytoreductive nephrectomy+ sunitinib (N = 49)
<b>Clinical N stage - Unknown</b>	n = 8 ; % = 16	n = 11 ; % = 22.5
No of events		
<b>Number of metastatic site - One</b>	n = 7 ; % = 14	n = 3 ; % = 6.1
No of events		
<b>Number of metastatic site - <math>\geq 2</math></b>	n = 43 ; % = 86	n = 46 ; % = 93.9
No of events		

1

2 **Outcomes**3 **Survival**

Outcome	Deferred cytoreductive nephrectomy+ sunitinib vs Immediate cytoreductive nephrectomy + sunitinib, , N2 = 49, N1 = 50
<b>Progression-free survival</b>	0.88 (0.56 to 1.37)
Hazard ratio/95% CI	
<b>Overall survival</b>	0.57 (0.34 to 0.95)
Hazard ratio/95% CI	

4 Progression-free survival - Polarity - Higher values are better

5 Overall survival - Polarity - Higher values are better

6

7 **Postoperative complications**

Outcome	Immediate cytoreductive nephrectomy + sunitinib, , N = 46	Deferred cytoreductive nephrectomy+ sunitinib, , N = 34
<b>Clavien-Dindo postoperative complications grade <math>\geq 3</math></b>	n = 3 ; % = 6.5	n = 1 ; % = 2.9
No of events		

8 Clavien-Dindo postoperative complications grade  $\geq 3$  - Polarity - Lower values are better

9

10

1 **Critical appraisal – Cochrane Risk of Bias tool (RoB 2.0)**

Question	Answer
Risk of bias judgement	Moderate (Patients in the deferred group were allowed presurgical sunitinib dose modification)
Overall Directness	Directly applicable

2

3 **De Bruijn, 2019**

<b>Bibliographic Reference</b>	De Bruijn, Roderick Emile; Mulders, Peter; Jewett, Michael A; Wagstaff, John; Van Thienen, Johan V; Blank, Christian U; Van Velthoven, Roland; Wood, Lori; van Melick, Harm E; Aarts, Maureen J; Lattouf, Jean B; Powles, Thomas; De Jong, Igle J; Rottey, Sylvie; Tombal, Bertrand; Marreaud, Sandrine; Collette, Sandra; Collette, Laurence; Haanen, John B; Bex, Axel; Surgical Safety of Cyto-reductive Nephrectomy Following Sunitinib: Results from the Multicentre, Randomised Controlled Trial of Immediate Versus Deferred Nephrectomy (SURTIME).; European urology; 2019; vol. 76 (no. 4); 437-440
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5 **Study details**

<b>Other publications associated with this study included in review</b>	Paper published by Bexl, 2018 reported progression-free survival, overall survival outcomes from SURTIME trial
<b>Trial registration number and/or trial name</b>	SURTIME (NCT01099423)
<b>Study type</b>	Randomised Controlled Trial
<b>Study location</b>	Multicentre study with 19 institutions in the Netherlands, Belgium, the United Kingdom, and Canada
<b>Study dates</b>	This randomised clinical trial began on July 14, 2010, and continued until March 24, 2016.
<b>Sources of funding</b>	This study was supported by Pfizer and Kankerbestrijding/KWF from the Netherlands through the Cancer Research Fund of the European Organisation for Research and Treatment of Cancer
<b>Inclusion criteria</b>	People aged 18 years or older

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	<p>Histologically confirmed, previously untreated clear cell metastatic RCC</p> <p>Resectable asymptomatic primary tumour in situ</p> <p>Required therapy with sunitinib</p> <p>World Health Organization (WHO) performance status of 0 or 1</p> <p>Measurable disease according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1</p> <p>No clinical signs of central nervous system involvement</p> <p>A life expectancy greater than 3 months</p> <p>Adequate bone marrow, liver, cardiac, and renal function</p> <p>3 or fewer surgical risk factors</p>
<b>Intervention(s)</b>	Immediate cytoreductive nephrectomy followed by sunitinib therapy
<b>Comparator</b>	Treatment with 3 cycles of sunitinib followed by cytoreductive nephrectomy
<b>Outcome measures</b>	Severe adverse events
<b>Number of participants</b>	<p>N = 99</p> <p>Immediate cytoreductive nephrectomy + sunitinib = 50</p> <p>Deferred cytoreductive nephrectomy + sunitinib = 49</p> <p>Analysis per protocol</p> <p>N = 74</p> <p>Immediate cytoreductive nephrectomy + sunitinib = 40</p> <p>Deferred cytoreductive nephrectomy + sunitinib = 34</p>
<b>Duration of follow-up</b>	5.7 years
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Surgical postoperative complication rates in both arms were reported as percentages with 95% confidence intervals.
<b>Additional comments</b>	

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2 **Study arms**3 **Immediate cytoreductive nephrectomy+ sunitinib (Per Protocol) (N = 46)**4 **Deferred cytoreductive nephrectomy+ sunitinib (Per Protocol) (N = 34)**5 **Immediate cytoreductive nephrectomy+ sunitinib (N = 50)**6 **Deferred cytoreductive nephrectomy+ sunitinib (N = 49)**

7

8 **Characteristics**9 **Arm-level characteristics**

Characteristic	Immediate cytoreductive nephrectomy+ sunitinib (Per Protocol) (N = 46)	Deferred cytoreductive nephrectomy+ sunitinib (Per Protocol) (N = 34)	Immediate cytoreductive nephrectomy+ sunitinib (N = 50)	Deferred cytoreductive nephrectomy+ sunitinib (N = 49)
<b>% Female</b>	<i>empty data</i>	<i>empty data</i>	n = 9 ; % = 18	n = 10 ; % = 20
No of events				
<b>Age</b>	<i>empty data</i> ( <i>empty data to</i> <i>empty data</i> )	<i>empty data</i> ( <i>empty data to</i> <i>empty data</i> )	60 (39 to 78)	58 (43 to 74)
Median (IQR)				
<b>MSKCC risk score - Intermediate risk (0-2 factors)</b>	<i>empty data</i>	<i>empty data</i>	n = 43 ; % = 86	n = 44 ; % = 90
No of events				
<b>MSKCC risk score - Poor risk (3 factors)</b>	<i>empty data</i>	<i>empty data</i>	n = 7 ; % = 14	n = 5 ; % = 10
No of events				
<b>Clinical T stage - T1</b>	<i>empty data</i>	<i>empty data</i>	n = 9 ; % = 18	n = 8 ; % = 16
No of events				
<b>Clinical T stage - T2</b>	<i>empty data</i>	<i>empty data</i>	n = 15 ; % = 30	n = 23 ; % = 47
No of events				

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<b>Characteristic</b>	<b>Immediate cytoreductive nephrectomy+ sunitinib (Per Protocol) (N = 46)</b>	<b>Deferred cytoreductive nephrectomy+ sunitinib (Per Protocol) (N = 34)</b>	<b>Immediate cytoreductive nephrectomy+ sunitinib (N = 50)</b>	<b>Deferred cytoreductive nephrectomy+ sunitinib (N = 49)</b>
<b>Clinical T stage - T3</b>	<i>empty data</i>	<i>empty data</i>	n = 22 ; % = 44	n = 15 ; % = 31
No of events				
<b>Clinical T stage - T4</b>	<i>empty data</i>	<i>empty data</i>	n = 4 ; % = 8	n = 3 ; % = 6
No of events				
<b>Clinical N stage - N0</b>	<i>empty data</i>	<i>empty data</i>	n = 17 ; % = 34	n = 20 ; % = 41
No of events				
<b>Clinical N stage - N1</b>	<i>empty data</i>	<i>empty data</i>	n = 15 ; % = 30	n = 10 ; % = 20
No of events				
<b>Clinical N stage - N2</b>	<i>empty data</i>	<i>empty data</i>	n = 10 ; % = 20	n = 8 ; % = 16
No of events				
<b>Clinical N stage - Unknown</b>	<i>empty data</i>	<i>empty data</i>	n = 8 ; % = 16	n = 11 ; % = 23
No of events				
<b>Number of metastatic site - One</b>	<i>empty data</i>	<i>empty data</i>	n = 7 ; % = 14	n = 3 ; % = 6
No of events				
<b>Number of metastatic site - ≥2</b>	<i>empty data</i>	<i>empty data</i>	n = 43 ; % = 86	n = 46 ; % = 94
No of events				

1 **Outcomes**2 **Duration of hospital stay**

Outcome	Immediate cytoreductive nephrectomy+ sunitinib (Per Protocol), , N =	Deferred cytoreductive nephrectomy+ sunitinib (Per Protocol), , N =	Immediate cytoreductive nephrectomy+ sunitinib, , N = 46	Deferred cytoreductive nephrectomy+ sunitinib, , N = 34
Duration of hospital stay	<i>empty data</i>	<i>empty data</i>	8.4 (7.1)	7.4 (3.4)
Mean (SD)				

3 Duration of hospital stay - Polarity - Lower values are better

4

5 **Critical appraisal –Cochrane Risk of Bias tool (RoB 2.0)**

Question	Answer
Risk of bias judgement	Moderate <i>(Patients in the deferred group were allowed presurgical sunitinib dose modification)</i>
Overall Directness	Directly applicable

6

7 **Mejean, 2021**

<b>Bibliographic Reference</b>	Mejean, Arnaud; Ravaud, Alain; Thezenas, Simon; Chevreau, Christine; Bensalah, Karim; Geoffrois, Lionnel; Thiery-Vuillemin, Antoine; Cormier, Luc; Lang, Herve; Guy, Laurent; Gravis, Gwenaelle; Rolland, Frederic; Linassier, Claude; Lechevallier, Eric; Oudard, Stephane; Laguerre, Brigitte; Gross-Goupil, Marine; Bernhard, Jean Christophe; Colas, Sandra; Albiges, Laurence; Lebre, Thierry; Treluyer, Jean-Marc; Timsit, Marc-Olivier; Escudier, Bernard; Sunitinib Alone or After Nephrectomy for Patients with Metastatic Renal Cell Carcinoma: Is There Still a Role for Cytoreductive Nephrectomy?.; European urology; 2021; vol. 80 (no. 4); 417-424
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9 **Study details**

<b>Other publications associated with this study</b>	CARMENA trial data has been published previously by Mejean A, 2018
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<b>included in review</b>	
<b>Trial registration number and/or trial name</b>	CARMENA trial - NCT00930033
<b>Study type</b>	Randomised Controlled Trial
<b>Study location</b>	Multicentre - Not reported where the centres were based
<b>Study dates</b>	2009 to October 2018
<b>Sources of funding</b>	Funded by Assistance Publique–Hôpitaux de Paris and others
<b>Inclusion criteria</b>	<p>Eastern Cooperative Oncology Group (ECOG) status score of 0 to 1</p> <p>Patients with clear cell renal cell carcinoma confirmed on mandatory biopsy and documented metastatic disease</p> <p>Absence of brain metastases or treated brain metastases without recurrence 3 weeks after treatment</p> <p>Acceptable organ function</p>
<b>Exclusion criteria</b>	<p>Patients who received previous systemic treatment for kidney cancer (including VEGF-targeted therapy) or anticoagulants</p> <p>Patients with any medical condition, including cardiovascular disease, that ruled them out as candidates for treatment</p>
<b>Intervention(s)</b>	Cytoreductive nephrectomy associated with sunitinib
<b>Comparator</b>	Sunitinib alone
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	<p>N = 450</p> <p>Cytoreductive nephrectomy + sunitinib = 226</p> <p>Sunitinib alone = 224</p>
<b>Duration of follow-up</b>	36.6 months, cut-off (October 2018)
<b>Loss to follow-up</b>	There is 1(0.4%) missing patient in the CN + sunitinib arm
<b>Methods of analysis</b>	The overall survival analyses were estimated using the Kaplan-Meier method. Treatment arms were compared using a log-rank test. The post hoc analyses for efficacy were carried out on the intent to treat population.

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Treatment with sunitinib alone was considered to be non-inferior to cytoreductive nephrectomy followed by sunitinib treatment if the upper bound of the 95% CI of the HR for death was  $\leq 1.20$ .

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2 **Study arms**3 **Nephrectomy + sunitinib (ITT) (N = 226)**4 **Sunitinib alone (ITT) (N = 224)**

5

6 **Characteristics**7 **Arm-level characteristics**

Characteristic	Nephrectomy + sunitinib (ITT) (N = 226)	Sunitinib alone (ITT) (N = 224)
<b>% Female</b>	n = 57 ; % = 25.2	n = 57 ; % = 35.4
No of events		
<b>Age</b>	63 (33 to 84)	62 (30 to 87)
Median (IQR)		
<b>Location of metastases - lung</b>	n = 172 ; % = 79.3	n = 161 ; % = 72.9
No of events		
<b>Location of metastases - bone</b>	n = 78 ; % = 35.9	n = 82 ; % = 37.1
No of events		
<b>Location of metastases - Lymph nodes</b>	n = 76 ; % = 35	n = 86 ; % = 38.9
No of events		
<b>Location of metastases - Other</b>	n = 78 ; % = 35.9	n = 90 ; % = 40.7
No of events		
<b>Baseline performance status - ECOG 0</b>	n = 130 ; % = 57.5	n = 122 ; % = 54.5
No of events		
<b>Baseline performance status - ECOG 1</b>	n = 96 ; % = 42.5	n = 102 ; % = 45.5
No of events		
<b>Tumour stage - T1</b>	n = 5 ; % = 7.5	n = 7 ; % = 14.3

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Characteristic	Nephrectomy + sunitinib (ITT) (N = 226)	Sunitinib alone (ITT) (N = 224)
No of events		
<b>Tumour stage - T2</b>	n = 13 ; % = 19.4	n = 13 ; % = 26.5
No of events		
<b>Tumour stage - T3 or T4</b>	n = 47 ; % = 70.1	n = 25 ; % = 51
No of events		
<b>Tumour stage - Tx</b>	n = 2 ; % = 3	n = 4 ; % = 8.2
No of events		
<b>MSKCC risk category - Intermediate risk</b>	n = 125 ; % = 55.6	n = 131 ; % = 58.5
No of events		
<b>MSKCC risk category - Poor risk</b>	n = 100 ; % = 44.4	n = 93 ; % = 41.5
No of events		
<b>Node stage - N0</b>	n = 23 ; % = 34.8	n = 18 ; % = 36.7
No of events		
<b>Node stage - N1</b>	n = 13 ; % = 19.7	n = 6 ; % = 12.2
No of events		
<b>Node stage - N2</b>	n = 7 ; % = 10.6	n = 13 ; % = 26.5
No of events		
<b>Node stage - Nx</b>	n = 23 ; % = 34.8	n = 12 ; % = 24.5
No of events		

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2 **Outcomes**3 **Survival**

Outcome	Sunitinib alone (ITT) vs Nephrectomy + sunitinib (ITT), , N2 = 224, N1 = 226
<b>Overall survival</b>	0.97 (0.79 to 1.19)
Hazard ratio/95% CI	

4 Overall survival - Polarity - Higher values are better

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2 **Critical appraisal –Cochrane Risk of Bias tool (RoB 2.0)**

Question	Answer
Risk of bias judgement	Moderate ( <i>There is some concern related to the unclear randomisation process</i> )
Overall Directness	Directly applicable

3

4 **Mejean, 2018**

<b>Bibliographic Reference</b>	Mejean, Arnaud; Ravaud, Alain; Thezenas, Simon; Colas, Sandra; Beauval, Jean-Baptiste; Bensalah, Karim; Geoffrois, Lionnel; Thiery-Vuillemin, Antoine; Cormier, Luc; Lang, Herve; Guy, Laurent; Gravis, Gwenaëlle; Rolland, Frederic; Linassier, Claude; Lechevallier, Eric; Beisland, Christian; Aitchison, Michael; Oudard, Stephane; Patard, Jean-Jacques; Theodore, Christine; Chevreau, Christine; Laguerre, Brigitte; Hubert, Jacques; Gross-Goupil, Marine; Bernhard, Jean-Christophe; Albiges, Laurence; Timsit, Marc-Olivier; Lebre, Thierry; Escudier, Bernard; Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma.; The New England journal of medicine; 2018; vol. 379 (no. 5); 417-427
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6 **Study details**

<b>Trial registration number and/or trial name</b>	CARMENA trial - NCT00930033
<b>Study type</b>	Randomised Controlled Trial
<b>Study location</b>	Multicentre - Not reported where the centres were based
<b>Study dates</b>	2009-2017
<b>Sources of funding</b>	Funded by Assistance Publique–Hôpitaux de Paris and others
<b>Inclusion criteria</b>	<p>Eastern Cooperative Oncology Group (ECOG) status score of 0 to 1</p> <p>Patients with clear cell renal cell carcinoma confirmed on mandatory biopsy and documented metastatic disease</p> <p>Absence of brain metastases or treated brain metastases without recurrence 3 weeks after treatment</p> <p>Acceptable organ function</p>

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<b>Exclusion criteria</b>	Patients who received previous systemic treatment for kidney cancer (including VEGF-targeted therapy) or anticoagulants  Patients with any medical condition, including cardiovascular disease, that ruled them out as candidates for treatment
<b>Intervention(s)</b>	Cytoreductive nephrectomy associated with sunitinib
<b>Comparator</b>	Sunitinib alone
<b>Outcome measures</b>	Progression-free survival  Severe adverse events
<b>Number of participants</b>	N = 450  Cytoreductive nephrectomy + sunitinib = 226  Sunitinib alone = 224
<b>Duration of follow-up</b>	50.9 months, at the time of data cutoff (December 12, 2017)
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	The rates and 95% confidence intervals for the analyses of overall survival and progression-free survival were estimated by the Kaplan–Meier method in the intention-to-treat population. Tumour response and safety data were analysed in patients who received sunitinib.

1

2 **Study arms**3 **Nephrectomy + sunitinib (N = 226)**4 **Sunitinib alone (N = 224)**

5

6 **Characteristics**7 **Arm-level characteristics**

<b>Characteristic</b>	<b>Nephrectomy + sunitinib (N = 226)</b>	<b>Sunitinib alone (N = 224)</b>
<b>% Female</b>	n = 57 ; % = 25.2	n = 57 ; % = 35.4
No of events		
<b>Age</b>	63 (33 to 84)	62 (30 to 87)
Median (IQR)		
<b>Location of metastases - Lung</b>	n = 172 ; % = 79.3	n = 161 ; % = 72.9

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<b>Characteristic</b>	<b>Nephrectomy + sunitinib (N = 226)</b>	<b>Sunitinib alone (N = 224)</b>
No of events		
<b>Location of metastases - bone</b>	n = 78 ; % = 35.9	n = 82 ; % = 37.1
No of events		
<b>Location of metastases - Lymph nodes</b>	n = 76 ; % = 35	n = 86 ; % = 38.9
No of events		
<b>Location of metastases - Other</b>	n = 78 ; % = 35.9	n = 90 ; % = 40.7
No of events		
<b>Baseline performance status - ECOG 0</b>	n = 130 ; % = 57.5	n = 122 ; % = 54.5
No of events		
<b>Baseline performance status - ECOG 1</b>	n = 92 ; % = 42.5	n = 102 ; % = 45.3
No of events		
<b>Tumour stage - T1</b>	n = 5 ; % = 7.5	n = 7 ; % = 14.3
No of events		
<b>Tumour stage - T2</b>	n = 13 ; % = 19.4	n = 13 ; % = 26.5
No of events		
<b>Tumour stage - T3 or T4</b>	n = 47 ; % = 70.1	n = 25 ; % = 51
No of events		
<b>Tumour stage - Tx</b>	n = 2 ; % = 3	n = 4 ; % = 8.2
No of events		
<b>MSKCC risk category - Intermediate risk</b>	n = 125 ; % = 55.6	n = 131 ; % = 58.5
No of events		
<b>MSKCC risk category - Poor risk</b>	n = 100 ; % = 44.4	n = 93 ; % = 41.5
No of events		
<b>Node stage - N0</b>	n = 23 ; % = 34.8	n = 18 ; % = 36.7
No of events		

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Characteristic	Nephrectomy + sunitinib (N = 226)	Sunitinib alone (N = 224)
<b>Node stage - N1</b>	n = 13 ; % = 19.7	n = 6 ; % = 12.2
No of events		
<b>Node stage - N2</b>	n = 7 ; % = 10.6	n = 13 ; % = 26.5
No of events		
<b>Node stage - Nx</b>	n = 23 ; % = 34.8	n = 12 ; % = 24.5
No of events		

1

2 **Outcomes**3 **Survival**

Outcome	Sunitinib alone vs Nephrectomy + sunitinib, , N2 = 224, N1 = 226
<b>Progression-free survival</b>	0.82 (0.67 to 1)
Hazard ratio/95% CI	

4 Progression-free survival - Polarity - Higher values are better

5

6 **Adverse events**

Outcome	Nephrectomy + sunitinib, , N = 186	Sunitinib alone, , N = 213
<b>Any adverse event of grade 3 or 4 (Clavien Dindo)</b>	n = 61 ; % = 32.8	n = 91 ; % = 42.7
No of events		

7 Any adverse event of grade 3 or 4 (Clavien Dindo) - Polarity - Lower values are  
8 better

9

10 **Critical appraisal –Cochrane Risk of Bias tool (RoB 2.0)**

Question	Answer
Risk of bias judgement	Moderate (There is some concern related to the unclear randomisation process)
Overall Directness	Directly applicable

11

1 **Shen, 2023**

**Bibliographic Reference** Shen, X-P; Xie, M; Wang, J-S; Guo, X; Efficacy of immunotherapy-based immediate cytoreductive nephrectomy vs. deferred cytoreductive nephrectomy in metastatic renal cell carcinoma.; European review for medical and pharmacological sciences; 2023; vol. 27 (no. 12); 5684-5691

2

3 **Study details**

<b>Study type</b>	Randomised Controlled Trial
<b>Study location</b>	China
<b>Study dates</b>	2018 to 2020
<b>Sources of funding</b>	Not received.
<b>Inclusion criteria</b>	<p>Histologically or cytologically confirmed clear cell renal cell carcinoma</p> <p>measurable disease according to RECIST 1.1 criteria, including primary and metastatic lesions</p> <p>Eastern Cooperative Oncology Group (ECOG) status score of 0 to 1</p> <p>Life expectancy &gt; 24 weeks</p> <p>Primary resectable tumour at first diagnosis</p>
<b>Exclusion criteria</b>	<p>Brain or liver metastases</p> <p>Poor prognosis as defined by Memorial Sloan-Kettering Cancer Center (MSKCC) or Heng criteria</p> <p>Severe hepatic or renal insufficiency or uncontrolled hypertension or diabetes mellitus</p> <p>Active infection</p> <p>Primary tumors from other sites</p> <p>Previous surgical or systemic treatment for metastatic renal cell carcinoma</p>
<b>Intervention(s)</b>	Immediate cytoreductive nephrectomy
<b>Comparator</b>	Delayed cytoreductive nephrectomy
<b>Outcome measures</b>	<p>Progression-free survival</p> <p>Overall survival</p>
<b>Number of participants</b>	N = 84

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	Immediate cytoreductive nephrectomy = 42
	Delayed cytoreductive nephrectomy = 42
<b>Duration of follow-up</b>	Patients were followed up for 10-52 months, with a median follow-up period of 40.50 months.
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Count data were expressed as rates (%), and differences between groups were compared using the Chi-square test. Survival data were expressed using the Kaplan Meier test.

1

2 **Study arms**3 **Immediate cytoreductive nephrectomy (N = 42)**4 **Delayed cytoreductive nephrectomy (N = 42)**

5

6 **Characteristics**7 **Arm-level characteristics**

<b>Characteristic</b>	<b>Immediate cytoreductive nephrectomy (N = 42)</b>	<b>Delayed cytoreductive nephrectomy (N = 42)</b>
<b>% Female</b>	n = 10 ; % = 23.8	n = 14 ; % = 33.3
No of events		
<b>Age</b>	65.58 (11.52)	61.29 (14.36)
Mean (SD)		
<b>TNM classification - T3a</b>	n = 22 ; % = 52.4	n = 18 ; % = 42.9
No of events		
<b>TNM classification - T3b</b>	n = 10 ; % = 23.8	n = 14 ; % = 33.3
No of events		
<b>TNM classification - T3c</b>	n = 5 ; % = 11.9	n = 6 ; % = 14.3
No of events		
<b>TNM classification - T4</b>	n = 5 ; % = 11.9	n = 4 ; % = 9.5
No of events		
<b>Baseline performance status - ECOG 0</b>	n = 29 ; % = 69.04	n = 24 ; % = 57.1

Characteristic	Immediate cytoreductive nephrectomy (N = 42)	Delayed cytoreductive nephrectomy (N = 42)
No of events		
<b>Baseline performance status - ECOG 1</b>	n = 13 ; % = 31	n = 12 ; % = 42.9
No of events		

1

2 **Outcomes**3 **Survival**

Outcome	Delayed cytoreductive nephrectomy vs Upfront cytoreductive nephrectomy, , N2 = 42, N1 = 42
<b>Progression-free survival</b>	0.53 (0.28 to 0.99)
Hazard ratio/95% CI	
<b>Overall survival</b>	0.81 (0.41 to 1.61)
Hazard ratio/95% CI	

4 Progression-free survival - Polarity - Higher values are better

5 Overall survival - Polarity - Higher values are better

6

7 **Critical appraisal –Cochrane Risk of Bias tool (RoB 2.0)**

Question	Answer
Risk of bias judgement	Moderate <i>(There is some concern related to the unclear randomisation process, also, there is no information on whether the trial analysis was performed in accordance with a pre-specified plan)</i>
Overall Directness	Directly applicable

8

9

10 **Non-randomised controlled trials evidence**11 **Bakouny, 2023**

**Bibliographic Reference** Bakouny, Ziad; El Zarif, Talal; Dudani, Shaan; Connor Wells, J; Gan, Chun Loo; Donskov, Frede; Shapiro, Julia; Davis, Ian D; Parnis, Francis; Ravi, Praful; Steinharter, John A; Agarwal, Neeraj; Alva, Ajjai; Wood, Lori; Kapoor, Anil; Ruiz Morales, Jose M; Kollmannsberger, Christian;

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Beuselinck, Benoit; Xie, Wanling; Heng, Daniel Y C; Choueiri, Toni K; Upfront Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma Treated with Immune Checkpoint Inhibitors or Targeted Therapy: An Observational Study from the International Metastatic Renal Cell Carcinoma Database Consortium.; European urology; 2023; vol. 83 (no. 2); 145-151

1

2 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	US - uses the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) database
<b>Study dates</b>	January 2020
<b>Sources of funding</b>	None
<b>Inclusion criteria</b>	<p>Treated with a first-line immune checkpoint inhibitor (including monotherapy and combination therapy with other immune check-point inhibitors or other agents) or targeted therapy regimen</p> <p>Initiated first-line systemic therapy on or after January 1, 2009</p> <p>Diagnosed with de novo metastatic renal cell carcinoma or had not received a nephrectomy for localised renal cell carcinoma</p>
<b>Exclusion criteria</b>	<p>Missing dates of diagnosis or dates of metastatic disease</p> <p>Missing information on whether they had a nephrectomy or the date of nephrectomy</p> <p>Missing dates of death or last follow-up</p>
<b>Intervention(s)</b>	Immune checkpoint inhibitors with upfront cytoreductive nephrectomy
<b>Comparator</b>	Immune checkpoint inhibitors no upfront cytoreductive nephrectomy
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	<p>N = 437</p> <p>Immune checkpoint inhibitors with upfront cytoreductive nephrectomy = 234</p> <p>Immune checkpoint inhibitors no upfront cytoreductive nephrectomy = 203</p>

<b>Duration of follow-up</b>	The median follow-up for surviving patients treated with immune checkpoint inhibitors was 12 months.
<b>Methods of analysis</b>	<p>For overall survival, the Kaplan-Meier methodology was used to summarise the survival distribution, and median overall survival and 95% confidence intervals (95% CIs) were computed.</p> <p>A multivariable logistic regression model with receipt of cytoreductive nephrectomy as the dependent variable (cytoreductive nephrectomy versus no cytoreductive nephrectomy), with the predictor variables chosen a priori: age (&lt;65, 65–74, or &gt;75 yr); presence of bone, brain, or liver metastases (yes or no); non– clear cell or sarcomatoid histology (yes or no); Karnofsky Performance Scale (KPS: ≥80 or &lt;80); and the number of IMDC risk factors (≤1, 2, 3, or ≥4). Cox regressions were computed in each treatment group separately to determine the relationship between the receipt of cytoreductive nephrectomy and overall survival.</p>
<b>Additional comments</b>	This study also reported results for people who received targeted therapy and upfront nephrectomy compared with targeted therapy only. These results are not extracted as there are reported in another study (Bhindi 2020).

1

2 **Study arms**3 **Immune checkpoint inhibitors with upfront cytoreductive nephrectomy (N =**  
4 **234)**5 **Immune checkpoint inhibitors no upfront cytoreductive nephrectomy (N = 203)**

6

7 **Characteristics**8 **Arm-level characteristics**

<b>Characteristic</b>	<b>Immune checkpoint inhibitors with upfront cytoreductive nephrectomy (N = 234)</b>	<b>Immune checkpoint inhibitors no upfront cytoreductive nephrectomy (N = 203)</b>
<b>% Female</b>	n = 61 ; % = 26	n = 57 ; % = 28
No of events		
<b>Age</b>	60 (53 to 66)	63 (56 to 70)
Median (IQR)		
<b>Primary RCC type - Clear cell</b>	n = 204 ; % = 89	n = 110 ; % = 73
No of events		

<b>Characteristic</b>	<b>Immune checkpoint inhibitors with upfront cytoreductive nephrectomy (N = 234)</b>	<b>Immune checkpoint inhibitors no upfront cytoreductive nephrectomy (N = 203)</b>
<b>Primary RCC type - Non-clear cell</b>	n = 26 ; % = 11	n = 41 ; % = 27
No of events		
<b>IMDC - Favorable (0 risk factor)</b>	n = 18 ; % = 9	n = 1 ; % = 0.6
No of events		
<b>IMDC - Intermediate (1–2 risk factors)</b>	n = 143 ; % = 72	n = 78 ; % = 47
No of events		
<b>IMDC - Poor (3 risk factors)</b>	n = 39 ; % = 19	n = 88 ; % = 53
No of events		
<b>Sites of metastasis - One</b>	n = 52 ; % = 23	n = 39 ; % = 20
No of events		
<b>Sites of metastasis - ≥2</b>	n = 171 ; % = 77	n = 155 ; % = 80
No of events		
<b>Presence of bone, brain, or liver metastases - Yes</b>	n = 87 ; % = 45	n = 120 ; % = 71
No of events		
<b>Presence of bone, brain, or liver metastases - No</b>	n = 108 ; % = 55	n = 48 ; % = 29
No of events		



1 **Outcomes**2 **Survival**

Outcome	Immune checkpoint inhibitors with upfront cytoreductive nephrectomy vs Immune checkpoint inhibitors no upfront cytoreductive nephrectomy , , N2 = 203, N1 = 234
Overall survival	0.61 (0.41 to 0.9)
Hazard ratio/95% CI	

3 Overall survival - Polarity - Higher values are better

4

5 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest)
Directness	Directly applicable

6

7 **Bhindi, 2018**

<b>Bibliographic Reference</b>	Bhindi, B.; Habermann, E.B.; Mason, R.J.; Costello, B.A.; Pagliaro, L.C.; Thompson, R.H.; Leibovich, B.C.; Boorjian, S.A.; Comparative Survival following Initial Cytoreductive Nephrectomy versus Initial Targeted Therapy for Metastatic Renal Cell Carcinoma; Journal of Urology; 2018; vol. 200 (no. 3); 528-534
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8

9 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	US - uses national clinical oncology (NCDB) database
<b>Study dates</b>	2006 and 2013
<b>Sources of funding</b>	Not reported
<b>Inclusion criteria</b>	Metastatic patients at diagnosis
<b>Exclusion criteria</b>	Another prior cancer history NonRCC or unknown histology

	<p>Missing vital status or follow-up</p> <p>Renal ablative procedure</p> <p>Inability to determine cytoreductive nephrectomy status</p> <p>Missing time to surgery in patients who underwent cytoreductive nephrectomy</p> <p>Missing time to targeted therapy in those who received targeted therapy</p> <p>No treatment (cytoreductive nephrectomy or targeted therapy) within 3 months of diagnosis</p>
<b>Intervention(s)</b>	Initial cytoreductive nephrectomy + targeted therapy
<b>Comparator</b>	Initial targeted therapy + cytoreductive nephrectomy
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	<p>N = 15,068</p> <p>Initial cytoreductive nephrectomy + targeted therapy = 6,731</p> <p>Initial targeted therapy + cytoreductive nephrectomy = 8,337</p>
<b>Duration of follow-up</b>	Median follow-up in survivors was 31 months (IQR 19-50)
<b>Methods of analysis</b>	<p>Overall survival was compared between the initial cytoreductive nephrectomy and initial targeted therapy groups using Kaplan-Meier analysis and Cox regression models with censoring at end of the study period or due to loss to follow-up. To account for differences in baseline characteristics which may have influenced the initial treatment selection the author performed inverse probability of treatment weighting based on the propensity to receive initial cytoreductive nephrectomy vs initial targeted therapy, which was in turn estimated by logistic regression.</p> <p>Included variables in the inverse probability of treatment weighting were: age, sex, race/ethnicity, year of diagnosis, insurance status, income quartile, education, county of residence, Charlson-Deyo score, facility location, facility type, histology, clinical T-stage, and clinical N-stage</p>
<b>Additional comments</b>	

1 **Study arms**2 **Initial cytoreductive nephrectomy + targeted therapy (N = 6731)**3 **Initial targeted therapy + cytoreductive nephrectomy (N = 8337)**

4

5 **Characteristics**6 **Arm-level characteristics**

<b>Characteristic</b>	<b>Initial cytoreductive nephrectomy + targeted therapy (N = 6731)</b>	<b>Initial targeted therapy + cytoreductive nephrectomy (N = 8337)</b>
<b>% Female</b>	n = 2081 ; % = 30.9	n = 2581 ; % = 31
No of events		
<b>Primary RCC type - clear cell</b>	n = 3647 ; % = 54.2	n = 2727 ; % = 32.7
No of events		
<b>Primary RCC type - Non-clear cell</b>	n = 817 ; % = 12.1	n = 600 ; % = 7.2
No of events		
<b>Primary RCC type - RCC, unknown subtype</b>	n = 2267 ; % = 33.7	n = 5010 ; % = 60.1
No of events		
<b>Clinical T-stage - cT1</b>	n = 1024 ; % = 15.2	n = 1513 ; % = 18.2
No of events		
<b>Clinical T-stage - cT2</b>	n = 1812 ; % = 26.9	n = 1735 ; % = 20.8
No of events		
<b>Clinical T-stage - cT3</b>	n = 2503 ; % = 37.2	n = 1903 ; % = 22.8
No of events		
<b>Clinical T-stage - cT4</b>	n = 488 ; % = 7.2	n = 990 ; % = 11.9
No of events		
<b>Clinical T-stage - cTx</b>	n = 904 ; % = 13.4	n = 2196 ; % = 26.3
No of events		
<b>Clinical N-stage - cN0</b>	n = 3872 ; % = 57.5	n = 3328 ; % = 39.9

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Characteristic	Initial cytoreductive nephrectomy + targeted therapy (N = 6731)	Initial targeted therapy + cytoreductive nephrectomy (N = 8337)
No of events		
<b>Clinical N-stage - cN1</b>	n = 1701 ; % = 25.3	n = 2935 ; % = 35.2
No of events		
<b>Clinical N-stage - cNx</b>	n = 1158 ; % = 17.2	n = 2074 ; % = 24.9
No of events		

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2 **Outcomes**3 **Survival**

Outcome	Initial cytoreductive nephrectomy + targeted therapy vs Initial targeted therapy + cytoreductive nephrectomy, , N2 = 6731, N1 = 8337
<b>Overall survival - Entire mRCC cohort</b>	0.62 (0.59 to 0.65)
Hazard ratio/95% CI	
<b>Overall survival - Clear cell RCC subset</b>	0.61 (0.58 to 0.65)
Hazard ratio/95% CI	
<b>Overall survival - Nonclear cell RCC subset</b>	0.73 (0.64 to 0.84)
Hazard ratio/95% CI	

4 Overall survival - Polarity - Higher values are better

5

6 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest)
Directness	Directly applicable

7

1 **Bhindi, 2020**

**Bibliographic Reference** Bhindi, Bimal; Graham, Jeffrey; Wells, J Connor; Bakouny, Ziad; Donskov, Frede; Fraccon, Anna; Pasini, Felice; Lee, Jae Lyun; Basappa, Naveen S; Hansen, Aaron; Kollmannsberger, Christian K; Kanesvaran, Ravindran; Yuasa, Takeshi; Ernst, D Scott; Srinivas, Sandy; Rini, Brian I; Bowman, Isaac; Pal, Sumanta K; Choueiri, Toni K; Heng, Daniel Y C; Deferred Cytoreductive Nephrectomy in Patients with Newly Diagnosed Metastatic Renal Cell Carcinoma.; European urology; 2020; vol. 78 (no. 4); 615-623

2

3 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	33 centres in Canada, the USA, Belgium, Denmark, Germany, Greece, Italy, South Korea, Singapore, Japan, New Zealand, and Australia
<b>Study dates</b>	2006-2018
<b>Sources of funding</b>	None
<b>Inclusion criteria</b>	Only patients whose first systemic therapy was sunitinib
<b>Exclusion criteria</b>	Missing data on confounder variables  First treatment (sunitinib or upfront cytoreductive nephrectomy) >12 months after diagnosis  A period of surveillance of >6 months after upfront cytoreductive nephrectomy  Unknown timing of deferred cytoreductive nephrectomy
<b>Intervention(s)</b>	Upfront cytoreductive nephrectomy + sunitinib
<b>Comparator</b>	Sunitinib + deferred cytoreductive nephrectomy
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	N = 1,541  Upfront cytoreductive nephrectomy + sunitinib N = 805  Sunitinib + deferred cytoreductive nephrectomy N = 85  Sunitinib alone N = 651
<b>Duration of follow-up</b>	Median follow-up among survivors from first treatment initiation was 25 months (IQR 10–49)

<b>Methods of analysis</b>	<p>Survival curves were plotted using the Kaplan-Meier method in order to describe benchmark OS outcomes, and were compared using the log-rank test.</p> <p>Multivariable Cox proportional hazards models were created including the following a priori selected potential confounders: upfront cytoreductive nephrectomy and deferred cytoreductive nephrectomy, age at diagnosis (continuous), sex, year of diagnosis (continuous), Karnofsky performance status (<math>\geq 80</math> vs <math>&lt; 80</math>), IMDC risk group (intermediate vs poor risk; by definition, favorable-risk patients were not included), clear cell versus non-clear cell histology, sarcomatoid dedifferentiation, number of metastatic sites (continuous), and location of metastases (lung, brain, liver, bone, and lymph node). In order to account for immortal time bias, deferred cytoreductive nephrectomy was operationalized as a time-varying covariate</p>
<b>Additional comments</b>	Arm level baseline characteristics were not reported in the study

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**Study arms**

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**Upfront cytoreductive nephrectomy + sunitinib (N = 805)**

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**Sunitinib + deferred cytoreductive nephrectomy (N = 85)**

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**Sunitinib alone (N = 651)**

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7

**Characteristics**

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**Study-level characteristics**

<b>Characteristic</b>	<b>Study (N = 1541)</b>
<b>% Female</b>	n = 403 ; % = 26
No of events	
<b>Age</b>	61 (54 to 68)
Median (IQR)	
<b>Primary RCC type - Clear cell histology</b>	n = 1311 ; % = 85
No of events	
<b>Primary RCC type - Sarcomatoid dedifferentiation</b>	n = 232 ; % = 15
No of events	
<b>Location of metastases - Brain</b>	n = 130 ; % = 8

<b>Characteristic</b>	<b>Study (N = 1541)</b>
No of events	
<b>Location of metastases - lung</b>	n = 1141 ; % = 74
No of events	
<b>Location of metastases - Liver</b>	n = 333 ; % = 22
No of events	
<b>Location of metastases - bone</b>	n = 593 ; % = 38
No of events	
<b>Location of metastases - Nodal</b>	n = 785 ; % = 51
No of events	
<b>Location of metastases - Other sites</b>	n = 461 ; % = 30
No of events	
<b>IMDC risk - Poor IMDC risk</b>	n = 618 ; % = 40
No of events	
<b>Number of metastatic sites - One</b>	n = 435 ; % = 28
No of events	
<b>Number of metastatic sites - Two</b>	n = 546 ; % = 35
No of events	
<b>Number of metastatic sites - Three</b>	n = 371 ; % = 24
No of events	
<b>Number of metastatic sites - Four</b>	n = 147 ; % = 10
No of events	
<b>Number of metastatic sites - Five +</b>	n = 42 ; % = 3
No of events	

1 **Outcomes**2 **Survival**

Outcome	Upfront cytoreductive nephrectomy + sunitinib vs Sunitinib alone, , N2 = 651, N1 = 805	Sunitinib + deferred cytoreductive nephrectomy vs Upfront cytoreductive nephrectomy + sunitinib, , N2 = 805, N1 = 85
<b>Overall survival</b>	0.6 (0.53 to 0.68)	0.52 (0.39 to 0.7)
Hazard ratio/95% CI		

3 Overall survival - Polarity - Higher values are better

4

5 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest)
Directness	Directly applicable

6

7 **Chakiryan, 2022**

**Bibliographic Reference** Chakiryan, Nicholas H; Gore, L Robert; Reich, Richard R; Dunn, Rodney L; Jiang, Da David; Gillis, Kyle A; Green, Elizabeth; Hajiran, Ali; Hugar, Lee; Zemp, Logan; Zhang, Jingsong; Jain, Rohit K; Chahoud, Jad; Spiess, Philippe E; Manley, Brandon J; Sexton, Wade J; Hollenbeck, Brent K; Gilbert, Scott M; Survival Outcomes Associated With Cytoreductive Nephrectomy in Patients With Metastatic Clear Cell Renal Cell Carcinoma.; JAMA network open; 2022; vol. 5 (no. 5); e2212347

8

9 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	United States - Uses the National Clinical Data Base (NCDB)
<b>Study dates</b>	January 2006 to December 2016
<b>Sources of funding</b>	NR
<b>Inclusion criteria</b>	Clinical stage IV metastatic renal cancer at diagnosis; age of 18 to 100 years; availability of complete staging and demographic data; and receipt of targeted therapy as first-line treatment  Diagnosis with clear cell renal cell carcinoma

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<b>Exclusion criteria</b>	NCDB codes indicated that the patient was treated on an experimental or blinded clinical trial protocol; data were missing on distance from the patient's residence to the treating facility; if The International Metastatic Renal Cell Carcinoma Database risk score were not available in the NCDB, and available data points are not adequate to calculate this score directly
<b>Intervention(s)</b>	Up-front cytoreductive nephrectomy (CN)
<b>Comparator</b>	First line systemic anti-cancer therapy only i.e. no cytoreductive nephrectomy
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	Overall - 12,154  Up-front cytoreductive nephrectomy= 4,393  Systemic anti-cancer therapy alone - 7,761
<b>Duration of follow-up</b>	Median follow-up time for patients who were alive at last contact was 36.0 months (IQR, 22.3-56.7 months)
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	<p>Patients were stratified according to the cytoreductive nephrectomy status. Wilcoxon rank sum testing was used to compare continuous variables, and the <math>\chi^2</math> test of independence was used to compare categorical variables. Kaplan-Meier estimates were used to generate survival functions. Propensity score matching carried out. Univariable analysis was repeated in the post-matching cohorts to assess for balance between groups.</p> <p>Subgroup analysis was conducted for each of the 3 methods (multivariable Cox proportional hazards regression, propensity score matching, and instrumental variable analysis) to test whether the cytoreductive nephrectomy sequence with targeted therapy administration was associated with overall survival</p> <p>Adjusted covariates: age, sex, race, Charlson-Deyo score, facility type, year of diagnosis, cT stage, cN stage, and cytoreductive nephrectomy status</p>
<b>Additional comments</b>	Study included 12,766 participants in total with 5,005 in the cytoreductive nephrectomy arm and 7,761 in no cytoreductive nephrectomy arm. The protocol relevant outcomes were extracted from the subset of the cytoreductive nephrectomy arm who received up-front cytoreductive nephrectomy compared to no cytoreductive nephrectomy arm (4,393 vs. 7,761). However, the baseline data was not reported for this subset but as an overall for the participants who had received cytoreductive nephrectomy and was extracted (5,005 and 7,761).

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Study uses and reports the protocol relevant outcomes based on both multiple-cox regression and propensity score matching model. The extracted results came from the propensity score matching model.

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2 **Study arms**3 **Cytoreductive nephrectomy (N = 5005)**4 **Upfront nephrectomy + SACT - N= 4393**5 **SACT Alone (N = 7761)**

6

7 **Characteristics**8 **Arm-level characteristics**

Characteristic	Cytoreductive nephrectomy (N = 5005)	SACT Alone (N = 7761)
% Female	n = 1540 ; % = 31	n = 2482 ; % = 32
No of events		
Age	61 (54 to 67)	65 (57 to 72)
Median (IQR)		
<b>TNM classification - cT1</b>	n = 887 ; % = 18	n = 2295 ; % = 30
No of events		
<b>TNM classification - cT2</b>	n = 1721 ; % = 34	n = 2213 ; % = 29
No of events		
<b>TNM classification - cT3</b>	n = 2049 ; % = 41	n = 2101 ; % = 27
No of events		
<b>TNM classification - cT4</b>	n = 348 ; % = 7	n = 1152 ; % = 15
No of events		
<b>TNM classification - cN0</b>	n = 3579 ; % = 72	n = 4366 ; % = 56
No of events		
<b>TNM classification - cN+</b>	n = 1426 ; % = 28	n = 3395 ; % = 44
No of events		

9

1 **Outcomes**2 **Survival**

Outcome	Cytoreductive nephrectomy vs SACT Alone, , N2 = 4393, N1 = 7761
Overall survival Upfront	0.5 (0.48 to 0.52)
Hazard ratio/95% CI	

3 Overall survival - Polarity - Higher values are better

4 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious ( <i>Insufficient adjustment for confounders, limited reporting on missing data and protocol not identified</i> )
Directness	Directly applicable

5

6 **Choueiri, 2011**

<b>Bibliographic Reference</b>	Choueiri, Toni K; Xie, Wanling; Kollmannsberger, Christian; North, Scott; Knox, Jennifer J; Lampard, J Geoffrey; McDermott, David F; Rini, Brian I; Heng, Daniel Y C; The impact of cytoreductive nephrectomy on survival of patients with metastatic renal cell carcinoma receiving vascular endothelial growth factor targeted therapy.; The Journal of urology; 2011; vol. 185 (no. 1); 60-6
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8 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	US and Canada
<b>Study dates</b>	August 2004 and July 2008
<b>Inclusion criteria</b>	Patients diagnosis of metastatic renal cell carcinoma of any pathological subtype  Patients treated with sunitinib, sorafenib or bevacizumab
<b>Exclusion criteria</b>	Patients who had undergone nephrectomy for early stage disease and metastases had subsequently developed
<b>Intervention(s)</b>	Cytoreductive nephrectomy, before systemic anti-cancer therapy
<b>Comparator</b>	No cytoreductive nephrectomy, only systemic anti-cancer therapy
<b>Number of participants</b>	N = 314

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	Cytoreductive nephrectomy N=201
	No cytoreductive nephrectomy N = 113
<b>Duration of follow-up</b>	Median followup after treatment initiation in those alive was 16.3 months
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Distributions of overall survival were estimated using the Kaplan-Meier method and medians with 95% confidence intervals were reported. Proportional hazards regression was used to examine the association between cytoreductive nephrectomy and overall survival when adjusted for the Heng et al. or Memorial Sloan-Kettering Cancer Centre criteria. Survival curves were constructed for each of the Heng et al, and Memorial Sloan-Kettering Cancer Centre favorable, intermediate and poor risk groups, and hazard ratio and Wald chi-square test from Cox regression were performed. This was also performed in different subgroups including patients with or without brain metastases, those with Karnofsky performance status 80% or greater vs less than 80%, those with more than 1 site of metastasis vs 1 site of metastasis, and those on different types of vascular endothelial growth factor targeted therapy

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2 **Study arms**3 **Cytoreductive nephrectomy, before systemic anti-cancer therapy (N = 201)**4 **No cytoreductive nephrectomy, only systemic anti-cancer therapy (N = 113)**

5

6 **Characteristics**7 **Arm-level characteristics**

<b>Characteristic</b>	<b>Cytoreductive nephrectomy, before systemic anti-cancer therapy (N = 201)</b>	<b>No cytoreductive nephrectomy, only systemic anti-cancer therapy (N = 113)</b>
<b>% Female</b>	n = 62 ; % = 30.8	n = 30 ; % = 26.5
No of events		
<b>Number of metastatic sites - One</b>	n = 45 ; % = 22.4	n = 37 ; % = 32.7
No of events		
<b>Number of metastatic sites - More than 1</b>	n = 156 ; % = 77.6	n = 76 ; % = 67.3
No of events		

<b>Characteristic</b>	<b>Cytoreductive nephrectomy, before systemic anti-cancer therapy (N = 201)</b>	<b>No cytoreductive nephrectomy, only systemic anti-cancer therapy (N = 113)</b>
<b>Brain metastases - No</b>	n = 180 ; % = 89.6	n = 105 ; % = 92.9
No of events		
<b>Brain metastases - Yes</b>	n = 21 ; % = 10.4	n = 8 ; % = 7.1
No of events		
<b>Nonclear cell pathology - No</b>	n = 180 ; % = 91.4	n = 89 ; % = 96.7
No of events		
<b>Nonclear cell pathology - Yes</b>	n = 17 ; % = 8.6	n = 3 ; % = 3.3
No of events		
<b>Sarcomatoid features - No</b>	n = 182 ; % = 92.4	n = 85 ; % = 94.4
No of events		
<b>Sarcomatoid features - Yes</b>	n = 15 ; % = 7.6	n = 5 ; % = 5.6
No of events		
<b>Type of therapy - Sunitinib</b>	n = 114 ; % = 56.7	n = 84 ; % = 74.3
No of events		
<b>Type of therapy - Sorafenib</b>	n = 72 ; % = 35.8	n = 22 ; % = 19.5
No of events		
<b>Type of therapy - Bevacizumab</b>	n = 15 ; % = 7.5	n = 7 ; % = 6.2
No of events		
<b>Diagnosis to targeted therapy less than 1 yr - No</b>	n = 63 ; % = 31.3	n = 9 ; % = 8
No of events		

<b>Characteristic</b>	<b>Cytoreductive nephrectomy, before systemic anti-cancer therapy (N = 201)</b>	<b>No cytoreductive nephrectomy, only systemic anti-cancer therapy (N = 113)</b>
<b>Diagnosis to targeted therapy less than 1 yr - Yes</b>	n = 138 ; % = 68.7	n = 104 ; % = 92
No of events		
<b>Hemoglobin less than lower level normal - No</b>	n = 68 ; % = 35.6	n = 34 ; % = 32.1
No of events		
<b>Hemoglobin less than lower level normal - Yes</b>	n = 123 ; % = 64.4	n = 72 ; % = 67.9
No of events		
<b>Serum corrected calcium greater than upper limit normal - No</b>	n = 178 ; % = 93.7	n = 76 ; % = 74.5
No of events		
<b>Serum corrected calcium greater than upper limit normal - Yes</b>	n = 12 ; % = 6.3	n = 26 ; % = 25.5
No of events		
<b>LDH greater than 1.5 upper limit normal - No</b>	n = 144 ; % = 85.7	n = 73 ; % = 83
No of events		
<b>LDH greater than 1.5 upper limit normal - Yes</b>	n = 24 ; % = 14.3	n = 15 ; % = 17
No of events		
<b>Neutrophils greater than upper limit normal - No</b>	n = 159 ; % = 87.9	n = 77 ; % = 79.4
No of events		
<b>Neutrophils greater than upper limit normal - Yes</b>	n = 22 ; % = 12.1	n = 20 ; % = 20.6
No of events		

Characteristic	Cytoreductive nephrectomy, before systemic anti-cancer therapy (N = 201)	No cytoreductive nephrectomy, only systemic anti-cancer therapy (N = 113)
<b>Platelets greater than upper limit normal - No</b>	n = 141 ; % = 74.6	n = 71 ; % = 68.3
No of events		
<b>Platelets greater than upper limit normal - Yes</b>	n = 48 ; % = 25.4	n = 33 ; % = 31.7
No of events		

1

2 **Outcomes**3 **Survival**

Outcome	Cytoreductive nephrectomy, before systemic anti-cancer therapy vs No cytoreductive nephrectomy, only systemic anti-cancer therapy, , N2 = 113, N1 = 201
<b>OS</b>	0.68 (0.46 to 0.99)
Hazard ratio/95% CI	

4 OS - Polarity - Higher values are better

5

6 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest)
Directness	Directly applicable

7

8 **de Groot, 2016**

<b>Bibliographic Reference</b>	de Groot, Saskia; Redekop, William K; Sleijfer, Stefan; Oosterwijk, Egbert; Bex, Axel; Kiemeny, Lambertus A L M; Uyl-de Groot, Carin A; Survival in Patients With Primary Metastatic Renal Cell Carcinoma Treated With Sunitinib With or Without Previous Cytoreductive Nephrectomy: Results From a Population-based Registry.; Urology; 2016; vol. 95; 121-7
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10 **Study details**

<b>Trial registration</b>	PERCEPTION-registry
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<b>number and/or trial name</b>	
<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Netherlands - Patients registried from the Dutch Cancer Registry
<b>Study dates</b>	January 2008 and December 2010
<b>Sources of funding</b>	The PERCEPTION-registry was supported by grants from the Netherlands Organisation for Health Research and Development (grant number 152001014), Pfizer (formerly Wyeth Pharmaceuticals BV), and Roche Nederland BV. From the Institute of Health Policy and Management, Erasmus University Rotterdam, Rotterdam, The Netherlands; the Department of Medical Oncology and Cancer Genomics Netherlands, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; the Radboud Institute for Molecular Life Sciences, Radboud University Medical Center, Department of Urology, Nijmegen, The Netherlands; the Department of Urology, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands; and the Radboud Institute for Health Sciences, Radboud University Medical Center, Department for Health Evidence, Nijmegen, The Netherlands
<b>Inclusion criteria</b>	<p>Patients treated with first-line sunitinib</p> <p>Patients diagnosed with metastatic renal cell carcinoma (ie, metastases at initial presentation) of any histologic subtype</p>
<b>Intervention(s)</b>	Cytoreductive nephrectomy + sunitinib
<b>Comparator</b>	Sunitinib only
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	<p>N = 146</p> <p>Cytoreductive nephrectomy + sunitinib N=73</p> <p>Sunitinib only N=73</p>
<b>Methods of analysis</b>	<p>Overall survival was calculated from the date of the start of treatment (i.e., cytoreductive nephrectomy or start of first-line sunitinib) until the date of death from any cause or last follow-up using the Kaplan-Meier method. The first approach to evaluate the effect of cytoreductive nephrectomy was a Cox proportional hazards model using the propensity score as a covariate.</p> <p>Baseline demographics (age at diagnosis and gender) and 3 additional clinical factors (histology, clinical tumour stage, and regional lymph node</p>



involvement) were incorporated as covariates because these factors could have influenced the decision to conduct a nephrectomy

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2 **Study arms**3 **Cytoreductive nephrectomy + sunitinib (N = 73)**4 **Sunitinib only (N = 73)**

5

6 **Characteristics**7 **Arm-level characteristics**

Characteristic	Cytoreductive nephrectomy + sunitinib (N = 73)	Sunitinib only (N = 73)
<b>% Female</b>	n = 60 ; % = 82	n = 60 ; % = 83
No of events		
<b>Age</b>	62 (28 to 77)	64 (24 to 89)
Median (IQR)		
<b>TNM classification - cT1-T3a</b>	n = 60 ; % = 82	n = 59 ; % = 81
No of events		
<b>TNM classification - cT3b-T4</b>	n = 13 ; % = 18	n = 14 ; % = 19
No of events		
<b>TNM classification - cN0</b>	n = 37 ; % = 50	n = 32 ; % = 44
No of events		
<b>TNM classification - cN1</b>	n = 36 ; % = 50	n = 41 ; % = 56
No of events		
<b>Primary RCC type - Clear cell</b>	n = 57 ; % = 78	n = 57 ; % = 78
No of events		
<b>Primary RCC type - other</b>	n = 16 ; % = 22	n = 16 ; % = 22
No of events		
<b>Site of metastasis - One</b>	n = 33 ; % = 45	n = 39 ; % = 54
No of events		

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Characteristic	Cytoreductive nephrectomy + sunitinib (N = 73)	Sunitinib only (N = 73)
<b>Site of metastasis - More than one</b>	n = 40 ; % = 55	n = 34 ; % = 46
No of events		
<b>Liver metastasis - No</b>	n = 67 ; % = 92	n = 68 ; % = 94
No of events		
<b>Liver metastasis - Yes</b>	n = 6 ; % = 8	n = 5 ; % = 6
No of events		
<b>Lung metastasis - No</b>	n = 16 ; % = 22	n = 24 ; % = 32
No of events		
<b>Lung metastasis - Yes</b>	n = 57 ; % = 78	n = 49 ; % = 68
No of events		
<b>Bone metastasis - No</b>	n = 58 ; % = 79	n = 61 ; % = 84
No of events		
<b>Bone metastasis - Yes</b>	n = 15 ; % = 21	n = 12 ; % = 16
No of events		

1

2 **Outcomes**3 **Survival**

Outcome	Cytoreductive nephrectomy + sunitinib vs Sunitinib only, , N2 = 73, N1 = 73
<b>Overall survival - Cytoreductive nephrectomy</b>	0.61 (0.41 to 0.92)
Hazard ratio/95% CI	

4 Overall survival - Cytoreductive nephrectomy - Polarity - Higher values are better

5

6

7 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest)

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Question	Answer
Directness	Directly applicable

1

2 **Dragomir, 2022**

**Bibliographic Reference** Dragomir, A.; Nazha, S.; Tanguay, S.; Breau, R.H.; Bhindi, B.; Rendon, R.A.; Kapoor, A.; Hotte, S.J.; Basappa, N.; Fairey, A.; So, A.I.; Kollmannsberger, C.; Finelli, A.; Hansen, A.; Canil, C.; Heng, D.; Lattouf, J.-B.; Bjarnason, G.; Power, N.; Pouliot, F.; Wood, L.A.; Outcomes of Cytoreductive Nephrectomy for Patients with Metastatic Renal Cell Carcinoma: Real World Data from Canadian Centers; European Urology Focus; 2022; vol. 8 (no. 6); 1703-1710

3

4 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Canada - Data retrieved from the Canadian Kidney Cancer information system (CKCis)
<b>Study dates</b>	January 2011 and April 2020
<b>Sources of funding</b>	The Kidney Cancer Research Network of Canada and the Canadian Kidney Cancer information system (CKCis) have received unrestricted grants from BMS, Eisai, EMD Serono, GSK, Ipsen, Pfizer, Merck, Novartis, and Roche. These sponsors had no direct role in or influence on this work
<b>Inclusion criteria</b>	Diagnosis of renal cell carcinoma was made on the basis of histopathological evaluations; patients with synchronous disease (i.e., metastases found 3 months before or within 6 months after the primary tumour diagnosis); treated (with cytoreductive nephrectomy or/and systemic therapy) within 12 months of the initial renal cell carcinoma diagnosis
<b>Exclusion criteria</b>	Patients who had indolent metastatic disease
<b>Intervention(s)</b>	Cytoreductive nephrectomy followed by systemic therapy (cytoreductive nephrectomy before systemic therapy)
<b>Comparator</b>	Systemic therapy followed by cytoreductive nephrectomy (cytoreductive nephrectomy after systemic therapy) and systemic therapy alone (systemic therapy only)
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	N = 708  Cytoreductive nephrectomy before systemic therapy - N = 383

	Cytoreductive nephrectomy after systemic therapy - N = 73
	Systemic therapy only - N = 252
<b>Duration of follow-up</b>	Earliest date of death, loss to follow-up, or the end of the study period (April 2020)
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	<p>Kaplan Meier curve analysis was performed to estimate overall survival from the index date until death (any causes) or loss to follow-up. A log-rank test was used to evaluate differences in overall survival. Uses Inverse probability of treatment weighting to account for the differences in the distribution among baseline characteristics.</p> <p>It uses the inverse probability of treatment weighting and Cox proportional hazard model to adjust only for age, gender, sites and number of organs with metastasis, histology, International Metastatic Consortium (IMDC) scores and Charlson comorbidity index.</p>

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2 **Study arms**3 **Cytoreductive nephrectomy before systemic therapy (N = 383)**4 **Cytoreductive nephrectomy after systemic therapy (N = 73)**5 **Systemic therapy only (N = 252)**

6

7 **Characteristics**8 **Arm-level characteristics**

<b>Characteristic</b>	<b>Cytoreductive nephrectomy before systemic therapy (N = 383)</b>	<b>Cytoreductive nephrectomy after systemic therapy (N = 73)</b>	<b>Systemic therapy only (N = 252)</b>
<b>% Female</b>	n = 104 ; % = 27.1	n = 19 ; % = 26	n = 128 ; % = 50.8
No of events			
<b>Age</b>	61 (54 to 68)	62 (55 to 68)	64 (57 to 70)
Median (IQR)			
<b>Primary RCC type - Clear cell histology</b>	n = 314 ; % = 82	n = 61 ; % = 83.6	n = 169 ; % = 67.1
No of events			

<b>Characteristic</b>	<b>Cytoreductive nephrectomy before systemic therapy (N = 383)</b>	<b>Cytoreductive nephrectomy after systemic therapy (N = 73)</b>	<b>Systemic therapy only (N = 252)</b>
<b>Location of metastases - lung</b>	n = 215 ; % = 56.1	n = 39 ; % = 53.4	n = 135 ; % = 53.6
No of events			
<b>Location of metastases - bone</b>	n = 75 ; % = 19.6	n = 14 ; % = 19.2	n = 66 ; % = 26.2
No of events			
<b>Location of metastases - Brain</b>	n = 7 ; % = 1.8	n = 2 ; % = 2.7	n = 16 ; % = 6.4
No of events			
<b>Location of metastases - Adrenal gland</b>	n = 41 ; % = 10.7	n = 10 ; % = 13.7	n = 29 ; % = 11.5
No of events			
<b>Location of metastases - Liver</b>	n = 36 ; % = 9.4	n = 9 ; % = 12.3	n = 41 ; % = 16.3
No of events			
<b>Location of metastases - Lymph nodes</b>	n = 122 ; % = 31.9	n = 28 ; % = 38.4	n = 104 ; % = 41.3
No of events			
<b>Systemic therapy type - Sunitinib</b>	n = 230 ; % = 60.1	n = 52 ; % = 71.2	n = 121 ; % = 48
No of events			
<b>Systemic therapy type - Pazopanib</b>	n = 72 ; % = 18.8	n = 8 ; % = 11	n = 52 ; % = 20.6
No of events			
<b>Systemic therapy type - Ipilimumab/nivolumab</b>	n = 44 ; % = 11.5	n = 3 ; % = 4.1	n = 57 ; % = 22.6
No of events			
<b>Systemic therapy type - Other</b>	n = 37 ; % = 9.6	n = 10 ; % = 13.7	n = 22 ; % = 8.8
No of events			

<b>Characteristic</b>	<b>Cytoreductive nephrectomy before systemic therapy (N = 383)</b>	<b>Cytoreductive nephrectomy after systemic therapy (N = 73)</b>	<b>Systemic therapy only (N = 252)</b>
<b>IMDC Score - 0 (good)</b>	n = 0 ; % = 0	n = 0 ; % = 0	n = 0 ; % = 0
No of events			
<b>IMDC Score - 1–2 (intermediate)</b>	n = 253 ; % = 66.1	n = 48 ; % = 65.8	n = 133 ; % = 52.8
No of events			
<b>IMDC Score - 3-5 (poor)</b>	n = 130 ; % = 33.9	n = 25 ; % = 34.2	n = 119 ; % = 47.2
No of events			
<b>Charlson comorbidity index - 0 or 1</b>	n = 95 ; % = 27	n = 20 ; % = 28.6	n = 55 ; % = 23.8
No of events			
<b>Charlson comorbidity index - &gt;1</b>	n = 257 ; % = 73	n = 50 ; % = 71.4	n = 175 ; % = 76.2
No of events			
<b>Comorbidities - Hypertension</b>	n = 204 ; % = 53.3	n = 28 ; % = 38.4	n = 121 ; % = 48
No of events			
<b>Comorbidities - Diabetes</b>	n = 83 ; % = 21.7	n = 16 ; % = 21.9	n = 57 ; % = 22.6
No of events			
<b>Comorbidities - Obesity</b>	n = 12 ; % = 3.1	n = 2 ; % = 2.7	n = 11 ; % = 4.4
No of events			
<b>Comorbidities - Hypercholesterolemia</b>	n = 89 ; % = 23.2	n = 11 ; % = 15.1	n = 47 ; % = 18.7
No of events			
<b>Comorbidities - Smoker</b>	n = 8 ; % = 2.1	n = 3 ; % = 4.1	n = 2 ; % = 0.8
No of events			

1 **Outcomes**2 **Survival**

Outcome	Cytoreductive nephrectomy before systemic therapy vs Systemic therapy only, , N2 = 252, N1 = 383	Cytoreductive nephrectomy after systemic therapy vs Cytoreductive nephrectomy before systemic therapy, , N2 = 383, N1 = 73
<b>Overall survival</b>	0.65 (0.52 to 0.82)	0.66 (0.42 to 1.04)
Hazard ratio/95% CI		

3 Overall survival - Polarity - Higher values are better

4

5

6 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (No adjustment for confounders or matching undertaken. Limited information about missing data or inclusion criteria. No protocol identified so unable to fully assess bias in selection of reported result.)
Directness	Directly applicable

7

8 **Ghatalia, 2022**

<b>Bibliographic Reference</b>	Ghatalia, Pooja; Handorf, Elizabeth A; Geynisman, Daniel M; Deng, Mengying; Zibelman, Matthew R; Abbosh, Philip; Anari, Fern; Greenberg, Richard E; Viterbo, Rosalia; Chen, David; Smaldone, Marc C; Kutikov, Alexander; Uzzo, Robert G; The Role of Cytoreductive Nephrectomy in Metastatic Renal Cell Carcinoma: A Real-World Multi-Institutional Analysis.; The Journal of urology; 2022; vol. 208 (no. 1); 71-79
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9

10 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	US - uses the nationwide US Flatiron Health (FH) electronic health record (EHR)-derived deidentified database.
<b>Study dates</b>	2011-2020
<b>Sources of funding</b>	This work was not supported by external funding

<b>Inclusion criteria</b>	Patients with clear cell histology and synchronous metastases
<b>Intervention(s)</b>	Upfront cytoreductive nephrectomy
<b>Comparator</b>	Deferred cytoreductive nephrectomy Systemic therapy alone
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	N = 1,719  Upfront cytoreductive nephrectomy - N = 605  Deferred cytoreductive nephrectomy - N = 142  Systemic therapy alone - N = 972
<b>Duration of follow-up</b>	Not reported
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Kaplan-Meier curves, log-rank tests, and Cox proportional hazards regressions were used to assess the effect of therapy on survival. Adjusted analyses were conducted via Inverse Probability of Treatment Weighing (IPTW) based on the generalized propensity score, with propensity scores estimated via Bayesian Additive Regression Trees. Covariates in the propensity score model were age, gender, race, insurance at diagnosis, and IMDC risk group. Where covariates were missing, we used a missing category in the propensity score model. Propensity scores were assessed for overlap, and weighted observations were assessed for covariate balance, with a standardized difference of <0.1 taken to indicate sufficient balance. Weighted Kaplan-Meier curves and Cox models were then used.



1 **Study arms**2 **Upfront cytoreductive nephrectomy (N = 605)**3 **Deferred cytoreductive nephrectomy (N = 142)**4 **Systemic therapy alone (N = 972)**

5

6 **Characteristics**7 **Arm-level characteristics**

Characteristic	Upfront cytoreductive nephrectomy (N = 605)	Deferred cytoreductive nephrectomy (N = 142)	Systemic therapy alone (N = 972)
<b>% Female</b>	n = 187 ; % = 31	n = 41 ; % = 29	n = 297 ; % = 31
No of events			
<b>Age</b>	62.3 (56 to 69)	63.2 (58 to 70)	67 (60 to 75)
Median (IQR)			
<b>Baseline performance status - ECOG 0</b>	n = 160 ; % = 26	n = 37 ; % = 26	n = 213 ; % = 22
No of events			
<b>Baseline performance status - ECOG 1</b>	n = 144 ; % = 24	n = 29 ; % = 20	n = 264 ; % = 27
No of events			
<b>Baseline performance status - ECOG 2</b>	n = 36 ; % = 6	n = 11 ; % = 8	n = 116 ; % = 12
No of events			
<b>Baseline performance status - ECOG 3</b>	n = 7 ; % = 1	<i>empty data</i>	n = 32
No of events			
<b>Baseline performance status - ECOG 4</b>	<i>empty data</i>	<i>empty data</i>	n = 3 ; % = 0.3
No of events			
<b>Baseline performance status - Missing</b>	n = 258 ; % = 43	n = 59 ; % = 42	n = 344 ; % = 35
No of events			

<b>Characteristic</b>	<b>Upfront cytoreductive nephrectomy (N = 605)</b>	<b>Deferred cytoreductive nephrectomy (N = 142)</b>	<b>Systemic therapy alone (N = 972)</b>
<b>Race - white</b>	n = 438 ; % = 72	n = 101 ; % = 71	n = 670 ; % = 70
No of events			
<b>Race - Black</b>	n = 23 ; % = 4	n = 8 ; % = 6	n = 55 ; % = 6
No of events			
<b>Race - Hispanic</b>	n = 6 ; % = 1	n = 0 ; % = 0	n = 2 ; % = 0.2
No of events			
<b>Race - Asian</b>	n = 10 ; % = 2	n = 2 ; % = 2	n = 13 ; % = 2
No of events			
<b>Race - Other</b>	n = 84 ; % = 14	n = 21 ; % = 15	n = 130 ; % = 13
No of events			
<b>Race - Missing</b>	n = 44 ; % = 7	n = 10 ; % = 7	n = 102 ; % = 11
No of events			
<b>IMDC risk category - Intermediate</b>	n = 90 ; % = 15	n = 29 ; % = 20	n = 149 ; % = 15
No of events			
<b>IMDC risk category - Poor</b>	n = 211 ; % = 35	n = 47 ; % = 33	n = 443 ; % = 46
No of events			
<b>IMDC risk category - Poor/Intermediate</b>	n = 304 ; % = 50	n = 66 ; % = 47	n = 380 ; % = 39
No of events			

**Outcomes**

**Survival**

Outcome	Upfront cytoreductive nephrectomy vs Systemic therapy alone, , N2 = 972, N1 = 605	Upfront cytoreductive nephrectomy vs Deferred cytoreductive nephrectomy, , N2 = 142, N1 = 605
Overall survival	0.83 (0.7 to 0.96)	1 (0.76 to 1.32)
Hazard ratio/95% CI		

Overall survival - Polarity - Higher values are better

**Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious ( <i>Insufficient adjustment for confounders, limited reporting on missing data and protocol not identified</i> )
Directness	Directly applicable

**Gunenc, 2024**

**Bibliographic Reference** Gunenc, Damla; Issa, Wadih; Gerald, Thomas; Zhou, Qinhan; Zhang, Song; Ibezue, I Chidera; Bhanvadia, Raj; Tachibana, Isamu; Brugarolas, James; Hammers, Hans; Qin, Qian; Kapur, Payal; Woldu, Solomon; Gaston, Kris; Lotan, Yair; Cadeddu, Jeffrey; Wang, Andrew Z; Margulis, Vitaly; Zhang, Tian; Pathological Response and Outcomes in Patients With Metastatic Renal Cell Carcinoma (mRCC) Receiving Immunotherapy-Based Therapies and Undergoing Deferred Cytoreductive Nephrectomy (CN).; Clinical genitourinary cancer; 2024; vol. 22 (no. 5); 102177

**Study details**

Study type	Retrospective cohort study
Study location	US
Study dates	April 2016 - October 2022
Sources of funding	Bristol-Myers Squibb, Merck & Co, Aravive, Surface oncology, NGM Biopharmaceutical, CPRIT, Janssen, Astra Zeneca, Pfizer, Astellas, Eli Lilly, Tempus, ALX Oncology, Janux Therapeutics, Exelixis, FBD Biologics, Guardant, OncoC4

<b>Inclusion criteria</b>	Patients with metastatic RCC receiving immunotherapy-based therapies and undergoing deferred or upfront CN
<b>Exclusion criteria</b>	Patients who did not receive immunotherapy based therapies
<b>Intervention(s)</b>	Upfront CN - patients who were started on immunotherapy inhibitor-based therapies after surgery
<b>Comparator</b>	Deferred CN - patients who were receiving immunotherapy-based therapies before surgery
<b>Outcome measures</b>	Progression-free survival Overall survival
<b>Number of participants</b>	N=51
<b>Duration of follow-up</b>	Median follow-up of 21 months
<b>Loss to follow-up</b>	No additional information
<b>Methods of analysis</b>	Kaplan Meier analysis was performed for Progression Free Survival (PFS) and Overall Survival (OS) estimates over time.  Estimated Blood Loss (EBL) were evaluated using the Mann-Whitney-U test.
<b>Additional comments</b>	The baseline timepoint was defined as the initiation of immune checkpoint inhibitor therapies for the deferred CN group and the time of nephrectomy for the upfront CN group. Categorical variables between the two groups were compared using the Chi-square test.

1

2 **Study arms**3 **Upfront CN (N = 13)**

4 **Upfront cytoreductive nephrectomy group included those who were receiving**  
5 **immunotherapy based therapies after surgery**

6

7 **Deferred CN (N = 38)**

8 **Deferred cytoreductive nephrectomy group included those who were receiving**  
9 **immunotherapy based therapies in the preoperative setting**

10

1 **Characteristics**2 **Arm-level characteristics**

<b>Characteristic</b>	<b>Upfront CN (N = 13)</b>	<b>Deferred CN (N = 38)</b>
<b>% Female</b>	n = 3 ; % = 13	n = 9 ; % = 23.7
No of events		
<b>Age (years)</b>	59.62 (NR)	62.53 (NR)
Mean (SD)		
<b>TNM classification - T1 stage</b>	n = 1 ; % = 7.7	n = 2 ; % = 5.3
No of events		
<b>TNM classification - T2 stage</b>	n = 0 ; % = 0	n = 6 ; % = 15.8
No of events		
<b>TNM classification - T3 stage</b>	n = 9 ; % = 69.2	n = 19 ; % = 50
No of events		
<b>TNM classification - T4 stage</b>	n = 3 ; % = 23.1	n = 11 ; % = 28.9
No of events		
<b>TNM classification - N0 stage</b>	n = 5 ; % = 38.5	n = 23 ; % = 60.5
No of events		
<b>TNM classification - N1 stage</b>	n = 7 ; % = 53.8	n = 13 ; % = 39.5
No of events		
<b>Primary RCC type - clear cell</b>	n = 10 ; % = 76.9	n = 34 ; % = 89.5
No of events		
<b>Primary RCC type - Papillary</b>	n = 2 ; % = 15.4	n = 1 ; % = 2.6
No of events		
<b>Primary RCC type - Other</b>	n = 1 ; % = 7.7	n = 3 ; % = 7.9
No of events		
<b>Location of metastases - Bone, brain, or liver metastases</b>	n = 4 ; % = 30.8	n = 19 ; % = 50
No of events		

1

2 **Outcomes**3 **Progression free survival**

Outcome	Upfront CN vs Deferred CN, , N2 = 38, N1 = 13
<b>Progression free survival</b>	0.7 (0.29 to 1.98)
Hazard ratio/95% CI	
<b>Overall survival</b>	0.4 (0.13 to 1.57)
Hazard ratio/95% CI	

4

5 **Critical appraisal - ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious <i>(Retrospective study design so difficult to account for confounders and not clear if there was selection bias in the selection of patients for upfront or deferred CN. There was no mention of adjusting for selection biases. The systemic therapies varied. Different follow-up durations but only median follow-up reported.)</i>
Directness	Directly applicable

6

7 **Hara, 2023**

<b>Bibliographic Reference</b>	Hara, Takuto; Furukawa, Junya; Shiraishi, Yusuke; Okamura, Yasuyoshi; Bando, Yukari; Terakawa, Tomoaki; Harada, Kenichi; Nakano, Yuzo; Fujisawa, Masato; Impact of cytoreductive nephrectomy prior to combination therapy of ipilimumab plus nivolumab in metastatic renal cell carcinoma.; International journal of urology : official journal of the Japanese Urological Association; 2023; vol. 30 (no. 9); 746-752
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8

9 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Japan - used the institutional medical record database at Kobe University Hospital and five affiliated hospitals
<b>Study dates</b>	October 2018 and December 2021
<b>Sources of funding</b>	Not reported
<b>Inclusion criteria</b>	Patients who received nivolumab plus ipilimumab for synchronous metastatic renal cell carcinoma

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<b>Exclusion criteria</b>	Patients who received deferred cytoreductive nephrectomy
<b>Intervention(s)</b>	Cytoreductive nephrectomy before ipilimumab plus nivolumab
<b>Comparator</b>	Without cytoreductive nephrectomy
<b>Outcome measures</b>	Progression-free survival Overall survival
<b>Number of participants</b>	N = 54  Cytoreductive nephrectomy prior to ipilimumab plus nivolumab - N = 21  Without cytoreductive nephrectomy - N = 33
<b>Duration of follow-up</b>	Median follow-up was 15.7 months
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	<p>The progression-free survival and overall survival rates were calculated by the Kaplan–Meier method, and differences were analyzed by the log-rank test. progression-free survival and overall survival of the patients treated with either prior cytoreductive nephrectomy or not were compared after propensity score matching of patient cohorts to reduce potential confounding effects and treatment selection bias.</p> <p>The covariates were age, body mass index (BMI), sex, International Metastatic RCC Database Consortium (IMDC) risk classification, histology, presence of liver, brain, or bone metastasis, clinical T stage, neutrophil lymphocyte ratio (NLR), PS, number of metastasis and presence of tumour associated symptoms (e.g., pain, paralysis, fever, weight loss). Nearest-neighbor matching with a 1:1 ratio and a caliper distance of 0.2 was used.</p>

1 **Study arms**2 **Cytoreductive nephrectomy before ipilimumab plus nivolumab (N = 21)**3 **Without cytoreductive nephrectomy (N = 33)**

4

5 **Characteristics**6 **Arm-level characteristics**

Characteristic	Cytoreductive nephrectomy before ipilimumab plus nivolumab (N = 21)	Without cytoreductive nephrectomy (N = 33)
<b>% Female</b>	n = 2 ; % = 15.4	n = 2 ; % = 15.4
No of events		
<b>Age</b>	71 (42 to 80)	71 (30 to 81)
Median (IQR)		
<b>Primary RCC type - Clear cell</b>	n = 10 ; % = 76.9	n = 8 ; % = 61.5
No of events		
<b>Primary RCC type - Non-clear cell</b>	n = 3 ; % = 23.1	n = 5 ; % = 38.5
No of events		
<b>IMDC risk - Intermediate</b>	n = 6 ; % = 46.2	n = 6 ; % = 46.2
No of events		
<b>IMDC risk - Poor</b>	n = 7 ; % = 53.8	n = 7 ; % = 53.8
No of events		

7

8 **Outcomes**9 **Survival**

Outcome	Cytoreductive nephrectomy before ipilimumab plus nivolumab vs Without cytoreductive nephrectomy, , N2 = 33, N1 = 21
<b>Progression-free survival</b>	0.41 (0.18 to 0.91)
Hazard ratio/95% CI	
<b>Overall survival</b>	0.21 (0.06746 to 0.63)

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Outcome	Cytoreductive nephrectomy before ipilimumab plus nivolumab vs Without cytoreductive nephrectomy, , N2 = 33, N1 = 21
Hazard ratio/95% CI	

Progression-free survival - Polarity - Higher values are better

Overall survival - Polarity - Higher values are better

#### Adverse events ≥ grade 3

Outcome	Cytoreductive nephrectomy before ipilimumab plus nivolumab, , N = 21	Without cytoreductive nephrectomy, , N = 33
Adverse events ≥ grade 3	n = 10 ; % = 47.6	n = 9 ; % = 27.3
No of events		

Adverse events ≥ grade 3 - Polarity - Lower values are better

#### Critical appraisal –ROBINS-I checklist

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest.)
Directness	Directly applicable

#### Hatakeyama, 2021

<b>Bibliographic Reference</b>	Hatakeyama, Shingo; Naito, Sei; Numakura, Kazuyuki; Kato, Renpei; Koguchi, Tomoyuki; Kojima, Takahiro; Kawasaki, Yoshihide; Kandori, Shuya; Kawamura, Sadafumi; Tsushima, Eiki; Nishiyama, Hiroyuki; Ito, Akihiro; Kojima, Yoshiyuki; Habuchi, Tomonori; Obara, Wataru; Tsuchiya, Norihiko; Ohyama, Chikara; Impact of cytoreductive nephrectomy in patients with primary metastatic renal cell carcinoma receiving systemic tyrosine kinase inhibitor therapy: A multicenter retrospective study.; International journal of urology : official journal of the Japanese Urological Association; 2021; vol. 28 (no. 4); 369-375
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#### Study details

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Japan - Michinoku Japan Urological Cancer Study Group database
<b>Study dates</b>	January 2008 - November 2019
<b>Sources of funding</b>	Japan Society for the Promotion of Science

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<b>Inclusion criteria</b>	Patients with primary metastatic renal cell carcinoma initially treated with first-line sunitinib, sorafenib, axitinib, and pazopanib were included
<b>Exclusion criteria</b>	Treatment with first-line interferon, mammalian target of rapamycin inhibitors, immunotherapy, or chemotherapy; a period from diagnosis to first treatment (tyrosine kinase inhibitors or immediate cytoreductive nephrectomy) of more than 3 months; a period of surveillance after immediate cytoreductive nephrectomy of more than 3 months; a follow-up period from the first treatment of less than 3 months; and missing data on confounder variables
<b>Intervention(s)</b>	Immediate cytoreductive nephrectomy followed by first-line tyrosine kinase inhibitors
<b>Comparator</b>	Deferred cytoreductive nephrectomy - after receiving tyrosine kinase inhibitors  Systemic anti-cancer therapy alone - tyrosine kinase inhibitors
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	N = 278  Immediate cytoreductive nephrectomy followed by first-line tyrosine kinase inhibitors - N = 107  Deferred cytoreductive nephrectomy - after receiving tyrosine kinase inhibitors - N = 39  Systemic anti-cancer therapy alone - tyrosine kinase inhibitors - N = 132
<b>Duration of follow-up</b>	Until death
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Overall survival from the initial treatment until death was estimated using Kaplan–Meier curves and the log-rank test. Uses inverse probability of treatment weighting (inverse probability of treatment weighting) -adjusted Cox regression analysis.  Adjusted confounders - age, sex, performance status, number of IMDC risk factors, clinical stage (cT3b–4), and number of metastatic organs

1 **Study arms**2 **Immediate cytoreductive nephrectomy (N = 107)**3 **Deferred cytoreductive nephrectomy (N = 39)**4 **Systemic anti-cancer therapy alone (N = 132)**

5

6 **Characteristics**7 **Arm-level characteristics**

Characteristic	Immediate cytoreductive nephrectomy (N = 107)	Deferred cytoreductive nephrectomy (N = 39)	Systemic anti-cancer therapy alone (N = 132)
% Female	n = 28 ; % = 26.2	n = 17 ; % = 43.6	n = 32 ; % = 24.2
No of events			
Age	62 (56 to 69)	67 (62 to 72)	67 (61 to 76)
Median (IQR)			
Intervention subtype - Sunitinib	n = 72 ; % = 67	n = 17 ; % = 44	n = 65 ; % = 49
No of events			
Intervention subtype - Sorafenib	n = 10 ; % = 9.3	n = 2 ; % = 5.2	n = 16 ; % = 12
No of events			
Intervention subtype - Axitinib	n = 15 ; % = 14	n = 19 ; % = 49	n = 47 ; % = 36
No of events			
Intervention subtype - Pazopanib	n = 10 ; % = 9.3	n = 1 ; % = 2.6	n = 4 ; % = 3
No of events			
TNM classification - cT1–2	n = 37 ; % = 35	n = 14 ; % = 36	n = 32 ; % = 24
No of events			
TNM classification - cT3a	n = 47 ; % = 44	n = 8 ; % = 21	n = 34 ; % = 26
No of events			

<b>Characteristic</b>	<b>Immediate cytoreductive nephrectomy (N = 107)</b>	<b>Deferred cytoreductive nephrectomy (N = 39)</b>	<b>Systemic anti- cancer therapy alone (N = 132)</b>
<b>TNM classification - cT3b–4</b>	n = 19 ; % = 18	n = 17 ; % = 44	n = 63 ; % = 48
No of events			
<b>TNM classification - cTx (unknown)</b>	n = 4 ; % = 4	n = 0 ; % = 0	n = 3 ; % = 2
No of events			
<b>TNM classification - cN+</b>	n = 40 ; % = 37	n = 11 ; % = 28	n = 65 ; % = 49
No of events			
<b>Primary RCC type - Non–clear cell</b>	n = 12 ; % = 11	n = 3 ; % = 7.7	n = 21 ; % = 16
No of events			
<b>Location of metastases - lung</b>	n = 74 ; % = 69	n = 23 ; % = 59	n = 77 ; % = 58
No of events			
<b>Location of metastases - Distant lymph node</b>	n = 40 ; % = 37	n = 11 ; % = 28	n = 49 ; % = 37
No of events			
<b>Location of metastases - bone</b>	n = 38 ; % = 36	n = 14 ; % = 36	n = 38 ; % = 29
No of events			
<b>Location of metastases - Liver</b>	n = 11 ; % = 10	n = 3 ; % = 8	n = 23 ; % = 17
No of events			
<b>Location of metastases - Adrenal</b>	n = 11 ; % = 10	n = 1 ; % = 3	n = 16 ; % = 12
No of events			
<b>Location of metastases - Brain</b>	n = 11 ; % = 10	n = 2 ; % = 5	n = 9 ; % = 7

Characteristic	Immediate cytoreductive nephrectomy (N = 107)	Deferred cytoreductive nephrectomy (N = 39)	Systemic anti-cancer therapy alone (N = 132)
No of events			
<b>Location of metastases - Pancreas</b>	n = 5 ; % = 5	n = 0 ; % = 0	n = 5 ; % = 4
No of events			
<b>Location of metastases - Others</b>	n = 23 ; % = 21	n = 8 ; % = 21	n = 46 ; % = 35
No of events			

1

2 **Outcomes**3 **Survival**

Outcome	Immediate cytoreductive nephrectomy vs Systemic anti-cancer therapy alone, , N2 = 132, N1 = 107	Deferred cytoreductive nephrectomy vs Immediate cytoreductive nephrectomy, , N2 = 39, N1 = 107
<b>Overall survival</b>	0.63 (0.42 to 0.93)	0.61 (0.32 to 1.14)
Hazard ratio/95% CI		

4 Overall survival - Polarity - Higher values are better

5

6 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest)
Directness	Directly applicable

7

8 **Macleod, 2018**

**Bibliographic Reference** Macleod, Liam C; Odisho, Anobel Y; Tykodi, Scott S; Holt, Sarah K; Harper, Jonathan D; Gore, John L; Comparative Effectiveness of Initial Surgery vs Initial Systemic Therapy for Metastatic Kidney Cancer in the Targeted Therapy Era: Analysis of a Population-based Cohort.; Urology; 2018; vol. 113; 146-152

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1

2 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	US - data use agreement set forth by The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program data linked with Medicare claims
<b>Study dates</b>	2006 - 2011
<b>Sources of funding</b>	This work was funded in part by a seed grant from the AMA Foundation
<b>Inclusion criteria</b>	Patients with continuous Medicare fee-for-service coverage
<b>Exclusion criteria</b>	<p>Incomplete treatment claims data</p> <p>Under 66 years of age</p> <p>Patients receiving cytoreductive nephrectomy but no additional therapy</p> <p>Competing non-metastatic renal cell carcinoma stage IV cancer</p>
<b>Intervention(s)</b>	Initial cytoreductive nephrectomy
<b>Comparator</b>	Initial systemic therapy
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	<p>N = 537</p> <p>Initial cytoreductive nephrectomy N=190</p> <p>Initial systemic therapy N=347</p>
<b>Duration of follow-up</b>	Median follow-up 12 months (IQR 5.2, 22 months)
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	<p>Kaplan-Meier estimates the overall survival, stratified by treatment, and compared mortality with the log-rank test. Propensity for initial cytoreductive nephrectomy was calculated based on age, gender, race, marital status, urban or rural status, histologic subtype, clinical T and N classification, comorbidity index, and grade. A propensity score adjusted model was performed using Cox proportional hazards regression.</p> <p>Covariates were selected a priori based on proven impact on overall survival and included demographic factors (age, race, ethnicity, rural status), treatment era (first half and latter half of study period), cancer</p>

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severity (tumor stage, nodal status, histology), comorbidity (Charlson-Klabunde index), and SEER registry

1

2 **Study arms**3 **Initial cytoreductive nephrectomy (N = 190)**4 **Initial systemic therapy (N = 347)**

5

6 **Characteristics**7 **Arm-level characteristics**

Characteristic	Initial cytoreductive nephrectomy (N = 190)	Initial systemic therapy (N = 347)
<b>% Female</b>	n = 68 ; % = 35.8	n = 163 ; % = 47
No of events		
<b>TNM classification - 1-2</b>	n = 84 ; % = 44.2	n = 196 ; % = 56.5
No of events		
<b>TNM classification - 3-4</b>	n = 103 ; % = 54.2	n = 88 ; % = 25.4
No of events		
<b>TNM classification - missing</b>	n = 3 ; % = 1.6	n = 63 ; % = 18.1
No of events		
<b>Primary RCC type - Clear cell</b>	n = 56 ; % = 29.5	n = 215 ; % = 62
No of events		
<b>Primary RCC type - Other RCC</b>	n = 134 ; % = 70.5	n = 132 ; % = 38
No of events		
<b>Race - white</b>	n = 165 ; % = 86.8	n = 289 ; % = 83.3
No of events		
<b>Race - Non white</b>	n = 25 ; % = 13.2	n = 58 ; % = 16.7
No of events		
<b>Grade - 1-2</b>	n = 45 ; % = 23.7	n = 38 ; % = 11
No of events		

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Characteristic	Initial cytoreductive nephrectomy (N = 190)	Initial systemic therapy (N = 347)
<b>Grade - 3-4</b>	n = 115 ; % = 60.5	n = 40 ; % = 11.5
No of events		
<b>Grade - Missing</b>	n = 30 ; % = 15.8	n = 269 ; % = 77.5
No of events		

1

2 **Outcomes**3 **Survival**

Outcome	Initial cytoreductive nephrectomy vs Initial systemic therapy, , N2 = 347, N1 = 190
<b>Overall survival</b>	1.94 (1.49 to 2.53)
Hazard ratio/95% CI	

4 Overall survival - Polarity - Higher values are better

5

6 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious ( <i>Insufficient adjustment for confounders,</i> )
Directness	Directly applicable

7

8 **Manley, 2017**

**Bibliographic Reference** Manley, Brandon J; Kim, Eric H; Vetter, Joel M; Potretzke, Aaron M; Strobe, Seth A; Validation of preoperative variables and stratification of patients to help predict benefit of cytoreductive nephrectomy in the targeted therapy ERA.; International braz j urol : official journal of the Brazilian Society of Urology; 2017; vol. 43 (no. 3); 432-439

9

10 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	United States
<b>Study dates</b>	2005 - 2013
<b>Sources of funding</b>	Not reported

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<b>Inclusion criteria</b>	Patients with metastatic renal cell carcinoma who received systemic targeted therapy
<b>Exclusion criteria</b>	Patients with missing survival data Patients with incomplete clinical data Patients who received prior immunotherapy
<b>Intervention(s)</b>	Cytoreductive nephrectomy + targeted therapy
<b>Comparator</b>	Targeted therapy alone
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	N = 123 Cytoreductive nephrectomy + targeted therapy N=88 Targeted therapy alone N=35
<b>Duration of follow-up</b>	Not reported
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Kaplan-Meier estimated overall survival was compared between cytoreductive nephrectomy and targeted therapy groups. Log rank p-values were calculated to compare survival curves. Multivariate cox proportional hazards analysis was also performed adjusting for age and comorbidity

1

2 **Study arms**3 **Cytoreductive nephrectomy + targeted therapy (N = 88)**4 **Targeted therapy alone (N = 35)**

5

6 **Characteristics**7 **Arm-level characteristics**

<b>Characteristic</b>	<b>Cytoreductive nephrectomy + targeted therapy (N = 88)</b>	<b>Targeted therapy alone (N = 35)</b>
<b>Age</b>	57.4 (10.4)	57.8 (10.4)
Mean (SD)		
<b>TNM classification</b>	n = 36 ; % = 41	n = 13 ; % = 37

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Characteristic	Cytoreductive nephrectomy + targeted therapy (N = 88)	Targeted therapy alone (N = 35)
No of events		
Location of metastases - Liver	n = 18 ; % = 20	n = 11 ; % = 31
No of events		

1

2 **Outcomes**

3 **Survival**

Outcome	Cytoreductive nephrectomy + targeted therapy vs Targeted therapy alone, , N2 = 35, N1 = 88
Overall survival	0.39 (0.23 to 0.65)
Hazard ratio/95% CI	

4 Overall survival - Polarity - Higher values are better

5

6 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest)
Directness	Directly applicable

7 **Meagher, 2024**

<b>Bibliographic Reference</b>	Meagher, Margaret F; Minervini, Andrea; Mir, Maria C; Cerrato, Clara; Rebez, Giacomo; Autorino, Riccardo; Hampton, Lance; Campi, Riccardo; Kriegmair, Maximilian; Linares, Estefania; Hevia, Vital; Musquera, Maria; D'Anna, Mauricio; Roussel, Eduard; Albersen, Maarten; Pavan, Nicola; Claps, Francesco; Antonelli, Alessandro; Marchioni, Michele; Paksoy, Nail; Erdem, Selcuk; Derweesh, Ithaar H; Does the Timing of Cytoreductive Nephrectomy Impact Outcomes? Analysis of REMARCC Registry Data for Patients Receiving Tyrosine Kinase Inhibitor Versus Immune Checkpoint Inhibitor Therapy.; European urology open science; 2024; vol. 63; 71-80
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8 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Italy
	Spain

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<b>Study dates</b>	January 2006 - October 2019
<b>Sources of funding</b>	Stephen Weissman Kidney Cancer Research Fund. The funding body played a role in management and analysis of the data.
<b>Inclusion criteria</b>	Patients with metastatic RCC receiving tyrosine kinase inhibitor or immunotherapy as systemic treatment and undergoing deferred or upfront CN
<b>Exclusion criteria</b>	Exclusion criteria not reported
<b>Intervention(s)</b>	Upfront cytoreductive nephrectomy (CN)  CN prior to first line systemic therapy with tyrosine kinase inhibitor or immunotherapy.
<b>Comparator</b>	Deferred cytoreductive nephrectomy (CN)  CN following first line systemic therapy with tyrosine kinase inhibitor or immunotherapy.
<b>Outcome measures</b>	Overall survival  Mortality reported  Cancer-specific survival  Cancer specific mortality reported
<b>Number of participants</b>	N=189
<b>Duration of follow-up</b>	23.2 months median follow-up
<b>Loss to follow-up</b>	None
<b>Methods of analysis</b>	Multivariable proportional-hazards regression analysis was conducted for ACM and CSM.  The Kaplan-Meier method was used to analyse median OS and CSS, with stratification by type of systemic therapy and the timing of CN.
<b>Additional comments</b>	International multi-institutional analysis using Registry of Metastatic RCC (REMARCC) data for patients presenting with metastatic RCC (mRCC) between January 2006 and October 2019 who underwent CN.  Patients received either TKI or ICI first-line therapy. The type of systemic therapy provided and the treatment protocol were chosen at an institutional level.  The type of surgery, CN timing, and surgical approach were at the surgeon's discretion.

1

2 **Study arms**3 **Upfront CN (N = 141)**4 **Systemic therapy with tyrosine kinase inhibitor or immunotherapy following**  
5 **cytoreductive nephrectomy**

6

7 **Deferred CN (N = 48)**8 **Cytoreductive nephrectomy following systemic therapy with tyrosine kinase**  
9 **inhibitor or immunotherapy**

10

11 **Characteristics**12 **Study-level characteristics**

<b>Characteristic</b>	<b>Study (N = 189)</b>
<b>% Female</b>	n = 44 ; % = 23
No of events	
<b>Age (years)</b>	62.13 (11.07)
Mean (SD)	
<b>TNM classification - cT1</b>	n = 27 ; % = 14.3
No of events	
<b>TNM classification - cT2</b>	n = 50 ; % = 26.5
No of events	
<b>TNM classification - cT3</b>	n = 90 ; % = 47.6
No of events	
<b>TNM classification - cT4</b>	n = 21 ; % = 11.1
No of events	
<b>TNM classification - N0</b>	n = 107 ; % = 56.6
No of events	
<b>TNM classification - N1</b>	n = 79 ; % = 41.8
No of events	
<b>TNM classification - NX</b>	n = 3 ; % = 1.6

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Characteristic	Study (N = 189)
No of events	

1

2 **Outcomes**3 **Mortality**

Outcome	Upfront CN vs Deferred CN, , N2 = 48, N1 = 141
<b>All-cause mortality</b>	1.49 (1.02 to 2.17)
Hazard ratio/95% CI	
<b>Cancer-specific mortality</b>	2.04 (1.35 to 3.13)
Hazard ratio/95% CI	

4 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious <i>(Retrospective study using data from registry. It isn't clear how participants were selected. Potential confounding due to different therapeutic approaches and follow-up protocols. The systemic agents varied according to centre.)</i>
Directness	Directly applicable

5

6 **Patel, 2016**

<b>Bibliographic Reference</b>	Patel, Nishant; Woo, Jason; Liss, Michael A; Palazzi, Kerrin L; Randall, J Michael; Mehrazin, Reza; Jabaj, Ramzi; Mirheydar, Hossein S; Gillis, Kyle; Lee, Hak J; Patterson, Anthony L; Kane, Christopher J; Millard, Frederick; Derweesh, Ithaar H; Does timing of targeted therapy for metastatic renal cell carcinoma impact treatment toxicity and surgical complications? A comparison of primary and adjuvant approaches.; The Canadian journal of urology; 2016; vol. 23 (no. 2); 8227-33
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7

8 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	United States
<b>Study dates</b>	July 2007 to January 2014
<b>Sources of funding</b>	Not reported
<b>Inclusion criteria</b>	Primary systemic therapy was offered to all patients

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	Patients diagnosed with metastatic renal cell carcinoma
<b>Exclusion criteria</b>	<p>Patients with overwhelming burden of metastatic disease, with poor performance status, who proceeded to systemic therapy after the initial evaluation without a plan to offer cytoreductive nephrectomy</p> <p>Patients who undergone prior chemotherapy or immunotherapy</p> <p>Patients in whom the primary targeted treatment was other than sunitinib</p> <p>Patients were also excluded if tumour histology was not clear cell renal cell carcinoma</p> <p>Patients with &lt; 3 months follow-up with no clear evidence of death or progression within that period</p>
<b>Intervention(s)</b>	Cytoreductive nephrectomy + sunitinib
<b>Comparator</b>	Sunitinib + cytoreductive nephrectomy
<b>Outcome measures</b>	Severe adverse events
<b>Number of participants</b>	<p>N = 48</p> <p>Cytoreductive nephrectomy + sunitinib N=27</p> <p>Sunitinib + cytoreductive nephrectomy N=21</p>
<b>Duration of follow-up</b>	<p>Median follow-up from first treatment (IQR), months:</p> <p>Cytoreductive nephrectomy + sunitinib = 28.1 (11.8-36.9)</p> <p>Sunitinib + cytoreductive nephrectomy = 42.5 (8.7-61.0)</p>
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Tests performed included the independent t-test, analysis of variance, MannWhitney U test, and Kruskal-Wallace tests for continuous variables (dependent on distribution), and Chi-square and Fisher exact tests for categorical values.

Variables entered into the model included treatment group, age, race, BMI, ECOG, type of procedure performed, surgical approach, RENAL nephrometry score, tumour grade, and presence of thrombus.

## Study arms

**Cytoreductive nephrectomy + sunitinib (N = 27)**

**Sunitinib + cytoreductive nephrectomy (N = 21)**

## Characteristics

### Arm-level characteristics

Characteristic	Cytoreductive nephrectomy + sunitinib (N = 27)	Sunitinib + cytoreductive nephrectomy (N = 21)
<b>% Female</b>	n = 10 ; % = 37	n = 7 ; % = 33.3
No of events		
<b>Age</b>	59 (14.9)	57 (12.5)
Mean (SD)		
<b>Race - Caucasian</b>	n = 19 ; % = 70.4	n = 8 ; % = 40
No of events		
<b>Race - Other</b>	n = 8 ; % = 29.6	n = 12 ; % = 60
No of events		
<b>ECOG performance status - 0-1</b>	n = 19 ; % = 70.4	n = 19 ; % = 90.5
No of events		
<b>ECOG performance status - &gt;1</b>	n = 8 ; % = 29.6	n = 2 ; % = 9.5
No of events		
<b>Number of metastases - 1-5</b>	n = 13 ; % = 61.9	n = 15 ; % = 88.2
No of events		
<b>Number of metastases - &gt;5</b>	n = 8 ; % = 38.1	n = 2 ; % = 11.8
No of events		

1 **Outcomes**2 **Duration of hospital stay**

Outcome	Cytoreductive nephrectomy + sunitinib, , N = 27	Sunitinib + cytoreductive nephrectomy, , N = 21
Duration of hospital stay	4.5 (3 to 8)	7 (5 to 11)
Median (IQR)		
Surgical complications - High grade 3a/b (Clavien-Dindo)	n = 0 ; % = 0	n = 6 ; % = 26.8
No of events		

3 Duration of hospital stay - Polarity - Lower values are better

4 Surgical complications - High grade 3a/b (Clavien-Dindo) - Polarity - Lower values  
5 are better

6

7 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest. No protocol identified so unable to fully assess bias in selection of reported result.)
Directness	Directly applicable

8

9 **Poprach, 2020**

<b>Bibliographic Reference</b>	Poprach, Alexandr; Holanek, Milos; Chloupkova, Renata; Lakomy, Radek; Stanik, Michal; Fiala, Ondrej; Melichar, Bohuslav; Kopeckova, Katerina; Zemanova, Milada; Kiss, Igor; Penka, Igor; Bohosova, Julia; Buchler, Tomas; Cytoreductive Nephrectomy and Overall Survival of Patients with Metastatic Renal Cell Carcinoma Treated with Targeted Therapy-Data from the National Renis Registry.; Cancers; 2020; vol. 12 (no. 10)
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10

11 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Czech Republic - RenIS Registry database
<b>Study dates</b>	2007 to 2018
<b>Sources of funding</b>	This work was supported in part by the Ministry of Health, Czech Republic—Conceptual Development of Research Organization (MMCI 00209805) and supported by grant NV18-03-00554 and NV19-08-00250 from the Ministry of Health of Czech Republic. The RenIS registry is funded

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	in part by pharmaceutical companies producing targeted agents for renal cancer (Pfizer, Bayer, Glaxo Smith Kline, Roche, and Novartis).
<b>Inclusion criteria</b>	<p>Patients with synchronous metastatic disease subsequently treated with first-line targeted therapies with pazopanib or sunitinib</p> <p>Patients having cytoreductive nephrectomy within 3 months from the metastatic renal cell carcinoma diagnosis and subsequently treated with targeted therapies</p>
<b>Intervention(s)</b>	Cytoreductive nephrectomy + targeted therapies
<b>Comparator</b>	Targeted therapies
<b>Outcome measures</b>	<p>Progression-free survival</p> <p>Overall survival</p>
<b>Number of participants</b>	<p>N = 730</p> <p>Cytoreductive nephrectomy + targeted therapies N=458</p> <p>Targeted therapies N=272</p>
<b>Duration of follow-up</b>	Not reported
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Progression-free survival and overall survival were estimated using the Kaplan–Meier method, and all point estimates include 95% confidence intervals (95% CI). Statistical significance of differences in survival among subgroups was assessed using the log-rank test. Multivariable Cox proportional hazards models were used to evaluate the effect of all potential prognostic factors on the survival measures

1

2 **Study arms**3 **Cytoreductive nephrectomy + targeted therapies (N = 458)**4 **Targeted therapies (N = 272)**

5

6 **Characteristics**7 **Arm-level characteristics**

<b>Characteristic</b>	<b>Cytoreductive nephrectomy + targeted therapies (N = 458)</b>	<b>Targeted therapies (N = 272)</b>
<b>% Female</b>	n = 120 ; % = 26.2	n = 72 ; % = 26.5
<b>No of events</b>		

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<b>Characteristic</b>	<b>Cytoreductive nephrectomy + targeted therapies (N = 458)</b>	<b>Targeted therapies (N = 272)</b>
<b>Age</b>	62 (25 to 83)	64 (35 to 85)
Median (IQR)		
<b>Intervention subtype - Sunitinib</b>	n = 361 ; % = 78.8	n = 210 ; % = 72.2
No of events		
<b>Intervention subtype - Pazopanib</b>	n = 97 ; % = 21.2	n = 62 ; % = 22.8
No of events		
<b>Primary RCC type - Clear cell carcinoma</b>	n = 431 ; % = 94.1	n = 261 ; % = 96
No of events		
<b>Primary RCC type - Papillary cell carcinoma</b>	n = 22 ; % = 4.8	n = 8 ; % = 2.9
No of events		
<b>Primary RCC type - Chromophobe cell carcinoma</b>	n = 2 ; % = 0.4	n = 2 ; % = 0.7
No of events		
<b>Primary RCC type - Bellini duct carcinoma</b>	n = 2 ; % = 0.4	n = 0 ; % = 0
No of events		
<b>Primary RCC type - unknown</b>	n = 1 ; % = 0.2	n = 1 ; % = 0.4
No of events		
<b>MSKCC score - Good</b>	n = 3 ; % = 0.7	n = 7 ; % = 2.6
No of events		
<b>MSKCC score - Intermediate</b>	n = 417 ; % = 91	n = 215 ; % = 79
No of events		
<b>MSKCC score - Poor</b>	n = 38 ; % = 8.3	n = 50 ; % = 18.4
No of events		

Characteristic	Cytoreductive nephrectomy + targeted therapies (N = 458)	Targeted therapies (N = 272)
<b>ECog - &lt; 2</b>	n = 433 ; % = 94.5	n = 258 ; % = 94.9
No of events		
<b>ECog - ≥ 2</b>	n = 25 ; % = 5.5	n = 14 ; % = 5.1
No of events		

1

2 **Outcomes**3 **Survival**

Outcome	Cytoreductive nephrectomy + targeted therapies vs Targeted therapies, , N2 = 272, N1 = 458
<b>Progression-free survival</b>	0.63 (0.53 to 0.76)
Hazard ratio/95% CI	
<b>Overall survival</b>	0.55 (0.45 to 0.68)
Hazard ratio/95% CI	

4 Progression-free survival - Polarity - Higher values are better

5 Overall survival - Polarity - Higher values are better

6

7 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest. No protocol identified so unable to fully assess bias in selection of reported result.)
Directness	Directly applicable

8

9 **Singla, 2020**

<b>Bibliographic Reference</b>	Singla, Nirmish; Hutchinson, Ryan C; Ghandour, Rashed A; Freifeld, Yuval; Fang, Dong; Sagalowsky, Arthur I; Lotan, Yair; Bagrodia, Aditya; Margulis, Vitaly; Hammers, Hans J; Woldu, Solomon L; Improved survival after cytoreductive nephrectomy for metastatic renal cell carcinoma in the contemporary immunotherapy era: An analysis of the National Cancer Database.; Urologic oncology; 2020; vol. 38 (no. 6); 604e9-604e17
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10

1 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	US - uses the National Cancer Database (NCDB)
<b>Study dates</b>	2015 - 2016
<b>Sources of funding</b>	This work was supported, in part, by the Ruth L. Kirschstein National Research Service Award T32 CA136515-09 (N.S.), the University of Texas Southwestern Medical Center Physician Scientist Training Program (N.S.), and Dedman Family Scholarship in Clinical Care (A.B.).
<b>Inclusion criteria</b>	Patients diagnosed with metastatic renal clear cell carcinoma  Patients who received immunotherapy
<b>Exclusion criteria</b>	Patients who received any non-immunotherapy systemic therapies
<b>Intervention(s)</b>	Cytoreductive nephrectomy + immunotherapy
<b>Comparator</b>	Immunotherapy + cytoreductive nephrectomy
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	N = 221  Cytoreductive nephrectomy + immunotherapy N=197  Immunotherapy + cytoreductive nephrectomy N=24
<b>Duration of follow-up</b>	Median follow-up of 14.7 months
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Overall survival was compared between the two cohorts using Kaplan-Meier methods, and differences were analysed with the log-rank statistic. Clinicopathologic predictors for overall survival were assessed using multivariable Cox regression analyses.  Missing data were excluded from comparative analyses.  Variables of interest included patient demographics, performance of cytoreductive nephrectomy, presence of sarcomatoid features, primary tumour size, cT stage, cN stage, presence of bone, brain, liver, or lung metastases, number of known metastatic sites, and time to receipt of

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immunotherapy from diagnosis. Among patients who underwent cytoreductive nephrectomy, additional variables of interest included performance of lymph node dissection, Fuhrman grade, pT stage, pN stage, lymphovascular invasion, time to surgery from diagnosis, surgical margin status, inpatient length of stay for the operative admission, 30-day readmission rates following surgery, and timing of cytoreductive nephrectomy in relation to immunotherapy administration (immunotherapy administered before cytoreductive nephrectomy (delayed cytoreductive nephrectomy) versus upfront cytoreductive nephrectomy before immunotherapy)

1

2 **Study arms**3 **Cytoreductive nephrectomy + immunotherapy (N = 197)**4 **Immunotherapy + cytoreductive nephrectomy (N = 24)**

5

6 **Characteristics**7 **Arm-level characteristics**

Characteristic	Cytoreductive nephrectomy + immunotherapy (N = 197)	Immunotherapy + cytoreductive nephrectomy (N = 24)
<b>% Female</b>	n = 47 ; % = 23.9	n = 17 ; % = 29.2
No of events		
<b>Age</b>	56 (51 to 63)	65 (56 to 70)
Median (IQR)		
<b>TNM classification - cT1</b>	n = 25 ; % = 12.7	n = 9 ; % = 37.5
No of events		
<b>TNM classification - cT2</b>	n = 75 ; % = 38.1	n = 4 ; % = 16.7
No of events		
<b>TNM classification - cT3</b>	n = 70 ; % = 35.5	n = 9 ; % = 37.5
No of events		
<b>TNM classification - cT4</b>	n = 10 ; % = 5.1	n = 1 ; % = 4.2
No of events		
<b>TNM classification - cTx</b>	n = 17 ; % = 8.6	n = 1 ; % = 4.2
No of events		

<b>Characteristic</b>	<b>Cytoreductive nephrectomy + immunotherapy (N = 197)</b>	<b>Immunotherapy + cytoreductive nephrectomy (N = 24)</b>
<b>TNM classification - cN0</b>	n = 130 ; % = 66	n = 18 ; % = 75
No of events		
<b>TNM classification - cN1</b>	n = 49 ; % = 24.9	n = 5 ; % = 20.8
No of events		
<b>TNM classification - cNx</b>	n = 18 ; % = 9.1	n = 1 ; % = 4.2
No of events		
<b>Race - white</b>	n = 169 ; % = 85.8	n = 19 ; % = 79.2
No of events		
<b>Race - Black</b>	n = 7 ; % = 3.6	n = 3 ; % = 12.5
No of events		
<b>Race - Hispanic</b>	n = 13 ; % = 6.6	n = 2 ; % = 8.3
No of events		
<b>Race - Asian/Other</b>	n = 8 ; % = 4.1	n = 0 ; % = 0
No of events		
<b>Presence of bone metastases - Yes</b>	n = 56 ; % = 28.4	n = 17 ; % = 70.8
No of events		
<b>Presence of bone metastases - No</b>	n = 129 ; % = 65	n = 7 ; % = 29.2
No of events		
<b>Presence of bone metastases - Unknown</b>	n = 13 ; % = 6.6	n = 0 ; % = 0
No of events		
<b>Presence of brain metastases - Yes</b>	n = 14 ; % = 7.1	n = 0 ; % = 0
No of events		
<b>Presence of brain metastases - No</b>	n = 171 ; % = 86.8	n = 24 ; % = 100

<b>Characteristic</b>	<b>Cytoreductive nephrectomy + immunotherapy (N = 197)</b>	<b>Immunotherapy + cytoreductive nephrectomy (N = 24)</b>
No of events		
<b>Presence of brain metastases - Unknown</b>	n = 12 ; % = 6.1	n = 0 ; % = 0
No of events		
<b>Presence of liver metastases - Yes</b>	n = 15 ; % = 7.6	n = 2 ; % = 8.3
No of events		
<b>Presence of liver metastases - No</b>	n = 170 ; % = 86.3	n = 22 ; % = 91.7
No of events		
<b>Presence of liver metastases - Unknown</b>	n = 12 ; % = 6.1	n = 0 ; % = 0
No of events		
<b>Presence of lung metastases - Yes</b>	n = 135 ; % = 68.5	n = 12 ; % = 50
No of events		
<b>Presence of lung metastases - No</b>	n = 49 ; % = 24.9	n = 12 ; % = 50
No of events		
<b>Presence of lung metastases - Unknown</b>	n = 13 ; % = 6.6	n = 0 ; % = 0
No of events		
<b>Presence of bone, liver, or brain metastases - Yes</b>	n = 76 ; % = 38.6	n = 17 ; % = 70.8
No of events		
<b>Presence of bone, liver, or brain metastases - No</b>	n = 109 ; % = 55.3	n = 7 ; % = 29.2
No of events		
<b>Presence of bone, liver, or brain metastases - Unknown</b>	n = 12 ; % = 6.1	n = 0 ; % = 0

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Characteristic	Cytoreductive nephrectomy + immunotherapy (N = 197)	Immunotherapy + cytoreductive nephrectomy (N = 24)
No of events		

1

2 **Outcomes**3 **Survival**

Outcome	Cytoreductive nephrectomy + immunotherapy vs Immunotherapy + cytoreductive nephrectomy, , N2 = 24, N1 = 197
Overall survival	0.25 (0.03 to 1.83)
Hazard ratio/95% CI	

4 Overall survival - Polarity - Higher values are better

5

6 **Critical appraisal – ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious ( <i>Insufficient adjustment for confounders, missing data were excluded from comparative analyses, and limited reporting on missing data and protocol not identified</i> )
Directness	Directly applicable

7

8 **Stroup, 2013**

<b>Bibliographic Reference</b>	Stroup, Sean P; Raheem, Omer A; Palazzi, Kerrin L; Liss, Michael A; Mehrazin, Reza; Kopp, Ryan P; Patel, Nishant; Cohen, Seth A; Park, Samuel K; Patterson, Anthony L; Kane, Christopher J; Millard, Frederick; Derweesh, Ithaar H; Does timing of cytoreductive nephrectomy impact patient survival with metastatic renal cell carcinoma in the tyrosine kinase inhibitor era? A multi-institutional study.; Urology; 2013; vol. 81 (no. 4); 805-11
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10 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	US - multi-institutional (University of California San Diego Medical Centre; San Diego Veterans Administration Medical Centre; University of Tennessee Health Sciences Centre Memphis)
<b>Study dates</b>	May 2005 to August 2009

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<b>Sources of funding</b>	Not reported
<b>Inclusion criteria</b>	Patients diagnosed with metastatic renal cell carcinoma
<b>Exclusion criteria</b>	<p>Patients with an overwhelming burden of metastatic disease, with poor performance status, who proceeded to systemic therapy after the initial evaluation without a plan to offer cytoreductive nephrectomy</p> <p>Patients who had undergone prior chemotherapy or immunotherapy</p> <p>Patients in whom the primary targeted treatment was other than sunitinib</p> <p>Patients with &lt;3 months follow-up with no clear evidence of death or progression within that period</p> <p>Tumour histology was not clear cell renal cell carcinoma</p>
<b>Intervention(s)</b>	Cytoreductive nephrectomy + sunitinib
<b>Comparator</b>	<p>Sunitinib + cytoreductive nephrectomy</p> <p>Sunitinib alone</p>
<b>Outcome measures</b>	<p>Overall survival</p> <p>Cancer-specific survival</p>
<b>Number of participants</b>	<p>N = 35</p> <p>Cytoreductive nephrectomy + sunitinib N=17</p> <p>Sunitinib + cytoreductive nephrectomy N=11</p> <p>Sunitinib alone N = 7</p>
<b>Duration of follow-up</b>	<p>Follow-up from first treatment, month</p> <p>Cytoreductive nephrectomy + sunitinib = 29.9 (IQR: 16.9-46.8)</p> <p>Sunitinib + cytoreductive nephrectomy = 32 (IQR: 24.5-70.8)</p> <p>Sunitinib alone = 4.6 (IQR: 3.5-7.5)</p> <p>Follow-up from surgery, month</p>

	Cytoreductive nephrectomy + sunitinib = 29.9 (IQR: 16.9-46.8)
	Sunitinib + cytoreductive nephrectomy = 22.8 (IQR: 16.8-34.7)
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	<p>Kaplan-Meier analysis was used to demonstrate unadjusted survival outcomes, and Cox regression was used to examine associations between survival outcomes and predictors of interest.</p> <p>The following variables were tried in the multivariate Cox regression models and removed if nonsignificant: age, race, BMI, ECOG score (0 or 1 vs &gt;1), tumour size (&lt;7 vs ≥7 cm), tumour grade, inferior vena cava thrombus, and number of metastatic lesions (&lt;5 vs ≥5)</p>

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2 **Study arms**3 **Cytoreductive nephrectomy + sunitinib (N = 17)**4 **Sunitinib + cytoreductive nephrectomy (N = 18)**5 **Sunitinib alone (N = 7)**6 **Sunitinib + cytoreductive nephrectomy (Outcome) (N = 11)**

7

8 **Characteristics**9 **Arm-level characteristics**

Characteristic	Cytoreductive nephrectomy + sunitinib (N = 17)	Sunitinib + cytoreductive nephrectomy (N = 18)	Sunitinib alone (N = 7)	Sunitinib + cytoreductive nephrectomy (Outcome) (N = 11)
<b>% Female</b>	n = 7 ; % = 41.2	n = 10 ; % = 55.6	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Age</b>	57 (17.2)	55 (9.9)	<i>empty data</i>	<i>empty data</i>
Mean (SE)				
<b>TNM classification - pT1</b>	n = 0 ; % = 0	n = 4 ; % = 36.4	<i>empty data</i>	<i>empty data</i>
No of events				
<b>TNM classification - pT2</b>	n = 2 ; % = 28.6	n = 4 ; % = 36.4	<i>empty data</i>	<i>empty data</i>
No of events				

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<b>Characteristic</b>	<b>Cytoreductive nephrectomy + sunitinib (N = 17)</b>	<b>Sunitinib + cytoreductive nephrectomy (N = 18)</b>	<b>Sunitinib alone (N = 7)</b>	<b>Sunitinib + cytoreductive nephrectomy (Outcome) (N = 11)</b>
<b>TNM classification - pT3</b>	n = 4 ; % = 57.1	n = 2 ; % = 18.2	<i>empty data</i>	<i>empty data</i>
No of events				
<b>TNM classification - pT4</b>	n = 1 ; % = 14.3	n = 1 ; % = 9.1	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Location of metastases - lung</b>	n = 13 ; % = 76.5	n = 11 ; % = 61.1	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Location of metastases - Liver</b>	n = 5 ; % = 29.4	n = 7 ; % = 38.9	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Location of metastases - Lymphadenopathy</b>	n = 5 ; % = 29.4	n = 5 ; % = 27.8	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Location of metastases - Brain</b>	n = 1 ; % = 5.9	n = 2 ; % = 11.1	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Location of metastases - bone</b>	n = 6 ; % = 35.3	n = 3 ; % = 16.7	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Location of metastases - Adrenal</b>	n = 3 ; % = 17.6	n = 6 ; % = 33.3	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Race - Caucasian</b>	n = 8 ; % = 72.7	n = 9 ; % = 50	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Race - Other</b>	n = 3 ; % = 27.3	n = 9 ; % = 50	<i>empty data</i>	<i>empty data</i>

Characteristic	Cytoreductive nephrectomy + sunitinib (N = 17)	Sunitinib + cytoreductive nephrectomy (N = 18)	Sunitinib alone (N = 7)	Sunitinib + cytoreductive nephrectomy (Outcome) (N = 11)
No of events				
<b>ECOG status - 0-1</b>	n = 14 ; % = 82.4	n = 12 ; % = 66.7	<i>empty data</i>	<i>empty data</i>
No of events				
<b>ECOG status - 2-3</b>	n = 3 ; % = 17.6	n = 6 ; % = 33.3	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Number of metastases - 1-5</b>	n = 8 ; % = 53.3	n = 10 ; % = 58.8	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Number of metastases - &gt;5</b>	n = 7 ; % = 46.7	n = 7 ; % = 41.2	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Nephrectomy - Radical</b>	n = 17 ; % = 100	n = 5 ; % = 45.5	<i>empty data</i>	<i>empty data</i>
No of events				
<b>Nephrectomy - Partial</b>	n = 0 ; % = 0	n = 6 ; % = 54.4	<i>empty data</i>	<i>empty data</i>
No of events				

1

2 **Outcomes**3 **Survival**

Outcome	Cytoreductive nephrectomy + sunitinib vs Sunitinib + cytoreductive nephrectomy (Outcome), , N2 = 17, N1 = 11	Sunitinib alone vs Cytoreductive nephrectomy + sunitinib, , N2 = 7, N1 = 17
<b>Cancer specific survival</b>	7.24 (0.93 to 56.63)	10.17 (2.39 to 43.3)
Hazard ratio/95% CI		

Outcome	Cytoreductive nephrectomy + sunitinib vs Sunitinib + cytoreductive nephrectomy (Outcome), , N2 = 17, N1 = 11	Sunitinib alone vs Cytoreductive nephrectomy + sunitinib, , N2 = 7, N1 = 17
Overall death	7.95 (1.03 to 61.63)	8.38 (2.2 to 31.9)
Hazard ratio/95% CI		

1 Cancer specific survival - Polarity - Higher values are better

2 Overall death - Polarity - Lower values are better

3

#### 4 Critical appraisal – ROBINS-I checklist

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest and limited reporting on missing data and protocol not identified)
Directness	Directly applicable

5

#### 6 Takemura, 2023

**Bibliographic Reference** Takemura, Kosuke; Ernst, Matthew S; Navani, Vishal; Wells, J Connor; Bakouny, Ziad; Donskov, Frede; Basappa, Naveen S; Wood, Lori A; Meza, Luis; Pal, Sumanta K; Szabados, Bernadett; Powles, Thomas; Beuselinck, Benoit; McKay, Rana R; Lee, Jae-Lyun; Ernst, D Scott; Kapoor, Anil; Yuasa, Takeshi; Choueiri, Toni K; Heng, Daniel Y C; Characterization of Patients with Metastatic Renal Cell Carcinoma Undergoing Deferred, Upfront, or No Cytoreductive Nephrectomy in the Era of Combination Immunotherapy: Results from the International Metastatic Renal Cell Carcinoma Database Consortium.; European urology oncology; 2023

7

#### 8 Study details

Study type	Retrospective cohort study
Study location	Multicentre collaboration involving participants from more than 40 institutions worldwide: Australia, Belgium, Canada, Denmark, Germany, Greece, Italy, Japan, Mexico, Netherlands, New Zealand, Singapore, South Korea, Spain, UK, and the United States
Study dates	Not reported
Sources of funding	This study was supported by the Yasuda Medical Foundation (grant to Kosuke Takemura). The sponsor played no direct role in the study

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<b>Inclusion criteria</b>	<p>Patients received frontline immuno-oncology based combinations, including immuno-oncology/immuno-oncology doublet therapy (ie, nivolumab plus ipilimumab) and immuno-oncology/tyrosine kinase inhibitor combination therapy (ie, pembrolizumab plus axitinib, avelumab plus axitinib, nivolumab plus cabozantinib, or pembrolizumab plus lenvatinib)</p> <p>Patients diagnosed with either synchronous metastatic renal cell carcinoma or metachronous metastatic renal cell carcinoma without previous nephrectomy for localized renal cell carcinoma</p> <p>Patient did not die nor were censored within a fixed landmark time, with different landmark time periods (6, 9, 12, and 18 months) examined</p>
<b>Exclusion criteria</b>	<p>Patients with missing data for the date of diagnosis or metastasis</p> <p>Patients with missing data for whether they underwent nephrectomy, or the date of nephrectomy</p> <p>Patients with missing data for whether they are dead or alive, or the date of death or last follow-up</p>
<b>Intervention(s)</b>	Deferred cytoreductive nephrectomy
<b>Comparator</b>	<p>Upfront cytoreductive nephrectomy</p> <p>Immuno-oncology alone</p>
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	<p>N = 807</p> <p>Deferred cytoreductive nephrectomy N=40</p> <p>Upfront cytoreductive nephrectomy N=327</p> <p>Immuno-oncology alone N=440</p>
<b>Duration of follow-up</b>	12 months
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Kaplan-Meier curves were constructed, and the log-rank test was carried out to compare post-landmark overall survival curves by cytoreductive nephrectomy status. Cox proportional-hazards regression was used to assess overall survival hazard ratios by cytoreductive nephrectomy status, operationalised as a time-varying covariate to account for immortal time bias.

1 **Study arms**2 **Deferred cytoreductive nephrectomy (N = 40)**3 **Upfront cytoreductive nephrectomy (N = 327)**4 **Immuno-oncology alone (N = 440)**

5

6 **Characteristics**7 **Arm-level characteristics**

<b>Characteristic</b>	<b>Deferred cytoreductive nephrectomy (N = 40)</b>	<b>Upfront cytoreductive nephrectomy (N = 327)</b>	<b>Immuno-oncology alone (N = 440)</b>
<b>% Female</b>	n = 6 ; % = 25	n = 45 ; % = 25	n = 52 ; % = 29
No of events			
<b>Age</b>	57 (50 to 65)	60 (52 to 67)	63 (57 to 70)
Median (IQR)			
<b>Primary RCC type - Non-clear cell</b>	n = 9 ; % = 45	n = 21 ; % = 14	n = 9 ; % = 7.6
No of events			
<b>Location of metastases - Brain</b>	n = 2 ; % = 8.7	n = 9 ; % = 5.2	n = 14 ; % = 8.1
No of events			
<b>Location of metastases - bone</b>	n = 6 ; % = 26	n = 41 ; % = 23	n = 77 ; % = 44
No of events			
<b>Location of metastases - Liver</b>	n = 1 ; % = 4.3	n = 23 ; % = 13	n = 32 ; % = 19
No of events			
<b>IMDC prognostic - Favorable</b>	n = 0 ; % = 0	n = 13 ; % = 7.7	n = 3 ; % = 2
No of events			
<b>IMDC prognostic - Intermediate</b>	n = 10 ; % = 53	n = 116 ; % = 69	n = 83 ; % = 54
No of events			

Characteristic	Deferred cytoreductive nephrectomy (N = 40)	Upfront cytoreductive nephrectomy (N = 327)	Immuno-oncology alone (N = 440)
<b>IMDC prognostic - Poor</b>	n = 9 ; % = 47	n = 39 ; % = 23	n = 67 ; % = 44
No of events			

1

2 **Outcomes**3 **Mortality**

Outcome	Deferred cytoreductive nephrectomy, , N = 40	Upfront cytoreductive nephrectomy, , N = 327	Immuno-oncology alone, , N = 440
<b>Mortality</b>	n = 1 ; % = 2.5	n = 43 ; % = 13	n = 107 ; % = 24
No of events			

4 Mortality - Polarity - Lower values are better

5

6 **Critical appraisal – ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious ( <i>Insufficient adjustment for confounders and protocol not identified</i> )
Directness	Directly applicable

7

8 **Xu, 2019**

<b>Bibliographic Reference</b>	Xu, W.-H.; Wang, J.; Huo, D.-Z.; Yin, G.-C.; Cao, D.-L.; Shi, G.-H.; Qu, Y.-Y.; Ye, D.-W.; Zhang, H.-L.; C-reactive protein levels and survival following cytoreductive nephrectomy in 118 patients with metastatic renal cell carcinoma treated with sunitinib: A retrospective study; Medical Science Monitor; 2019; vol. 25; 8984-8994
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10 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	China - Department of Urology, Fudan University Shanghai Cancer Centre (FUSCC) Shanghai,
<b>Study dates</b>	May 2009 and June 2018
<b>Sources of funding</b>	Not reported

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<b>Inclusion criteria</b>	Patients who had metastases on initial diagnosis and who were treated by urologists according to the standard treatment at our institution
<b>Intervention(s)</b>	Cytoreductive nephrectomy+ sunitinib
<b>Comparator</b>	Sunitinib alone
<b>Outcome measures</b>	Progression-free survival Overall survival
<b>Number of participants</b>	N = 118  Cytoreductive nephrectomy+ sunitinib N=70  Sunitinib alone N=48
<b>Duration of follow-up</b>	Last day of follow-up (8th July 2018)
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	The follow-up duration was determined using the Kaplan-Meier method with 95% confidence intervals and assessed using a log-rank test.

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2 **Study arms**3 **Cytoreductive nephrectomy+ sunitinib (N = 70)**4 **Sunitinib alone (N = 48)**

5

6 **Characteristics**7 **Arm-level characteristics**

<b>Characteristic</b>	<b>Cytoreductive nephrectomy+ sunitinib (N = 70)</b>	<b>Sunitinib alone (N = 48)</b>
<b>% Female</b>	n = 14 ; % = 34.3	n = 10 ; % = 20.8
No of events		
<b>TNM classification - T1</b>	n = 0 ; % = 0	n = 2 ; % = 4.2
No of events		
<b>TNM classification - T2</b>	n = 6 ; % = 8.6	n = 9 ; % = 18.8
No of events		
<b>TNM classification - T3</b>	n = 35 ; % = 50	n = 27 ; % = 56.2

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<b>Characteristic</b>	<b>Cytoreductive nephrectomy+ sunitinib (N = 70)</b>	<b>Sunitinib alone (N = 48)</b>
No of events		
<b>TNM classification - T4</b>	n = 29 ; % = 41.4	n = 10 ; % = 20.48
No of events		
<b>TNM classification - N0</b>	n = 38 ; % = 54.3	n = 21 ; % = 43.8
No of events		
<b>TNM classification - N1</b>	n = 32 ; % = 45.7	n = 27 ; % = 56.3
No of events		
<b>Primary RCC type - Clear cell</b>	n = 55 ; % = 78.6	n = 37 ; % = 77.1
No of events		
<b>Primary RCC type - Non-clear cell</b>	n = 15 ; % = 21.4	n = 11 ; % = 22.9
No of events		
<b>Location of metastases - lung</b>	n = 39 ; % = 55.7	n = 28 ; % = 58.3
No of events		
<b>Location of metastases - Bone</b>	n = 26 ; % = 37.1	n = 14 ; % = 29.2
No of events		
<b>Location of metastases - Liver</b>	n = 8 ; % = 11.4	n = 8 ; % = 16.7
No of events		
<b>Location of metastases - Brain</b>	n = 1 ; % = 1.4	n = 2 ; % = 4.2
No of events		
<b>Location of metastases - Pleural</b>	n = 3 ; % = 4.3	n = 2 ; % = 4.2
No of events		
<b>Location of metastases - Vena cava</b>	n = 2 ; % = 2.9	n = 8 ; % = 16.7
No of events		
<b>Location of metastases - Retroperitoneal</b>	n = 2 ; % = 2.9	n = 7 ; % = 14.6
No of events		

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Characteristic	Cytoreductive nephrectomy+ sunitinib (N = 70)	Sunitinib alone (N = 48)
<b>Location of metastases - Other</b>	n = 12 ; % = 17.1	n = 10 ; % = 20.8
No of events		
<b>IMDC risk category - Intermediate-risk</b>	n = 36 ; % = 51.4	n = 20 ; % = 41.7
No of events		
<b>IMDC risk category - High-risk</b>	n = 34 ; % = 48.6	n = 27 ; % = 58.3
No of events		

1

2 **Outcomes**3 **Survival**

Outcome	Cytoreductive nephrectomy+ sunitinib vs Sunitinib alone, , N2 = 48, N1 = 70
<b>Progression-free survival</b>	1.13 (0.77 to 1.67)
Hazard ratio/95% CI	
<b>Overall survival</b>	0.96 (0.67 to 1.41)
Hazard ratio/95% CI	

4 Progression-free survival - Polarity - Higher values are better

5 Overall survival - Polarity - Higher values are better

6

7 **Critical appraisal – ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest and limited reporting on missing data and protocol not identified)
Directness	Directly applicable

8

9 **Yoshino, 2022**

**Bibliographic Reference** Yoshino, Maki; Ishihara, Hiroki; Nemoto, Yuki; Nakamura, Kazutaka; Nishimura, Koichi; Tachibana, Hidekazu; Fukuda, Hironori; Toki, Daisuke; Yoshida, Kazuhiko; Kobayashi, Hirohito; Iizuka, Junpei; Shimmura, Hiroaki; Hashimoto, Yasunobu; Tanabe, Kazunari; Kondo, Tsunenori;

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Takagi, Toshio; Therapeutic role of deferred cytoreductive nephrectomy in patients with metastatic renal cell carcinoma treated with nivolumab plus ipilimumab.; Japanese journal of clinical oncology; 2022; vol. 52 (no. 10); 1208-1214

1

2 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Japan - five affiliated institutions (Tokyo Women's Medical University Hospital, Tokyo Women's Medical University Adachi Medical Centre, Saiseikai Kawaguchi General Hospital, Saiseikai Kurihashi Hospital and Tokiwakai Joban Hospital).
<b>Study dates</b>	September 2016 and July 2021
<b>Sources of funding</b>	Not reported
<b>Inclusion criteria</b>	Patients with synchronous metastatic renal cell carcinoma received nivolumab plus ipilimumab as first-line therapy
<b>Exclusion criteria</b>	Patients whose duration of post-treatment follow-up was short (i.e. <1 month) or whose clinical data were missing
<b>Intervention(s)</b>	Upfront cytoreductive nephrectomy + nivolumab plus ipilimumab initiation
<b>Comparator</b>	No cytoreductive nephrectomy Nivolumab plus ipilimumab + deferred cytoreductive nephrectomy
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	N = 41 Upfront cytoreductive nephrectomy + nivolumab plus ipilimumab initiation N=21 No cytoreductive nephrectomy N=13 Nivolumab plus ipilimumab + deferred cytoreductive nephrectomy N=7
<b>Duration of follow-up</b>	Median of 12.0 months (interquartile range: 7.0–21.0 months)

<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Survival was calculated using the Kaplan–Meier method and compared using the log-rank test.

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2 **Study arms**3 **Upfront cytoreductive nephrectomy + nivolumab plus ipilimumab initiation (N =**  
4 **21)**5 **No cytoreductive nephrectomy (N = 13)**6 **Nivolumab plus ipilimumab + deferred cytoreductive nephrectomy (N = 7)**

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8 **Characteristics**9 **Arm-level characteristics**

<b>Characteristic</b>	<b>Upfront cytoreductive nephrectomy + nivolumab plus ipilimumab initiation (N = 21)</b>	<b>No cytoreductive nephrectomy (N = 13)</b>	<b>Nivolumab plus ipilimumab + deferred cytoreductive nephrectomy (N = 7)</b>
<b>% Female</b>	n = 8 ; % = 38.1	n = 5 ; % = 38.5	n = 1 ; % = 14.3
No of events			
<b>Age</b>	64 (53.5 to 69.5)	70 (56.5 to 69.5)	56 (47 to 64)
Median (IQR)			
<b>Primary RCC type - Clear-cell carcinoma</b>	n = 18 ; % = 85.7	n = 8 ; % = 61.5	n = 5 ; % = 71.4
No of events			
<b>Primary RCC type - Non-clear-cell carcinoma</b>	n = 3 ; % = 14.3	n = 2 ; % = 20	n = 1 ; % = 14.3
No of events			
<b>Primary RCC type - Papillary renal cell carcinoma</b>	n = 2 ; % = 9.52	n = 1 ; % = 7.7	n = 0 ; % = 0
No of events			

Characteristic	Upfront cytoreductive nephrectomy + nivolumab plus ipilimumab initiation (N = 21)	No cytoreductive nephrectomy (N = 13)	Nivolumab plus ipilimumab + deferred cytoreductive nephrectomy (N = 7)
<b>Primary RCC type - Others</b>	n = 1 ; % = 4.76	n = 1 ; % = 7.7	n = 1 ; % = 14.3
No of events			
<b>Primary RCC type - unknown</b>	n = 0 ; % = 0	n = 3 ; % = 23.1	n = 1 ; % = 14.3
No of events			
<b>Location of metastases - Liver</b>	n = 3 ; % = 14.3	n = 1 ; % = 7.7	n = 1 ; % = 14.3
No of events			
<b>Location of metastases - bone</b>	n = 7 ; % = 33.3	n = 0 ; % = 0	n = 1 ; % = 14.3
No of events			
<b>IMDC risk - Intermediate</b>	n = 14 ; % = 66.7	n = 4 ; % = 30.8	n = 1 ; % = 14.3
No of events			
<b>IMDC risk - Poor</b>	n = 7 ; % = 33.3	n = 9 ; % = 69.2	n = 5 ; % = 71.4
No of events			
<b>IMDC risk - Unknown</b>	n = 0 ; % = 0	n = 0 ; % = 0	n = 1 ; % = 14.3
No of events			

1

2 **Outcomes**3 **Survival**

Outcome	Upfront cytoreductive nephrectomy + nivolumab plus ipilimumab initiation, , N = 21	No cytoreductive nephrectomy, , N = 13	Nivolumab plus ipilimumab + deferred cytoreductive nephrectomy, , N = 7
<b>Overall survival - Nivolumab plus ipilimumab</b>	n = 15 ; % = 72.4	<i>empty data</i>	n = 7 ; % = 100

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Outcome	Upfront cytoreductive nephrectomy + nivolumab plus ipilimumab initiation, , N = 21	No cytoreductive nephrectomy, , N = 13	Nivolumab plus ipilimumab + deferred cytoreductive nephrectomy, , N = 7
<b>+ deferred cytoreductive nephrectomy vs. Upfront cytoreductive nephrectomy + nivolumab plus ipilimumab initiation</b>			
No of events			
<b>Overall survival - Nivolumab plus ipilimumab + deferred cytoreductive nephrectomy vs. No cytoreductive nephrectomy</b>	<i>empty data</i>	n = 8 ; % = 58.2	n = 7 ; % = 100
No of events			

1 Overall survival - Polarity - Higher values are better

2

### 3 Critical appraisal – ROBINS-I checklist

Question	Answer
Risk of bias judgement	Serious (Analyses were not controlled for all confounding variables of interest)
Directness	Directly applicable

4

### 5 You, 2011

<b>Bibliographic Reference</b>	You, Dalsan; Jeong, In Gab; Ahn, Jin-Hee; Lee, Dae Ho; Lee, Jae-Lyun; Hong, Jun Hyuk; Ahn, Hanjong; Kim, Choung-Soo; The value of cytoreductive nephrectomy for metastatic renal cell carcinoma in the era of targeted therapy.; The Journal of urology; 2011; vol. 185 (no. 1); 54-9
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### 7 Study details

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Republic of Korea
<b>Study dates</b>	November 2006 to December 2009

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<b>Sources of funding</b>	Not reported
<b>Inclusion criteria</b>	Patients diagnosed with metastatic renal clear cell carcinoma  Patient with observable disease, and adequate haematological, coagulation, hepatic, renal and cardiopulmonary function
<b>Exclusion criteria</b>	Non-clear cell type renal cell carcinoma  No evidence of residual disease due to complete nephrectomy and metastasectomy
<b>Intervention(s)</b>	Cytoreductive nephrectomy + targeted therapy
<b>Comparator</b>	Targeted therapy alone
<b>Outcome measures</b>	Progression-free survival  Overall survival
<b>Number of participants</b>	N = 78  Cytoreductive nephrectomy + targeted therapy N=45  Targeted therapy alone N=33
<b>Duration of follow-up</b>	Not reported
<b>Loss to follow-up</b>	Not reported
<b>Methods of analysis</b>	Kaplan-Meier survival curves were used to estimate progression-free survival and overall survival, which were compared using the log-rank test. Cox proportional hazards model estimates the prognostic significance of each variable, including the Memorial Sloan-Kettering Cancer Centre prognostic factors
<b>Additional comments</b>	



1 **Study arms**2 **Cytoreductive nephrectomy + targeted therapy (N = 45)**3 **Targeted therapy alone (N = 33)**

4

5 **Characteristics**6 **Arm-level characteristics**

<b>Characteristic</b>	<b>Cytoreductive nephrectomy + targeted therapy (N = 45)</b>	<b>Targeted therapy alone (N = 33)</b>
<b>% Female</b>	n = 36 ; % = 80	n = 21 ; % = 64
No of events		
<b>Location of metastases - Brain</b>	n = 3 ; % = 7	n = 1 ; % = 3
No of events		
<b>Targeted agent - Sunitinib</b>	n = 34 ; % = 76	n = 29 ; % = 88
No of events		
<b>Targeted agent - Sorafenib</b>	n = 11 ; % = 24	n = 4 ; % = 12
No of events		
<b>Number metastatic sites - One</b>	n = 30 ; % = 67	n = 15 ; % = 45
No of events		
<b>Number metastatic sites - Greater than 1</b>	n = 15 ; % = 33	n = 18 ; % = 55
No of events		
<b>Liver metastasis - No</b>	n = 43 ; % = 96	n = 28 ; % = 85
No of events		
<b>Liver metastasis - Yes</b>	n = 2 ; % = 4	n = 5 ; % = 15
No of events		

7

1 **Outcomes**

2 **Survival**

Outcome	Cytoreductive nephrectomy + targeted therapy vs Targeted therapy alone, , N2 = 33, N1 = 45
Progression-free survival	1.5 (0.7 to 3.5)
Hazard ratio/95% CI	
Overall survival	1.9 (0.9 to 4.3)
Hazard ratio/95% CI	

3 Progression-free survival - Polarity - Higher values are better

4 Overall survival - Polarity - Higher values are better

5

6 **Critical appraisal –ROBINS-I checklist**

Question	Answer
Risk of bias judgement	Serious <i>(Analyses were not controlled for all confounding variables of interest)</i>
Directness	Directly applicable

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1 **Review 2 Systemic anti-cancer therapy then cytoreductive nephrectomy**2 **Non-randomised controlled trials evidence**3 **Bhindi, 2018**

**Bibliographic Reference** Bhindi, B.; Habermann, E.B.; Mason, R.J.; Costello, B.A.; Pagliaro, L.C.; Thompson, R.H.; Leibovich, B.C.; Boorjian, S.A.; Comparative Survival following Initial Cytoreductive Nephrectomy versus Initial Targeted Therapy for Metastatic Renal Cell Carcinoma; Journal of Urology; 2018; vol. 200 (no. 3); 528-534

4

5 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	United States - uses national clinical oncology (NCDB) database
<b>Study dates</b>	2006 - 2013
<b>Sources of funding</b>	Not reported
<b>Inclusion criteria</b>	Diagnosis with kidney cancer between 2006 and 2013 with being metastatic at the diagnosis
<b>Exclusion criteria</b>	another prior cancer history, non RCC or unknown histology, missing vital status or follow-up, a renal ablative procedure, inability to determine cytoreductive nephrectomy (CN) status, missing time to surgery in patients who underwent CN, missing time to targeted therapy (TT) in those who received TT and no treatment (CN or TT) within 3 months of diagnosis
<b>Intervention(s)</b>	Deferred cytoreductive nephrectomy - no information about the SACT
<b>Comparator</b>	SACT alone
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	Deferred cytoreductive nephrectomy - 7526 SACT alone - not reported
<b>Duration of follow-up</b>	Until death
<b>Methods of analysis</b>	Cohort characteristics were compared between groups using the Wilcoxon rank sum test and the chi-square test. Factors associated with TT after initial CN and CN after initial TT were evaluated in separate multivariable Cox regression models. Overall survival was compared between the initial CN and initial TT groups using Kaplan-Meier analysis and Cox regression models with censoring at end of the study period or due to loss to follow-up. To account for differences in baseline characteristics which may have influenced the initial treatment selection authors used inverse probability of treatment weighting (IPTW) based on the propensity to receive initial CN vs

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	initial TT, which was in turn estimated by logistic regression. Additional sensitivity analysis was also performed without assumptions to evaluate the potential impact of unmeasured confounders on the study conclusion.
<b>Additional comments</b>	The study does not report the number of participants in the SACT alone arm and baseline data for the protocol relevant comparison arm (deferred CN and SACT alone). Therefore, the baseline data extracted in EPPI is for the overall participants included in the study.

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2 **Study arms**3 **Deferred cytoreductive nephrectomy (N = 7520)**

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5 **SACT alone (N = NR)**

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7 **Characteristics**8 **Study-level characteristics**

<b>Characteristic</b>	<b>Study (N = 15068)</b>
<b>% Female</b>	n = 4662 ; % = 30.9
Sample size	
<b>Age - ≤50</b>	n = 2456 ; % = 16.3
Sample size	
<b>Age - 51–60</b>	n = 4629 ; % = 30.7
Sample size	
<b>Age - 61–70</b>	n = 4758 ; % = 31.6
Sample size	
<b>Age - &gt;70</b>	n = 3225 ; % = 21.4
Sample size	
<b>TNM classification - cT1</b>	n = 2537 ; % = 16.8
Sample size	
<b>TNM classification - cT2</b>	n = 3547 ; % = 23.5
Sample size	
<b>TNM classification - cT3</b>	n = 4406 ; % = 29.2
Sample size	

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Characteristic	Study (N = 15068)
<b>TNM classification - cT4</b>	n = 1478 ; % = 9.8
Sample size	
<b>TNM classification - cTx</b>	n = 3100 ; % = 20.6
Sample size	
<b>Primary RCC type - Clear cell</b>	n = 6374 ; % = 42.3
Sample size	
<b>Primary RCC type - Non-clear cell</b>	n = 1417 ; % = 9.4
Sample size	
<b>Primary RCC type - RCC- unknown subtype</b>	n = 7227 ; % = 48.3
Sample size	

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3 **Outcomes**

4 **Overall survival**

Outcome	Deferred cytoreductive nephrectomy vs SACT alone, , N2 = , N1 =
<b>Overall survival</b>	0.53 (0.46 to 0.6)
Hazard ratio/95% CI	

5 Overall survival - Polarity - Lower values are better

6

7 **Critical appraisal - ROBIS checklist**

Question	Answer
Risk of bias judgement	Serious <i>Insufficient adjustment for confounders, limited reporting on missing data and protocol not identified</i>
Directness	Directly applicable

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1 **Bhindi, 2020**

**Bibliographic Reference** Bhindi, Bimal; Graham, Jeffrey; Wells, J Connor; Bakouny, Ziad; Donskov, Frede; Fraccon, Anna; Pasini, Felice; Lee, Jae Lyun; Basappa, Naveen S; Hansen, Aaron; Kollmannsberger, Christian K; Kanesvaran, Ravindran; Yuasa, Takeshi; Ernst, D Scott; Srinivas, Sandy; Rini, Brian I; Bowman, Isaac; Pal, Sumanta K; Choueiri, Toni K; Heng, Daniel Y C; Deferred Cyto-reductive Nephrectomy in Patients with Newly Diagnosed Metastatic Renal Cell Carcinoma.; European urology; 2020; vol. 78 (no. 4); 615-623

2

3 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	International mRCC Database Consortium (IMDC) databased used. This covers 33 centres in Canada, the USA, Belgium, Denmark, Germany, Greece, Italy, South Korea, Singapore, Japan, New Zealand, and Australia
<b>Study dates</b>	2006-2018
<b>Sources of funding</b>	No funding received
<b>Inclusion criteria</b>	first systemic therapy was sunitinib
<b>Exclusion criteria</b>	first treatment with sunitinib greater than 12 months after diagnosis; unknown timings of deferred cytoreductive nephrectomy (CN); missing data on confounding variables
<b>Intervention(s)</b>	Deferred cytoreductive nephrectomy - followed by initial treatment with sunitinib; median time to receive CN after sunitinib was 7.8 months.
<b>Comparator</b>	SACT alone - first-line treatment with sunitinib
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	Deferred CN arm - 85 SACT alone arm - 651
<b>Duration of follow-up</b>	Not reported - Median follow-up time for the survivors was 25 months (IQR 10–49)
<b>Methods of analysis</b>	Baseline cohort characteristics were compared between groups using the Kruskal-Wallis and the chi-square tests for continuous and categorical variables. Survival curves were plotted using the Kaplan-Meier method for OS outcomes, and were compared using the log-rank test. Multivariable Cox proportional hazards models were to adjust for the covariates for the deferred CN vs sunitinib alone arms. Furthermore, sensitivity analyses was carried out by using backward selection (with threshold for model inclusion set at $p < 0.05$ ) and the change-of-estimate approach (whereby only covariates that changed the main effect estimate by $>10\%$ were included) as a variable reduction strategy. A sensitivity analysis for unmeasured

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	covariates was also conducted to evaluates the joint magnitude of the association between deferred CN and unmeasured confounders.
	Adjusted confounder: age at diagnosis, sex, year of diagnosis, Karnofsky performance status (>80 vs <80), IMDC risk group (intermediate vs poor risk), clear cell versus non-clear cell histology, sarcomatoid dedifferentiation, number of metastatic sites, and location of metastases (lung, brain, liver, bone, and lymph node).
<b>Additional comments</b>	Baseline data is reported for the overall participants included in the study and not for the population subsets.

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2 **Study arms**3 **Deferred cytoreductive nephrectomy (N = 85)**

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5 **SACT alone (N = 651)**

6

7 **Characteristics**8 **Study-level characteristics**

<b>Characteristic</b>	<b>Study (N = 1541)</b>
<b>% Female</b>	n = 403 ; % = 26
Sample size	
<b>Age</b>	61 (54 to 68)
Median (IQR)	
<b>Primary RCC type - Clear cell histology</b>	n = 1311 ; % = 85
Sample size	
<b>Primary RCC type - Sarcomatoid dedifferentiation</b>	n = 232 ; % = 15
Sample size	
<b>Location of metastases - Brain</b>	n = 130 ; % = 8
Sample size	
<b>Location of metastases - lung</b>	n = 1141 ; % = 74
Sample size	
<b>Location of metastases - Liver</b>	n = 333 ; % = 22
Sample size	

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Characteristic	Study (N = 1541)
Location of metastases - bone	n = 593 ; % = 38
Sample size	
Location of metastases - Nodal	n = 785 ; % = 51
Sample size	
Location of metastases - Other	n = 461 ; % = 30
Sample size	

1

2 **Outcomes**3 **Overall survival**

Outcome	Deferred cytoreductive nephrectomy vs SACT alone, , N2 = 85, N1 = 651
Overall survival	0.45 (0.33 to 0.6)
Hazard ratio/95% CI	

4 Overall survival - Polarity - Lower values are better

5

6

7 **Critical appraisal - ROBIS checklist**

Question	Answer
Risk of bias judgement	Serious ( <i>Insufficient adjustment for confounders, limited reporting on missing data and protocol not identified</i> )
Directness	Directly applicable

8 **Chakiryan, 2022**

**Bibliographic Reference** Chakiryan, Nicholas H; Gore, L Robert; Reich, Richard R; Dunn, Rodney L; Jiang, Da David; Gillis, Kyle A; Green, Elizabeth; Hajiran, Ali; Hugar, Lee; Zemp, Logan; Zhang, Jingsong; Jain, Rohit K; Chahoud, Jad; Spiess, Philippe E; Manley, Brandon J; Sexton, Wade J; Hollenbeck, Brent K; Gilbert, Scott M; Survival Outcomes Associated With Cytoreductive Nephrectomy in Patients With Metastatic Clear Cell Renal Cell Carcinoma.; JAMA network open; 2022; vol. 5 (no. 5); e2212347

9

10 **Study details**

<b>Study type</b>	Retrospective cohort study
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<b>Study location</b>	United States - Uses the National Clinical Data Base (NCDB)
<b>Study dates</b>	January 2006 to December 2016
<b>Sources of funding</b>	NR
<b>Inclusion criteria</b>	clinical stage IV metastatic renal cancer at diagnosis; age of 18 to 100 years; availability of complete staging and demographic data; and receipt of targeted therapy as first-line treatment  Diagnosis with clear cell renal cell carcinoma
<b>Exclusion criteria</b>	NCDB codes indicated that the patient was treated on an experimental or blinded clinical trial protocol; data were missing on distance from the patient's residence to the treating facility; if The International Metastatic Renal Cell Carcinoma Database risk score were not available in the NCDB, and available data points are not adequate to calculate this score directly
<b>Intervention(s)</b>	Deferred Cytoreductive nephrectomy (CN) - median time to nephrectomy after the first-line systemic therapy was 23 days with inter-quartile range of 68 to 193 days; type of SACT not reported in the paper
<b>Comparator</b>	First line SACT only i.e no CN
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	Overall - 12766  Deferred CN - 612  SACT alone - 7761
<b>Duration of follow-up</b>	From the date of diagnosis to death or censoring at last follow-up
<b>Methods of analysis</b>	Patients were stratified according to the CN status. Wilcoxon rank sum testing was used to compare continuous variables, and the $\chi^2$ test of independence was used to compare categorical variables. Kaplan-Meier estimates were used to generate survival functions. Propensity score matching carried out. Univariable analysis was repeated in the post-matching cohorts to assess for balance between groups.  Subgroup analysis was conducted for each of the 3 methods (multivariable Cox proportional hazards regression, propensity score matching, and instrumental variable analysis). The results for OS outcome were extracted using the subgroup analysis using multivariable Cox regression model.  Adjusted covariates: age, sex, race, Charlson-Deyo score, facility type, year of diagnosis, cT stage, cN stage, and cytoreductive nephrectomy status
<b>Additional comments</b>	Study included 12, 766 participants in total with 5,005 in the CN arm and 7,761 in no CN arm. The protocol relevant outcomes were extracted from the subset of the CN arm who received delayed CN compared to no CN

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	arm (612 vs. 7,761) . However, the baseline data was not reported for this subset but as an overall for the participants who had received cytoreductive nephrectomy and was extracted (5,005 and 7,761).
	Study uses and reports the protocol relevant outcomes based on both multiple-cox regression and propensity score matching model. The extracted results came from the propensity score matching model.

1

2 **Study arms**

3 **Cytoreductive nephrectomy (N = 5005)**

4 Deferred Cytoreductive nephrectomy - 612

5

6 **SACT alone (N = 7761)**

7

8 **Characteristics**

9 **Arm-level characteristics**

Characteristic	Cytoreductive nephrectomy (N = 5005)	SACT alone (N = 7761)
% Female	n = 1540 ; % = 31	n = 2482 ; % = 32
Sample size		
Age	61 (54 to 67)	65 (57 to 72)
Median (IQR)		
TNM classification - cT1	n = 887 ; % = 18	n = 2295 ; % = 30
Sample size		
TNM classification - cT2	n = 1721 ; % = 34	n = 2213 ; % = 29
Sample size		
TNM classification - cT3	n = 2049 ; % = 41	n = 2101 ; % = 27
Sample size		
TNM classification - cT4	n = 348 ; % = 7	n = 1152 ; % = 15
Sample size		

10

1 **Outcomes**2 **Overall Survival**

Outcome	Cytoreductive nephrectomy vs SACT alone, , N2 = 612, N1 = 7716
<b>Overall survival</b> Deferred cytoreductive nephrectomy	0.39 (0.36 to 0.43)
Hazard ratio/95% CI	

3 Overall survival - Polarity - Lower values are better

4

5 **Critical appraisal - ROBIS checklist**

Question	Answer
Risk of bias judgement	Serious ( <i>Insufficient adjustment for confounders, limited reporting on missing data and protocol not identified</i> )
Directness	Directly applicable

6 **Day, 2016**

**Bibliographic Reference** Day, D; Kanjanapan, Y; Kwan, E; Yip, D; Lawrentschuk, N; Davis, I D; Azad, A A; Wong, S; Rosenthal, M; Gibbs, P; Tran, B; Benefit from cytoreductive nephrectomy and the prognostic role of neutrophil-to-lymphocyte ratio in patients with metastatic renal cell carcinoma.; Internal medicine journal; 2016; vol. 46 (no. 11); 1291-1297

7

8 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Australia - locally conducted at four Australian hospitals
<b>Study dates</b>	January 2006 - December 2012
<b>Sources of funding</b>	Institute of Health and Biomedical Innovation of Queensland University of Technology
<b>Inclusion criteria</b>	Patients with metastatic disease at diagnosis (de novo mRCC) and with complete information on survival and treatment data, neutrophil-to-lymphocyte ratio and other preoperative variables were included
<b>Exclusion criteria</b>	Patients who had received systemic therapy before 1 January 2006 were excluded
<b>Intervention(s)</b>	Cytoreductive nephrectomy who had received first-line systemic therapy. All participants received cytoreductive nephrectomy within 3 months of the diagnosis

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<b>Comparator</b>	SACT alone i.e., no cytoreductive nephrectomy. (76 out of 91 received sunitinib, others received pazopanib, everolimus, bevacizumab, interferon and temsirolimus – treatment combinations unclear).
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	<p>Overall - 91</p> <ul style="list-style-type: none"> <li>• Cytoreductive nephrectomy arm - 46</li> <li>• No Cytoreductive nephrectomy arm - 45</li> </ul> <p>Subset receiving SACT</p> <ul style="list-style-type: none"> <li>• Cytoreductive nephrectomy arm - 42</li> <li>• No Cytoreductive nephrectomy arm (SACT alone) - 34</li> </ul>
<b>Duration of follow-up</b>	NR
<b>Methods of analysis</b>	<p>Descriptive statistics were used to summaries patient characteristics. Survival analyses were performed by calculating hazard ratios using the Cox proportional hazards model. Median survival was determined using the Kaplan–Meier method. Comparisons between groups were made using Fisher's exact test. Univariate analysis was used to determine the statistically significant factors for the overall survival.</p> <p>Adjustment was carried out for: Cytoreductive nephrectomy (CN), MSKCC risk classification, neutrophil-to-lymphocyte ratio, histology and systemic treatment.</p>
<b>Additional comments</b>	Study included 91 participants in total. The protocol relevant outcomes were extracted from the subset of participants who had the history of receiving systemic therapy with or without cytoreductive nephrectomy (42 and 34 participants). However, the baseline data was not reported for this subset but as an overall for the participants who had or not had cytoreductive nephrectomy (46 and 45).

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**Study arms**

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**Cytoreductive nephrectomy (N = 46)**

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**No Cytoreductive nephrectomy (N = 45)**

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1 **Characteristics**2 **Arm-level characteristics**

<b>Characteristic</b>	<b>Cytoreductive nephrectomy (N = 46)</b>	<b>No Cytoreductive nephrectomy (N = 45)</b>
<b>Age (years)</b>	59 (NR to NR)	64.6 (NR to NR)
Median (IQR)		
<b>Intervention subtype - Sunitinib</b>	n = 33 ; % = 72	n = 34 ; % = 76
Sample size		
<b>Intervention subtype - Pazopanib</b>	n = 4 ; % = 9	n = 0 ; % = 0
Sample size		
<b>Intervention subtype - Everolimus</b>	n = 0 ; % = 0	n = 4 ; % = 9
Sample size		
<b>Intervention subtype - Bevacizumab</b>	n = 2 ; % = 4	n = 0 ; % = 0
Sample size		
<b>Intervention subtype - Interferon</b>	n = 2 ; % = 4	n = 0 ; % = 0
Sample size		
<b>Intervention subtype - Temsirolimus</b>	n = 1 ; % = 2	n = 0 ; % = 0
Sample size		
<b>Primary RCC type - Clear cell histology</b>	n = 37 ; % = 80	n = 27 ; % = 60
Sample size		
<b>Primary RCC type - Non-clear cell histology</b>	n = 6 ; % = 13	n = 5 ; % = 11
Sample size		
<b>Primary RCC type - unknown</b>	n = 3 ; % = 7	n = 13 ; % = 29
Sample size		

## 3

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

1 **Outcomes**2 **Overall survival**

Outcome	Cytoreductive nephrectomy vs No Cytoreductive nephrectomy, , N2 = 42, N1 = 34
Overall survival	0.41 (0.19 to 0.6)
Hazard ratio/95% CI	

3 Overall survival - Polarity - Lower values are better

4 **Critical appraisal - ROBIS checklist**

Question	Answer
Risk of bias judgement	Serious (No adjustment for confounders or matching undertaken. Limited information about missing data or inclusion criteria. No protocol identified so unable to fully assess bias in selection of reported result.)
Directness	Directly applicable

5

6 **Dragomir, 2022**

**Bibliographic Reference** Dragomir, A.; Nazha, S.; Tanguay, S.; Breau, R.H.; Bhindi, B.; Rendon, R.A.; Kapoor, A.; Hotte, S.J.; Basappa, N.; Fairey, A.; So, A.I.; Kollmannsberger, C.; Finelli, A.; Hansen, A.; Canil, C.; Heng, D.; Lattouf, J.-B.; Bjarnason, G.; Power, N.; Pouliot, F.; Wood, L.A.; Outcomes of Cytoreductive Nephrectomy for Patients with Metastatic Renal Cell Carcinoma: Real World Data from Canadian Centers; European Urology Focus; 2022; vol. 8 (no. 6); 1703-1710

7

8 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Canada - Data retrieved from the Canadian Kidney Cancer information system (CKCis)
<b>Study dates</b>	January 2011 and April 2020
<b>Sources of funding</b>	None
<b>Inclusion criteria</b>	Diagnosis of RCC was made on the basis of histopathological evaluations; patients with synchronous disease (i.e, metastases found 3 months before or within 6 months after the primary tumour diagnosis); treated (with cytoreductive nephrectomy (CN) or/and systemic therapy (ST)) within 12 months of the initial RCC diagnosis  Edit: IMDC intermediate or high risk

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<b>Exclusion criteria</b>	patients who had indolent metastatic disease
<b>Intervention(s)</b>	Deferred Cyto-reductive nephrectomy after systemic therapy
<b>Comparator</b>	Systemic therapy alone (overall across the study, 51% had sunitinib, others had pazopanib, ipilimumab / nivolumab combination, or other).
<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	Overall n= 325  Intervention arm (CN) - 73  Comparator arm (SACT alone) - 252
<b>Duration of follow-up</b>	Earliest date of death, loss to follow-up, or the end of the study period (April 2020)
<b>Methods of analysis</b>	Frequency and percentage for categorical variables and as the median with interquartile range for continuous variables; Chi-square test or Fisher's exact test for categorical variables for categorical variables; non-parametric Wilcoxon rank-sum test was used for continuous variables. Kaplan Meier curve analysis was performed to estimate OS from the index date until death (any causes) or loss to follow-up. A log-rank test was used to evaluate differences in overall survival. Uses IPTW to account for the differences in the distribution among baseline characteristics.  Adjusted confounders: Age, sex, sites and number of organs for metastasis, cell histology, IMDC risk and Charlson comorbidity index
<b>Additional comments</b>	

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2 **Study arms**3 **Cyto-reductive nephrectomy (N = 73)**

4 After SACT

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6 **SACT alone (N = 252)**

7

8 **Characteristics**9 **Arm-level characteristics**

<b>Characteristic</b>	<b>Cyto-reductive nephrectomy (N = 73)</b>	<b>SACT alone (N = 252)</b>
<b>% Female</b>	n = 19 ; % = 26	n = 184 ; % = 27
<b>Sample size</b>		

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<b>Characteristic</b>	<b>Cytoreductive nephrectomy (N = 73)</b>	<b>SACT alone (N = 252)</b>
<b>Age (Years (IQR))</b>	62 (55 to 68)	64 (57 to 70)
Median (IQR)		
<b>Intervention subtype - Sunitinib</b>	n = 52 ; % = 71.2	n = 121 ; % = 48
Sample size		
<b>Intervention subtype - Pazopanib</b>	n = 8 ; % = 11	n = 52 ; % = 20.6
Sample size		
<b>Intervention subtype - Ipilimumab/nivolumab</b>	n = 3 ; % = 4.1	n = 57 ; % = 22.6
Sample size		
<b>Intervention subtype - Others</b> Nivolumab, everolimus, pembrolizumab, temsirolimus, atezolizumab, axitinib, lenvatinib	n = 10 ; % = 13.7	n = 22 ; % = 8.8
Sample size		
<b>Primary RCC type - Clear-cell RCC</b>	n = 61 ; % = 83.6	n = 169 ; % = 67.1
Sample size		
<b>Location of metastases - lung</b>	n = 39 ; % = 53.4	n = 135 ; % = 53.6
Sample size		
<b>Location of metastases - bone</b>	n = 14 ; % = 19.2	n = 66 ; % = 26.2
Sample size		
<b>Location of metastases - Brain</b>	n = 2 ; % = 2.7	n = 16 ; % = 6.4
Sample size		
<b>Location of metastases - Adrenal gland</b>	n = 10 ; % = 13.7	n = 29 ; % = 11.5
Sample size		
<b>Location of metastases - Liver</b>	n = 9 ; % = 12.3	n = 41 ; % = 16.3
Sample size		
<b>Location of metastases - Lymph nodes</b>	n = 28 ; % = 38.4	n = 104 ; % = 41.3
Sample size		



1 **Outcomes**2 **Overall Survival**

Outcome	Cytoreductive nephrectomy vs SACT alone, , N2 = 73, N1 = 252
Overall survival	0.41 (0.28 to 0.6)
Hazard ratio/95% CI	

3 Overall survival - Polarity - Lower values are better

4

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6 **Critical appraisal - ROBIS checklist**

Question	Answer
Risk of bias judgement	Serious (No adjustment for confounders or matching undertaken. Limited information about missing data or inclusion criteria. No protocol identified so unable to fully assess bias in selection of reported result.)
Directness	Directly applicable

7 **Fransen van de Putte, 2023**

**Bibliographic Reference** Fransen van de Putte, Elisabeth E; van den Brink, Luna; Mansour, Mohamed A; van der Mijn, Johannes C; Wilgenhof, Sofie; van Thienen, Johannes V; Haanen, John B A G; Boleti, Ekaterini; Powles, Thomas; Zondervan, Patricia J; Graafland, Niels M; Bex, Axel; Indications and Outcomes for Deferred Cytoreductive Nephrectomy Following Immune Checkpoint Inhibitor Combination Therapy: Can Systemic Therapy be Withdrawn in Patients with No Evidence of Disease?.; European urology open science; 2023; vol. 55; 15-22

8

9 **Study details**

Study type	Retrospective cohort study
Study location	Four European centres; two in Netherlands and two in England
Study dates	March 2019 - June 2022
Sources of funding	No funding received
Inclusion criteria	Biopsy-confirmed synchronous metastatic renal cell carcinoma; receiving first-line ipilimumab-nivolumab
Intervention(s)	Deferred cytoreductive nephrectomy
Comparator	SACT alone - receiving first-line ICI therapy (ipilimumab-nivolumab)
Outcome measures	Cancer-specific survival

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<b>Number of participants</b>	Deferred cytoreductive nephrectomy - 19 SACT alone - 7
<b>Duration of follow-up</b>	3 years
<b>Loss to follow-up</b>	No loss to follow up
<b>Methods of analysis</b>	Kaplan-Meier data for disease-free survival, progression-free survival, and cancer-specific survival were compared between IMDC risk groups and between modalities using log-rank tests
<b>Additional comments</b>	Study included 125 participants in total. The protocol relevant outcomes were extracted from the subset of participants who had near complete or complete response to at the metastatic site (a >80% reduction in the cumulative metastatic volume) with or without cytoreductive nephrectomy (19 and 7 participants). However, the baseline data was not reported for this subset but as an overall for the participants who had or not had cytoreductive nephrectomy (23 and 7).

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2 **Study arms**3 **Deferred Cytoreductive nephrectomy (N = 23)**4 **SACT (N = 7)**5 **Characteristics**6 **Arm-level characteristics**

<b>Characteristic</b>	<b>Deferred Cytoreductive nephrectomy (N = 23)</b>	<b>SACT (N = 7)</b>
<b>% Female</b>	n = 10 ; % = 43	n = 3 ; % = 42
Sample size		
<b>Age</b>	62 (10)	71 (12)
Mean (SD)		
<b>Primary RCC type - Papillary type 2</b>	n = 0 ; % = 0	n = 1 ; % = 14
Sample size		
<b>Primary RCC type - Clear cell RCC with sarcomatoid variant</b>	n = 1 ; % = 4	n = 1 ; % = 14
Sample size		
<b>Primary RCC type - Clear cell RCC with other variant</b>	n = 0 ; % = 0	n = 0 ; % = 0

Characteristic	Deferred Cytoreductive nephrectomy (N = 23)	SACT (N = 7)
Sample size		
<b>Primary RCC type - Poorly differentiated</b>	n = 0 ; % = 0	n = 1 ; % = 14
Sample size		
<b>Primary RCC type - clear cell RCC</b>	n = 21 ; % = 92	n = 4 ; % = 57
Sample size		
<b>Primary RCC type - Sarcomatoid</b>	n = 1 ; % = 4	n = 0 ; % = 0
Sample size		
<b>Baseline performance status - 0 ( )</b> ECOG performance status	n = 12 ; % = 52	n = 2 ; % = 29
Sample size		
<b>Baseline performance status - 1 ( )</b> ECOG performance status	n = 9 ; % = 39	n = 5 ; % = 71
Sample size		
<b>Baseline performance status - ≥ 2</b> ECOG performance status	n = 1 ; % = 4	n = 0 ; % = 0
Sample size		
<b>Baseline performance status - Unknown</b> ECOG performance status	n = 2 ; % = 9	n = 0 ; % = 0
Sample size		

1

2 **Outcomes**3 **Cancer specific mortality**

Outcome	Deferred Cytoreductive nephrectomy , , N = 19	SACT, , N = 7
<b>Cancer specific mortality</b> At 3 years	n = 15 ; % = 80	n = 7 ; % = 100
No of events		

4 Cancer specific mortality - Polarity - Lower values are better

1 **Critical appraisal - ROBIS checklist**

Question	Answer
Risk of bias judgement	Serious (No adjustment for confounders or matching undertaken. Limited information about missing data or inclusion criteria. No protocol identified so unable to fully assess bias in selection of reported result.)
Directness	Directly applicable

2

3

4 **Hatakeyama, 2021**

**Bibliographic Reference** Hatakeyama, Shingo; Naito, Sei; Numakura, Kazuyuki; Kato, Renpei; Koguchi, Tomoyuki; Kojima, Takahiro; Kawasaki, Yoshihide; Kandori, Shuya; Kawamura, Sadafumi; Tsushima, Eiki; Nishiyama, Hiroyuki; Ito, Akihiro; Kojima, Yoshiyuki; Habuchi, Tomonori; Obara, Wataru; Tsuchiya, Norihiko; Ohyama, Chikara; Impact of cytoreductive nephrectomy in patients with primary metastatic renal cell carcinoma receiving systemic tyrosine kinase inhibitor therapy: A multicenter retrospective study.; International journal of urology : official journal of the Japanese Urological Association; 2021; vol. 28 (no. 4); 369-375

5

6 **Study details**

<b>Study type</b>	Retrospective cohort study
<b>Study location</b>	Japan - Michinoku Japan Urological Cancer Study Group database
<b>Study dates</b>	January 2008 - November 2019
<b>Sources of funding</b>	Japan Society for the Promotion of Science
<b>Inclusion criteria</b>	Patients with primary metastatic RCC initially treated with first-line sunitinib, sorafenib, axitinib, and pazopanib were included
<b>Exclusion criteria</b>	Treatment with first-line interferon, mammalian target of rapamycin inhibitors, immunotherapy, or chemotherapy; a period from diagnosis to first treatment (TKIs or immediate CN) of more than 3 months; a period of surveillance after immediate CN of more than 3 months; a follow-up period from the first treatment of less than 3 months; and missing data on confounder variables
<b>Intervention(s)</b>	Deferred cytoreductive nephrectomy - after receiving tyrosine kinase inhibitors (TKI); Median time to CN was 5.1 months with inter-quartile range of 3.5-6.3 months
<b>Comparator</b>	SACT alone - TKI

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<b>Outcome measures</b>	Overall survival
<b>Number of participants</b>	Overall n= 171 Deferred CN - 39 SACT only - 132
<b>Duration of follow-up</b>	Until death
<b>Methods of analysis</b>	Quantitative variables were expressed as median values with IQRs; intergroup difference was tested using Student's t-test or the Mann–Whitney U-test to compare continuous variables; Fisher's exact test or the chi-squared test was used to compare categorical variables; and OS from the initial treatment until death was estimated using Kaplan–Meier curves and the log rank test.  Uses inverse probability of treatment weighting (IPTW) -adjusted Cox regression analysis.  Adjusted confounders - age, sex, performance status, number of IMDC risk factors, clinical stage (cT3b–4), and number of metastatic organs

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2 **Study arms**3 **Deferred cytoreductive nephrectomy (N = 39)**

4

5 **SACT (N = 132)**6 **Characteristics**7 **Arm-level characteristics**

<b>Characteristic</b>	<b>Deferred cytoreductive nephrectomy (N = 39)</b>	<b>SACT (N = 132)</b>
<b>% Female</b>	n = 17 ; % = 44	n = 32 ; % = 24
Sample size		
<b>Age</b>	67 (62 to 72)	67 (61 to 76)
Median (IQR)		
<b>Intervention subtype - Sunitinib</b>	n = 17 ; % = 44	n = 65 ; % = 49
Sample size		
<b>Intervention subtype - Sorafenib</b>	n = 2 ; % = 5.2	n = 16 ; % = 12

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

<b>Characteristic</b>	<b>Deferred cytoreductive nephrectomy (N = 39)</b>	<b>SACT (N = 132)</b>
Sample size		
<b>Intervention subtype - Axitinib</b>	n = 19 ; % = 49	n = 47 ; % = 36
Sample size		
<b>Intervention subtype - Pazopanib</b>	n = 1 ; % = 2.6	n = 4 ; % = 3
Sample size		
<b>TNM classification - T1-2</b>	n = 14 ; % = 36	n = 32 ; % = 24
Sample size		
<b>TNM classification - T3a</b>	n = 8 ; % = 21	n = 34 ; % = 26
Sample size		
<b>TNM classification - T3b-4</b>	n = 17 ; % = 44	n = 63 ; % = 48
Sample size		
<b>TNM classification - Unknown</b>	n = 0 ; % = 0	n = 3 ; % = 2
Sample size		
<b>Location of metastases - lung</b>	n = 23 ; % = 59	n = 77 ; % = 58
Sample size		
<b>Location of metastases - Distant lymph node</b>	n = 11 ; % = 28	n = 49 ; % = 37
Sample size		
<b>Location of metastases - bone</b>	n = 14 ; % = 36	n = 38 ; % = 29
Sample size		
<b>Location of metastases - Liver</b>	n = 3 ; % = 8	n = 23 ; % = 17
Sample size		
<b>Location of metastases - Adrenal</b>	n = 1 ; % = 3	n = 16 ; % = 12
Sample size		
<b>Location of metastases - Brain</b>	n = 2 ; % = 5	n = 9 ; % = 7
Sample size		
<b>Location of metastases - Pancreas</b>	n = 0 ; % = 0	n = 5 ; % = 4

Characteristic	Deferred cytoreductive nephrectomy (N = 39)	SACT (N = 132)
Sample size		
<b>Location of metastases - Others</b>	n = 8 ; % = 21	n = 46 ; % = 35
Sample size		
<b>Location of metastases - Nonclear histology</b>	n = 3 ; % = 7.7	n = 21 ; % = 16
Sample size		
<b>Baseline performance status</b>	n = NR ; % = NR	n = NR ; % = NR
Sample size		

1

2 **Outcomes**3 **Overall survival**

Outcome	Deferred cytoreductive nephrectomy vs SACT, , N2 = 39, N1 = 132
<b>Overall survival</b> deferred cytoreductive nephrectomy vs. SACT alone	0.34 (0.2 to 0.61)
Hazard ratio/95% CI	

4 Overall survival - Polarity - Lower values are better

5

6

7 **Critical appraisal - ROBIS checklist**

Question	Answer
Risk of bias judgement	Moderate ( <i>Insufficient adjustment for confounders</i> )
Directness	Directly applicable

Appendix E – Forest plots

Review H1: Upfront cytoreductive nephrectomy (CN) vs. deferred CN

Survival outcomes

Figure 1. Progression-free survival, ≤5 years - Clear cell - Randomised controlled trial

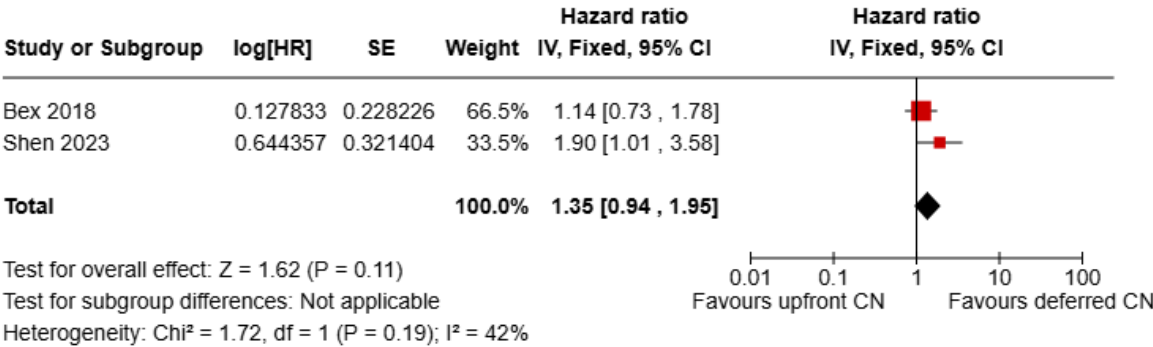
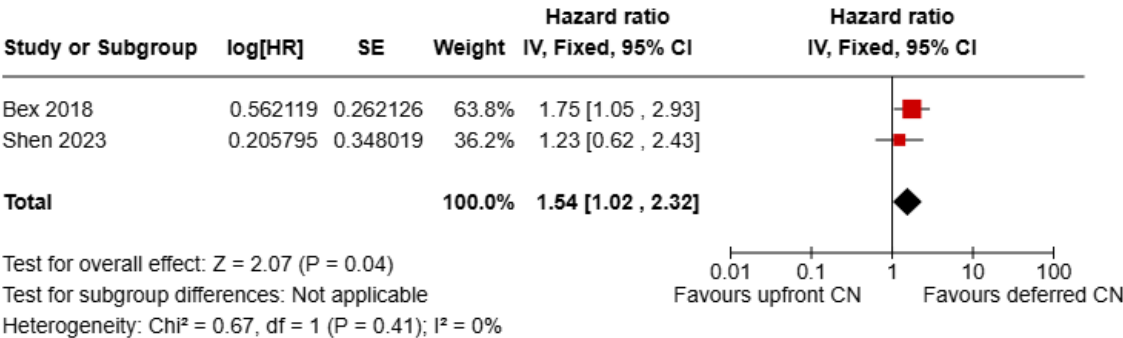
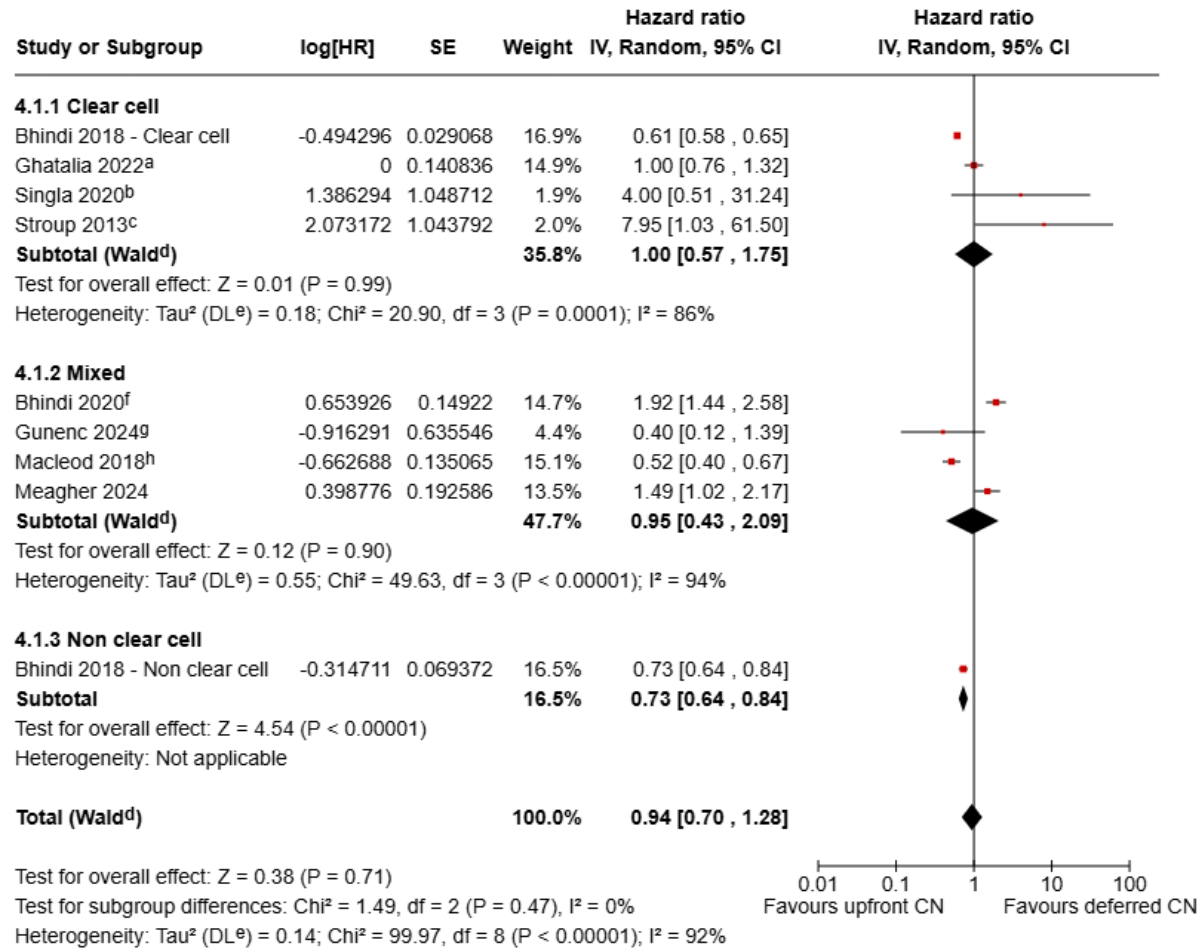


Figure 2. Overall survival, ≤5 years - Clear cell population - Randomised controlled trial





**Figure 3. Overall survival, ≤5 years - Mixed population – Non-randomised controlled trial**



**Footnotes**

<sup>a</sup>Follow-up was not reported

<sup>b</sup>Median follow-up was 14.7 months

<sup>c</sup>Median follow-up was 4.6 months (sunitinib); 22.8 months (sunitinib + CN)

<sup>d</sup>CI calculated by Wald-type method.

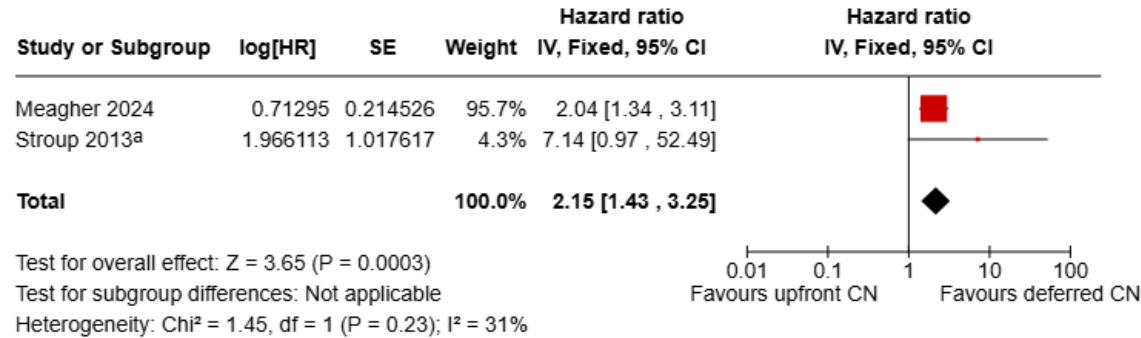
<sup>e</sup>Tau<sup>2</sup> calculated by DerSimonian and Laird method.

<sup>f</sup>Median follow-up was 25 months

<sup>g</sup>Median follow-up was 21 months

<sup>h</sup>Median follow-up was 12 months

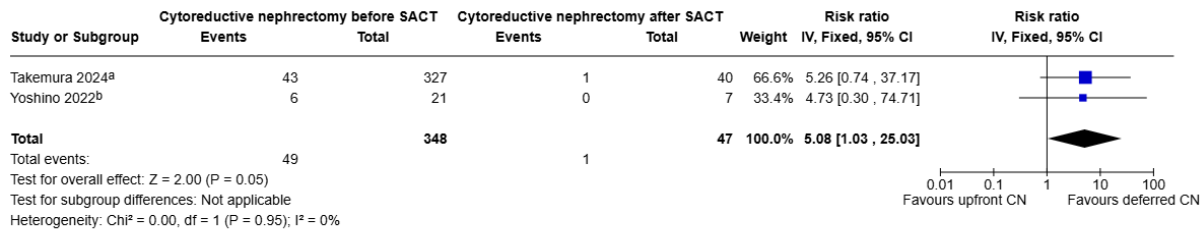
**Figure 4. Cancer specific survival, ≤5 years - Clear cell population - Non-randomised controlled trial**



**Footnotes**

<sup>a</sup>Median follow-up was 4.6 months (sunitinib); 22.8 months (sunitinib + CN)

**Figure 5. Mortality, ≤5 years - Mixed population - Non-randomised controlled trial**



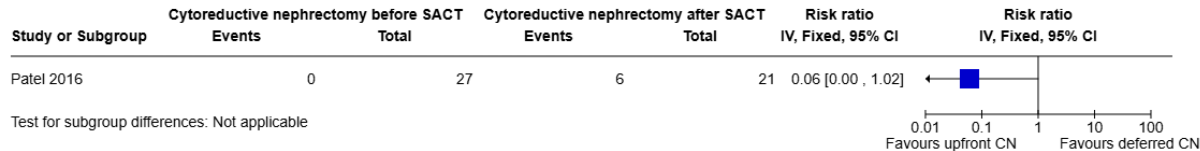
**Footnotes**

<sup>a</sup>Median follow-up was 12 months

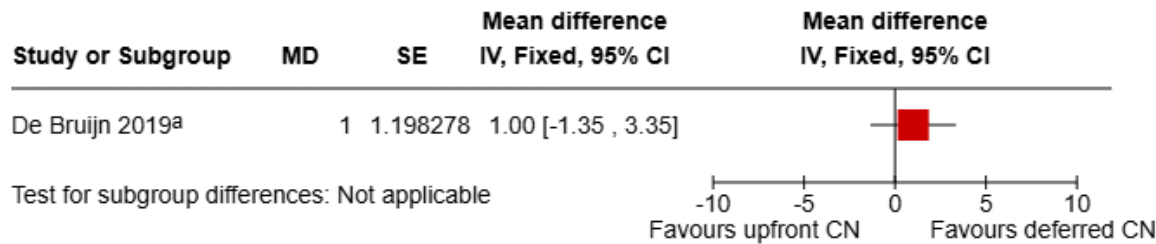
<sup>b</sup>Converted from 'overall survival' reported as events; median follow-up was 12.0 months

**All other outcomes**

**Figure 6. Adverse Events grade ≥ 3 (Clavien Dindo) - Clear cell population - Non-randomised controlled trial**



1 **Figure 7. Duration of hospital stay (days) - Clear cell - Randomised controlled**  
2 **trial**

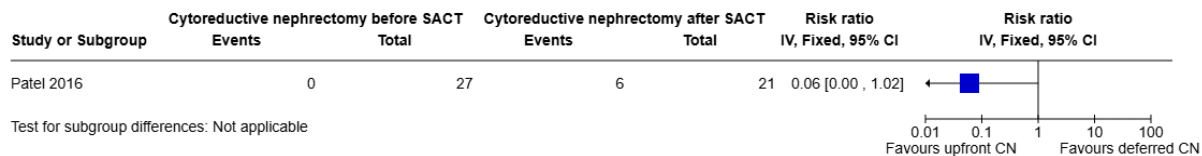


**Footnotes**

<sup>a</sup>Publications from the SURTIME study

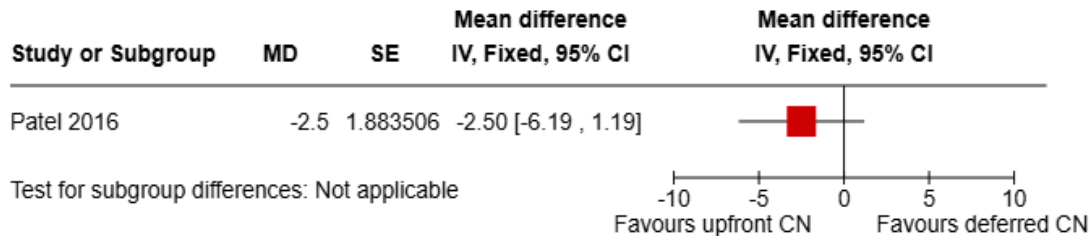
3

4 **Figure 8. Adverse Events grade  $\geq 3$  (Clavien Dindo) - Clear cell population -**  
5 **Non-randomised controlled trial**



6

7 **Figure 9. Duration of hospital stay (days) - Clear cell - Non-randomised**  
8 **controlled trial**

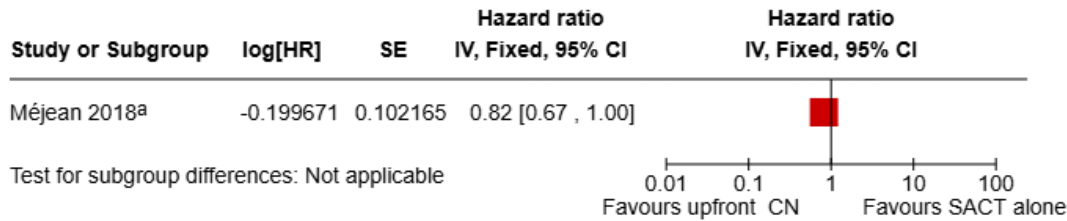


9

**Review H1: Upfront cytoreductive nephrectomy (CN) vs. systemic anti-cancer therapy (SACT) alone**

**Survival outcomes**

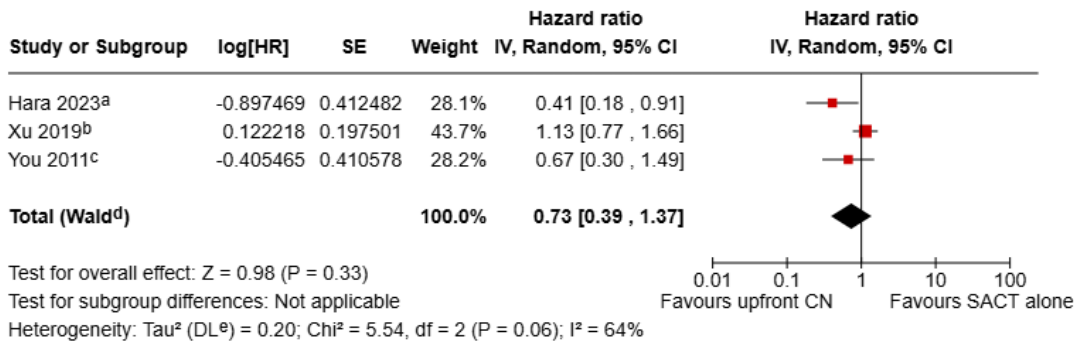
**Figure 10. Progression-free survival, ≤5 years - Clear cell - Randomised controlled trial**



**Footnotes**

<sup>a</sup>Median follow-up was 50.9 months; publications from the CARMENA study

**Figure 11. Progression-free survival, ≤5 years - Clear cell - Non-randomised controlled trial**



**Footnotes**

<sup>a</sup>Median follow-up was 15.7 months

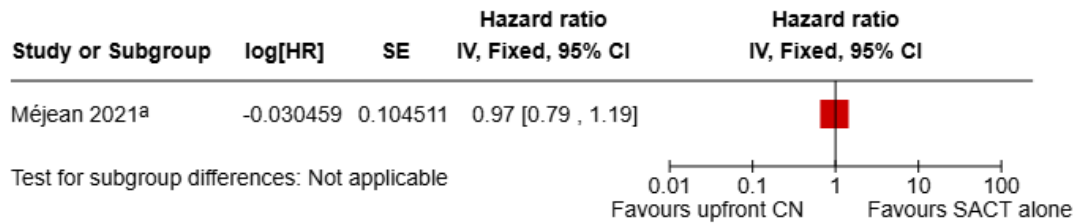
<sup>b</sup>Last day of follow-up (8th July 2018)

<sup>c</sup>Follow-up not reported

<sup>d</sup>CI calculated by Wald-type method.

<sup>e</sup> $\text{Tau}^2$  calculated by DerSimonian and Laird method.

1 **Figure 12. Overall survival, ≤5 years - Clear cell population - Randomised**  
2 **controlled trial**

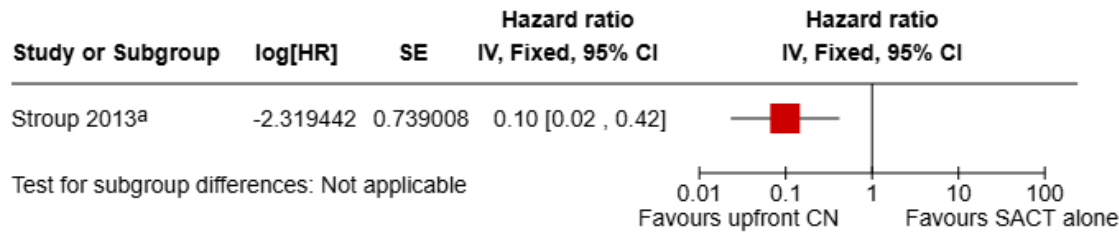


**Footnotes**

<sup>a</sup>Median follow-up was 36.6 months; publications from the CARMENA study

3

4 **Figure 13. Cancer specific survival, ≤5 years - Clear cell population - Non-**  
5 **randomised controlled trial**

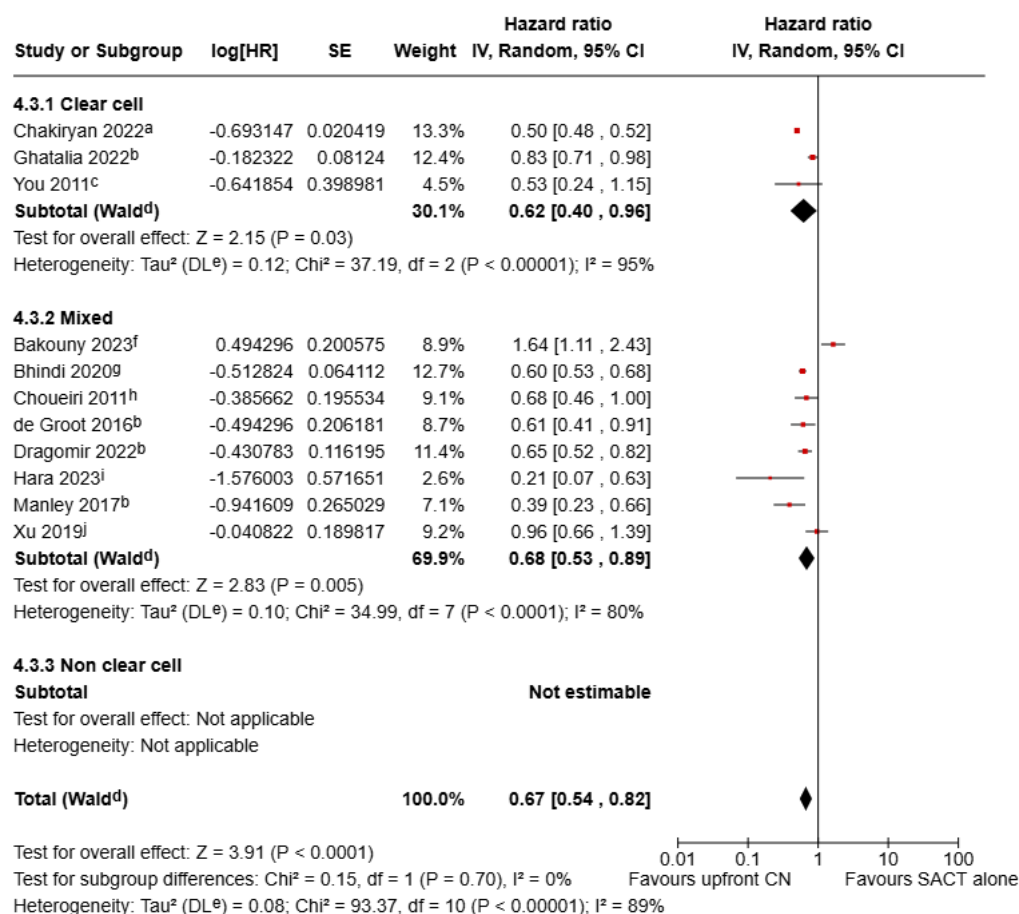


**Footnotes**

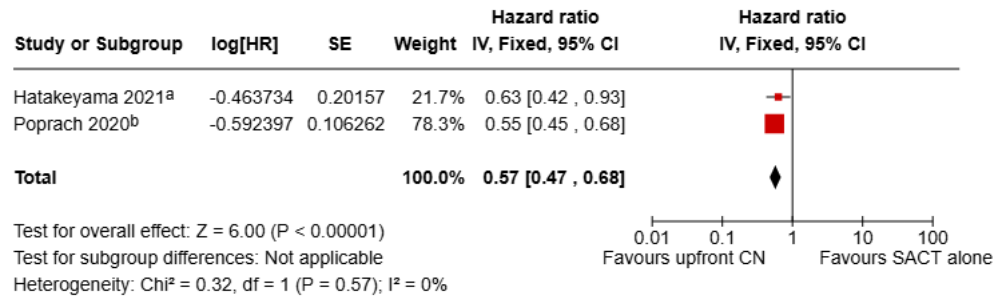
<sup>a</sup>Median follow-up was 4.6 months (sunitinib); 22.8 months (sunitinib + CN)

6

**Figure 14. Overall survival, ≤5 years - Clear cell/mixed population - Non-randomised controlled trial**

**Footnotes**<sup>a</sup>Median follow-up was 36.0 months<sup>b</sup>Follow-up was not reported<sup>c</sup>Follow-up not reported<sup>d</sup>CI calculated by Wald-type method.<sup>e</sup>Tau<sup>2</sup> calculated by DerSimonian and Laird method.<sup>f</sup>Median follow-up was 12 months<sup>g</sup>Median follow-up was 25 months<sup>h</sup>Median follow-up was 16.3 months<sup>i</sup>Median follow-up was 15.7 months<sup>j</sup>Last day of follow-up (8th July 2018)

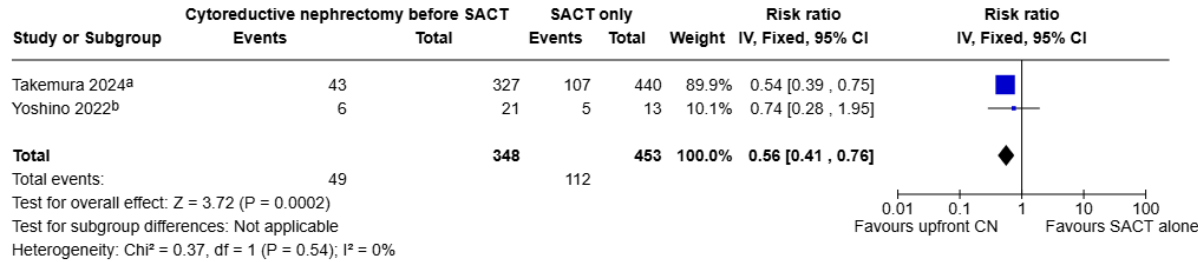
**Figure 15. Overall survival, >5 years - Mixed population - Non-randomised controlled trial**



**Footnotes**

<sup>a</sup>Exact follow-up period was not reported  
<sup>b</sup>Follow-up was not reported

**Figure 16. Mortality, ≤5 years - Mixed population - Non-randomised controlled trial**

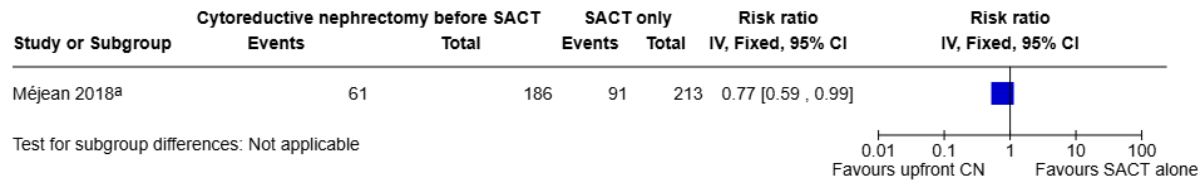


**Footnotes**

<sup>a</sup>Median follow-up was 12 months  
<sup>b</sup>Converted from 'overall survival' reported as events; median follow-up was 12.0 months

**All other outcomes**

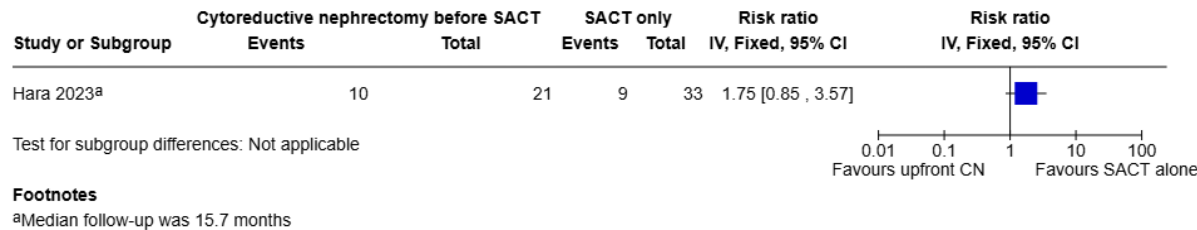
**Figure 17. Adverse Events grade ≥ 3 - Mixed population - Randomised controlled trial**



**Footnotes**

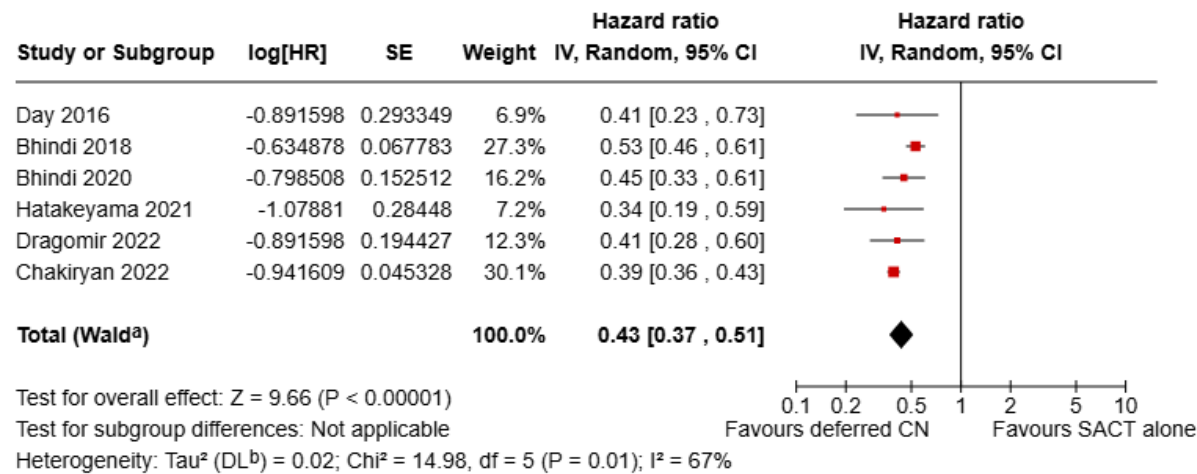
<sup>a</sup>Median follow-up was 50.9 months; publications from the CARMENA study

**Figure 18. Adverse Events grade  $\geq 3$  - Mixed population - Non-randomised controlled trial**



**Review H2: Deferred cytoreductive nephrectomy (CN) vs. systemic anti-cancer therapy (SACT) alone**

**Figure 19. Overall survival  $\leq 5$  years**





- 1 **Appendix F – GRADE tables**
- 2 **Review H1**
- 3 **Upfront cytoreductive nephrectomy (CN) vs. deferred CN**
- 4 **Survival outcomes**

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Upfront CN + SACT	Deferred CN	Relative (95% CI)	Absolute (95% CI)	
Progression-free survival, ≤5 years – Clear cell population											
2 (Bex 2028, Shen 2023)	randomised studies	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>c,d</sup>	none	92	91	HR 1.35 (0.94 to 1.95)	NR	Very low
1 (Gunenc 2024)	non-randomised studies	Serious <sup>a</sup>	Serious <sup>g</sup>	not serious	very serious <sup>c,d</sup>	none	13	38	HR 0.40 (0.12 to 1.39)	NR	Very low
Overall survival, ≤5 years - Clear cell population											
2 (Bex 2028, Shen 2023)	randomised studies	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	92	91	HR 1.54 (1.02 to 2.32)	NR	Low
Overall survival, ≤5 years – Mixed population											

Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Upfront CN + SACT	Deferred CN	Relative (95% CI)	Absolute (95% CI)	
8 (Bhindi 2018, Bhindi 2020, Ghatalia 2022, Gunenc 2024, Macleod 2018, Meagher 2024, Singla 2020, Stroup 2013)	non-randomised studies	very serious <sup>e</sup>	very serious <sup>f</sup>	not serious	serious <sup>c</sup>	none	8699	9032	HR 0.94 (0.70 to 1.28)	NR	Very low
<b>Overall survival, &gt;5 years – Mixed population</b>											
1 (Hatakeyama 2021)	non-randomised studies	very serious <sup>e</sup>	serious <sup>g</sup>	not serious	very serious <sup>c,d</sup>	none	107	39	HR 1.64 (0.87 to 3.09)	NR	Very low
<b>Cancer specific survival, ≤5 years - Clear cell population</b>											
2 (Meagher 2024, Stroup 2013)	non-randomised studies	very serious <sup>e</sup>	not serious	not serious	Serious <sup>d</sup>	none	158	59	HR 2.15 (1.43 to 3.25)	NR	Very low
<b>Mortality, ≤5 years – Mixed population</b>											
2 (Takemura 2024,	non-randomised studies	very serious <sup>e</sup>	not serious	not serious	serious <sup>d</sup>	none	49/348 (14.1%)	1/47 (2.1%)	RR 5.08 (1.03 to 25.03)	NR	Very low

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Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Upfront CN + SACT	Deferred CN	Relative (95% CI)	Absolute (95% CI)	
Yoshino 2022*)											

**CN:** cytoreductive nephrectomy; **CI:** confidence interval; **HR:** hazard ratio; **NR:** not reported; **RR:** risk ratio; **SACT:** systemic anti-cancer therapy

## Explanations

- Downgraded once for risk of bias. Greater than 50% of the weight in meta-analysis came from studies with some concerns or high risk of bias
- Downgraded once for inconsistency.  $I^2$  was between 40% and 60%
- Downgraded once for imprecision. 95% confidence interval for the effect size crossed the line of no effect
- Downgraded once for imprecision. Result comes from a study with a small sample size (sample size <576 participants)
- Downgraded twice for risk of bias. Greater than 50% of the weight in meta-analysis came from studies at high risk of bias
- Downgraded twice for inconsistency.  $I^2$  greater than 60%
- Downgraded once for inconsistency. Single study only

## All other outcomes

Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Upfront CN + SACT	Deferred CN	Relative (95% CI)	Absolute (95% CI)	
Adverse events grade ≥3 (Clavien Dindo) – Clear cell population											
1 (Bex 2018)	randomised trials	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>c,d</sup>	none	1/34 (2.9%)	3/46 (6.5%)	RR 0.45 (0.05 to 4.15)	NR	Very low
Adverse events grade ≥3 (Clavien Dindo) – Clear cell population											

Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Upfront CN + SACT	Deferred CN	Relative (95% CI)	Absolute (95% CI)	
1 (Patel 2016)	non-randomised studies	very serious <sup>e</sup>	serious <sup>b</sup>	not serious	very serious <sup>c,d</sup>	none	0/27 (0.0%)	6/21 (28.6%)	RR 0.06 (0.00 to 1.02)	NR	Very low
<b>Duration of hospital stay (days) – Clear cell population</b>											
1 (De Bruijn 2019)	randomised trials	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>c,d</sup>	none	46	34	NR	MD 1 higher (1.35 lower to 3.35 higher)	Very low
<b>Duration of hospital stay (days) – Clear cell population</b>											
1 (Patel 2016)	non-randomised studies	very serious <sup>e</sup>	serious <sup>b</sup>	not serious	very serious <sup>c,d</sup>	none	27	21	NR	MD 2.5 lower (6.19 lower to 1.19 higher)	Very low

1 **CN:** cytoreductive nephrectomy; **CI:** confidence interval; **MD:** mean difference; **NR:** not reported; **RR:** risk ratio; **SACT:** systemic anti-cancer therapy

## 2 Explanations

- 3 a. Downgraded once for risk of bias. Greater than 50% of the weight in meta-analysis came from studies with some concerns or high risk of bias
- 4 b. Downgraded once for inconsistency. Analysis included a single study
- 5 c. Downgraded once for imprecision. 95% confidence interval for the effect size crossed the line of no effect
- 6 d. Downgraded once for imprecision. Result comes from a study with a small sample size (sample size <576 participants)
- 7 e. Downgraded twice for risk of bias. Greater than 50% of the weight in meta-analysis came from studies at serious or high risk of bias

8

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1 **Upfront cytoreductive nephrectomy (CN) vs. systemic anti-cancer therapy (SACT) alone**2 **Survival outcomes**

Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Upfront CN + SACT	SACT alone	Relative (95% CI)	Absolute (95% CI)	
Progression-free survival, ≤5 years – Clear cell population											
1 (Méjean 2018)	randomised trials	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>c,d</sup>	None	226	224	HR 0.82 (0.67 to 1.00)	NR	Very low
Progression-free survival, ≤5 years - Clear cell population											
3 (Hara 2023, Xu 2019, You 2011)	non-randomised studies	very serious <sup>e</sup>	serious <sup>f</sup>	not serious	very serious <sup>c,d</sup>	None	136	114	HR 0.73 (0.39 to 1.37)	NR	Very low
Overall survival, ≤5 years – Clear cell population											
1 (Méjean 2018)	randomised trials	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>c</sup>	None	226	224	HR 0.97 (0.79 to 1.19)	NR	Very low
Overall survival, ≤5 years - Mixed population											
11 (Bakouny 2023, Bhindi 2020, Chakiryan 2022, Choueiri 2011, Dragomir 2022, de	non-randomised studies	very serious <sup>e</sup>	very serious <sup>f</sup>	not serious	not serious	None	6918	10174	HR 0.67 (0.54 to 0.82)	NR	Very low

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Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Upfront CN + SACT	SACT alone	Relative (95% CI)	Absolute (95% CI)	
Groot 2016, Ghatalia 2022, Hara 2023, Manley 2017, Xu 2019, You 2011)											
<b>Overall survival, &gt;5 years – Mixed population</b>											
2 (Hatakeyama 2021, Poprach 2020)	non-randomised studies	very serious <sup>e</sup>	not serious	not serious	not serious	None	565	404	HR 0.57 (0.47 to 0.68)	NR	Low
<b>Cancer specific survival, ≤5 years - Clear cell population</b>											
1 (Stroup 2013)	non-randomised studies	serious <sup>e</sup>	serious <sup>b</sup>	not serious	serious <sup>d</sup>	None	17	7	HR 0.10 (0.02 to 0.42)	NR	Very low
<b>Mortality, ≤5 years – Mixed population</b>											
2 (Takemura 2024, Yoshino 2022)	non-randomised studies	very serious <sup>e</sup>	not serious	not serious	not serious	none	49/348 (14.1%)	112/453 (24.7%)	RR 0.56 (0.41 to 0.76)	NR	Low

1 **CN:** cytoreductive nephrectomy; **CI:** confidence interval; **HR:** hazard ratio; **NR:** not reported; **RR:** risk ratio; **SACT:** systemic anti-cancer therapy

## 1 Explanations

- 2 a. Downgraded once for risk of bias. Greater than 50% of the weight in meta-analysis came from studies with some concerns or high risk of bias  
 3 b. Downgraded once for inconsistency. Analysis included a single study.  
 4 c. Downgraded once for imprecision. 95% confidence interval for the effect size crossed the line of no effect  
 5 d. Downgraded once for imprecision. Result comes from a study with a small sample size (sample size <576 participants)  
 6 e. Downgraded twice for imprecision. Greater than 50% of the weight in meta-analysis came from studies at serious or high risk of bias  
 7 f. Downgraded twice for inconsistency.  $I^2$  greater than 60%.

## 8 All other outcomes

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Upfront CN + SACT	SACT alone	Relative (95% CI)	Absolute (95% CI)	
Adverse events grade ≥3 (Clavien Dindo) – Mixed population											
1 (Méjean 2018)	randomised trials	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>c</sup>	none	61/186 (32.8%)	91/213 (42.7%)	RR 0.77 (0.59 to 0.99)	NR	Very low
Adverse events grade ≥3 (Clavien Dindo)– Mixed population											
1 (Hara 2023)	non-randomised studies	very serious <sup>d</sup>	serious <sup>b</sup>	not serious	very serious <sup>c,e</sup>	none	10/21 (47.6%)	9/33 (27.3%)	RR 1.75 (0.85 to 3.57)	NR	Very low

9 **CN:** cytoreductive nephrectomy; **CI:** confidence interval; **NR:** not reported; **RR:** risk ratio; **SACT:** systemic anti-cancer therapy

## 10 Explanations

- 11 a. Downgraded once for risk of bias. Greater than 50% of the weight in meta-analysis came from studies with some concerns or high risk of bias  
 12 b. Downgraded once for inconsistency.  $I^2$  was between 40% and 60%  
 13 c. Downgraded once for imprecision. 95% confidence interval for the effect size crossed the line of no effect  
 14 d. Greater than 50% of the weight in meta-analysis came from studies at serious or high risk of bias

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1 e. Result comes from a study with a small sample size (sample size <576 participants)

## 2 Review H2

### 3 Deferred cytoreductive nephrectomy (CN) vs. systemic anti-cancer therapy (SACT) alone

#### 4 Table 13 Overall survival

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Deferred CN	SACT alone	Relative (95% CI)	Absolute (95% CI)	
Overall survival ≤ 5 years											
6 (Bhindi 2018, Bhindi 2020, Chakiryan 2022, Day 2016, Dragomir 2022, Hatakeyama 2021)	non-randomised studies	very serious <sup>a</sup>	not serious	not serious	not serious	none	8,464	8,692 <sup>b</sup>	HR 0.43 (0.37 to 0.51)	NR	Low

5 **CI:** confidence interval; **HR:** hazard ratio; **MD:** mean difference; **OR:** odds ratio; **RR:** risk ratio; **NR:** not reported

#### 6 Explanations

7 a. Downgraded twice for risk of bias. Greater than 50% of the weight in meta-analysis came from studies at high risk of bias

8 b. Bhindi et al. 2018 does not report number of participants in SACT alone arm.

9



1 **Table 14 Cancer-specific mortality**

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Deferred CN	SACT alone	Relative (95% CI)	Absolute (95% CI)	
1 (Fransen 2023)	non-randomised studies	very serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>c,d</sup>	none	15/19 (78.9%)	7/7 (100.0%)	RR 0.83 (0.61 to 1.11)	170 fewer per 1,000 (from 390 fewer to 110 more)	Very low

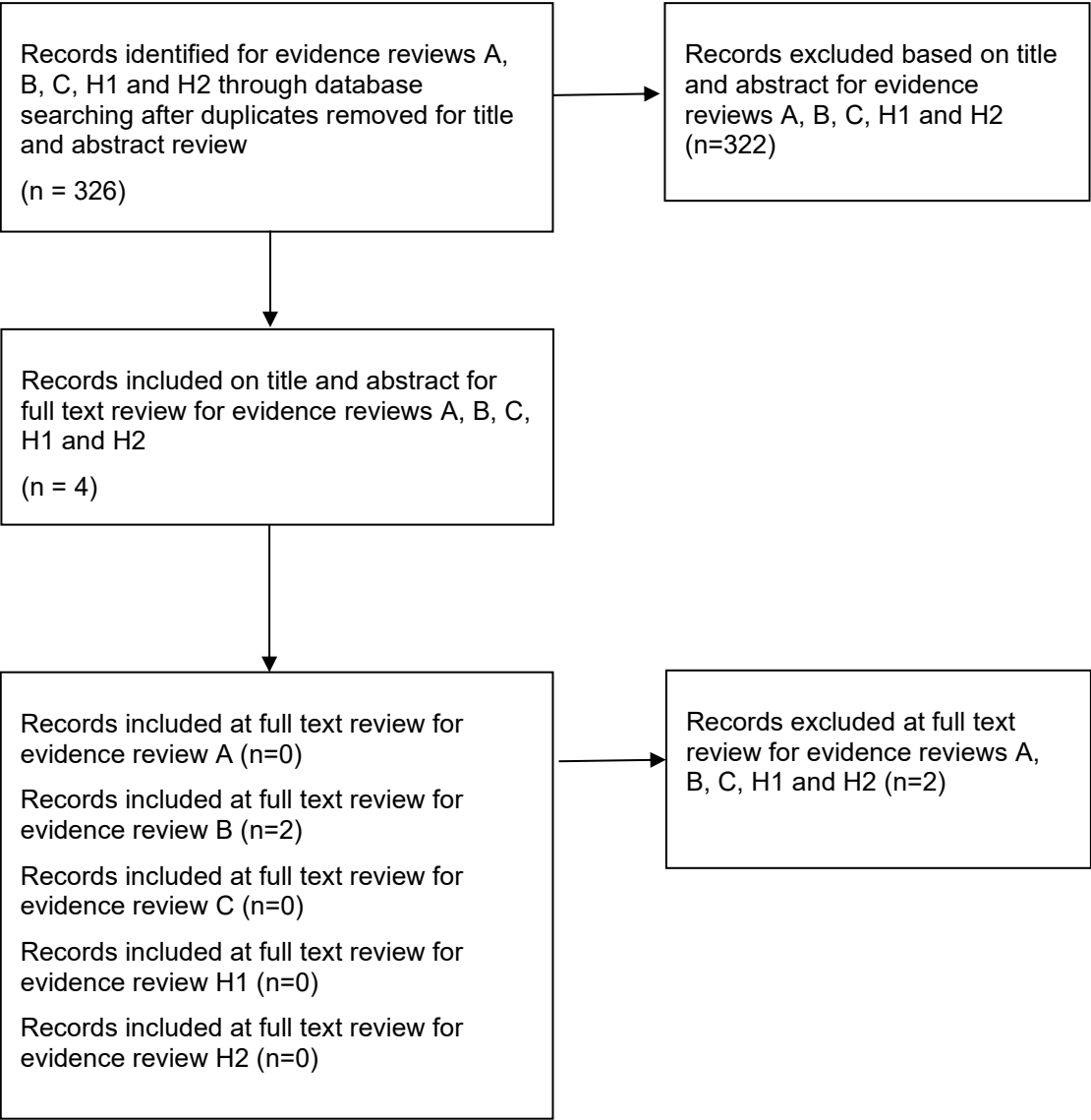
2 **CI:** confidence interval; **HR:** hazard ratio; **RR:** risk ratio

3 **Explanations**

- 4 a. Downgraded twice for risk of bias. Greater than 50% of the weight in meta-analysis came from studies at high risk of bias
- 5 b. Downgraded once for inconsistency. Analysis included a single study
- 6 c. Downgraded once for imprecision. 95% confidence interval for the effect size crossed the line of no effect
- 7 d. Downgraded once for imprecision. Result comes from a study with a small sample size (sample size <576 participants)

1 **Appendix G – Economic evidence study selection**

2 **Figure 20: Economic evidence study selection**



3

4

- 1 **Appendix H – Economic evidence tables**
- 2 No economic evidence was identified for review questions H1 and H2.

- 1 **Appendix I – Health economic model**
- 2 No original economic modelling was conducted for this review question.

## 1 Appendix J – Excluded studies

### 2 Effectiveness evidence excluded at full text (n=147)

Study	Reason
<a href="#">Abdel Raheem, Ali, Chang, Ki Don, Alenzi, Mohammed Jayed et al. (2019) Robot-Assisted Partial Nephrectomy for Totally Endophytic Renal Tumors: Step by Step Standardized Surgical Technique and Long-Term Outcomes with a Median 59-Month Follow-Up.</a> Journal of laparoendoscopic & advanced surgical techniques. Part A 29(1): 1-11	- Exclude review C- Study included only patients T1-T2
<a href="#">Abdollah, Firas, Sun, Maxine, Thuret, Rodolphe et al. (2011) Mortality and morbidity after cytoreductive nephrectomy for metastatic renal cell carcinoma: a population-based study.</a> Annals of surgical oncology 18(10): 2988-96	- Comparator in study does not match that specified in protocol <i>Compares radical nephrectomy Vs. cytoreductive nephrectomy. Unclear about the use of SACT</i>
<a href="#">Abedali, Zain A, Monn, M Francesca, Huddleston, Patrick et al. (2020) Robotic and open partial nephrectomy for intermediate and high complexity tumors: a matched-pairs comparison of surgical outcomes at a single institution.</a> Scandinavian journal of urology 54(4): 313-317	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Abu-Ghanem, Yasmin, Fernandez-Pello, Sergio, Bex, Axel et al. (2020) Limitations of Available Studies Prevent Reliable Comparison Between Tumour Ablation and Partial Nephrectomy for Patients with Localised Renal Masses: A Systematic Review from the European Association of Urology Renal Cell Cancer Guideline Panel.</a> European urology oncology 3(4): 433-452	- Data not reported in an extractable format
<a href="#">Abu-Ghanem, Yasmin, van Thienen, Johannes V, Blank, Christian et al. (2022) Cytoreductive nephrectomy and exposure to sunitinib - a post hoc analysis of the Immediate Surgery or Surgery After Sunitinib Malate in Treating Patients With Metastatic Kidney Cancer (SURTIME) trial.</a> BJU international 130(1): 68-75	- Study does not contain a relevant outcome <i>No additional outcomes to reported</i>
<a href="#">Acosta Ruiz, Vanessa, Ladjevardi, Sam, Brekkan, Einar et al. (2019) Periprocedural outcome after laparoscopic partial nephrectomy versus radiofrequency ablation for T1 renal tumors: a modified R.E.N.A.L nephrometry score adjusted comparison.</a> Acta radiologica (Stockholm, Sweden : 1987) 60(2): 260-268	- Study published before included SR/s for the outcome/s reported

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Study	Reason
<a href="#">Aeppli, S., Engeler, D.S., Fischer, S. et al. (2022) Incidence and outcome of patients with renal cell carcinoma treated with partial or radical nephrectomy in the Cantons St Gallen and Appenzell 2009-2018. Swiss Medical Weekly 152(2324): w30175</a>	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Ahn, Thomas, Ellis, Robert J, White, Victoria M et al. (2018) Predictors of new-onset chronic kidney disease in patients managed surgically for T1a renal cell carcinoma: An Australian population-based analysis. Journal of surgical oncology 117(7): 1597-1610</a>	- Primary study covered fully by an included systematic review
<a href="#">Alasker, Ahmed, Alnafisah, Turki Rashed, Alghafees, Mohammad et al. (2023) Preserving Renal Function without Compromising Oncological Outcomes: A Comparative Study of Partial and Total Nephrectomies in T3 Stage Renal Cell Carcinoma. Journal of kidney cancer and VHL 10(4): 28-32</a>	- Comparator in study does not match that specified in protocol <i>Compared PN vs RN in T3a RCC: not relevant for review C</i>
<a href="#">Ali, Muhammad, Kwon, Young Suk, Koo, Kendrick et al. (2025) Salvage stereotactic ablative body radiotherapy after thermal ablation of primary kidney cancer. BJU international 135(1): 110-116</a>	- Study did not compare the interventions of interest
<a href="#">Alnimer, Yanal, Qasrawi, Ayman, Yan, Donglin et al. (2021) Prognostic Impact of Cytoreductive Nephrectomy in Patients with Metastatic Renal Cell Carcinoma: Data from a Large Population-Based Database. Urology journal 19(2): 111-119</a>	- Exclude - Outcome was measured using a measure out of scope
<a href="#">Alper, Isik and Yuksel, Esra (2016) Comparison of Acute and Chronic Pain after Open Nephrectomy versus Laparoscopic Nephrectomy: A Prospective Clinical Trial. Medicine 95(16): e3433</a>	- There is no information on cT or pT stage
<a href="#">Alshyarba, M.H.M., Alamri, A., Assiri, J.M.M. et al. (2020) Treatment and overall survival in renal cell carcinoma. Bahrain Medical Bulletin 42(2): 113-115</a>	- Data not reported in an extractable format <i>Kaplan-Meier for overall survival</i>
<a href="#">Althaus, Adam B, Chang, Peter, Mao, Jialin et al. (2020) Patient-Reported Quality of Life and Convalescence After Minimally Invasive Kidney Cancer Surgery. Urology 144: 123-129</a>	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Alvim, Ricardo, Tin, Amy, Nogueira, Lucas et al. (2021) A comparison of oncologic and functional</a>	- Comparator in study does not match that specified in protocol

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Study	Reason
<a href="#">outcomes in patients with pt3a renal cell carcinoma treated with partial and radical nephrectomy</a> . International braz j urol : official journal of the Brazilian Society of Urology 47(4): 777-783	<i>Compared RN with PN in T3a tumours - not relevant for review C.</i>
<a href="#">Alzamzami, M, Geirbely, A, Ahmed, MB et al. (2023) A Literature Review of Perioperative Outcomes of Robotic Radical Nephrectomy (RRN) Versus Laparoscopic Radical Nephrectomy (LRN) for Renal Cell Carcinoma (RCC)</a> . Cureus 15(11): e49077	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Amin, C., Wallen, E., Pruthi, R.S. et al. (2008) Preoperative Tyrosine Kinase Inhibition as an Adjunct to Debulking Nephrectomy</a> . Urology 72(4): 864-868	- Study does not contain a relevant intervention <i>Irrelevant nephrectomy type. Study observes the patients undergone laparoscopic and radical nephrectomy</i>
<a href="#">Andrade, Hiury S, Zargar, Homayoun, Akca, Oktay et al. (2017) Is Robotic Partial Nephrectomy Safe for T3a Renal Cell Carcinoma? Experience of a High-Volume Center</a> . Journal of endourology 31(2): 153-157	- Comparator in study does not match that specified in protocol <i>Compares RN and PN in T3a RCC - not relevant for review C.</i>
<a href="#">Andrews, Jack R, Lohse, Christine M, Boorjian, Stephen A et al. (2022) Outcomes following cytoreductive nephrectomy without immediate postoperative systemic therapy for patients with synchronous metastatic renal cell carcinoma</a> . Urologic oncology 40(4): 166e1-166e8	- Comparator in study does not match that specified in protocol <i>None of the participants had SACT</i>
<a href="#">Anele, Uzoma A, Marchioni, Michele, Yang, Bo et al. (2019) Robotic versus laparoscopic radical nephrectomy: a large multi-institutional analysis (ROSULA Collaborative Group)</a> . World journal of urology 37(11): 2439-2450	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Ansari, Jawaher, Farrag, Ashraf, Ali, Arwa et al. (2021) Concurrent use of nivolumab and radiotherapy for patients with metastatic non-small cell lung cancer and renal cell carcinoma with oligometastatic disease progression on nivolumab</a> . Molecular and clinical oncology 15(4): 214	- Study does not contain a relevant outcome
<a href="#">Antonelli, Alessandro, Palumbo, Carlotta, Sandri, Marco et al. (2020) Renal Function Impairment Below Safety Limits Correlates With Cancer-specific Mortality in Localized Renal Cell Carcinoma: Results From a Single-center Study</a> . Clinical genitourinary cancer 18(4): e360-e367	- Study does not contain a relevant outcome

Study	Reason
<a href="#">Antonelli, Alessandro, Veccia, Alessandro, Pavan, Nicola et al. (2019) Outcomes of Partial and Radical Nephrectomy in Octogenarians - A Multicenter International Study (Resurge).</a> Urology 129: 139-145	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Aron, Monish, Koenig, Phillipe, Kaouk, Jihad H et al. (2008) Robotic and laparoscopic partial nephrectomy: a matched-pair comparison from a high-volume centre.</a> BJU international 102(1): 86-92	- There is no information on cT or pT stage
<a href="#">Artsitas, Sotirios, Artsitas, Dimitrios, Segkou, Ioanna et al. (2022) Considering "Trifecta" as a Single Outcome when Comparing Robotic With Open Partial Nephrectomy: A Mathematical Model of Volume Conservation and Systematic Review.</a> In vivo (Athens, Greece) 36(6): 2558-2578	- Exclude - assessed outcome is out of scope
<a href="#">Bacic, Janine, Liu, Tao, Thompson, R Houston et al. (2020) Emulating Target Clinical Trials of Radical Nephrectomy With or Without Lymph Node Dissection for Renal Cell Carcinoma.</a> Urology 140: 98-106	- Comparator in study does not match that specified in protocol <i>LND vs no LND</i>
<a href="#">Badrigilan, S., Meola, A., Chang, S.D. et al. (2023) Stereotactic radiosurgery with immune checkpoint inhibitors for brain metastases: a meta-analysis study.</a> British Journal of Neurosurgery 37(6): 1533-1543	- Exclude - wrong population
<a href="#">Baio, Raffaele, Molisso, Giovanni, Caruana, Christian et al. (2023) "Could Patient Age and Gender, along with Mass Size, Be Predictive Factors for Benign Kidney Tumors?": A Retrospective Analysis of 307 Consecutive Single Renal Masses Treated with Partial or Radical Nephrectomy.</a> Bioengineering (Basel, Switzerland) 10(7)	- Study does not contain a relevant outcome
<a href="#">Bamias, Aristotle, Tzannis, Kimon, Papatsoris, Athanasios et al. (2014) Prognostic significance of cytoreductive nephrectomy in patients with synchronous metastases from renal cell carcinoma treated with first-line sunitinib: a European multiinstitutional study.</a> Clinical genitourinary cancer 12(5): 373-83	- Mixed population of SACT pre/post non-pharmacological regimens <i>No information available to interpret if the SACT was given before or after CN</i>
<a href="#">Baudo, A., Incesu, R.-B., Morra, S. et al. (2023) Other-Cause Mortality, According to Partial vs. Radical Nephrectomy: Age and Stage Analyses.</a> Clinical Genitourinary Cancer	- Study does not contain a relevant outcome

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# DRAFT FOR CONSULTATION

Study	Reason
<a href="#">Bayrak, Omer, Seckiner, Ilker, Erturhan, Sakip et al. (2014) Comparison of the complications and the cost of open and laparoscopic radical nephrectomy in renal tumors larger than 7 centimeters. Urology journal 11(1): 1222-7</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Bazzi, Wassim M, Sjoberg, Daniel D, Feuerstein, Michael A et al. (2015) Long-term survival rates after resection for locally advanced kidney cancer: Memorial Sloan Kettering Cancer Center 1989 to 2012 experience. The Journal of urology 193(6): 1911-6</a>	- Comparator in study does not match that specified in protocol
<a href="#">Bekema, Hendrika J, MacLennan, Steven, Imamura, Mari et al. (2013) Systematic review of adrenalectomy and lymph node dissection in locally advanced renal cell carcinoma. European urology 64(5): 799-810</a>	- Comparator in study does not match that specified in protocol
<a href="#">Beksac, Alp T, Okhawere, Kennedy E, Abou Zeinab, Mahmoud et al. (2022) Robotic partial nephrectomy for management of renal mass in patients with a solitary kidney: can we expand the indication to T2 and T3 disease?. Minerva urology and nephrology 74(2): 203-208</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Benichou, Ygal, Audenet, Francois, Bensalah, Karim et al. (2023) Partial nephrectomy in solitary kidneys: comparison between open surgery and robotic-assisted laparoscopy on perioperative and functional outcomes (UroCCR-54 study). World journal of urology 41(2): 315-324</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Bianchi, Lorenzo, Chessa, Francesco, Piazza, Pietro et al. (2022) Percutaneous ablation or minimally invasive partial nephrectomy for cT1a renal masses? A propensity score-matched analysis. International journal of urology : official journal of the Japanese Urological Association 29(3): 222-228</a>	- Secondary publication of an included study that does not provide any additional relevant information
<a href="#">Binsaleh, Saleh, Madbouly, Khaled, Matsumoto, Edward D et al. (2015) A Prospective Randomized Study of Pfannenstiel Versus Expanded Port Site Incision for Intact Specimen Extraction in Laparoscopic Radical Nephrectomy. Journal of endourology 29(8): 913-8</a>	- Exclude - Intervention is out of scope
<a href="#">Blom, Jan H M, van Poppel, Hein, Marechal, Jean M et al. (2009) Radical nephrectomy with</a>	- Comparator in study does not match that specified in protocol

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Study	Reason
<a href="#">and without lymph-node dissection: final results of European Organization for Research and Treatment of Cancer (EORTC) randomized phase 3 trial 30881</a> . <i>European urology</i> 55(1): 28-34	<i>Lymphadenectomy vs no lymphadenectomy</i>
<a href="#">Bosse, Dominick, Lin, Xun, Simantov, Ronit et al. (2019) Response of Primary Renal Cell Carcinoma to Systemic Therapy</a> . <i>European urology</i> 76(6): 852-860	- Not a relevant study design <i>Pooled Analysis</i>
<a href="#">Boylu, U., Basatac, C., Yildirim, U. et al. (2015) Comparison of surgical, functional, and oncological outcomes of open and robot-assisted partial nephrectomy</a> . <i>Journal of Minimal Access Surgery</i> 11(1): 72-77	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Bravi, C.A., on behalf of the Junior ERUS/Young Academic Urologist Working Group on Robot-Assisted, Surgery, Dell'Oglio, P. et al. (2024) Surgical Experience and Functional Outcomes after Laparoscopic and Robot-Assisted Partial Nephrectomy: Results from a Multi-Institutional Collaboration</a> . <i>Journal of Clinical Medicine</i> 13(19): 6016	- Exclude - review C. Patients with localised tumour
<a href="#">Breda, Alberto; Anterasian, Christine; Beldegrun, Arie (2010) Management and outcomes of tumor recurrence after focal ablation renal therapy</a> . <i>Journal of endourology</i> 24(5): 749-52	- More recent systematic review included that covers the same topic
<a href="#">Britton, Cameron J, Sharma, Vidit, Lohse, Christine M et al. (2022) Progression of Chronic Kidney Disease Following Radical and Partial Nephrectomy</a> . <i>Urology</i> 169: 125-133	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Brown, Janet E, Royle, Kara-Louise, Gregory, Walter et al. (2023) Temporary treatment cessation versus continuation of first-line tyrosine kinase inhibitor in patients with advanced clear cell renal cell carcinoma (STAR): an open-label, non-inferiority, randomised, controlled, phase 2/3 trial</a> . <i>The Lancet. Oncology</i> 24(3): 213-227	- Study does not contain a relevant intervention
<a href="#">Buckland, Benjamin, Tree, Kevin, Best, Oliver et al. (2024) Robotic versus Laparoscopic Partial Nephrectomy: A Systematic Review and Meta-Analysis of Randomised Trials</a> . <i>Surgical technology international</i> 45	- Exclude - review C. Patients with localised tumour

Study	Reason
<a href="#">Burgess, Neil A, Koo, Brendan C, Calvert, Robert C et al. (2007) Randomized trial of laparoscopic v open nephrectomy. Journal of endourology 21(6): 610-3</a>	- There is no information on cT or pT stage
<a href="#">Cacciamani, Giovanni E, Medina, Luis G, Gill, Tania et al. (2018) Impact of Surgical Factors on Robotic Partial Nephrectomy Outcomes: Comprehensive Systematic Review and Meta-Analysis. The Journal of urology 200(2): 258-274</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Cai, Yi; Li, Han-Zhong; Zhang, Yu-Shi (2018) Comparison of Partial and Radical Laparoscopic Nephrectomy: Long-Term Outcomes for Clinical T1b Renal Cell Carcinoma. Urology journal 15(2): 16-20</a>	- Non-OECD country
<a href="#">Calpin, Gavin G, Ryan, Fintan R, McHugh, Fiachra T et al. (2023) Comparing the outcomes of open, laparoscopic and robot-assisted partial nephrectomy: a network meta-analysis. BJU international 132(4): 353-364</a>	- Exclude - For C. Proportion of patients stage T3 < 90%
<a href="#">Calpin, GG, Ryan, FR, McHugh, FT et al. (2023) Comparing the Outcomes of Open, Laparoscopic &amp; Robotic Partial Nephrectomy: A Network Meta-Analysis. BJU international</a>	- Duplicate reference
<a href="#">Campi, Riccardo, Berni, Alessandro, Amparore, Daniele et al. (2022) Impact of frailty on perioperative and oncologic outcomes in patients undergoing surgery or ablation for renal cancer: a systematic review. Minerva urology and nephrology 74(2): 146-160</a>	- More recent systematic review included that covers the same topic
<a href="#">Cao, Dalong, Huang, Yongqiang, Zhang, Chuankai et al. (2019) Adverse Effect of Lymph Node Dissection in Metastatic Renal Cell Cancer Patients Treated with Cytoreductive Nephrectomy: A Contemporary Analysis of Survival. Journal of Cancer 10(19): 4639-4646</a>	- Study did not compare the interventions of interest
<a href="#">Capitanio, U., Larcher, A., Cianflone, F. et al. (2020) Hypertension and Cardiovascular Morbidity Following Surgery for Kidney Cancer. European Urology Oncology 3(2): 209-215</a>	- Primary study covered fully by an included systematic review
<a href="#">Capitanio, Umberto, Zini, Laurent, Perrotte, Paul et al. (2008) Cytoreductive partial nephrectomy does not undermine cancer control in metastatic renal cell carcinoma: a population-based study. Urology 72(5): 1090-5</a>	- Study does not contain a relevant intervention <i>Compares partial nephrectomy with radical nephrectomy</i>

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Study	Reason
<a href="#">Carvalho, Filipe L F, Zheng, Chaoyi, Witmer, Kenneth et al. (2019) Complications associated with perioperative use of tyrosine kinase inhibitor in cytoreductive nephrectomy.</a> Scientific reports 9(1): 15272	- Study does not contain a relevant intervention <i>Compares nephrectomy followed by SACT vs. nephrectomy alone.</i> - study evaluates the effect of preoperative SACT. It's unclear whether SACT was given before or after the surgery.
<a href="#">Castilho, Tiago Mendonca Lopez, Lemos, Gustavo Caserta, Cha, Jonathan Doyun et al. (2020) Transition from open partial nephrectomy directly to robotic surgery: experience of a single surgeon to achieve "TRIFECTA".</a> International braz j urol : official journal of the Brazilian Society of Urology 46(5): 814-821	- Exclude - Study with a single arm
<a href="#">Cerrato, Clara, Meagher, Margaret F, Autorino, Riccardo et al. (2023) Partial versus radical nephrectomy for complex renal mass: multicenter comparative analysis of functional outcomes (Rosula collaborative group).</a> Minerva urology and nephrology 75(4): 425-433	- Study does not contain a relevant outcome <i>Outcomes presented for T1, T2 and T3 combined</i>
<a href="#">Chan, Vinson Wai-Shun, Tan, Wei Shen, Leow, Jeffrey J et al. (2021) Delayed surgery for localised and metastatic renal cell carcinoma: a systematic review and meta-analysis for the COVID-19 pandemic.</a> World journal of urology 39(12): 4295-4303	- Exclude - Result reported in the most updated MA
<a href="#">Chanbour, Hani, Chen, Jeffrey W, Bendfeldt, Gabriel A et al. (2024) Impact of Targeted Systemic Therapy and Radiotherapy on Patients Undergoing Spine Surgery for Metastatic Renal Cell Carcinoma.</a> International journal of spine surgery 18(3): 343-352	- Exclude - Intervention is out of scope <i>Spinal surgery</i>
<a href="#">Chang, Ki Don, Abdel Raheem, Ali, Kim, Kwang Hyun et al. (2018) Functional and oncological outcomes of open, laparoscopic and robot-assisted partial nephrectomy: a multicentre comparative matched-pair analyses with a median of 5 years' follow-up.</a> BJU international 122(4): 618-626	- Exclude review C - Study included only patients T1-T2
<a href="#">Chang, Xiaofeng, Liu, Tieshi, Zhang, Fan et al. (2015) Radiofrequency ablation versus partial nephrectomy for clinical T1a renal-cell carcinoma: long-term clinical and oncologic outcomes based on a propensity score analysis.</a> Journal of endourology 29(5): 518-25	- Non-OECD country
<a href="#">Chang, Xiaofeng, Zhang, Fan, Liu, Tieshi et al. (2015) Radio frequency ablation versus partial</a>	- Non-OECD country

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Study	Reason
<a href="#">nephrectomy for clinical T1b renal cell carcinoma: long-term clinical and oncologic outcomes.</a> The Journal of urology 193(2): 430-5	
<a href="#">Chang, Ying-Hsu, Chang, Su-Wei, Liu, Chung-Yi et al. (2018) Demographic characteristics and complications of open and minimally invasive surgeries for renal cell carcinoma: a population-based case-control study in Taiwan.</a> Therapeutics and clinical risk management 14: 1235-1241	- Non-OECD country
<a href="#">Chapin, Brian F, Delacroix, Scott E Jr, Culp, Stephen H et al. (2011) Safety of presurgical targeted therapy in the setting of metastatic renal cell carcinoma.</a> European urology 60(5): 964-71	- Comparator in study does not match that specified in protocol <i>Study compares SACT followed by CN with immediate CN. Results section indicates that both groups received SACT post surgery as well.</i>
<a href="#">Chapman, Terence N, Sharma, Satish, Zhang, Shaozeng et al. (2008) Laparoscopic lymph node dissection in clinically node-negative patients undergoing laparoscopic nephrectomy for renal carcinoma.</a> Urology 71(2): 287-91	- Comparator in study does not match that specified in protocol <i>LND vs no LND</i>
<a href="#">Chen, Bo, Li, Jinze, Huang, Yin et al. (2023) The role of cytoreductive nephrectomy in metastatic renal cell carcinoma in the targeted therapy and immunological therapy era: a systematic review and meta-analysis.</a> International journal of surgery (London, England) 109(4): 982-994	- Exclude - error in the paper
<a href="#">Chen, Yonghui, Wu, Xiaorong, Zhou, Jiale et al. (2022) Thermal ablation assisted laparoscopic partial nephrectomy for clinical T1b renal tumors.</a> Minimally invasive therapy & allied technologies : MITAT : official journal of the Society for Minimally Invasive Therapy 31(2): 179-184	- Non-OECD country
<a href="#">Cheung, Douglas C and Finelli, Antonio (2017) Active Surveillance in Small Renal Masses in the Elderly: A Literature Review.</a> European urology focus 3(45): 340-351	- More recent systematic review included that covers the same topic
<a href="#">Cheung, Patrick, Patel, Samir, North, Scott A et al. (2021) Stereotactic Radiotherapy for Oligoprogression in Metastatic Renal Cell Cancer Patients Receiving Tyrosine Kinase Inhibitor Therapy: A Phase 2 Prospective Multicenter Study.</a> European urology 80(6): 693-700	- Not a relevant study design

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Study	Reason
<a href="#">Chiancone, Francesco, Fabiano, Marco, Meccariello, Clemente et al. (2021) Laparoscopic versus open partial nephrectomy for the management of highly complex renal tumors with PADUA score 10: A single center analysis.</a> Urologia 88(4): 343-347	- Exclude review C- Study included only patients T1-T2
<a href="#">Chiou, Jiun-Kai, Chang, Li-Wen, Li, Jian-Ri et al. (2023) Metastasectomy Improves Overall Survival in Metastatic Renal Cell Carcinoma: A Retrospective Cohort Study.</a> Anticancer research 43(7): 3193-3201	- Mixed population of SACT pre/post non-pharmacological regimens <i>All participants received SACT. Not sufficient information to know the timeline of SACT. Compares patients undergone metastasectomy vs. non-metastasectomy.</i>
<a href="#">Chlorogiannis, David-Dimitris, Kratiras, Zisis, Efthymiou, Evgenia et al. (2024) Percutaneous Microwave Ablation Versus Robot-Assisted Partial Nephrectomy for Stage I Renal Cell Carcinoma: A Propensity-Matched Cohort Study Focusing Upon Long-Term Follow-Up of Oncologic Outcomes.</a> Cardiovascular and interventional radiology 47(5): 573-582	- Data not reported in an extractable format
<a href="#">Cho, C L, Ho, K L, Chu, S S M et al. (2011) Robot-assisted versus standard laparoscopic partial nephrectomy: comparison of perioperative outcomes from a single institution.</a> Hong Kong medical journal = Xianggang yi xue za zhi 17(1): 33-8	- Non-OECD country  - Not a relevant study design <i>Consecutive case series</i>
<a href="#">Choi, Chang Il, Kang, Minyong, Sung, Hyun Hwan et al. (2018) Oncologic Outcomes of Cytoreductive Nephrectomy in Synchronous Metastatic Renal-Cell Carcinoma: A Single-Center Experience.</a> Clinical genitourinary cancer 16(6): e1189-e1199	- Mixed population of SACT pre/post non-pharmacological regimens <i>All participants received SACT. Not sufficient information to know the timeline of SACT.</i>
<a href="#">Choi, J.D., Park, J.W., Lee, H.W. et al. (2013) A comparison of surgical and functional outcomes of robot-assisted versus pure laparoscopic partial nephrectomy.</a> Journal of the Society of Laparoendoscopic Surgeons 17(2): 292-299	- Exclude review C. Study included only patients T1-T2
<a href="#">Choi, J.E., You, J.H., Kim, D.K. et al. (2015) Comparison of perioperative outcomes between robotic and laparoscopic partial nephrectomy: A systematic review and meta-analysis.</a> European Urology 67(5): 891-901	- Exclude - review C. Patients with localised tumour
<a href="#">Choi, Se Young, Ha, Moon Soo, Lee, Jeong Woo et al. (2023) Shifting role of cytoreductive nephrectomy according to type of systemic</a>	- Mixed population of SACT pre/post non-pharmacological regimens <i>All participants received SACT. Not sufficient information to know the timeline of SACT.</i>

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Study	Reason
<a href="#">therapy: A nationwide cohort study.</a> Asian journal of surgery 46(1): 328-336	
<a href="#">Choi, Se Young, Jung, Han, You, Dalsan et al. (2019) Robot-assisted partial nephrectomy is associated with early recovery of renal function: Comparison of open, laparoscopic, and robot-assisted partial nephrectomy using DTPA renal scintigraphy.</a> Journal of surgical oncology 119(7): 1016-1023	- There is no information on cT or pT stage
<a href="#">Chung, Doo Yong, Kang, Dong Hyuk, Kim, Jong Won et al. (2020) Comparison of oncologic outcomes between partial nephrectomy and radical nephrectomy in patients who were upstaged from cT1 renal tumor to pT3a renal cell carcinoma: an updated systematic review and meta-analysis.</a> Therapeutic advances in urology 12: 1756287220981508	- Comparator in study does not match that specified in protocol <i>PN vs RN for upstaged pT3 tumour</i>
<a href="#">Chung, Jae-Seung, Son, Nak Hoon, Lee, Sang Eun et al. (2018) Partial versus Radical Nephrectomy for T1-T2 Renal Cell Carcinoma in Patients with Chronic Kidney Disease Stage III: a Multiinstitutional Analysis of Kidney Function and Survival Rate.</a> Journal of Korean medical science 33(43): e277	- More recent systematic review included that covers the same topic <i>already included by Ochoa but also reports HR in people with CKD <math>30 \leq eGFR &lt; 60</math> in table 2 Looks like Ochoa only included new onset CKD which is why they've only used the stage i-iii values - can exclude</i>
<a href="#">Cinar, O., Bolat, M.S., Cicek, M.C. et al. (2020) Experiences of Laparoscopic Partial Nephrectomy for T1a Kidney Tumours: Results of Two Hundred and Fifteen Patients.</a> Bulletin of Urooncology 19(3): 130-135	- Exclude - review C. Study included only patients T1-T2
<a href="#">Colombo, Jose R Jr, Haber, Georges-Pascal, Jelovsek, John E et al. (2008) Seven years after laparoscopic radical nephrectomy: oncologic and renal functional outcomes.</a> Urology 71(6): 1149-54	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Correa, Rohann J M, Louie, Alexander V, Zaorsky, Nicholas G et al. (2019) The Emerging Role of Stereotactic Ablative Radiotherapy for Primary Renal Cell Carcinoma: A Systematic Review and Meta-Analysis.</a> European urology focus 5(6): 958-969	- More recent systematic review included that covers the same topic
<a href="#">Cotta, Brittney H, Meagher, Margaret F, Patil, Dattatraya et al. (2021) Elevated preoperative C-reactive protein is associated with renal functional decline and non-cancer mortality in surgically treated renal cell carcinoma: analysis from the INternational Marker Consortium for</a>	- Primary study covered fully by an included systematic review

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Study	Reason
<a href="#">Renal Cancer (INMARC)</a> . BJU international 127(3): 311-317	
<a href="#">Crocerossa, Fabio, Autorino, Riccardo, Derweesh, Ithaar et al. (2023) Management of renal cell carcinoma in transplant kidney: a systematic review and meta-analysis</a> . Minerva urology and nephrology 75(1): 1-16	- Does not contain a population of people with kidney cancer <i>Transplanted kidneys only</i>
<a href="#">Crocerossa, Fabio, Carbonara, Umberto, Cantiello, Francesco et al. (2021) Robot-assisted Radical Nephrectomy: A Systematic Review and Meta-analysis of Comparative Studies</a> . European urology 80(4): 428-439	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Culp, Stephen H, Tannir, Nizar M, Abel, E Jason et al. (2010) Can we better select patients with metastatic renal cell carcinoma for cytoreductive nephrectomy?</a> . Cancer 116(14): 3378-88	- Mixed population of SACT pre/post non-pharmacological regimens <i>All participants received SACT. Not sufficient information to know the timeline of SACT received before or after CN.</i>
<a href="#">Dabestani, Saeed, Marconi, Lorenzo, Hofmann, Fabian et al. (2014) Local treatments for metastases of renal cell carcinoma: a systematic review</a> . The Lancet. Oncology 15(12): e549-61	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Dahm, P., Ergun, O., Uhlig, A. et al. (2024) Cytoreductive nephrectomy in metastatic renal cell carcinoma</a> . Cochrane Database of Systematic Reviews 2024(6): cd013773	- Systematic review used as source of primary studies
<a href="#">Dahm, Philipp, Ergun, Onuralp, Uhlig, Annemarie et al. (2024) Cytoreductive nephrectomy in metastatic renal cell carcinoma</a> . The Cochrane database of systematic reviews 6: cd013773	- Duplicate reference
<a href="#">Danzig, Matthew R, Ghandour, Rashed A, Chang, Peter et al. (2015) Active Surveillance is Superior to Radical Nephrectomy and Equivalent to Partial Nephrectomy for Preserving Renal Function in Patients with Small Renal Masses: Results from the DISSRM Registry</a> . The Journal of urology 194(4): 903-9	- Primary study covered fully by an included systematic review
<a href="#">Darlane, Charles; Timsit, Marc-Olivier; Mejean, Arnaud (2018) Position of cytoreductive nephrectomy in the setting of metastatic renal cell carcinoma patients: does the CARMENA trial lead to a paradigm shift?</a> . Bulletin du cancer 105suppl3: 229-s234	- Systematic review used as source of primary studies



Study	Reason
<a href="#">Das, Manoj K, Rohith, Gorrepati, Mandal, Swarnendu et al. (2024) Intraoperative ultrasonography (IOUS)-guided vs conventional laparoscopic nephrectomy: a randomised control trial. BJU international 133(1): 71-78</a>	- Exclude - Intervention is out of scope
<a href="#">Dash, A., Vickers, A.J., Schachter, L.R. et al. (2006) Comparison of outcomes in elective partial vs radical nephrectomy for clear cell renal cell carcinoma of 4-7 cm. BJU International 97(5): 939-945</a>	- For review A. Study published before 2016 (search date for disease-free survival)
<a href="#">de Bruijn, Roderick, Wimalasingham, Akhila, Szabados, Bernadett et al. (2020) Deferred Cytoreductive Nephrectomy Following Presurgical Vascular Endothelial Growth Factor Receptor-targeted Therapy in Patients with Primary Metastatic Clear Cell Renal Cell Carcinoma: A Pooled Analysis of Prospective Trial Data. European urology oncology 3(2): 168-173</a>	- Systematic review used as source of primary studies
<a href="#">De Gobbi, Alberto, BIASONI, Davide, Catanzaro, Mario et al. (2018) Surgery of locally advanced and metastatic kidney cancer after tyrosine kinase inhibitors therapy: single institute experience. Tumori 104(5): 388-393</a>	- Not a relevant study design <i>observational study</i>
<a href="#">de Saint Aubert, N, Audenet, F, Mccaig, F et al. (2018) Nephron sparing surgery in tumours greater than 7cm. Progres en urologie : journal de l'Association francaise d'urologie et de la Societe francaise d'urologie 28(6): 336-343</a>	- Primary study covered fully by an included systematic review
<a href="#">Deka, H., Medam, N.M., Ginil Kumar, P. et al. (2024) Comparison of Trifecta and Pentafecta Outcomes across 3 Surgical Modalities of Partial Nephrectomy (PN) - Open, Lap, and Robotic. Journal of Kidney Cancer and VHL 11(3): 27</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Deng, Huan, Fan, Yan, Yuan, Feifei et al. (2021) Partial nephrectomy provides equivalent oncologic outcomes and better renal function preservation than radical nephrectomy for pathological T3a renal cell carcinoma: A meta-analysis. International braz j urol : official journal of the Brazilian Society of Urology 47(1): 46-60</a>	- Comparator in study does not match that specified in protocol <i>Compares RN vs PN for T3 tumours</i>
<a href="#">Deng, Wen, Chen, Luyao, Wang, Yibing et al. (2019) Cryoablation versus Partial Nephrectomy for Clinical Stage T1 Renal Masses: A Systematic Review and Meta-Analysis. Journal of Cancer 10(5): 1226-1236</a>	- More recent systematic review included that covers the same topic

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Study	Reason
<a href="#">Deng, Wen, Zhou, Zhengtao, Zhong, Jian et al. (2020) Retroperitoneal laparoscopic partial versus radical nephrectomy for large (<math>\geq 4</math> cm) and anatomically complex renal tumors: A propensity score matching study.</a> European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 46(7): 1360-1365	- Non-OECD country
<a href="#">Dengina, N., Mitin, T., Gamayunov, S. et al. (2019) Stereotactic body radiation therapy in combination with systemic therapy for metastatic renal cell carcinoma: A prospective multicentre study.</a> ESMO Open 4(5): e000535	- Not a relevant study design
<a href="#">Desideri, I, Francolini, G, Scotti, V et al. (2019) Benefit of ablative versus palliative-only radiotherapy in combination with nivolumab in patients affected by metastatic kidney and lung cancer.</a> Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico 21(7): 933-938	- Does not contain a population of people with kidney cancer <i>Mix of non-small cell lung cancer and RCC. No separate results for participants with RCC reported. No comparator group. Participants received RT and SACT simultaneously. Or RT given at least 60 days after the last dose of SACT.</i>
<a href="#">Dillenburger, Wolfgang, Poulakis, Vassilis, Skriapas, Konstantinos et al. (2006) Retroperitoneoscopic versus open surgical radical nephrectomy for large renal cell carcinoma in clinical stage cT2 or cT3a: quality of life, pain and reconvalescence.</a> European urology 49(2): 314-3	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Dong, Bao Nan, Song, Jie, Yang, Wen Li et al. (2024) Comparison of Outcomes Between Partial and Radical Laparoscopic Nephrectomy for Localized Renal Tumors Larger Than Four Centimeters: A Systematic Review and Meta-Analysis.</a> World journal of oncology 15(4): 625-639	- Systematic review with case control studies
<a href="#">Dong, Hanzhi, Cao, Yuan, Jian, Yan et al. (2023) Patients with metastatic renal cell carcinoma who receive immune-targeted therapy may derive survival benefit from nephrectomy.</a> BMC cancer 23(1): 943	- Study does not contain a relevant intervention <i>Compares SACT vs. non pharma (nephrectomy). Only 40% of the patients in the nephrectomy arm underwent CN with rest of them arm receiving radical nephrectomy. No subgroup data available.</i>
<a href="#">Dong, Lin, Liang, Wang You, Ya, Lu et al. (2022) A Systematic Review and Meta-Analysis of Minimally Invasive Partial Nephrectomy Versus Focal Therapy for Small Renal Masses.</a> Frontiers in oncology 12: 732714	- Does not contain a population of people with kidney cancer <i>SR focussing on small renal masses</i>

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Study	Reason
<a href="#">Dragomir, Alice, Nazha, Sara, Wood, Lori A et al. (2020) Outcomes of complete metastasectomy in metastatic renal cell carcinoma patients: The Canadian Kidney Cancer information system experience.</a> Urologic oncology 38(10): 799e1-799e10	- Study does not contain a relevant intervention <i>compares mastectomy Vs. no mastectomy. No information regarding the use of SACT prior or during the mastectomy is given. Baseline data reports percentage of patients used SCAT during follow-up, which can not be used to determine the timeline of SCAT</i>
<a href="#">El-Ghazaly, Tarek H; Mason, Ross J; Rendon, Ricardo A (2014) Oncological outcomes of partial nephrectomy for tumours larger than 4 cm: A systematic review.</a> Canadian Urological Association journal = Journal de l'Association des urologues du Canada 8(12): 61-6	- There is no information on cT or pT stage
<a href="#">Ellis, E.E. and Messing, E. (2021) Active Surveillance of Small Renal Masses: A Systematic Review.</a> Kidney Cancer 5(3): 139-152	- More recent systematic review included that covers the same topic
<a href="#">Ellison, Jonathan S, Montgomery, Jeffrey S, Wolf, J Stuart Jr et al. (2012) A matched comparison of perioperative outcomes of a single laparoscopic surgeon versus a multisurgeon robot-assisted cohort for partial nephrectomy.</a> The Journal of urology 188(1): 45-50	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Enikeev, Dmitry, Morozov, Andrey, Bazarkin, Andrey et al. (2023) Thermal ablation vs. active surveillance for renal masses: a systematic review and network meta-analysis.</a> Minerva urology and nephrology 75(2): 154-162	- More recent systematic review included that covers the same topic <i>Reports unadjusted outcomes only</i>
<a href="#">Ergun, Muslum, Sagir, Suleyman, Akyuz, Osman et al. (2024) Evolving Approach in Nephron-Sparing Surgery: Has Anything Changed from Open Surgery to Laparoscopy?.</a> Archivos espanoles de urologia 77(7): 726-731	- Exclude - review C. Patients with localised tumour
<a href="#">Faddegon, Stephen, Ju, Tom, Olweny, Ephrem O et al. (2013) A comparison of long term renal functional outcomes following partial nephrectomy and radiofrequency ablation.</a> The Canadian journal of urology 20(3): 6785-9	- Study published before included SR/s for the outcome/s reported
<a href="#">Faena, Izak, Salmasi, Amirali, Lenis, Andrew T et al. (2018) Overall survival in patients with metastatic renal cell carcinoma and clinical N1 disease undergoing cytoreductive nephrectomy and lymph node dissection.</a> Urologic oncology 36(2): 79e19-79e26	- Study does not contain a relevant intervention <i>Compares lymphadenectomy vs. No lymphadenectomy. All had previously received CN, no information of background use of SACT given. No additional sub-group analysis</i>

Study	Reason
<a href="#">Fallah, Jaleh, Gittleman, Haley, Weinstock, Chana et al. (2024) Cytoreductive nephrectomy in the era of immune checkpoint inhibitors: a US Food and Drug Administration pooled analysis.</a> Journal of the National Cancer Institute 116(7): 1043-1050	- Exclude - Intervention is out of scope <i>Pooled analysis of trials comparing pharmaceuticals only.</i>
<a href="#">Feder, Marc T, Patel, Manoj B, Melman, Arnold et al. (2008) Comparison of open and laparoscopic nephrectomy in obese and nonobese patients: outcomes stratified by body mass index.</a> The Journal of urology 180(1): 79-83	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Feuerstein, Michael A, Kent, Matthew, Bazzi, Wassim M et al. (2014) Analysis of lymph node dissection in patients with &gt;=7-cm renal tumors.</a> World journal of urology 32(6): 1531-6	- Comparator in study does not match that specified in protocol  - Study did not compare the interventions of interest
<a href="#">Feuerstein, Michael A, Kent, Matthew, Bernstein, Melanie et al. (2014) Lymph node dissection during cytoreductive nephrectomy: a retrospective analysis.</a> International journal of urology : official journal of the Japanese Urological Association 21(9): 874-9	- Study does not contain a relevant intervention <i>Compares lymphadenectomy vs. No lymphadenectomy. All had previously received CN, no information of background use of SACT given.</i>
<a href="#">Ficarra, V., Crestani, A., Inferrera, A. et al. (2018) Positive surgical margins after partial nephrectomy: A systematic review and meta-analysis of comparative studies.</a> Kidney Cancer 2(2): 133-145	- Exclude - assessed outcome is out of scope
<a href="#">Ficarra, Vincenzo, Minervini, Andrea, Antonelli, Alessandro et al. (2014) A multicentre matched-pair analysis comparing robot-assisted versus open partial nephrectomy.</a> BJU international 113(6): 936-41	- Exclude review C Study included only patients T1-T2
<a href="#">Figaroa, Orlane, Zondervan, Patricia, Kessels, Rob et al. (2024) PrimerX: A Bayesian Multistage Cohort Embedded Randomised Trial to Evaluate the Role of Deferred Local Therapy of the Primary Tumour in Combination with Immune Checkpoint Inhibitor-based First-line Therapy in Metastatic Renal Cell Carcinoma Patients.</a> European urology open science 70: 28-35	- Comparator in study does not match that specified in protocol <i>People in the comparator group were allowed to receive deferred CN if primary tumour was progressing</i>
<a href="#">Fossati, Nicola, Larcher, Alessandro, Gadda, Giulio M et al. (2015) Minimally Invasive Partial Nephrectomy Versus Laparoscopic Cryoablation for Patients Newly Diagnosed with a Single</a>	- Primary study covered fully by an included systematic review

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Study	Reason
<a href="#">Small Renal Mass.</a> European urology focus 1(1): 66-72	
<a href="#">Franzese, Ciro, Marini, Beatrice, Baldaccini, Davide et al. (2023) The impact of stereotactic ablative radiotherapy on oligoprogressive metastases from renal cell carcinoma.</a> Journal of cancer research and clinical oncology 149(8): 4411-4417	- Review H - SABR exclude <i>All patients received active SCAT during SABR</i>
<a href="#">Franzese, Ciro, Marvaso, Giulia, Francolini, Giulio et al. (2021) The role of stereotactic body radiation therapy and its integration with systemic therapies in metastatic kidney cancer: a multicenter study on behalf of the AIRO (Italian Association of Radiotherapy and Clinical Oncology) genitourinary study group.</a> Clinical & experimental metastasis 38(6): 527-537	- Review H - SABR exclude
<a href="#">Gandi, C., Totaro, A., Bientinesi, R. et al. (2022) Purely Off-Clamp Partial Nephrectomy: Robotic Approach Better than Open Using a Pentafecta Outcome with Propensity Score Matching.</a> Journal of Clinical Medicine 11(21): 6241	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Gao, HuiYu, Zhou, Lin, Zhang, JiaBin et al. (2024) Comparative efficacy of cryoablation versus robot-assisted partial nephrectomy in the treatment of cT1 renal tumors: a systematic review and meta-analysis.</a> BMC cancer 24(1): 1150	- Systematic review used as source of primary studies
<a href="#">Gao, X., Hu, L., Pan, Y. et al. (2018) Surgical outcomes of nephrectomy for elderly patients with renal cell carcinoma.</a> Pakistan Journal of Medical Sciences 34(2): 288-293	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Garcia-Perdomo, Herney A; Zapata-Copete, James A; Castillo-Cobaleda, Diego F (2018) Role of cytoreductive nephrectomy in the targeted therapy era: A systematic review and meta-analysis.</a> Investigative and clinical urology 59(1): 2-9	- Exclude - Result reported in the most updated MA
<a href="#">Garg, Harshit, Das, Bhabatosh, Bansal, Amit et al. (2022) Trifecta and Pentafecta Outcomes in Laparoscopic and Robotic Nephron-Sparing Surgery for Highly Complex Renal Tumors: A Propensity Score-Matched Cohort Analysis.</a> Journal of endourology 36(8): 1050-1056	- Exclude - review C - Study included only patients T1-T2
<a href="#">Garg, Harshit, Tiwari, Deviprasad, Nayak, Brusabhanu et al. (2020) A comparative</a>	- Exclude -review C- Study included only patients T1-T2

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Study	Reason
<a href="#">analysis of various surgical approaches of nephron-sparing surgery and correlation of histopathological grade with RENAL nephrometry score in renal cell carcinoma.</a> Journal of minimal access surgery 16(2): 144-151	
<a href="#">Garisto, Juan, Bertolo, Riccardo, Dagenais, Julien et al. (2018) Robotic versus open partial nephrectomy for highly complex renal masses: Comparison of perioperative, functional, and oncological outcomes.</a> Urologic oncology 36(10): 471e1-471e9	- Exclude -review C- Study included only patients T1-T2
<a href="#">Ge, Si, Wang, Zuoping, Li, Yunxiang et al. (2025) Is Ablation Suitable For Small Renal Masses? A Meta-Analysis.</a> Academic radiology 32(1): 218-235	- Systematic review used as source of primary studies
<a href="#">Gebbia, Vittorio, Girlando, Andrea, DI Grazia, Alfio et al. (2020) Stereotactic Radiotherapy for the Treatment of Patients With Oligo-progressive Metastatic Renal Cell Carcinoma Receiving Vascular Endothelial Growth Factor Receptor Tyrosine Kinase Inhibitor: Data From the Real World.</a> Anticancer research 40(12): 7037-7043	- Review H - SABR exclude <i>All participants received concomitant SACT</i>
<a href="#">Gershman, Boris, Moreira, Daniel M, Thompson, R Houston et al. (2018) Perioperative Morbidity of Lymph Node Dissection for Renal Cell Carcinoma: A Propensity Score-based Analysis.</a> European urology 73(3): 469-475	- Comparator in study does not match that specified in protocol
<a href="#">Gershman, Boris, Thompson, R Houston, Boorjian, Stephen A et al. (2018) Radical Nephrectomy with or without Lymph Node Dissection for High Risk Nonmetastatic Renal Cell Carcinoma: A Multi-Institutional Analysis.</a> The Journal of urology 199(5): 1143-1148	- Exclude - For review C. Proportion of patients stage T3 < 90%  - Comparator in study does not match that specified in protocol <i>LND vs no LND</i>
<a href="#">Gershman, Boris, Thompson, R Houston, Moreira, Daniel M et al. (2017) Lymph Node Dissection is Not Associated with Improved Survival among Patients Undergoing Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma: A Propensity Score Based Analysis.</a> The Journal of urology 197(3pt1): 574-579	- Mixed population of SACT pre/post non-pharmacological regimens  - Study does not contain a relevant intervention <i>Compares CN with lymphadenectomy vs. CN without lymphadenectomy. Mixed population with pre and post non-pharmacological treatment.</i>
<a href="#">Gershman, Boris, Thompson, R Houston, Moreira, Daniel M et al. (2017) Radical Nephrectomy With or Without Lymph Node</a>	- Comparator in study does not match that specified in protocol <i>LND vs no LND</i>

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Study	Reason
<a href="#">Dissection for Nonmetastatic Renal Cell Carcinoma: A Propensity Score-based Analysis.</a> European urology 71(4): 560-567	
<a href="#">Ghani, Khurshid R, Sukumar, Shyam, Sammon, Jesse D et al. (2014) Practice patterns and outcomes of open and minimally invasive partial nephrectomy since the introduction of robotic partial nephrectomy: results from the nationwide inpatient sample.</a> The Journal of urology 191(4): 907-12	- There is no information on cT or pT stage
<a href="#">Gill, Inderbir S, Matin, Surena F, Desai, Mihir M et al. (2003) Comparative analysis of laparoscopic versus open partial nephrectomy for renal tumors in 200 patients.</a> The Journal of urology 170(1): 64-8	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Golombos, D.M., Chughtai, B., Trinh, Q.-D. et al. (2017) Adoption of technology and its impact on nephrectomy outcomes, a U.S. population-based analysis (2008-2012).</a> Journal of Endourology 31(1): 91-99	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Golombos, David M, Chughtai, Bilal, Trinh, Quoc-Dien et al. (2017) Minimally invasive vs open nephrectomy in the modern era: does approach matter?.</a> World journal of urology 35(10): 1557-1568	- Exclude - For review C. Proportion of patients stage T3 < 90% <i>Reported as stage 3</i>
<a href="#">Gonzalez-Ruiz de Leon, C., Pellejero-Perez, P., Quintas-Blanco, A. et al. (2017) Beneficio de la nefrectomia en el tratamiento del carcinoma de celulas renales metastasico, Benefit of on nephrectomy for treating metastatic renal cell carcinoma.</a> Actas urologicas espanolas 41(5): 338-342	- Exclude - non-English paper
<a href="#">Graham, Jeffrey, Wells, J Connor, Donskov, Frede et al. (2019) Cytoreductive Nephrectomy in Metastatic Papillary Renal Cell Carcinoma: Results from the International Metastatic Renal Cell Carcinoma Database Consortium.</a> European urology oncology 2(6): 643-648	- Exclude - Result reported in the most updated MA
<a href="#">Green, Harshani; Taylor, Alexandra; Khoo, Vincent (2023) Beyond the Knife in Renal Cell Carcinoma: A Systematic Review-To Ablate or Not to Ablate?.</a> Cancers 15(13)	- More recent systematic review included that covers the same topic
<a href="#">Grimaud, L.W., Chen, F.V., Chang, J. et al. (2021) Comparison of Perioperative Outcomes for Radical Nephrectomy Based on Surgical</a>	- Exclude - For review C. Proportion of patients stage T3 < 90% <i>Study excluded cT3b-4 disease</i>

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Study	Reason
<a href="#">Approach for Masses Greater Than 10 cm.</a> Journal of Endourology 35(12): 1785-1792	
<a href="#">Grimm, Marc-Oliver, Oya, Mototsugu, Choueiri, Toni K et al. (2024) Impact of Prior Cytoreductive Nephrectomy on Efficacy in Patients with Synchronous Metastatic Renal Cell Carcinoma Treated with Avelumab plus Axitinib or Sunitinib: Post Hoc Analysis from the JAVELIN Renal 101 Phase 3 Trial.</a> European urology 85(1): 8-12	- Not a relevant study design
<a href="#">Grivas, Nikolaos, Kalampokis, Nikolaos, Larcher, Alessandro et al. (2019) Robot-assisted versus open partial nephrectomy: comparison of outcomes. A systematic review.</a> Minerva urologica e nefrologica = The Italian journal of urology and nephrology 71(2): 113-120	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Gross, Evan E, Li, Mingjia, Yin, Ming et al. (2023) A multicenter study assessing survival in patients with metastatic renal cell carcinoma receiving immune checkpoint inhibitor therapy with and without cytoreductive nephrectomy.</a> Urologic oncology 41(1): 51e25-51e31	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Gu, Liangyou, Liu, Kan, Shen, Donglai et al. (2020) Comparison of Robot-Assisted and Laparoscopic Partial Nephrectomy for Completely Endophytic Renal Tumors: A High-Volume Center Experience.</a> Journal of endourology 34(5): 581-587	- Exclude review C - Study included only patients T1-T2
<a href="#">Gu, Liangyou, Ma, Xin, Gao, Yu et al. (2017) Robotic versus Open Level I-II Inferior Vena Cava Thrombectomy: A Matched Group Comparative Analysis.</a> The Journal of urology 198(6): 1241-1246	- Non-OECD country
<a href="#">Gu, Liangyou, Ma, Xin, Wang, Baojun et al. (2018) Laparoscopic vs robot-assisted partial nephrectomy for renal tumours of &gt;4 cm: a propensity score-based analysis.</a> BJU international 122(3): 449-455	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Guan, Wei, Bai, Jian, Liu, Jihong et al. (2012) Microwave ablation versus partial nephrectomy for small renal tumors: intermediate-term results.</a> Journal of surgical oncology 106(3): 316-21	- Non-OECD country
<a href="#">Guglielmetti, Giuliano B, Dos Anjos, Gabriel C, Sawczyn, Guilherme et al. (2022) A Prospective.</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%

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Study	Reason
<a href="#">Randomized Trial Comparing the Outcomes of Open vs Laparoscopic Partial Nephrectomy.</a> The Journal of urology 208(2): 259-267	
<a href="#">Guillotreau, Julien, Haber, Georges-Pascal, Autorino, Riccardo et al. (2012) Robotic partial nephrectomy versus laparoscopic cryoablation for the small renal mass.</a> European urology 61(5): 899-904	- Primary study covered fully by an included systematic review
<a href="#">Guner, E. and Sahin, S. (2019) Comparison of robotic and laparoscopic partial nephrectomy in robotic surgery era.</a> Bulletin of Urooncology 18(4): 154-157	- There is no information on cT or pT stage
<a href="#">Gupta, K., Omil-Lima, D., Sheyn, D. et al. (2021) Temporal improvements in renal surgery outcomes across surgical approaches.</a> International Urology and Nephrology 53(7): 1311-1316	- Study does not contain a relevant outcome
<a href="#">Haber, Georges-Pascal, White, Wesley M, Crouzet, Sebastien et al. (2010) Robotic versus laparoscopic partial nephrectomy: single-surgeon matched cohort study of 150 patients.</a> Urology 76(3): 754-8	- Not a relevant study design <i>Consecutive case series</i>
<a href="#">Hahn, Andrew W, Kotecha, Ritesh R, Viscuse, Paul V et al. (2023) Cytorreductive Nephrectomy for Patients with Metastatic Sarcomatoid and/or Rhabdoid Renal Cell Carcinoma Treated with Immune Checkpoint Therapy.</a> European urology focus 9(5): 734-741	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Hakam, Nizar, Heidar, Nassib Abou, El-Asmar, Jose et al. (2023) Comparative analysis of partial versus radical nephrectomy for renal cell carcinoma: Is oncologic safety compromised during nephron sparing in higher stage disease?.</a> Urology annals 15(2): 226-231	- Non-OECD country
<a href="#">Hall, Mary E, Bhindi, Bimal, Luckenbaugh, Amy N et al. (2021) Association between cytorreductive nephrectomy and survival among patients with metastatic renal cell carcinoma receiving modern therapies: a systematic review and meta-analysis examining effect modification according to systemic therapy approach.</a> Cancer causes & control : CCC 32(7): 675-680	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Haramis, Georgios, Graversen, Joseph A, Mues, Adam C et al. (2012) Retrospective comparison of laparoscopic partial nephrectomy</a>	- Primary study covered fully by an included systematic review

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Study	Reason
<a href="#">versus laparoscopic renal cryoablation for small (&lt;3.5 cm) cortical renal masses.</a> Journal of laparoendoscopic & advanced surgical techniques. Part A 22(2): 152-7	
<a href="#">Harke, N.N., Mandel, P., Witt, J.H. et al. (2018) Are there limits of robotic partial nephrectomy? TRIFECTA outcomes of open and robotic partial nephrectomy for completely endophytic renal tumors.</a> Journal of Surgical Oncology 118(1): 206-211	- Not a relevant study design <i>Consecutive case series</i>
<a href="#">Harryman, O.A., Davenport, K., Keoghane, S. et al. (2009) A Comparative Study of Quality of Life Issues Relating to Open Versus Laparoscopic Nephrectomy: A Prospective Pragmatic Study.</a> Journal of Urology 181(3): 998-1003	- There is no information on cT or pT stage
<a href="#">Harshman, Lauren C, Yu, R James, Allen, Genevera I et al. (2013) Surgical outcomes and complications associated with presurgical tyrosine kinase inhibition for advanced renal cell carcinoma (RCC).</a> Urologic oncology 31(3): 379-85	- Not a relevant study design <i>Reports case series</i>
<a href="#">Hatayama, Tomoya, Tasaka, Ryo, Mochizuki, Hideki et al. (2022) Comparison of surgical outcomes and split renal function between laparoscopic and robot-assisted partial nephrectomy: a propensity score-matched analysis.</a> International urology and nephrology 54(4): 805-811	- There is no information on cT or pT stage
<a href="#">He, Liru, Liu, Yang, Han, Hui et al. (2020) Survival Outcomes After Adding Stereotactic Body Radiotherapy to Metastatic Renal Cell Carcinoma Patients Treated With Tyrosine Kinase Inhibitors.</a> American journal of clinical oncology 43(1): 58-63	- Review H - SABR exclude <i>SABR and SACT given concomitantly</i>
<a href="#">Health Technology, Wales (2022) Stereotactic ablative radiotherapy (SABR) for the treatment of renal cell carcinoma.</a>	- Systematic review used as source of primary studies
<a href="#">Heng, Daniel Y C, Wells, J Connor, Rini, Brian I et al. (2014) Cytoreductive nephrectomy in patients with synchronous metastases from renal cell carcinoma: results from the International Metastatic Renal Cell Carcinoma Database Consortium.</a> European urology 66(4): 704-10	- Mixed population of SACT pre/post non-pharmacological regimens <i>Unclear if participants received SACT before or during or after the CN</i>

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Study	Reason
<a href="#">Hoeh, Benedikt, Wenzel, Mike, Eckart, Olivia et al. (2023) Comparison of peri- and intraoperative outcomes of open vs robotic-assisted partial nephrectomy for renal cell carcinoma: a propensity-matched analysis.</a> World journal of surgical oncology 21(1): 189	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Hong, Xuwei, Li, Fei, Tang, Kaiqiang et al. (2016) Prognostic value of cytoreductive nephrectomy combined with targeted therapy for metastatic renal cell carcinoma: a meta-analysis.</a> International urology and nephrology 48(6): 967-75	- Exclude - Result reported in the most updated MA
<a href="#">Hori, Shunta, Sakamoto, Keiichi, Onishi, Kenta et al. (2023) Perioperative outcomes of open and robot-assisted partial nephrectomy in patients with renal tumors of moderate to high complexity.</a> Asian journal of surgery 46(6): 2310-2318	- Exclude - review C. Patients with localised tumour
<a href="#">Hsieh, Po-Yen, Hung, Sheng-Chun, Li, Jian-Ri et al. (2021) The effect of metastasectomy on overall survival in metastatic renal cell carcinoma: A systematic review and meta-analysis.</a> Urologic oncology 39(7): 422-430	- Non-OECD country
<a href="#">Hu, Xu, Wang, Yaohui, Shao, Yanxiang et al. (2023) Radical versus partial nephrectomy for T1 non-clear cell renal cell carcinoma.</a> European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 49(8): 1519-1523	- SEER database overlap
<a href="#">Huang, Jiwei, Zhang, Jin, Wang, Yanqing et al. (2016) Comparing Zero Ischemia Laparoscopic Radio Frequency Ablation Assisted Tumor Enucleation and Laparoscopic Partial Nephrectomy for Clinical T1a Renal Tumor: A Randomized Clinical Trial.</a> The Journal of urology 195(6): 1677-83	- Study does not contain a relevant intervention <i>Radio frequency ablation group also had tumour enucleation</i>
<a href="#">Huang, Ryan S, Chow, Ronald, Benour, Ali et al. (2025) Comparative efficacy and safety of ablative therapies in the management of primary localised renal cell carcinoma: a systematic review and meta-analysis.</a> The Lancet. Oncology	- Data not reported in an extractable format
<a href="#">Hutchinson, Ryan, Singla, Nirmish, Krabbe, Laura-Maria et al. (2017) Increased use of antihypertensive medications after partial</a>	- Primary study covered fully by an included systematic review

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Study	Reason
<a href="#">nephrectomy vs. radical nephrectomy</a> . Urologic oncology 35(11): 660e17-660e25	
<a href="#">Iisager, Laura, Ahrenfeldt, Johanne, Donskov, Frede et al. (2024) Multicenter randomized trial of deferred cytoreductive nephrectomy in synchronous metastatic renal cell carcinoma receiving checkpoint inhibitors: the NORDIC-SUN-Trial</a> . BMC cancer 24(1): 260	- study protocol
<a href="#">Ingels, A, Bensalah, K, Beauval, J B et al. (2022) Comparison of open and robotic-assisted partial nephrectomy approaches using multicentric data (UroCCR-47 study)</a> . Scientific reports 12(1): 18981	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Ingrosso, Gianluca, Becherini, Carlotta, Francolini, Giulio et al. (2021) Stereotactic body radiotherapy (SBRT) in combination with drugs in metastatic kidney cancer: A systematic review</a> . Critical reviews in oncology/hematology 159: 103242	- Systematic review used as source of primary studies
<a href="#">Izol, Volkan, Gokalp, Fatih, Sozen, Sinan et al. (2021) Factors affecting long-term renal functions after partial vs radical nephrectomy for clinical T1 renal masses: A Multicentre Study of the Urooncology Association, Turkey</a> . International journal of clinical practice 75(5): e13960	- More recent systematic review included that covers the same topic <i>'requirement of dialysis' could mean eGFR &lt;15 see rec 1.1.3 within NG107. Also from Ochoa: "Due to the heterogeneity of defining CKD across studies, we pooled the studies for stages III-V or IV-V as determined by the EGFR or by renal replacement therapy and kidney transplant" Not included in Ochoa most likely because data not reported as HR/OR - to exclude</i>
<a href="#">Jang, Hoon Ah, Kim, Jin Wook, Byun, Seok Soo et al. (2016) Oncologic and Functional Outcomes after Partial Nephrectomy Versus Radical Nephrectomy in T1b Renal Cell Carcinoma: A Multicenter, Matched Case-Control Study in Korean Patients</a> . Cancer research and treatment 48(2): 612-20	- Primary study covered fully by an included systematic review
<a href="#">Jang, Hyeon Jun, Song, Wan, Suh, Yoon Seok et al. (2014) Comparison of perioperative outcomes of robotic versus laparoscopic partial nephrectomy for complex renal tumors (RENAL nephrometry score of 7 or higher)</a> . Korean journal of urology 55(12): 808-13	- There is no information on cT or pT stage
<a href="#">Janisch, Florian, Hillemacher, Tobias, Fuehner, Constantin et al. (2020) The impact of cytoreductive nephrectomy on survival</a>	- Data not reported in an extractable format <i>Reports OS, PFS and CSS as median months</i>

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Study	Reason
<a href="#">outcomes in patients treated with tyrosine kinase inhibitors for metastatic renal cell carcinoma in a real-world cohort.</a> Urologic oncology 38(9): 739e9-739e15	
<a href="#">Jelley, C.R., Kurukulaarachchi, K.A.S.H., Forster, L. et al. (2017) Comparison of open and robotic nephron sparing surgery: a single centre experience.</a> Journal of Clinical Urology 10(1): 28-35	- Exclude review C. Study included only patients T1-T2
<a href="#">Jeon, Hwang Gyun, Jeong, In Gab, Lee, Jeong Woo et al. (2009) Prognostic factors for chronic kidney disease after curative surgery in patients with small renal tumors.</a> Urology 74(5): 1064-8	- Primary study covered fully by an included systematic review
<a href="#">Jeong, In Gab, Khandwala, Yash S, Kim, Jae Heon et al. (2017) Association of Robotic-Assisted vs Laparoscopic Radical Nephrectomy With Perioperative Outcomes and Health Care Costs, 2003 to 2015.</a> JAMA 318(16): 1561-1568	- There is no information on cT or pT stage
<a href="#">Jeong, Seung-Hwan, Kim, Jung Kwon, Park, Juhyun et al. (2016) Pathological T3a Upstaging of Clinical T1 Renal Cell Carcinoma: Outcomes According to Surgical Technique and Predictors of Upstaging.</a> PloS one 11(11): e0166183	- Comparator in study does not match that specified in protocol
<a href="#">Ji, B., Li, D., Fu, S. et al. (2020) Propensity-score matched comparison of partial versus radical nephrectomy for T1N0M0 sarcomatoid renal cell carcinoma.</a> Translational Andrology and Urology 9(2): 250-257	- SEER database overlap
<a href="#">Ji, Changwei, Zhao, Xiaozhi, Zhang, Shiwei et al. (2016) Laparoscopic Radiofrequency Ablation versus Partial Nephrectomy for cT1a Renal Tumors: Long-Term Outcome of 179 Patients.</a> Urologia internationalis 96(3): 345-53	- Non-OECD country
<a href="#">Jiang, Jianping, Zheng, Xiangyi, Qin, Jie et al. (2009) Health-related quality of life after hand-assisted laparoscopic and open radical nephrectomies of renal cell carcinoma.</a> International urology and nephrology 41(1): 23-7	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Jiang, Yu-Li, Peng, Cheng-Xia, Wang, Heng-Zi et al. (2019) Comparison of the long-term follow-up and perioperative outcomes of partial nephrectomy and radical nephrectomy for 4 cm to 7 cm renal cell carcinoma: a systematic review and meta-analysis.</a> BMC urology 19(1): 48	- Systematic review used as source of primary studies

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Study	Reason
<a href="#">Jiang, Yu-Li, Yu, Dong-Dong, Xu, Yang et al. (2023) Comparison of perioperative outcomes of robotic vs. laparoscopic partial nephrectomy for renal tumors with a RENAL nephrometry score &gt;=7: A meta-analysis. Frontiers in surgery 10: 1138974</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Jin, Seok-Joon, Park, Jun-Young, Kim, Doo-Hwan et al. (2017) Comparison of postoperative pain between laparoscopic and robot-assisted partial nephrectomies for renal tumors: A propensity score matching analysis. Medicine 96(29): e7581</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Jokimaki, A., Hietala, H., Lemma, J. et al. (2023) Previous radiotherapy improves treatment responses and causes a trend toward longer time to progression among patients with immune checkpoint inhibitor-related adverse events. Cancer Immunology, Immunotherapy 72(10): 3337-3347</a>	- Review H - SABR exclude <i>Protocol relevant outcomes are not reported for RCC subgroup</i>
<a href="#">Jones, J.O., Ince, W.H.J., Welsh, S.J. et al. (2022) Activity of Immunotherapy Regimens on Primary Renal Tumours: A Systematic Review. Kidney Cancer 6(4): 221-236</a>	- Systematic review used as source of primary studies
<a href="#">Joslyn, Sue A; Sirintrapun, S Joseph; Konety, Badrinath R (2005) Impact of lymphadenectomy and nodal burden in renal cell carcinoma: retrospective analysis of the National Surveillance, Epidemiology, and End Results database. Urology 65(4): 675-80</a>	- There is no information on cT or pT stage
<a href="#">Junker, Theresa, Duus, Louise, Rasmussen, Benjamin S B et al. (2022) Quality of life and complications after nephron-sparing treatment of renal cell carcinoma stage T1-a systematic review. Systematic reviews 11(1): 4</a>	- Systematic review used as source of primary studies
<a href="#">Kalogirou, Charis, Fender, Hendrik, Muck, Patricia et al. (2017) Long-Term Outcome of Nephron-Sparing Surgery Compared to Radical Nephrectomy for Renal Cell Carcinoma &gt;=4 cm - A Matched-Pair Single Institution Analysis. Urologia internationalis 98(2): 138-147</a>	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Kandi, Maryam, Richard, Patrick O, Violette, Philippe D et al. (2024) Complications and blood loss after invasive treatments for small renal masses: A systematic review. Canadian Urological Association journal = Journal de l'Association des urologues du Canada</a>	- Comparator in study does not match that specified in protocol

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Study	Reason
<a href="#">Kaneko, Gou, Miyajima, Akira, Kikuchi, Eiji et al. (2012) The benefit of laparoscopic partial nephrectomy in high body mass index patients. Japanese journal of clinical oncology 42(7): 619-24</a>	- Exclude - review C - Study included only patients T1-T2
<a href="#">Kapoor, A., Wong, E.C.L., Fang, W. et al. (2019) Upfront cytoreductive nephrectomy vs. Upfront systemic therapy in metastatic kidney cancer. Canadian Urological Association Journal 13(11): e377-e381</a>	- Data not reported in an extractable format <i>Protocol relevant outcomes reported as median, no time to event data</i>
<a href="#">Kato, Daiki, Nakane, Keita, Enomoto, Torai et al. (2021) The utility of laparoscopic partial nephrectomy with renal function preservation, regardless of warm ischemia time, compared with laparoscopic radical nephrectomy. Asian journal of endoscopic surgery 14(3): 386-393</a>	- Data not reported in an extractable format
<a href="#">Kato, Renpei, Naito, Sei, Numakura, Kazuyuki et al. (2022) Significance of upfront cytoreductive nephrectomy stratified by IMDC risk for metastatic renal cell carcinoma in targeted therapy era - a multi-institutional retrospective study. International journal of clinical oncology 27(3): 563-573</a>	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Katsanos, K, Mailli, L, Krokidis, M et al. (2014) Systematic review and meta-analysis of thermal ablation versus surgical nephrectomy for small renal tumours. Cardiovascular and interventional radiology 37(2): 427-37</a>	- More recent systematic review included that covers the same topic
<a href="#">Katsimperis, Stamatios, Tzelves, Lazaros, Bellos, Themistoklis et al. (2022) Cytoreductive nephrectomy for synchronous metastatic renal cell carcinoma. Is there enough evidence?. Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica 94(4): 476-485</a>	- Systematic review used as source of primary studies
<a href="#">Kawase, Kota, Enomoto, Torai, Kawase, Makoto et al. (2022) The Impact of Postoperative Renal Function Recovery after Laparoscopic and Robot-Assisted Partial Nephrectomy in Patients with Renal Cell Carcinoma. Medicina (Kaunas, Lithuania) 58(4)</a>	- Exclude - For review C . Proportion of patients stage T3 < 90%
<a href="#">Khalifeh, Ali, Autorino, Riccardo, Hillyer, Shahab P et al. (2013) Comparative outcomes and assessment of trifecta in 500 robotic and laparoscopic partial nephrectomy cases: a</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%

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Study	Reason
<a href="#">single surgeon experience.</a> The Journal of urology 189(4): 1236-42	
<a href="#">Khalil, M.I., Ubeda, J., Soehner, T. et al. (2019) Contemporary Perioperative Morbidity and Mortality Rates of Minimally Invasive vs Open Partial Nephrectomy in Obese Patients with Kidney Cancer.</a> Journal of Endourology 33(11): 920-927	- There is no information on cT or pT stage
<a href="#">Khan, M.M.A., Patel, R.A., Jain, N. et al. (2019) Prospective analysis of laparoscopic versus open radical nephrectomy for renal tumours more than 7 cm.</a> Journal of Minimal Access Surgery 15(1): 14-18	- Non-OECD country - There is no information on cT or pT stage
<a href="#">Kim, Jeong Ho, Park, Yong Hyun, Kim, Yong June et al. (2015) Perioperative and long-term renal functional outcomes of robotic versus laparoscopic partial nephrectomy: a multicenter matched-pair comparison.</a> World journal of urology 33(10): 1579-84	- There is no information on cT or pT stage
<a href="#">Kim, Jung Kwon, Lee, Hakmin, Oh, Jong Jin et al. (2019) Comparison of robotic and open partial nephrectomy for highly complex renal tumors (RENAL nephrometry score &gt;=10).</a> PloS one 14(1): e0210413	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Kim, Na Young, Lee, Hye Sun, Park, Jin Ha et al. (2022) Influence of age on gender-related differences in acute kidney injury after minimally invasive radical or partial nephrectomy.</a> Surgical endoscopy 36(5): 2962-2972	- Study does not contain a relevant outcome
<a href="#">Kim, Simon P, Thompson, R Houston, Boorjian, Stephen A et al. (2012) Comparative effectiveness for survival and renal function of partial and radical nephrectomy for localized renal tumors: a systematic review and meta-analysis.</a> The Journal of urology 188(1): 51-7	- Systematic review used as source of primary studies
<a href="#">Kim, Sung Han, Jeong, Kyung-Chae, Joung, Jae Young et al. (2018) Prognostic significance of nephrectomy in metastatic renal cell carcinoma treated with systemic cytokine or targeted therapy: A 16-year retrospective analysis.</a> Scientific reports 8(1): 2974	- Study does not contain a relevant intervention <i>Mixed population, receiving radical nephrectomy and CN</i>
<a href="#">Kim, Sung Han, Lee, Eun-Sik, Kim, Hyeon Hoe et al. (2015) A propensity-matched comparison of perioperative complications and of chronic kidney disease between robot-assisted</a>	- Primary study covered fully by an included systematic review

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)



Study	Reason
<a href="#">laparoscopic partial nephrectomy and radiofrequency ablative therapy</a> . Asian journal of surgery 38(3): 126-33	
<a href="#">Kim, Sung Han, Park, Boram, Hwang, Eu Chang et al. (2021) A Retrospective, Multicenter, Long-Term Follow-Up Analysis of the Prognostic Characteristics of Recurring Non-Metastatic Renal Cell Carcinoma After Partial or Radical Nephrectomy</a> . Frontiers in oncology 11: 653002	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Kizilay, Fuat, Turna, Burak, Apaydin, Erdal et al. (2019) Comparison of long-term outcomes of laparoscopic and robot-assisted laparoscopic partial nephrectomy</a> . The Kaohsiung journal of medical sciences 35(4): 238-243	- Comparator in study does not match that specified in protocol
<a href="#">Klatte, Tobias, Berni, Alessandro, Serni, Sergio et al. (2021) Intermediate- and long-term oncological outcomes of active surveillance for localized renal masses: a systematic review and quantitative analysis</a> . BJU international 128(2): 131-143	- More recent systematic review included that covers the same topic <i>Single arm studies</i>
<a href="#">Klatte, Tobias, Fife, Kate, Welsh, Sarah J et al. (2018) Prognostic effect of cytoreductive nephrectomy in synchronous metastatic renal cell carcinoma: a comparative study using inverse probability of treatment weighting</a> . World journal of urology 36(3): 417-425	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Klatte, Tobias, Grubmuller, Bernhard, Waldert, Matthias et al. (2011) Laparoscopic cryoablation versus partial nephrectomy for the treatment of small renal masses: systematic review and cumulative analysis of observational studies</a> . European urology 60(3): 435-43	- Review article but not a systematic review
<a href="#">Klatte, Tobias; Shariat, Shahrokh F; Remzi, Mesut (2014) Systematic review and meta-analysis of perioperative and oncologic outcomes of laparoscopic cryoablation versus laparoscopic partial nephrectomy for the treatment of small renal tumors</a> . The Journal of urology 191(5): 1209-17	- More recent systematic review included that covers the same topic
<a href="#">Kobayashi, Satoshi, Mutaguchi, Jun, Kashiwagi, Eiji et al. (2021) Clinical advantages of robot-assisted partial nephrectomy versus laparoscopic partial nephrectomy in terms of global and split renal functions: A propensity score-matched comparative analysis</a> .	- Exclude - For review C. Proportion of patients stage T3 < 90%

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Study	Reason
International journal of urology : official journal of the Japanese Urological Association 28(6): 630-636	
<a href="#">Kokorovic, Andrea and Rendon, Ricardo A (2019) Cyto-reductive nephrectomy in metastatic kidney cancer: what do we do now?</a> . Current opinion in supportive and palliative care 13(3): 255-261	- Review article but not a systematic review
<a href="#">Komninos, Christos, Shin, Tae Young, Tulliao, Patrick et al. (2014) R-LESS partial nephrectomy trifecta outcome is inferior to multiport robotic partial nephrectomy: comparative analysis.</a> European urology 66(3): 512-7	- There is no information on cT or pT stage
<a href="#">Koo, Kyo Chul, Kim, Jong Chan, Cho, Kang Su et al. (2016) Oncological outcomes after partial vs radical nephrectomy in renal cell carcinomas of &lt;=7 cm with presumed renal sinus fat invasion on preoperative imaging.</a> BJU international 117(1): 87-93	- Not a relevant study design <i>Consecutive case series</i>
<a href="#">Kopp, Ryan P, Mehrazin, Reza, Palazzi, Kerrin L et al. (2014) Survival outcomes after radical and partial nephrectomy for clinical T2 renal tumours categorised by R.E.N.A.L. nephrometry score.</a> BJU international 114(5): 708-18	- Secondary publication of an included study that does not provide any additional relevant information
<a href="#">Kowalewski, Karl-Friedrich, Muller, Dennis, Kirchner, Marietta et al. (2021) Robotic-Assisted Versus Conventional Open Partial Nephrectomy (Robocop): A Propensity Score-Matched Analysis of 249 Patients.</a> Urologia internationalis 105(56): 490-498	- There is no information on cT or pT stage
<a href="#">Krabbe, Laura-Maria, Haddad, Ahmed Q, Westerman, Mary E et al. (2014) Surgical management of metastatic renal cell carcinoma in the era of targeted therapies.</a> World journal of urology 32(3): 615-22	- Review article but not a systematic review
<a href="#">Kroeze, Stephanie G C, Fritz, Corinna, Schaule, Jana et al. (2021) Stereotactic radiotherapy combined with immunotherapy or targeted therapy for metastatic renal cell carcinoma.</a> BJU international 127(6): 703-711	- Mixed population of SACT pre/post non-pharmacological regimens <i>76% of the participants received SACT before SRT, no subgroup results reported</i>
<a href="#">Kunath, Frank, Schmidt, Stefanie, Krabbe, Laura-Maria et al. (2017) Partial nephrectomy versus radical nephrectomy for clinical localised</a>	- Systematic review used as source of primary studies

Study	Reason
<a href="#">renal masses</a> . The Cochrane database of systematic reviews 5: cd012045	
<a href="#">Kunkle, David A; Egleston, Brian L; Uzzo, Robert G (2008) Excise, ablate or observe: the small renal mass dilemma--a meta-analysis and review</a> . The Journal of urology 179(4): 1227-4	- More recent systematic review included that covers the same topic
<a href="#">Kwak, Cheol, Park, Yong Hyun, Jeong, Chang Wook et al. (2007) No role of adjuvant systemic therapy after complete metastasectomy in metastatic renal cell carcinoma?</a> . Urologic oncology 25(4): 310-6	- Comparator in study does not match that specified in protocol <i>All included participants had undergone complete metastasectomy. Compares SACT vs. No SACT population.</i>
<a href="#">Kwak, Cheol, Park, Yong Hyun, Jeong, Chang Wook et al. (2007) Metastasectomy without systemic therapy in metastatic renal cell carcinoma: comparison with conservative treatment</a> . Urologia internationalis 79(2): 145-51	- Study does not contain a relevant intervention <i>None of the participants received SACT at anytime point. Study compares metastasectomy vs. no metastasectomy after nephrectomy</i>
<a href="#">La Vecchia, Maria, Federico, Manuela, Aiello, Dario et al. (2024) The Role of Stereotactic Body Radiotherapy (SBRT) in Oligoprogressive Renal Cell Carcinoma (RCC) Treated with ICIs-TKIs: A Retrospective Multicentric Study</a> . Journal of personalized medicine 14(10)	- Comparator in study does not match that specified in protocol <i>There isn't a defined comparator group. Outcomes were reported for some patients before SBRT but these outcomes did not meet the protocol criteria and these patients did go on to have SBRT also.</i>
<a href="#">Laganosky, D., Filson, C.P., Patil, D. et al. (2020) Survival benefit with extended lymphadenectomy for advanced renal malignancy: A population-based analysis</a> . Asian Journal of Urology 7(1): 29-36	- Comparator in study does not match that specified in protocol
<a href="#">Lai, G.-S., Li, J.-R., Wang, S.-S. et al. (2020) Survival analysis of pathological T3a upstaging in clinical T1 renal cell carcinoma</a> . In Vivo 34(2): 799-805	- Non-OECD country
<a href="#">Lai, Gu-Shun, Li, Jian-Ri, Wang, Shian-Shiang et al. (2024) Outcome benefits of upfront cytoreductive nephrectomy for patients with metastatic renal cell carcinoma: An analysis of the TriNetX database</a> . PloS one 19(3): e0299102	- Non-OECD country
<a href="#">Lai, T.C.T.; Ma, W.K.; Yiu, M.K. (2016) Partial nephrectomy for t1 renal cancer can achieve an equivalent oncological outcome to radical nephrectomy with better renal preservation: The way to go</a> . Hong Kong Medical Journal 22(1): 39-45	- Primary study covered fully by an included systematic review

Study	Reason
<a href="#">Lam, Jing Kai Jackie; Tan, Sher Yin; Chong, Kian Tai (2020) Is partial nephrectomy worth performing compared to radical nephrectomy for small, localised renal cortical tumours in geriatric patients?.</a> Singapore medical journal 61(4): 190-193	- Data not reported in an extractable format <i>reports CKD at 5 years but it was published within the search dates of Ochoa-Arviso - But N at 5yrs was not reported, which is likely why it wasn't included in Ochoa</i>
<a href="#">Larcher, A, Sun, M, Dell'Oglio, P et al. (2017) Mortality, morbidity and healthcare expenditures after local tumour ablation or partial nephrectomy for T1A kidney cancer.</a> European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 43(4): 815-822	- Data not reported in an extractable format <i>Insufficient data reported to assess study methodology</i>
<a href="#">Larcher, Alessandro, Meskawi, Malek, Valdivieso, Roger et al. (2016) Comparison of renal function detriments after local tumor ablation or partial nephrectomy for renal cell carcinoma.</a> World journal of urology 34(3): 383-9	- Data not reported in an extractable format <i>Insufficient information reported to assess study</i>
<a href="#">Laru, Lauri, Ronkainen, Hanna, Ohtonen, Pasi et al. (2021) Nephrectomy improves the survival of metastatic renal cell cancer patients with moderate to good performance status-results from a Finnish nation-wide population-based study from 2005 to 2010.</a> World journal of surgical oncology 19(1): 190	- Comparator in study does not match that specified in protocol <i>Study compares CN vs. metastasectomy. Does not report about the SACT status</i>
<a href="#">Lasorsa, Francesco, Bignante, Gabriele, Orsini, Angelo et al. (2024) Partial nephrectomy in elderly patients: a systematic review and analysis of comparative outcomes.</a> European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 50(10): 108578	- Systematic review used as source of primary studies
<a href="#">Le Guevelou, Jennifer, Sargos, Paul, Siva, Shankar et al. (2023) The Emerging Role of Extracranial Stereotactic Ablative Radiotherapy for Metastatic Renal Cell Carcinoma: A Systematic Review.</a> European urology focus 9(1): 114-124	- Systematic review used as source of primary studies
<a href="#">Lee, H., Lee, M., Lee, S.E. et al. (2018) Outcomes of pathologic stage T3a renal cell carcinoma up-staged from small renal tumor: Emphasis on partial nephrectomy.</a> BMC Cancer 18(1): 427	- Study does not contain a relevant intervention

Study	Reason
<a href="#">Lee, Nora G; Zampini, Anna; Tuerk, Ingolf (2012) Single surgeon's experience with laparoscopic versus robotic partial nephrectomy: perioperative outcomes/complications and influence of tumor characteristics on choice of therapy.</a> The Canadian journal of urology 19(5): 6465-70	- Exclude - review C - study included only patients T1-T2
<a href="#">Lee, Sangchul, Oh, Jongjin, Hong, Seong Kyu et al. (2011) Open versus robot-assisted partial nephrectomy: effect on clinical outcome.</a> Journal of endourology 25(7): 1181-5	- There is no information on cT or pT stage
<a href="#">Lee, Sangchul; Ryu, Hoyoung; Lee, Jeong Woo (2021) Open Partial Nephrectomy vs. Robot-assisted Partial Nephrectomy for a Renal Tumor Larger than 4 cm: a Propensity Score Matching Analysis.</a> Journal of Korean medical science 36(20): e135	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Lenis, A.T., Salmasi, A.H., Donin, N.M. et al. (2018) Trends in usage of cytoreductive partial nephrectomy and effect on overall survival in patients with metastatic renal cell carcinoma.</a> Urologic Oncology: Seminars and Original Investigations 36(2): 78e21-78e28	- Comparator in study does not match that specified in protocol <i>Compares partial CN Vs. radical CN</i>
<a href="#">Lesnyak, O., Stroy, O., Banyra, O. et al. (2020) Assessment of the effectiveness of radiofrequency ablation as a technique for destroying small renal tumors in patients older than 70.</a> Central European Journal of Urology 73(4): 1-7	- Non-OECD country
<a href="#">Li, G, Luo, Q, Lang, Z et al. (2018) Histopathologic analysis of stage pT1b kidney neoplasms for optimal surgical margins of nephron-sparing surgery.</a> Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico 20(9): 1196-1201	- Study does not contain a relevant outcome
<a href="#">Li, Jingdong, Zhang, Yanping, Teng, Zhihai et al. (2019) Partial nephrectomy versus radical nephrectomy for cT2 or greater renal tumors: a systematic review and meta-analysis.</a> Minerva urologica e nefrologica = The Italian journal of urology and nephrology 71(5): 435-444	- Systematic review used as source of primary studies
<a href="#">Li, Jinze, Peng, Lei, Cao, Dehong et al. (2020) Comparison of Perioperative Outcomes of Robot-Assisted vs. Laparoscopic Radical</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%

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Study	Reason
<a href="#">Nephrectomy: A Systematic Review and Meta-Analysis.</a> Frontiers in oncology 10: 551052	
<a href="#">Li, Kun-Peng, Chen, Si-Yu, Wan, Shun et al. (2024) Percutaneous ablation versus robotic-assisted partial nephrectomy for cT1 renal cell carcinoma: an evidence-based analysis of comparative outcomes.</a> Journal of robotic surgery 18(1): 301	- Systematic review used as source of primary studies
<a href="#">Li, Kun-Peng, Chen, Si-Yu, Wang, Chen-Yang et al. (2023) The impact of cytoreductive nephrectomy on survival outcomes in patients with metastatic renal cell carcinoma receiving immunotherapy: An evidence-based analysis of comparative outcomes.</a> Frontiers in immunology 14: 1132466	- Exclude - wrong population
<a href="#">Li, Kun-Peng, Chen, Si-Yu, Wang, Chen-Yang et al. (2023) Comparison between minimally invasive partial nephrectomy and open partial nephrectomy for complex renal tumors: a systematic review and meta-analysis.</a> International journal of surgery (London, England) 109(6): 1769-1782	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Li, Kun-Peng, Wan, Shun, Chen, Si-Yu et al. (2024) Perioperative, functional and oncologic outcomes of percutaneous ablation versus minimally invasive partial nephrectomy for clinical T1 renal tumors: outcomes from a pooled analysis.</a> Journal of robotic surgery 18(1): 306	- Systematic review used as source of primary studies
<a href="#">Li, Kun-Peng, Wan, Shun, Wang, Chen-Yang et al. (2023) Perioperative, functional, and oncologic outcomes of robot-assisted versus open partial nephrectomy for complex renal tumors (RENAL score <math>\geq 7</math>): an evidence-based analysis.</a> Journal of robotic surgery 17(4): 1247-1258	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Li, Pin, Peng, Cheng, Gu, Liangyou et al. (2019) Radical Nephrectomy with or without Lymph Node Dissection for pT3 Renal Cell Carcinoma: A Propensity Score-based Analysis.</a> Journal of Cancer 10(10): 2369-2375	- Non-OECD country - Comparator in study does not match that specified in protocol
<a href="#">Li, Wentao, Cheng, Yanlei, Cheng, Yi et al. (2014) Clinical efficacy of radical nephrectomy versus nephron-sparing surgery on localized renal cell carcinoma.</a> European journal of medical research 19: 58	- Systematic review used as source of primary studies

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# DRAFT FOR CONSULTATION

Study	Reason
<a href="#">Liao, Xinyang, Qiu, Shi, Wang, Wanyu et al. (2019) Partial nephrectomy vs cryoablation for T1a renal cell carcinoma: A comparison of survival benefit stratified by tumour size.</a> Cancer epidemiology 59: 221-226	- Non-OECD country
<a href="#">Liek, Elisabeth, Elsebach, Klaus, Gobel, Hubert et al. (2018) The Overall Survival Benefit for Patients with T1 Renal Cell Carcinoma after Nephron-Sparing Surgery Depends on Gender and Age.</a> Urologia internationalis 100(3): 309-316	- Data not reported in an extractable format <i>Overall survival reported as Kaplan-Meier and P values</i>
<a href="#">Lin, J., Song, A.J., Hoffman-Censits, J. et al. (2020) A Pilot Study of Radiation Therapy in Combination with Pembrolizumab in Patients with Metastatic Renal Cell Cancer.</a> American Journal of Clinical Oncology: Cancer Clinical Trials 43(2): 82-86	- Not a relevant study design <i>Reports a part of RCT. Reported subgroup irrelevant to the protocol</i>
<a href="#">Lin, Pengxiu, Wu, Minhong, Gu, Hongyong et al. (2021) Comparison of outcomes between laparoscopic and robot-assisted partial nephrectomy for complex renal tumors: RENAL score <math>\geq 7</math> or maximum tumor size <math>&gt;4</math> cm.</a> Minerva urology and nephrology 73(2): 154-164	- Exclude review C - Study included only patients T1-T2
<a href="#">Lin, Wenhao, Yang, Zhenggang, Yan, Ling et al. (2023) Comparison of partial nephrectomy and radical nephrectomy for cystic renal cell carcinoma: a SEER-based and retrospective study.</a> Scientific reports 13(1): 8052	- SEER database overlap
<a href="#">Liu, Changfu, Cao, Fei, Xing, Wenge et al. (2019) Efficacy of cryoablation combined with sorafenib for the treatment of advanced renal cell carcinoma.</a> International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group 36(1): 220-228	- Study does not contain a relevant intervention <i>SACT given along with cryotherapy</i>
<a href="#">Liu, Gang, Ma, Yulei, Wang, Shouhua et al. (2017) Laparoscopic Versus Open Radical Nephrectomy for Renal Cell Carcinoma: a Systematic Review and Meta-Analysis.</a> Translational oncology 10(4): 501-510	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Liu, H.; Gao, C.; Yu, H. (2016) Safety and effectiveness of percutaneous radiofrequency ablation in early stage renal cell carcinoma.</a> Oncology Letters 12(6): 4618-4622	- Non-OECD country

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Study	Reason
<a href="#">Liu, Hui, Kong, Qing-Fang, Li, Jian et al. (2021) A meta-analysis for comparison of partial nephrectomy vs. radical nephrectomy in patients with pT3a renal cell carcinoma.</a> Translational andrology and urology 10(3): 1170-1178	- Comparator in study does not match that specified in protocol <i>PN vs RN for T3 tumour</i>
<a href="#">Liu, Ning, Huang, Daoguang, Cheng, Xiangming et al. (2017) Percutaneous radiofrequency ablation for renal cell carcinoma vs. partial nephrectomy: Comparison of long-term oncologic outcomes in both clear cell and non-clear cell of the most common subtype.</a> Urologic oncology 35(8): 530e1-530e6	- Non-OECD country
<a href="#">Liu, Wing K, Lam, J M, Butters, T et al. (2020) Cytorreductive nephrectomy in metastatic renal cell carcinoma: outcome of patients treated with a multidisciplinary, algorithm-driven approach.</a> World journal of urology 38(12): 3199-3205	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Liu, X-H, Song, J, Ma, W-M et al. (2024) Comparison of perioperative outcomes between robot-assisted partial nephrectomy and laparoscopic partial nephrectomy in obese patients.</a> European review for medical and pharmacological sciences 28(10): 3583-3589	- Exclude - Review C. Patients with localised tumour
<a href="#">Liu, Y., Zhang, Z., Han, H. et al. (2021) Survival After Combining Stereotactic Body Radiation Therapy and Tyrosine Kinase Inhibitors in Patients With Metastatic Renal Cell Carcinoma.</a> Frontiers in Oncology 11: 607595	- Study does not contain a relevant outcome
<a href="#">Liu, Yang, Long, Wen, Zhang, Zhiling et al. (2021) Metastasis-directed stereotactic body radiotherapy for oligometastatic renal cell carcinoma: extent of tumor burden eradicated by radiotherapy.</a> World journal of urology 39(11): 4183-4190	- Mixed population of SACT pre/post non-pharmacological regimens  - Review H - SABR exclude
<a href="#">Liu, Yang, Zhang, Zhiling, Liu, Ruiqi et al. (2021) Stereotactic body radiotherapy in combination with non-frontline PD-1 inhibitors and targeted agents in metastatic renal cell carcinoma.</a> Radiation oncology (London, England) 16(1): 211	- Review H - SABR exclude <i>doesn't separate out SABR given before vs after SACT</i>
<a href="#">Liu, Ying, Wang, Li, Bao, Er-Hao et al. (2024) Perioperative, functional, and oncological outcomes after cryoablation or partial nephrectomy for small renal masses in solitary kidneys: a systematic review and meta-analysis.</a> BMC urology 24(1): 19	- Systematic review used as source of primary studies

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Study	Reason
<a href="#">Liu, Z., Wang, P., Xia, D. et al. (2013) Comparison between laparoscopic and open partial nephrectomy: Surgical, oncologic, and functional outcomes.</a> Kaohsiung Journal of Medical Sciences 29(11): 624-628	- Non-OECD country  - Exclude Review C - Study included only patients T1-T2
<a href="#">Liu, Zhenhua, Yang, Zhenyu, Li, Jibin et al. (2023) Partial versus radical nephrectomy for the treatment of pT3aN0M0 renal cell carcinoma: A propensity score analysis.</a> Asian journal of surgery 46(9): 3607-3613	- Comparator in study does not match that specified in protocol <i>For review C - comparison RN vs PN in T3 tumours which is not applicable for this question</i>
<a href="#">Ljungberg, Borje, Sundqvist, Pernilla, Lindblad, Per et al. (2020) Survival advantage of upfront cytoreductive nephrectomy in patients with primary metastatic renal cell carcinoma compared with systemic and palliative treatments in a real-world setting.</a> Scandinavian journal of urology 54(6): 487-492	- Comparator in study does not match that specified in protocol <i>Compares SACT alone with upfront CN.</i>
<a href="#">Long, Jean-Alexandre, Yakoubi, Rachid, Lee, Byron et al. (2012) Robotic versus laparoscopic partial nephrectomy for complex tumors: comparison of perioperative outcomes.</a> European urology 61(6): 1257-62	- Exclude - review C. Patients with localised tumour
<a href="#">Loo Gan, Chun, Huang, Jiaming, Pan, Elizabeth et al. (2023) Real-world Practice Patterns and Safety of Concurrent Radiotherapy and Cabozantinib in Metastatic Renal Cell Carcinoma: Results from the International Metastatic Renal Cell Carcinoma Database Consortium.</a> European urology oncology 6(2): 204-211	- Review H - SABR exclude  - Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Lounova, Veronika, Student, Vladimir Jr, Purova, Dana et al. (2024) Frequency of benign tumors after partial nephrectomy and the association between malignant tumor findings and preoperative clinical parameters.</a> BMC urology 24(1): 175	- Study did not compare the interventions of interest <i>Reporting results for benign and malignant tumours and not for the two different surgical techniques for nephrectomy</i>
<a href="#">Love, Harrison, Yong, Courtney, Slaven, James E et al. (2024) Outcomes of open versus robotic partial nephrectomy: a 20-year single institution experience.</a> Journal of robotic surgery 18(1): 315	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Lucas, Steven M, Mellon, Matthew J, Erntsberger, Luke et al. (2012) A comparison of robotic, laparoscopic and open partial nephrectomy.</a> JSLS : Journal of the Society of Laparoendoscopic Surgeons 16(4): 581-7	- Comparator in study does not match that specified in protocol

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Study	Reason
<a href="#">Luciani, Lorenzo G, Chiodini, Stefano, Mattevi, Daniele et al. (2017) Robotic-assisted partial nephrectomy provides better operative outcomes as compared to the laparoscopic and open approaches: results from a prospective cohort study.</a> Journal of robotic surgery 11(3): 333-339	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Luo, X., Yi, M., Hu, Q. et al. (2019) Is cytoreductive nephrectomy necessary for metastatic renal cell carcinoma: A systematic review and meta-analysis.</a> International Journal of Clinical and Experimental Medicine 12(6): 7029-7037	- Exclude - Result reported in the most updated MA
<a href="#">Luo, X, Li, J-X, Liu, Y-T et al. (2019) Influence of lymph node dissection in patients undergoing radical nephrectomy for non-metastatic renal cell carcinoma: a systematic review and meta-analysis.</a> European review for medical and pharmacological sciences 23(14): 6079-6090	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Luo, You, Chen, San-San, Bai, Liang et al. (2017) Nephron Sparing Surgery Has Better Oncologic Outcomes Than Extirpative Nephrectomy in T1a but Not in T1b or T2 Stage Renal Cell Carcinoma.</a> Medical science monitor : international medical journal of experimental and clinical research 23: 3480-3488	- SEER database overlap
<a href="#">Lv, ZongYing, Chen, GuiYuan, Chen, XiaoBin et al. (2023) Open versus robot-assisted partial nephrectomy for highly complex renal masses: a meta-analysis of perioperative and functional outcomes.</a> Journal of robotic surgery 17(5): 1955-1965	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Ma, Ming-Wei, Li, Hong-Zhen, Gao, Xian-Shu et al. (2022) Outcomes of High-Dose Stereotactic Ablative Radiotherapy to All/Multiple Sites for Oligometastatic Renal Cell Cancer Patients.</a> Current oncology (Toronto, Ont.) 29(10): 7832-7841	- Mixed population of SACT pre/post non-pharmacological regimens - Review H - SABR exclude
<a href="#">MacLennan, Steven, Imamura, Mari, Lapitan, Marie C et al. (2012) Systematic review of oncological outcomes following surgical management of localised renal cancer.</a> European urology 61(5): 972-93	- Systematic review used as source of primary studies
<a href="#">MacLennan, Steven, Imamura, Mari, Lapitan, Marie C et al. (2012) Systematic review of perioperative and quality-of-life outcomes</a>	- Systematic review used as source of primary studies

Kidney cancer: evidence review for non- pharmacological management of advanced renal cell carcinoma DRAFT FOR CONSULTATION (September 2025)

Study	Reason
<a href="#">following surgical management of localised renal cancer.</a> European urology 62(6): 1097-117	
<a href="#">Maisel, Franziska, Smolle, Maria A, Mollnar, Stefanie et al. (2022) Benefit of Metastasectomy in Renal Cell Carcinoma: A Propensity Score Analysis.</a> Clinical genitourinary cancer 20(4): 344-353	<ul style="list-style-type: none"> <li>- Comparator in study does not match that specified in protocol</li> <li>- Study does not contain a relevant intervention</li> </ul>
<a href="#">Malaeb, B.S., Sherwood, J.B., Taylor, G.D. et al. (2005) Hand-assisted laparoscopic nephrectomy for renal masses &gt;9.5 cm: Series comparison with open radical nephrectomy.</a> Urologic Oncology: Seminars and Original Investigations 23(5): 323-327	<ul style="list-style-type: none"> <li>- Exclude - Review C. Proportion of patients stage T3 &lt; 90%</li> </ul>
<a href="#">Manikandan, R; Srinivasan, V; Rane, A (2004) Which is the real gold standard for small-volume renal tumors? Radical nephrectomy versus nephron-sparing surgery.</a> Journal of endourology 18(1): 39-44	<ul style="list-style-type: none"> <li>- More recent systematic review included that covers the same topic</li> </ul>
<a href="#">Marchioni, M., Bandini, M., Pompe, R.S. et al. (2018) The impact of lymph node dissection and positive lymph nodes on cancer-specific mortality in contemporary pT2-3 non-metastatic renal cell carcinoma treated with radical nephrectomy.</a> BJU International 121(3): 383-392	<ul style="list-style-type: none"> <li>- Comparator in study does not match that specified in protocol <i>LND vs no LND</i></li> </ul>
<a href="#">Marchioni, Michele, Cheaib, Joseph G, Takagi, Toshio et al. (2021) Active surveillance for small renal masses in elderly patients does not increase overall mortality rates compared to primary intervention: a propensity score weighted analysis.</a> Minerva urology and nephrology 73(6): 781-788	<ul style="list-style-type: none"> <li>- Comparator in study does not match that specified in protocol <i>Ablation and partial nephrectomy groups combined in results vs active surveillance</i></li> </ul>
<a href="#">Marchioni, Michele, Preisser, Felix, Bandini, Marco et al. (2019) Comparison of Partial Versus Radical Nephrectomy Effect on Other-cause Mortality, Cancer-specific Mortality, and 30-day Mortality in Patients Older Than 75 Years.</a> European urology focus 5(3): 467-473	<ul style="list-style-type: none"> <li>- Study does not contain a relevant outcome</li> </ul>
<a href="#">Margulis, Vitaly, Tamboli, Pheroze, Jacobsohn, Kenneth M et al. (2007) Oncological efficacy and safety of nephron-sparing surgery for selected patients with locally advanced renal cell carcinoma.</a> BJU international 100(6): 1235-9	<ul style="list-style-type: none"> <li>- Comparator in study does not match that specified in protocol <i>Compares Rn vs PN in locally advanced RCC - not applicable for review C.</i></li> </ul>
<a href="#">Maric, P., Jovanovic, M., Milovic, N. et al. (2017) Complications of radical and partial</a>	<ul style="list-style-type: none"> <li>- Data not reported in an extractable format</li> </ul>

Study	Reason
<a href="#">nephrectomy for renal cell carcinoma up to 7 cm.</a> Vojnosanitetski Pregled 74(7): 639-643	<i>Severe complications (Clavien-Dindo <math>\geq</math> III) were only reported in a graph</i> Duration of hospital stay was reported as median and range
<a href="#">Mason, Ross J, Atwell, Thomas D, Lohse, Christine et al. (2017) Renal functional outcomes in patients undergoing percutaneous cryoablation or partial nephrectomy for a solitary renal mass.</a> BJU international 120(4): 544-549	- Study does not contain a relevant outcome
<a href="#">Massari, Francesco, Di Nunno, Vincenzo, Gatto, Lidia et al. (2018) Should CARMENA Really Change our Attitude Towards Cytoreductive Nephrectomy in Metastatic Renal Cell Carcinoma? A Systematic Review and Meta-Analysis Evaluating Cytoreductive Nephrectomy in the Era of Targeted Therapy.</a> Targeted oncology 13(6): 705-714	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Masson-Lecomte, Alexandra, Bensalah, Karim, Serigne, Elise et al. (2013) A prospective comparison of surgical and pathological outcomes obtained after robot-assisted or pure laparoscopic partial nephrectomy in moderate to complex renal tumours: results from a French multicentre collaborative study.</a> BJU international 111(2): 256-63	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Masson-Lecomte, Alexandra, Yates, David R, Hupertan, Vincent et al. (2013) A prospective comparison of the pathologic and surgical outcomes obtained after elective treatment of renal cell carcinoma by open or robot-assisted partial nephrectomy.</a> Urologic oncology 31(6): 924-9	- There is no information on cT or pT stage
<a href="#">Mastroianni, R., Chiacchio, G., Perpepaj, L. et al. (2024) Comparison of Perioperative, Functional, and Oncologic Outcomes of Open vs. Robot-Assisted Off-Clamp Partial Nephrectomy: A Propensity Score Match Analysis.</a> Sensors (Basel, Switzerland) 24(9)	- Exclude review C- Study included only patients T1-T2
<a href="#">Mathieu, Romain, Pignot, Geraldine, Ingles, Alexandre et al. (2015) Nephrectomy improves overall survival in patients with metastatic renal cell carcinoma in cases of favorable MSKCC or ECOG prognostic features.</a> Urologic oncology 33(8): 339e9-15	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">May, D.N., Hill, H., Matrana, M.R. et al. (2021) A Contemporary Analysis of the 30-day Morbidity</a>	- Comparator in study does not match that specified in protocol

Study	Reason
<a href="#">and Mortality Associated With Cytoreductive Nephrectomy.</a> Urology 147: 186-191	
<a href="#">Mearini, Luigi, Nunzi, Elisabetta, Vianello, Alberto et al. (2016) Margin and complication rates in clampless partial nephrectomy: a comparison of open, laparoscopic and robotic surgeries.</a> Journal of robotic surgery 10(2): 135-44	- There is no information on cT or pT stage
<a href="#">Mehra, Ketan, Manikandan, Ramanitharan, Dorairajan, Lalgudi Narayanan et al. (2019) Trifecta Outcomes in Open, Laparoscopy or Robotic Partial Nephrectomy: Does the Surgical Approach Matter?.</a> Journal of kidney cancer and VHL 6(1): 8-12	- Non-OECD country - There is no information on cT or pT stage
<a href="#">Mennitto, A, Verzoni, E, Cognetti, F et al. (2021) Radical metastasectomy followed by sorafenib versus observation in patients with clear cell renal cell carcinoma: extended follow-up of efficacy results from the randomized phase II RESORT trial.</a> Expert review of clinical pharmacology 14(2): 261-268	- Comparator in study does not match that specified in protocol <i>Compares patients with metastatic rcc treated with sorafenib vs. observation-alone after the radical surgery of metastases</i>
<a href="#">Mershon, J Patrick; Tuong, Mei N; Schenkman, Noah S (2020) Thermal ablation of the small renal mass: a critical analysis of current literature.</a> Minerva urologica e nefrologica = The Italian journal of urology and nephrology 72(2): 123-134	- More recent systematic review included that covers the same topic
<a href="#">Metcalf, Meredith R, Cheaib, Joseph G, Biles, Michael J et al. (2021) Outcomes of Active Surveillance for Young Patients with Small Renal Masses: Prospective Data from the DISSRM Registry.</a> The Journal of urology 205(5): 1286-1293	- Comparator in study does not match that specified in protocol <i>Surgery and cryoablation combined</i>
<a href="#">Metcalf, Meredith R, Pena, Vanessa N, Cheaib, Joseph G et al. (2022) Disparities in the Treatment and Survival of Metastatic Renal Cell Carcinoma.</a> Urology 165: 89-97	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Michalak, M., Kopczynska, A., Antczak, A. et al. (2024) Outcomes of treatment, laboratory results, adverse effects, and tolerability of cancer treatment in patients with metastatic renal cell carcinoma treated with ipilimumab and nivolumab after cytoreductive nephrectomy.</a> Nowotwory 74(6): 344	- Data not reported in an extractable format <i>Data for PFS was reported as mean and range only</i>

Study	Reason
<a href="#">Michalak, M., Tomczak, P., Milecki, T. et al. (2024) Outcomes of treatment, laboratory results, adverse effects, and tolerability of cancer treatment in patients with metastatic renal-cell carcinoma treated with sunitinib after cytoreductive nephrectomy. Nowotwory 74(2): 105</a>	- Exclude - assessed outcome is out of scope
<a href="#">Miller, Brady L, Mankowski Gettle, Lori, Van Roo, Jason R et al. (2018) Comparative Analysis of Surgery, Thermal Ablation, and Active Surveillance for Renal Oncocytic Neoplasms. Urology 112: 92-97</a>	- Does not contain a population of people with kidney cancer
<a href="#">Miller, Jacob A, Balagamwala, Ehsan H, Angelov, Lilyana et al. (2016) Spine stereotactic radiosurgery with concurrent tyrosine kinase inhibitors for metastatic renal cell carcinoma. Journal of neurosurgery. Spine 25(6): 766-774</a>	- Conference abstract
<a href="#">Minervini, Andrea, Vittori, Gianni, Antonelli, Alessandro et al. (2014) Open versus robotic-assisted partial nephrectomy: a multicenter comparison study of perioperative results and complications. World journal of urology 32(1): 287-93</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Mir, Maria Carmen, Derweesh, Ithaar, Porpiglia, Francesco et al. (2017) Partial Nephrectomy Versus Radical Nephrectomy for Clinical T1b and T2 Renal Tumors: A Systematic Review and Meta-analysis of Comparative Studies. European urology 71(4): 606-617</a>	- Systematic review used as source of primary studies
<a href="#">Mitchell, Christopher R, Atwell, Thomas D, Weisbrod, Adam J et al. (2011) Renal function outcomes in patients treated with partial nephrectomy versus percutaneous ablation for renal tumors in a solitary kidney. The Journal of urology 186(5): 1786-90</a>	- Study does not contain a relevant outcome <i>eGFR during postop period only</i>
<a href="#">Mittal, Abhenil, Al-Ezzi, Esmail, Li, Xuan et al. (2023) The role of cytoreductive nephrectomy and systemic therapy in the management of tumour thrombus in patients with metastatic renal cell carcinoma. British journal of cancer 128(10): 1888-1896</a>	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Miyake, Hideaki, Hinata, Nobuyuki, Imai, Satoshi et al. (2015) Partial nephrectomy for hilar tumors: comparison of conventional open and robot-assisted approaches. International journal of clinical oncology 20(4): 808-13</a>	- There is no information on cT or pT stage

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Study	Reason
<a href="#">Mo, Cheng-Qiang, Yu, Zhou, Tan, Wu-Lin et al. (2014) Comparison between laparoscopic partial nephrectomy and laparoscopic ablation therapy: a meta-analysis.</a> Minimally invasive therapy & allied technologies : MITAT : official journal of the Society for Minimally Invasive Therapy 23(6): 317-25	- More recent systematic review included that covers the same topic
<a href="#">Monda, S.; Lara, P.N.; Gulati, S. (2024) Post-Metastasectomy Adjuvant Therapy in Patients with Renal Cell Carcinoma: A Systematic Review.</a> Kidney Cancer 8(1): 115	- Comparator in study does not match that specified in protocol
<a href="#">Mori, Keiichiro, Quhal, Fahad, Yanagisawa, Takafumi et al. (2022) The effect of immune checkpoint inhibitor combination therapies in metastatic renal cell carcinoma patients with and without previous cytoreductive nephrectomy: A systematic review and meta-analysis.</a> International immunopharmacology 108: 108720	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Morkos, John, Porosnicu Rodriguez, Kori A, Zhou, Alice et al. (2020) Percutaneous Cryoablation for Stage 1 Renal Cell Carcinoma: Outcomes from a 10-year Prospective Study and Comparison with Matched Cohorts from the National Cancer Database.</a> Radiology 296(2): 452-459	- Secondary publication of an included study that does not provide any additional relevant information
<a href="#">Muhlbauer, Julia, de Gilde, Johannes, Mueller-Steinhardt, Michael et al. (2020) Perioperative Blood Transfusion Is a Predictor of Acute and Chronic Renal Function Deterioration after Partial and Radical Nephrectomy for Renal Cell Carcinoma.</a> Urologia internationalis 104(910): 775-780	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Muhlbauer, Julia, Kowalewski, Karl-Friedrich, Walach, Margarete T et al. (2020) Partial nephrectomy preserves renal function without increasing the risk of complications compared with radical nephrectomy for renal cell carcinomas of stages pT2-3a.</a> International journal of urology : official journal of the Japanese Urological Association 27(10): 906-913	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Nakada, S Y, Fadden, P, Jarrard, D F et al. (2001) Hand-assisted laparoscopic radical nephrectomy: comparison to open radical nephrectomy.</a> Urology 58(4): 517-20	- Exclude , review C. Patients with localised tumour

Study	Reason
<a href="#">Nandanan, N., Vecchia, A., Antonelli, A. et al. (2020) Outcomes and predictors of benign histology in patients undergoing robotic partial or radical nephrectomy for renal masses: A multicenter study.</a> Central European Journal of Urology 73(1): 33-38	- Study does not contain a relevant outcome
<a href="#">Nason, Gregory J, Walsh, Leon G, Redmond, Ciaran E et al. (2015) Comparative effectiveness of adrenal sparing radical nephrectomy and non-adrenal sparing radical nephrectomy in clear cell renal cell carcinoma: Observational study of survival outcomes.</a> Canadian Urological Association journal = Journal de l'Association des urologues du Canada 9(910): e583-8	- Comparator in study does not match that specified in protocol
<a href="#">Nayak, J.G., Patel, P., Saarela, O. et al. (2016) Pathological Upstaging of Clinical T1 to Pathological T3a Renal Cell Carcinoma: A Multi-institutional Analysis of Short-term Outcomes.</a> Urology 94: 154-160	- Primary study covered fully by an included systematic review
<a href="#">Nguyen, D.P., Vertosick, E.A., Corradi, R.B. et al. (2016) Histological subtype of renal cell carcinoma significantly affects survival in the era of partial nephrectomy.</a> Urologic Oncology: Seminars and Original Investigations 34(6): e1-259	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Nian, Xinwen, Ye, Huamao, Zhang, Wei et al. (2022) Propensity-matched pair analysis of safety and efficacy between laparoscopic and open radical nephrectomy for the treatment of large renal masses (&gt;10 cm): a retrospective cohort study.</a> Translational andrology and urology 11(8): 1148-1156	- Exclude, review C. Study included only patients T1-T2
<a href="#">Nicaise, Edouard, Feldman, Adam S, Gusev, Andrew et al. (2024) A contemporary comparison of laparoscopic versus open partial nephrectomy for renal cell carcinoma.</a> BMC urology 24(1): 58	- Exclude, review C - Study included only patients T1-T2
<a href="#">Nowak, Lukasz, Janczak, Dawid, Laszkiewicz, Jan et al. (2024) Clinical and Oncological Outcomes Following Percutaneous Cryoablation vs. Partial Nephrectomy for Clinical T1 Renal Tumours: Systematic Review and Meta-Analysis.</a> Cancers 16(6)	- Systematic review used as source of primary studies
<a href="#">Nunez Bragayrac, Luciano, Hoffmeyer, Jan, Abbotoy, Daniel et al. (2016) Minimally invasive</a>	- Comparator in study does not match that specified in protocol

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Study	Reason
<a href="#">cytoreductive nephrectomy: a multi-institutional experience.</a> World journal of urology 34(12): 1651-1656	No information about SACT
<a href="#">O'Malley, Rebecca L, Berger, Aaron D, Kanofsky, Jamie A et al. (2007) A matched-cohort comparison of laparoscopic cryoablation and laparoscopic partial nephrectomy for treating renal masses.</a> BJU international 99(2): 395-8	- Study published before included SR/s for the outcome/s reported
<a href="#">Ocak, Birol, Sahin, Ahmet Bilgehan, Erturk, Ismail et al. (2024) Can Cytoreductive Nephrectomy Improve Outcomes of Nivolumab Treatment in Patients with Metastatic Clear-Cell Renal Carcinoma?.</a> Current oncology (Toronto, Ont.) 31(9): 5195-5205	- Data not reported in an extractable format <i>Only median (95% CI) OS has been reported. Other data is time to treatment discontinuation for systemic treatments which is out of scope for this review.</i>
<a href="#">Oh, Jong Jin, Byun, Seoksoo, Hong, Sung Kyu et al. (2014) Comparison of robotic and open partial nephrectomy: Single-surgeon matched cohort study.</a> Canadian Urological Association journal = Journal de l'Association des urologues du Canada 8(78): e471-5	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Ohno, Y., Nakashima, J., Ohori, M. et al. (2014) Clinical variables for predicting metastatic renal cell carcinoma patients who might not benefit from cytoreductive nephrectomy: Neutrophil-to-lymphocyte ratio and performance status.</a> International Journal of Clinical Oncology 19(1): 139-145	- Mixed population of SACT pre/post non-pharmacological regimens <i>Unclear about the SACT treatment or any other treatment in no CN group</i>
<a href="#">Okita, Kazutaka, Hatakeyama, Shingo, Naito, Sei et al. (2021) External validation of the REMARCC model for the selection of cytoreductive nephrectomy in patients with primary metastatic renal cell carcinoma: A multicenter retrospective study.</a> Urologic oncology 39(12): 836e11-836e17	- Comparator in study does not match that specified in protocol <i>Study compares CN vs SACT. Combines upfront and deferred CN participants into one CN arm. No subgroup results reported</i>
<a href="#">Olweny, Ephrem O, Park, Samuel K, Tan, Yung K et al. (2012) Radiofrequency ablation versus partial nephrectomy in patients with solitary clinical T1a renal cell carcinoma: comparable oncologic outcomes at a minimum of 5 years of follow-up.</a> European urology 61(6): 1156-61	- Primary study covered fully by an included systematic review
<a href="#">Onal, Cem, Oymak, Ezgi, Guler, Ozan Cem et al. (2023) Stereotactic body radiotherapy and tyrosine kinase inhibitors in patients with oligometastatic renal cell carcinoma: a multi-institutional study.</a> Strahlentherapie und	- Review H - SABR exclude  - Mixed population of SACT pre/post non-pharmacological regimens

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Study	Reason
Onkologie : Organ der Deutschen Röntgengesellschaft ... [et al] 199(5): 456-464	
<a href="#">Onishi, Takehisa, Nishikawa, Kouhei, Hasegawa, Yoshihiro et al. (2007) Assessment of health-related quality of life after radiofrequency ablation or laparoscopic surgery for small renal cell carcinoma: a prospective study with medical outcomes Study 36-Item Health Survey (SF-36).</a> Japanese journal of clinical oncology 37(10): 750-4	- Study does not contain a relevant outcome <i>HRQoL reported as SF36</i>
<a href="#">Ontario, Health (2023) Robotic-assisted partial nephrectomy for kidney cancer.</a>	- Exclude - wrong population <i>Population too broad</i>
<a href="#">Pahouja, Gaurav, Sweigert, Sarah E, Sweigert, Patrick J et al. (2022) Does size matter? Comparing robotic versus open radical nephrectomy for very large renal masses.</a> Urologic oncology 40(10): 456e1-456e7	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Palacios, Diego Aguilar, Zabor, Emily C, Munoz-Lopez, Carlos et al. (2021) Does Reduced Renal Function Predispose to Cancer-specific Mortality from Renal Cell Carcinoma?.</a> European urology 79(6): 774-780	- Data not reported in an extractable format <i>No denominators for recurrence data</i>
<a href="#">Palumbo, Carlotta, Mistretta, Francesco A, Knipper, Sophie et al. (2020) Contemporary Cytoreductive Nephrectomy Provides Survival Benefit in Clear-cell Metastatic Renal Cell Carcinoma.</a> Clinical genitourinary cancer 18(6): e730-e738	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Pan, Xiu-Wu, Cui, Xin-Ming, Huang, Hai et al. (2015) Radiofrequency ablation versus partial nephrectomy for treatment of renal masses: A systematic review and meta-analysis.</a> The Kaohsiung journal of medical sciences 31(12): 649-58	- More recent systematic review included that covers the same topic
<a href="#">Panian, Justine, Saidian, Ava, Hakimi, Kevin et al. (2023) Pathological Outcomes of Patients With Advanced Renal Cell Carcinoma Who Receive Nephrectomy Following Immunotherapy.</a> The oncologist	- Not a relevant study design
<a href="#">Panumatrassamee, Kamol, Autorino, Riccardo, Laydner, Humberto et al. (2013) Robotic versus laparoscopic partial nephrectomy for tumor in a solitary kidney: a single institution comparative analysis.</a> International journal of urology : official	- Exclude - For review C. Proportion of patients stage T3 < 90%

Study	Reason
journal of the Japanese Urological Association 20(5): 484-91	
<a href="#">Papadopoulou, Ariadni, Campain, Nicholas, Abu-Ghanem, Yasmin et al. (2024) Not-so-simple nephrectomy: Comparative analysis of radical and simple nephrectomy in a high-volume tertiary referral center.</a> International journal of urology : official journal of the Japanese Urological Association 31(2): 160-168	- Comparator in study does not match that specified in protocol <i>Comparator is people who had simple nephrectomy; people who had partial nephrectomy were excluded.</i>
<a href="#">Patel, Hiten D, Kates, Max, Pierorazio, Phillip M et al. (2014) Survival after diagnosis of localized T1a kidney cancer: current population-based practice of surgery and nonsurgical management.</a> Urology 83(1): 126-32	- Study does not contain a relevant intervention <i>Not clearly active surveillance</i>
<a href="#">Patel, Hiten D, Riffon, Mark F, Joice, Gregory A et al. (2016) A Prospective, Comparative Study of Quality of Life among Patients with Small Renal Masses Choosing Active Surveillance and Primary Intervention.</a> The Journal of urology 196(5): 1356-1362	- Study does not contain a relevant outcome <i>QoL reported as SF12</i>
<a href="#">Patel, Sunil H, Uzzo, Robert G, Larcher, Alessandro et al. (2020) Oncologic and Functional Outcomes of Radical and Partial Nephrectomy in pT3a Pathologically Upstaged Renal Cell Carcinoma: A Multi-institutional Analysis.</a> Clinical genitourinary cancer 18(6): e723-e729	- Comparator in study does not match that specified in protocol <i>PN vs RN</i>
<a href="#">Patton, Michael W, Salevitz, Daniel A, Tyson, Mark D 2nd et al. (2016) Robot-assisted partial nephrectomy for complex renal masses.</a> Journal of robotic surgery 10(1): 27-31	- There is no information on cT or pT stage
<a href="#">Pecoraro, A., Roussel, E., Amparore, D. et al. (2023) New-onset Chronic Kidney Disease After Surgery for Localised Renal Masses in Patients with Two Kidneys and Preserved Renal Function: A Contemporary Multicentre Study.</a> European Urology Open Science 52: 100-108	- Data not reported in an extractable format <i>No information on participant split between I and C, or baseline characteristics by intervention.</i>
<a href="#">Pecoraro, A, Amparore, D, Manfredi, M et al. (2022) Partial vs. radical nephrectomy in non-metastatic pT3a kidney cancer patients: a population-based study.</a> Minerva urology and nephrology 74(4): 445-451	- Comparator in study does not match that specified in protocol <i>Compares PN vs RN in T3 tumours. Not applicable for review C.</i>
<a href="#">Peng, B, Zheng, J-H, Xu, D-F et al. (2006) Retroperitoneal laparoscopic nephrectomy and open nephrectomy for radical treatment of renal</a>	- Study not reported in English

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Study	Reason
<a href="#">cell carcinoma: a comparison of clinical outcomes.</a> Academic journal of second military medical university 27(11): 1167-1169	
<a href="#">Peng, Ding, He, Zhi-Song, Li, Xue-Song et al. (2017) Partial nephrectomy for T3aN0M0 renal cell carcinoma: shall we step forward?.</a> International braz j urol : official journal of the Brazilian Society of Urology 43(5): 849-856	- Non-OECD country  - Comparator in study does not match that specified in protocol <i>Compares PN vs RN in T3 tumours. Not applicable for review C.</i>
<a href="#">Peng, Jonathan; Lalani, Aly-Khan; Swaminath, Anand (2021) Cytoablative stereotactic body radiotherapy (SBRT) and combination SBRT with immune checkpoint inhibitors in metastatic renal cell carcinoma.</a> Canadian Urological Association journal = Journal de l'Association des urologues du Canada 15(8): 281-286	- Systematic review with single arm studies included only
<a href="#">Petrelli, Fausto, Coinu, Andrea, Vavassori, Ivano et al. (2016) Cytoablative Nephrectomy in Metastatic Renal Cell Carcinoma Treated With Targeted Therapies: A Systematic Review With a Meta-Analysis.</a> Clinical genitourinary cancer 14(6): 465-472	- Exclude - Result reported in the most updated MA
<a href="#">Petros, Firas G, Venkatesan, Aradhana M, Kaya, Diana et al. (2019) Conditional survival of patients with small renal masses undergoing active surveillance.</a> BJU international 123(3): 447-455	- Data not reported in an extractable format <i>Insufficient information about comparator arm to include</i>
<a href="#">Peyronnet, Benoit, Seisen, Thomas, Oger, Emmanuel et al. (2016) Comparison of 1800 Robotic and Open Partial Nephrectomies for Renal Tumors.</a> Annals of surgical oncology 23(13): 4277-4283	- There is no information on cT or pT stage
<a href="#">Piening, A., Al-Hammadi, N., Dombrowski, J. et al. (2023) Survival in Metastatic Renal Cell Carcinoma Treated With Immunotherapy and Stereotactic Radiation Therapy or Immunotherapy Alone: A National Cancer Database Analysis.</a> Advances in Radiation Oncology 8(5): 101238	- Mixed population of SACT pre/post non-pharmacological regimens <i>Combines participants receiving SACT and conventional radiotherapy in a single arm and compares it to SRT</i>
<a href="#">Pierorazio, Phillip M, Johnson, Michael H, Ball, Mark W et al. (2015) Five-year analysis of a multi-institutional prospective clinical trial of delayed intervention and surveillance for small renal masses: the DISSRM registry.</a> European urology 68(3): 408-15	- Comparator in study does not match that specified in protocol <i>Does not separate ablation and nephrectomy in comparator group</i>

Study	Reason
<a href="#">Pierorazio, Phillip M, Johnson, Michael H, Patel, Hiten D et al. (2016) Management of Renal Masses and Localized Renal Cancer: Systematic Review and Meta-Analysis.</a> The Journal of urology 196(4): 989-99	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>
<a href="#">Pignot, Geraldine, Margue, Gaelle, Bigot, Pierre et al. (2025) The effect of tumor downsizing on surgical complexity during nephrectomy after immune checkpoint inhibitors for metastatic renal cell carcinoma.</a> World journal of urology 43(1): 54	- Study did not compare the interventions of interest
<a href="#">Pignot, Geraldine, Mejean, Arnaud, Bernhard, Jean-Christophe et al. (2015) The use of partial nephrectomy: results from a contemporary national prospective multicenter study.</a> World journal of urology 33(1): 33-40	- Does not contain a population of people with kidney cancer <i>population has kidney cancer but &gt;10% of participants have stage 3 or higher</i>
<a href="#">Pignot, Geraldine, Thiery-Vuillemin, Antoine, Albiges, Laurence et al. (2022) Oncological Outcomes of Delayed Nephrectomy After Optimal Response to Immune Checkpoint Inhibitors for Metastatic Renal Cell Carcinoma.</a> European urology oncology 5(5): 577-584	- Comparator in study does not match that specified in protocol  - Study does not contain a relevant intervention
<a href="#">Poinas, G, Long, JA, Rébillard, X et al. (2018) [Place of partial nephrectomy assisted by robot: Review of the literature at the time of a request for a specific nomenclature].</a> Progres en urologie : journal de l'Association française d'urologie et de la Société française d'urologie 28(16): 890-899	- Study not reported in English
<a href="#">Posa, A., Lancellotta, V., Paoletti, F. et al. (2022) The Role of Focal Approach as Alternative to Nephron-Sparing Surgery in the Treatment of Stage I Cancer in Renal Graft: Results of a Systematic Review.</a> Turk Onkoloji Dergisi 37(3): 351-360	- More recent systematic review included that covers the same topic <i>kidney graft patients only</i>
<a href="#">Prata, F., Ragusa, A., Tedesco, F. et al. (2024) Trifecta Outcomes of Robot-Assisted Partial Nephrectomy Using the New Hugo™ RAS System Versus Laparoscopic Partial Nephrectomy.</a> Journal of Clinical Medicine 13(7): 2138	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Prins, Fieke M, Kerkmeijer, Linda G W, Pronk, Anne A et al. (2017) Renal Cell Carcinoma: Alternative Nephron-Sparing Treatment Options for Small Renal Masses, a Systematic Review.</a> Journal of endourology 31(10): 963-975	- More recent systematic review included that covers the same topic

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Study	Reason
<a href="#">Procopio, Giuseppe, Apollonio, Giulia, Cognetti, Francesco et al. (2019) Sorafenib Versus Observation Following Radical Metastasectomy for Clear-cell Renal Cell Carcinoma: Results from the Phase 2 Randomized Open-label RESORT Study.</a> European urology oncology 2(6): 699-707	- Comparator in study does not match that specified in protocol <i>Compares patients with metastatic rcc treated with sorafenib vs. observation-alone after the radical surgery of metastases</i>
<a href="#">Pyrgidis, N., Schulz, G.B., Stief, C. et al. (2024) Surgical Trends and Complications in Partial and Radical Nephrectomy: Results from the GRAND Study.</a> Cancers 16(1): 97	- Data not reported in an extractable format <i>no info on tumour stage (see highlighted text on page 9)study reports length of hospital stay (table 3)we could include and downgrade for applicability To exclude - as there is no information on tumour characteristics</i>
<a href="#">Qi, Nienie, Wu, Pengjie, Chen, Jinchao et al. (2017) Cytoreductive nephrectomy with thrombectomy before targeted therapy improves survival for metastatic renal cell carcinoma with venous tumor thrombus: a single-center experience.</a> World journal of surgical oncology 15(1): 4	- Study does not contain a relevant intervention
<a href="#">Qu, Hongchen; Wang, Kai; Hu, Bin (2023) Meta analysis of clinical prognosis of radiofrequency ablation versus partial nephrectomy in the treatment of early renal cell carcinoma.</a> Frontiers in oncology 13: 1105877	- Systematic review used as source of primary studies <i>Sources insufficient</i>
<a href="#">Qu, Hongchen; Wang, Kai; Hu, Bin (2024) Meta-analysis of clinical outcomes of robot-assisted partial nephrectomy and classical open partial nephrectomy.</a> International journal of surgery (London, England) 110(10): 6268-6281	- Exclude - review C. Patients with localised tumour
<a href="#">Raman, Jay D, Raj, Ganesh V, Lucas, Steven M et al. (2010) Renal functional outcomes for tumours in a solitary kidney managed by ablative or extirpative techniques.</a> BJU international 105(4): 496-500	- Study published before included SR/s for the outcome/s reported
<a href="#">Reese, Stephen W, Eismann, Lennert, White, Charlie et al. (2023) Surgical outcomes of cytoreductive nephrectomy in patients receiving systemic immunotherapy for advanced renal cell carcinoma.</a> Urologic oncology	- Comparator in study does not match that specified in protocol
<a href="#">Reifsnnyder, Jennifer E, Ramasamy, Ranjith, Ng, Casey K et al. (2012) Laparoscopic and open partial nephrectomy: complication comparison using the Clavien system.</a> JSLS : Journal of the Society of Laparoendoscopic Surgeons 16(1): 38-44	- There is no information on cT or pT stage

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Study	Reason
<a href="#">Ricciardulli, Stefano, Ding, Qiang, Zhang, Xu et al. (2015) Evaluation of laparoscopic vs robotic partial nephrectomy using the margin, ischemia and complications score system: a retrospective single center analysis.</a> Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica 87(1): 49-55	- Exclude, review C - Study included only patients T1-T2
<a href="#">Richey, S L, Culp, S H, Jonasch, E et al. (2011) Outcome of patients with metastatic renal cell carcinoma treated with targeted therapy without cytoreductive nephrectomy.</a> Annals of oncology : official journal of the European Society for Medical Oncology 22(5): 1048-1053	- Comparator in study does not match that specified in protocol <i>Compares targeted therapy with chemotherapy and other types of SACT</i>
<a href="#">Rim, C.H., Cho, W.K., Lee, J.H. et al. (2022) Role of Local Treatment for Oligometastasis: A Comparability-Based Meta-Analysis.</a> Cancer Research and Treatment 54(4): 953-969	- Exclude - wrong population - Exclude - Intervention is out of scope
<a href="#">Rini, Brian I and Campbell, Steven C (2007) The evolving role of surgery for advanced renal cell carcinoma in the era of molecular targeted therapy.</a> The Journal of urology 177(6): 1978-84	- Review article but not a systematic review
<a href="#">Rivero, J Ricardo, De La Cerda, Jose 3rd, Wang, Hanzhang et al. (2018) Partial Nephrectomy versus Thermal Ablation for Clinical Stage T1 Renal Masses: Systematic Review and Meta-Analysis of More than 3,900 Patients.</a> Journal of vascular and interventional radiology : JVIR 29(1): 18-29	- More recent systematic review included that covers the same topic
<a href="#">Roaldsen, Marius, Lohne, Vetle, Stenberg, Thor Allan et al. (2024) Comparing open and robot-assisted partial nephrectomy - a single institution report.</a> BMC urology 24(1): 197	- Exclude, review C. Study included only patients T1-T2
<a href="#">Roussel, Eduard, Laenen, Annouschka, Bhindi, Bimal et al. (2023) Predicting short- and long-term renal function following partial and radical nephrectomy.</a> Urologic oncology 41(2): 110e1-110e6	- Study does not contain a relevant outcome
<a href="#">Roussel, Eduard, Verbiest, Annelies, Milenkovic, Uros et al. (2020) Too good for CARMENA: criteria associated with long systemic therapy free intervals post cytoreductive nephrectomy for metastatic clear cell renal cell carcinoma.</a> Scandinavian journal of urology 54(6): 493-499	- Study does not contain a relevant outcome

Study	Reason
<a href="#">Russo, P. (2009) Radical nephrectomy with and without lymph node dissection: Final results of European Organization for Research and Treatment of Cancer (EORTC) randomized phase 3 trial 30881. Blom JH, van Poppel H, Marechal JM, Jacqmin D, Schroder FH, de Prijck L, Sylvester R, EORTC Genitourinary Tract Cancer Group, St. Franciscus Gasthuis, Rotterdam, The Netherlands. Urologic Oncology: Seminars and Original Investigations 27(1): 102</a>	- Conference abstract
<a href="#">Russo, P., Blum, K.A., Weng, S. et al. (2022) Outcomes for Atypical Tumor Recurrences Following Minimally Invasive Kidney Cancer Operations. European Urology Open Science 40: 125-132</a>	- Does not contain a population of people with kidney cancer <i>All participants were treated for recurrence after partial or radical nephrectomy</i>
<a href="#">Saeed, S., Shah, S.R., Najeebullah et al. (2024) THE ROLE OF NEPHRON-SPARING SURGERY IN THE MANAGEMENT OF SMALL RENAL MASSES COMPARING THE ONCOLOGICAL OUTCOMES, RENAL FUNCTION PRESERVATION, AND COMPLICATION RATES OF PARTIAL NEPHRECTOMY VERSUS RADICAL NEPHRECTOMY. Journal of Population Therapeutics and Clinical Pharmacology 31(9): 981</a>	- Non-OECD country
<a href="#">Sandbergen, Laura, Spriensma, Alette S, de la Rosette, Jean J et al. (2020) Health-related quality of life in localized renal masses: A matter of sparing nephrons or minimizing the incision?. Urologic oncology 38(2): 43e1-43e11</a>	- Study does not contain a relevant outcome <i>QoL as SF-36</i>
<a href="#">Schernuk, Jordan, Garcia Marchinena, Patricio A, Carminatti, Tomas et al. (2023) Renal Cell Carcinoma with Venous Extension: Safety of Laparoscopic Surgery for Thrombus Levels I- IIIa. Journal of endourology 37(7): 786-792</a>	- Comparator in study does not match that specified in protocol
<a href="#">Schiff, Jonathan D, Palese, Michael, Vaughan, E Darracott Jr et al. (2005) Laparoscopic vs open partial nephrectomy in consecutive patients: the Cornell experience. BJU international 96(6): 811-4</a>	- There is no information on cT or pT stage
<a href="#">Scosyrev, Emil, Messing, Edward M, Sylvester, Richard et al. (2014) Renal function after nephron-sparing surgery versus radical nephrectomy: results from EORTC randomized trial 30904. European urology 65(2): 372-7</a>	- Secondary publication of an included study that does not provide any additional relevant information

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Study	Reason
<a href="#">Scosyrev, Emil, Wu, Kevin, Levey, Helen R et al. (2014) Overall Survival after Partial Versus Radical Nephrectomy for a Small Renal Mass: Systematic Review of Observational Studies.</a> Urology practice 1(1): 27-34	- More recent systematic review included that covers the same topic
<a href="#">Selim, A.M., Zaghloul, A.S., Aboukassem, H.A. et al. (2020) Minimally invasive approach in surgical management of renal neoplasms national cancer institute experience.</a> Open Access Macedonian Journal of Medical Sciences 8(b): 1071-1076	- Study does not contain a relevant intervention <i>Laparoscopic &amp; robotic compared to open nephrectomy irrespective of being partial or radical</i>
<a href="#">Shah, Paras H, Leibovich, Bradley C, Van Houten, Holly et al. (2019) Association of Partial versus Radical Nephrectomy with Subsequent Hypertension Risk Following Renal Tumor Resection.</a> The Journal of urology 202(1): 69-75	- Primary study covered fully by an included systematic review
<a href="#">Shah, Paras H, Moreira, Daniel M, Patel, Vinay R et al. (2017) Partial Nephrectomy is Associated with Higher Risk of Relapse Compared with Radical Nephrectomy for Clinical Stage T1 Renal Cell Carcinoma Pathologically Up Staged to T3a.</a> The Journal of urology 198(2): 289-296	- Comparator in study does not match that specified in protocol <i>Compares RN and PN for upstaged T3 tumours.</i>
<a href="#">Sharma, Gopal, Sharma, Aditya Prakash, Tyagi, Shantanu et al. (2022) Robot-assisted partial nephrectomy for moderate to highly complex renal masses. A systematic review and meta-analysis.</a> Indian journal of urology : IJU : journal of the Urological Society of India 38(3): 174-183	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Shaw, Greg L, Hussain, Mahreen, Nair, Rajesh et al. (2012) Performing cytoreductive nephrectomy following targeted sunitinib therapy for metastatic renal cell carcinoma: a surgical perspective.</a> Urologia internationalis 89(1): 83-8	- Comparator in study does not match that specified in protocol
<a href="#">Shchukin, D.V., Lesovoy, V.N., Garagatiy, I.A. et al. (2017) Comparative analysis of oncologic outcomes of radical nephrectomy and nephron-sparing surgery in patients with intravenous extension of tumor into the renal vein.</a> New Armenian Medical Journal 11(2): 58-62	- Non-OECD country  - Comparator in study does not match that specified in protocol <i>Comparing RN vs PN in locally advanced tumours</i>
<a href="#">Shemshaki, Hamidreza, Al-Mamari, Said Abdallah, Al-Hooti, Qais et al. (2022) Comparison of cytoreductive partial versus radical nephrectomy in metastatic renal cell carcinoma: To be on the horns of a dilemma.</a> Urologia 89(2): 160-166	- Exclude - Intervention is out of scope

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Study	Reason
<a href="#">Shen, Zhonghua, Xie, Linguo, Xie, Wanqin et al. (2016) The comparison of perioperative outcomes of robot-assisted and open partial nephrectomy: a systematic review and meta-analysis.</a> World journal of surgical oncology 14(1): 220	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Shi, Xu, Feng, Dechao, Li, Dengxiong et al. (2021) The Role of Lymph Node Dissection for Non-Metastatic Renal Cell Carcinoma: An Updated Systematic Review and Meta-Analysis.</a> Frontiers in oncology 11: 790381	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Shinohara, N, Harabayashi, T, Sato, S et al. (2001) Impact of nephron-sparing surgery on quality of life in patients with localized renal cell carcinoma.</a> European urology 39(1): 114-9	- Data not reported in an extractable format
<a href="#">Shirotake, Suguru, Miyama, Y U, Baba, Yasutaka et al. (2022) Impact of Cytoreductive Nephrectomy Following Nivolumab Plus Ipilimumab Therapy for Patients With Advanced Renal Cell Carcinoma.</a> Anticancer research 42(5): 2727-2735	- Study does not contain a relevant outcome - Not a relevant study design
<a href="#">Shvero, Asaf, Nativ, Ofer, Abu-Ghanem, Yasmin et al. (2018) Oncologic Outcomes of Partial Nephrectomy for Stage T3a Renal Cell Cancer.</a> Clinical genitourinary cancer 16(3): e613-e617	- Comparator in study does not match that specified in protocol <i>Compared PN vs RN in locally advanced tumours</i>
<a href="#">Sidoti Abate, Marie Angela, Menold, Hanna Saskia, Neuberger, Manuel et al. (2024) Quality-of-life outcomes of the ROBOtic-assisted versus Conventional Open Partial nephrectomy (ROBOCOP) II trial.</a> BJU international 134(3): 434-441	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Simhan, J., Smaldone, M.C., Tsai, K.J. et al. (2012) Perioperative outcomes of robotic and open partial nephrectomy for moderately and highly complex renal lesions.</a> Journal of Urology 187(6): 2000-2004	- There is no information on cT or pT stage
<a href="#">Simone, Giuseppe, Tuderti, Gabriele, Anceschi, Umberto et al. (2017) Oncological outcomes of minimally invasive partial versus minimally invasive radical nephrectomy for cT1-2/N0/M0 clear cell renal cell carcinoma: a propensity score-matched analysis.</a> World journal of urology 35(5): 789-794	- Data not reported in an extractable format
<a href="#">Siva, Shankar, Ali, Muhammad, Correa, Rohann J M et al. (2022) 5-year outcomes after</a>	- Review article but not a systematic review

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Study	Reason
<a href="#">stereotactic ablative body radiotherapy for primary renal cell carcinoma: an individual patient data meta-analysis from IROCK (the International Radiosurgery Consortium of the Kidney)</a> . The Lancet. Oncology 23(12): 1508-1516	
<a href="#">Siva, Shankar, Louie, Alexander V, Kotecha, Rupesh et al. (2024) Stereotactic body radiotherapy for primary renal cell carcinoma: a systematic review and practice guideline from the International Society of Stereotactic Radiosurgery (ISRS)</a> . The Lancet. Oncology 25(1): e18-e28	- Not a relevant study design <i>Single arm studies only</i>
<a href="#">Siva, Shankar, Pham, Daniel, Gill, Suki et al. (2012) A systematic review of stereotactic radiotherapy ablation for primary renal cell carcinoma</a> . BJU international 110(11ptb): e737-43	- More recent systematic review included that covers the same topic
<a href="#">Soisrithong, C., Sirisreetreerux, P., Sangkum, P. et al. (2021) Comparative outcomes and predictive assessment of trifecta in open, laparoscopic, and robotic-assisted partial nephrectomy cases with renal cell carcinoma: A 10-year experience at ramathibodi hospital</a> . Research and Reports in Urology 13: 425-435	- Non-OECD country  - There is no information on cT or pT stage
<a href="#">Song, Y., Du, C.-X., Zhang, W. et al. (2016) Impact of cytoreductive nephrectomy on survival in patients with metastatic renal cell carcinoma treated by targeted therapy</a> . Chinese Medical Journal 129(5): 530-535	- Data not reported in an extractable format <i>OS data reported as median and range</i>
<a href="#">Soomro, Naeem, Lecouturier, Jan, Stocken, Deborah D et al. (2017) Surveillance versus ablation for incidentally diagnosed small renal tumours: the SURAB feasibility RCT</a> . Health technology assessment (Winchester, England) 21(81): 1-68	- Study does not contain a relevant outcome
<a href="#">Spaas, M, Sundahl, N, Rottey, S et al. (2021) Immuno-radiotherapy in solid tumors: preliminary results of the randomized phase 2 CHEERS trial</a> . Radiotherapy and oncology 161: S490-S491	- Conference abstract
<a href="#">Spaas, Mathieu, Sundahl, Nora, Kruse, Vibeke et al. (2023) Checkpoint Inhibitors in Combination With Stereotactic Body Radiotherapy in Patients With Advanced Solid</a>	- Review H - SABR exclude

Study	Reason
<a href="#">Tumors: The CHEERS Phase 2 Randomized Clinical Trial.</a> JAMA oncology 9(9): 1205-1213	
<a href="#">Spiess, Philippe E and Fishman, Mayer N (2010) Cyto-reductive nephrectomy vs medical therapy as initial treatment: a rational approach to the sequence question in metastatic renal cell carcinoma.</a> Cancer control : journal of the Moffitt Cancer Center 17(4): 269-78	- Review article but not a systematic review
<a href="#">Sprenkle, Preston C, Power, Nicholas, Ghoneim, Tarek et al. (2012) Comparison of open and minimally invasive partial nephrectomy for renal tumors 4-7 centimeters.</a> European urology 61(3): 593-9	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Stellato, M., Santini, D., Verzoni, E. et al. (2021) Impact of Previous Nephrectomy on Clinical Outcome of Metastatic Renal Carcinoma Treated With Immune-Oncology: A Real-World Study on Behalf of Meet-URO Group (MeetUro-7b).</a> Frontiers in Oncology 11: 682449	- Not a relevant study design - Study does not contain a relevant intervention <i>Mixed CN and radical nephrectomy population</i>
<a href="#">Stenman, M, Sinclair, G, Paavola, P et al. (2018) Overall survival after stereotactic radiotherapy or surgical metastasectomy in oligometastatic renal cell carcinoma patients treated at two Swedish centres 2005-2014.</a> Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology 127(3): 501-506	- Comparator in study does not match that specified in protocol <i>Compares SRT with metastasectomy. Mixed SACT population</i>
<a href="#">Stern, Joshua M, Svatek, Robert, Park, Sangtae et al. (2007) Intermediate comparison of partial nephrectomy and radiofrequency ablation for clinical T1a renal tumours.</a> BJU international 100(2): 287-90	- Primary study covered fully by an included systematic review
<a href="#">Steward, James E, Kern, Sean Q, Cheng, Liang et al. (2021) Clear cell papillary renal cell carcinoma: Characteristics and survival outcomes from a large single institutional series.</a> Urologic oncology 39(6): 370e21-370e25	- Not a relevant study design
<a href="#">Stewart, Grant D, Ang, W, Jensen, Laird, Alexander et al. (2012) The operative safety and oncological outcomes of laparoscopic nephrectomy for T3 renal cell cancer.</a> BJU international 110(6): 884-90	- Not a relevant study design <i>Non-comparative study</i>
<a href="#">Stroup, Sean P, Palazzi, Kerrin, Kopp, Ryan P et al. (2012) RENAL nephrometry score is associated with operative approach for partial</a>	- Exclude - For review C. Proportion of patients stage T3 < 90%

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Study	Reason
<a href="#">nephrectomy and urine leak</a> . Urology 80(1): 151-6	
<a href="#">Su, Jia-Rui, Zhu, Ding-Jun, Liang, Wu et al. (2012) Investigation on the indication of ipsilateral adrenalectomy in radical nephrectomy: a meta-analysis</a> . Chinese medical journal 125(21): 3885-90	- Comparator in study does not match that specified in protocol <i>Adrenalectomy vs no adrenalectomy</i>
<a href="#">Suk-Ouichai, Chalairat, Tanaka, Hajime, Wang, Yanbo et al. (2019) Renal Cancer Surgery in Patients without Preexisting Chronic Kidney Disease-Is There a Survival Benefit for Partial Nephrectomy?</a> . The Journal of urology 201(6): 1088-1096	- Data not reported in an extractable format <i>Stage of kidney cancer was not reported</i>
<a href="#">Sun, M, Abdollah, F, Shariat, S F et al. (2012) Propensity-score matched comparison of complications, blood transfusions, length of stay, and in-hospital mortality between open and laparoscopic partial nephrectomy: a national series</a> . European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 38(1): 80-7	- There is no information on cT or pT stage
<a href="#">Sun, Maxine, Becker, Andreas, Tian, Zhe et al. (2014) Management of localized kidney cancer: calculating cancer-specific mortality and competing risks of death for surgery and nonsurgical management</a> . European urology 65(1): 235-41	- Study does not contain a relevant intervention <i>Non-surgical management is unclear</i>
<a href="#">Sun, Zi-Jun, Liu, Feng, Wei, Hai-Bin et al. (2023) Laparoscopic partial versus radical nephrectomy for localized renal cell carcinoma over 4 cm</a> . Journal of cancer research and clinical oncology 149(20): 17837-17848	- Non-OECD country
<a href="#">Takagi, T., Kondo, T., Iizuka, J. et al. (2016) Comparison of survival rates in stage 1 renal cell carcinoma between partial nephrectomy and radical nephrectomy patients according to age distribution: A propensity score matching study</a> . BJU International 117(6): e52-e59	- For review A. Study published before 2016 (search date for overall survival)
<a href="#">Takagi, Toshio, Kondo, Tsunenori, Omae, Kenji et al. (2016) Comparison of progression to end-stage renal disease requiring dialysis after partial or radical nephrectomy for renal cell carcinoma in patients with severe chronic kidney disease</a> . International urology and nephrology 48(9): 1421-7	- Study does not contain a relevant outcome

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Study	Reason
<a href="#">Takahara, K., Fukaya, K., Nukaya, T. et al. (2022) Perioperative and long-term functional outcomes of robot-assisted versus open partial nephrectomy: A single-center retrospective study of a Japanese cohort.</a> Annals of Medicine and Surgery 75: 103482	- There is no information on cT or pT stage
<a href="#">Talenfeld, Adam D, Gennarelli, Renee L, Elkin, Elena B et al. (2018) Percutaneous Ablation Versus Partial and Radical Nephrectomy for T1a Renal Cancer: A Population-Based Analysis.</a> Annals of internal medicine 169(2): 69-77	- Secondary publication of an included study that does not provide any additional relevant information <i>SEER database - covered by other included studies</i>
<a href="#">Tam, Andrew W, Kutikov, Alexander, Winoker, Jared S et al. (2022) Propensity-score matched oncological outcomes and patterns of recurrence following open and minimally-invasive partial nephrectomy for renal cell carcinoma.</a> Urologic oncology 40(3): 111e19-111e25	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Tan, H.-J., Wolf Jr., J.S., Ye, Z. et al. (2011) Population-level comparative effectiveness of laparoscopic versus open radical nephrectomy for patients with kidney cancer.</a> Cancer 117(18): 4184-4193	- Exclude - review C. Patients with localised tumour
<a href="#">Tan, Jo-Lynn, Frydenberg, Mark, Grummet, Jeremy et al. (2018) Comparison of perioperative, renal and oncologic outcomes in robotic-assisted versus open partial nephrectomy.</a> ANZ journal of surgery 88(3): e194-e199	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Tang, Amber B, Lamaina, Margherita, Childers, Christopher P et al. (2021) Perioperative and Long-Term Outcomes of Robot-Assisted Partial Nephrectomy: A Systematic Review.</a> The American surgeon 87(1): 21-29	- Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Tang, Kun, Yao, Weimin, Li, Heng et al. (2014) Laparoscopic renal cryoablation versus laparoscopic partial nephrectomy for the treatment of small renal masses: a systematic review and meta-analysis of comparative studies.</a> Journal of laparoendoscopic & advanced surgical techniques. Part A 24(6): 403-10	- More recent systematic review included that covers the same topic
<a href="#">Tarkowska, M., Glowacka-Mrotek, I., Peterson, D. et al. (2023) Quality of life at 3 to 5 years after surgical treatment of renal cell carcinoma -</a>	- Study does not contain a relevant outcome <i>Quality of life was measured with the WHOQOL-BREF questionnaire</i>



Study	Reason
<a href="#">a pilot cross-sectional study</a> . Nowotwory 73(4): 201-212	
<a href="#">Tatsugami, Katsunori, Shinohara, Nobuo, Kondo, Tsunenori et al. (2015) Role of cytoreductive nephrectomy for Japanese patients with primary renal cell carcinoma in the cytokine and targeted therapy era</a> . International journal of urology : official journal of the Japanese Urological Association 22(8): 736-40	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Teishima, J., Hara, T., Tobe, T. et al. (2023) The impact of primary region resection on the therapeutic outcome of combination regimens for metastatic renal cell carcinoma</a> . Oncology Letters 26(5): 470	- Study does not contain a relevant outcome
<a href="#">Teishima, Jun, Goto, Keisuke, Sekino, Yohei et al. (2022) Prognostic model of upfront cytoreductive nephrectomy in patients with metastatic renal cell carcinoma treated with immune checkpoint inhibitors and/or targeted agents</a> . International urology and nephrology 54(6): 1225-1232	- Data not reported in an extractable format
<a href="#">Teishima, Jun, Ohara, Shinya, Shinmei, Shunsuke et al. (2018) Normalization of C-reactive protein levels following cytoreductive nephrectomy in patients with metastatic renal cell carcinoma treated with tyrosine kinase inhibitors is associated with improved overall survival</a> . Urologic oncology 36(7): 339e9-339e15	- Comparator in study does not match that specified in protocol
<a href="#">Thaidumrong, T. and Duangkae, S. (2018) Comparison of the outcomes of laparoscopic and open nephrectomy in Rajavithi hospital</a> . Journal of the Medical Association of Thailand 101(2supplement2): 103-s108	- Non-OECD country - Exclude - For review C. Proportion of patients stage T3 < 90%
<a href="#">Thompson, R Houston, Atwell, Tom, Schmit, Grant et al. (2015) Comparison of partial nephrectomy and percutaneous ablation for cT1 renal masses</a> . European urology 67(2): 252-9	- Primary study covered fully by an included systematic review
<a href="#">Tian, J., Zeng, X., Wan, J. et al. (2022) Partial and Radical Nephrectomy Provides Equivalent Oncologic Outcomes in pT3a Renal Cell Carcinoma: A Population-Based Study</a> . Frontiers in Oncology 11: 819098	- Comparator in study does not match that specified in protocol <i>Compares RN vs PN for upstaged T3 tumours</i>
<a href="#">Tobert, Conrad M; Riedinger, Christopher B; Lane, Brian R (2014) Do we know (or just</a>	- Review article but not a systematic review

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Study	Reason
<a href="#">believe) that partial nephrectomy leads to better survival than radical nephrectomy for renal cancer?</a> . World journal of urology 32(3): 573-9	
<a href="#">Tsai, Sheng-Han, Tseng, Ping-Tao, Sherer, Benjamin A et al. (2019) Open versus robotic partial nephrectomy: Systematic review and meta-analysis of contemporary studies.</a> The international journal of medical robotics + computer assisted surgery : MRCAS 15(1): e1963	- Exclude - For Review C. Proportion of patients stage T3 < 90%
<a href="#">Uhlig, A., Hahn, O., Strauss, A. et al. (2018) Treatment for Localized T1a Clear Cell Renal Cell Carcinoma: Survival Benefit for Cryosurgery and Thermal Ablation Compared to Deferred Therapy.</a> CardioVascular and Interventional Radiology 41(2): 277-283	- Secondary publication of an included study that does not provide any additional relevant information <i>NCDB database - more recent studies from this database included</i>
<a href="#">Uhlig, Johannes, Kokabi, Nima, Xing, Minzhi et al. (2018) Ablation versus Resection for Stage 1A Renal Cell Carcinoma: National Variation in Clinical Management and Selected Outcomes.</a> Radiology 288(3): 889-897	- Secondary publication of an included study that does not provide any additional relevant information
<a href="#">Uhlig, Johannes, Strauss, Arne, Rucker, Gerta et al. (2019) Partial nephrectomy versus ablative techniques for small renal masses: a systematic review and network meta-analysis.</a> European radiology 29(3): 1293-1307	- More recent systematic review included that covers the same topic
<a href="#">Upreti, Dipesh, Bista, Amir, Smith, Angela L et al. (2018) Cyto-reductive Nephrectomy in Elderly Patients with Metastatic Renal Cell Carcinoma in the Targeted Therapy Era.</a> Anticancer research 38(5): 3013-3018	- Study does not contain a relevant intervention <i>No information about SACT</i>  - Not a relevant study design <i>Case-control</i>
<a href="#">Van Poppel, Hein, Becker, Frank, Cadeddu, Jeffrey A et al. (2011) Treatment of localised renal cell carcinoma.</a> European urology 60(4): 662-72	- Review article but not a systematic review
<a href="#">Vartolomei, Liliana, Cotrus, Andrei, Stanciu, Camelia et al. (2022) Quality of Life and Psychological Distress among Patients with Small Renal Masses.</a> Journal of clinical medicine 11(14)	- Systematic review used as source of primary studies
<a href="#">Veccia, Alessandro, Dell'oglio, Paolo, Antonelli, Alessandro et al. (2020) Robotic partial nephrectomy versus radical nephrectomy in elderly patients with large renal masses.</a>	- Data not reported in an extractable format <i>Data was not reported by stage of kidney cancer</i>



Study	Reason
Minerva urologica e nefrologica = The Italian journal of urology and nephrology 72(1): 99-108	
<a href="#">Veltri, Andrea, Gazzera, Carlo, Busso, Marco et al. (2014) T1a as the sole selection criterion for RFA of renal masses: randomized controlled trials versus surgery should not be postponed. Cardiovascular and interventional radiology 37(5): 1292-8</a>	- Not a relevant study design <i>Noncomparative study</i>
<a href="#">Venkatramani, Vivek, Koru-Sengul, Tulay, Miao, Feng et al. (2018) A comparison of overall survival and perioperative outcomes between partial and radical nephrectomy for cT1b and cT2 renal cell carcinoma-Analysis of a national cancer registry. Urologic oncology 36(3): 90e9-90e14</a>	- Superseded by Ristau
<a href="#">Verbiest, A., De Meerleer, G., Albersen, M. et al. (2018) Non-surgical ablative treatment of distant extracranial metastases for renal cell carcinoma: A systematic review. Kidney Cancer 2(1): 57-67</a>	- Systematic review used as source of primary studies
<a href="#">Verbiest, A., Roussel, E., Tosco, L. et al. (2020) Long-Term Outcomes in Clear-Cell Renal Cell Carcinoma Patients Treated with Complete Metastasectomy. Kidney Cancer 4(4): 177-183</a>	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Verzoni, Elena, Ratta, Raffaele, Grassi, Paolo et al. (2018) TARIBO trial: targeted therapy with or without nephrectomy in metastatic renal cell carcinoma: liquid biopsy for biomarkers discovery. Tumori 104(5): 401-405</a>	- Not a relevant study design <i>Protocol for TARIBO trial. On going trial.</i>
<a href="#">Veys, Ralf, Abdollah, Firas, Briganti, Alberto et al. (2018) Oncological and functional efficacy of nephron-sparing surgery versus radical nephrectomy in renal cell carcinoma stages &gt;=cT1b: a single institution, matched analysis. Central European journal of urology 71(1): 48-57</a>	- Exclude - wrong population
<a href="#">Vilaseca, Antoni, Guglielmetti, Giuliano, Vertosick, Emily A et al. (2020) Value of Partial Nephrectomy for Renal Cortical Tumors of cT2 or Greater Stage: A Risk-benefit Analysis of Renal Function Preservation Versus Increased Postoperative Morbidity. European urology oncology 3(3): 365-371</a>	- Comparator in study does not match that specified in protocol <i>Compares RN vs PN in locally advanced RCC</i>
<a href="#">Vitruk, Iurii, Voylenko, Oleg, Stakhovsky, Oleksandr et al. (2023) Advantages of organ-sparing treatment approaches in metastatic</a>	- Comparator in study does not match that specified in protocol

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Study	Reason
<a href="#">kidney cancer</a> . Journal of cancer research and clinical oncology 149(7): 3131-3137	<i>Compares complete CN and partial CN. Inclusion criteria indicates all participants received SACT</i>
<a href="#">Wang, Agnes J and Bhayani, Sam B (2009) Robotic partial nephrectomy versus laparoscopic partial nephrectomy for renal cell carcinoma: single-surgeon analysis of &gt;100 consecutive procedures</a> . Urology 73(2): 306-10	- There is no information on cT or pT stage
<a href="#">Wang, Dong, Xiao, Zejun, Shou, Jianzhong et al. (2019) Comparison of Laparoscopy and Open Radical Nephrectomy of Renal Cell Cancer</a> . Open medicine (Warsaw, Poland) 14: 392-397	- Exclude - For Review C. Proportion of patients stage T3 < 90%
<a href="#">Wang, Li, Li, Kun-Peng, Yin, Shan et al. (2023) Oncologic and perioperative outcomes of laparoscopic versus open radical nephrectomy for the treatment of renal tumor (&gt; 7 cm): a systematic review and pooled analysis of comparative outcomes</a> . World journal of surgical oncology 21(1): 35	- Exclude - For Review C. Proportion of patients stage T3 < 90%
<a href="#">Wang, Luke L, Yuen, Kit L, Saitta, Cesare et al. (2024) Comparison of outcomes of radical and partial nephrectomy for sarcomatoid renal cell carcinoma: analysis of the national cancer database</a> . World journal of urology 42(1): 508	- Patients with sarcomatoid RCC and pT3 > 10% (61%)
<a href="#">Wang, Shanggian, Qin, Chao, Peng, Zhihang et al. (2014) Radiofrequency ablation versus partial nephrectomy for the treatment of clinical stage 1 renal masses: a systematic review and meta-analysis</a> . Chinese medical journal 127(13): 2497-503	- More recent systematic review included that covers the same topic
<a href="#">Wang, Yubin, Ma, Xin, Huang, Qingbo et al. (2016) Comparison of robot-assisted and laparoscopic partial nephrectomy for complex renal tumours with a RENAL nephrometry score &gt;=7: peri-operative and oncological outcomes</a> . BJU international 117(1): 126-30	- Non-OECD country - Exclude - For Review C. Proportion of patients stage T3 < 90%
<a href="#">Wang, Yubin, Shao, Jinkai, Ma, Xin et al. (2017) Robotic and open partial nephrectomy for complex renal tumors: a matched-pair comparison with a long-term follow-up</a> . World journal of urology 35(1): 73-80	- Non-OECD country - Exclude - For Review C. Proportion of patients stage T3 < 90%
<a href="#">Wang, Zheng, Wang, Ganggang, Xia, Qinghua et al. (2016) Partial nephrectomy vs. radical nephrectomy for renal tumors: A meta-analysis</a>	- More recent systematic review included that covers the same topic

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Study	Reason
<a href="#">of renal function and cardiovascular outcomes.</a> Urologic oncology 34(12): 533e11-533e19	
<a href="#">Webb, C.M., Kamel, M., Eltahawy, E. et al. (2015) A comparative study of open, laparoscopic and robotic partial nephrectomy in obese patients.</a> Urology Annals 7(2): 231-234	- There is no information on cT or pT stage
<a href="#">Wei, Xiyi, Ren, Xiaohan, Ding, Yichao et al. (2019) Comparative outcomes of radio frequency ablation versus partial nephrectomy for T1 renal tumors: a systematic review.</a> Translational andrology and urology 8(6): 601-608	- More recent systematic review included that covers the same topic
<a href="#">Weight, Christopher J, Lythgoe, Casey, Unnikrishnan, Raman et al. (2011) Partial nephrectomy does not compromise survival in patients with pathologic upstaging to pT2/pT3 or high-grade renal tumors compared with radical nephrectomy.</a> Urology 77(5): 1142-6	- Comparator in study does not match that specified in protocol <i>RN vs PN in upstaged T2/T3 tumours. Not applicable for Review C.</i>
<a href="#">Wen, Zhi, Wang, Li, Huang, Jing et al. (2023) Perioperative, functional, and oncologic outcomes after ablation or partial nephrectomy for solitary renal tumors: a systematic review and meta-analysis of comparative trials.</a> Frontiers in oncology 13: 1202587	- Systematic review used as source of primary studies <i>Solitary kidney only</i>
<a href="#">Whitson, Jared M; Harris, Catherine R; Meng, Maxwell V (2012) Population-based comparative effectiveness of nephron-sparing surgery vs ablation for small renal masses.</a> BJU international 110(10): 1438-1443	- Secondary publication of an included study that does not provide any additional relevant information <i>SEER database - more fully covered in another included study</i>
<a href="#">Wong, Ruby; Patel, Bijendra; Biyani, Chandra Shekhar (2023) Perioperative outcomes between laparoscopic versus open versus robotic partial nephrectomy: Current Review.</a> Urologia: 3915603231211975	- Exclude - For Review C. Proportion of patients stage T3 < 90%
<a href="#">Wu, Jing, Chang, Joshua, Bai, Harrison X et al. (2019) A Comparison of Cryoablation with Heat-Based Thermal Ablation for Treatment of Clinical T1a Renal Cell Carcinoma: A National Cancer Database Study.</a> Journal of vascular and interventional radiology : JVIR 30(7): 1027-1033e3	- Comparator in study does not match that specified in protocol <i>Compares cryoablation with thermal ablation</i>
<a href="#">Wu, Xiaorong, Chen, Wei, Huang, Jiwei et al. (2020) Zero ischemia laparoscopic microwave ablation assisted enucleation vs. laparoscopic partial nephrectomy in clinical T1a renal tumor:</a>	- Study does not contain a relevant intervention <i>Microwave ablation group also had tumour enucleation</i>

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Study	Reason
<a href="#">a randomized clinical trial.</a> Translational cancer research 9(1): 194-202	
<a href="#">Wu, Z., Li, M., Liu, B. et al. (2014) Robotic versus open partial nephrectomy: A systematic review and meta-analysis.</a> PLoS ONE 9(4): e94878	- There is no information on cT or pT stage
<a href="#">Wu, Zhenjie, Li, Mingmin, Qu, Le et al. (2014) A propensity-score matched comparison of perioperative and early renal functional outcomes of robotic versus open partial nephrectomy.</a> PloS one 9(4): e94195	- Non-OECD country - There is no information on cT or pT stage
<a href="#">Wu, Zhenjie, Li, Mingmin, Song, Shangqing et al. (2015) Propensity-score matched analysis comparing robot-assisted with laparoscopic partial nephrectomy.</a> BJU international 115(3): 437-45	- Non-OECD country - There is no information on cT or pT stage
<a href="#">Xia, Leilei, Wang, Xianjin, Xu, Tianyuan et al. (2017) Systematic Review and Meta-Analysis of Comparative Studies Reporting Perioperative Outcomes of Robot-Assisted Partial Nephrectomy Versus Open Partial Nephrectomy.</a> Journal of endourology 31(9): 893-909	- Exclude - For Review C. Proportion of patients stage T3 < 90%
<a href="#">Xiao, W.-J., Zhu, Y., Dai, B. et al. (2015) Assessment of survival of patients with metastatic clear cell renal cell carcinoma after radical cytoreductive nephrectomy versus no surgery: a seer analysis.</a> International braz j urol : official journal of the Brazilian Society of Urology 41(2): 288-295	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Xiaobing, Wu, Wentao, Gong, Guangxiang, Liu et al. (2017) Comparison of radiofrequency ablation and partial nephrectomy for tumor in a solitary kidney.</a> BMC urology 17(1): 79	- Non-OECD country
<a href="#">Xu, Haozhe, Xing, Zhuo, Ai, Kai et al. (2024) Patients with high nuclear grade pT1-ccRCC are more suitable for radical nephrectomy than partial nephrectomy: a multicenter retrospective study using propensity score.</a> World journal of surgical oncology 22(1): 24	- Non-OECD country
<a href="#">Xu, L. and Fan, W. (2020) Efficacy of sorafenib combined with radiofrequency ablation in renal cancer and its effects on immunity and inflammation in patients.</a> Journal of B.U.ON. 25(1): 514-519	- Mixed population of SACT pre/post non-pharmacological regimens <i>No information about SACT in the arm treated with radiofrequency ablation</i>

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# DRAFT FOR CONSULTATION

Study	Reason
	- Study does not contain a relevant outcome
<a href="#">Yan, Shuai, Yang, Wei, Zhu, Cheng-Mei et al. (2019) Comparison among cryoablation, radiofrequency ablation, and partial nephrectomy for renal cell carcinomas sized smaller than 2 cm or sized 2-4 cm: A population-based study. Medicine 98(21): e15610</a>	- Non-OECD country
<a href="#">Yang, Chao and Liao, Zhaolin (2018) Comparison of Radical Nephrectomy and Partial Nephrectomy for T1 Renal Cell Carcinoma: A Meta-Analysis. Urologia internationalis 101(2): 175-183</a>	- Systematic review used as source of primary studies
<a href="#">Yang, Chia-Min, Chung, Hsiao-Jen, Huang, Yi-Hsiu et al. (2014) Standardized analysis of laparoscopic and robotic-assisted partial nephrectomy complications with Clavien classification. Journal of the Chinese Medical Association : JCMA 77(12): 637-41</a>	- Non-OECD country - There is no information on cT or pT stage
<a href="#">Yang, Chuance, Wang, Zhenlong, Huang, Shanlong et al. (2018) Retroperitoneal Laparoscopic Partial Nephrectomy Versus Radical Nephrectomy for Clinical T1 Renal Hilar Tumor: Comparison of Perioperative Characteristics and Short-Term Functional and Oncologic Outcomes. Journal of laparoendoscopic &amp; advanced surgical techniques. Part A 28(10): 1183-1187</a>	- Non-OECD country
<a href="#">Yang, F.; Zhou, Q.; Xing, N. (2020) Comparison of survival and renal function between partial and radical laparoscopic nephrectomy for T1b renal cell carcinoma. Journal of Cancer Research and Clinical Oncology 146(1): 261-272</a>	- Non-OECD country
<a href="#">Yang, Quancheng, Meng, Fanzheng, Li, Kai et al. (2015) Safety and Efficacy of Thermal Ablation for Small Renal Masses in Solitary Kidney: Evidence from Meta-Analysis of Comparative Studies. PloS one 10(6): e0131290</a>	- More recent systematic review included that covers the same topic
<a href="#">Yang, Yong (2020) Partial Versus Radical Nephrectomy in Patients with Renal Cell Carcinoma: A Systematic Review and Meta-analysis. Urology journal 17(2): 109-117</a>	- More recent systematic review included that covers the same topic
<a href="#">Yang, Yue, Chen, Shouzhen, Chen, Fan et al. (2015) Outcome of radiofrequency ablation over</a>	- More recent systematic review included that covers the same topic

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Study	Reason
<a href="#">partial nephrectomy for small renal mass (&lt;4 cm): a systematic review and meta-analysis.</a> International journal of clinical and experimental medicine 8(11): 20670-4	
<a href="#">Yin, Xiaotao, Cui, Liang, Li, Fanglong et al. (2015) Radiofrequency Ablation Versus Partial Nephrectomy in Treating Small Renal Tumors: A Systematic Review and Meta-Analysis.</a> Medicine 94(50): e2255	- More recent systematic review included that covers the same topic
<a href="#">Yoo, Sangjun, You, Dalsan, Jeong, In Gab et al. (2017) Preserving Renal Function through Partial Nephrectomy Depends on Tumor Complexity in T1b Renal Tumors.</a> Journal of Korean medical science 32(3): 495-501	- Primary study covered fully by an included systematic review
<a href="#">Yoon, Young Eun, Lee, Hyung Ho, Kim, Ki Hong et al. (2018) Focal therapy versus robot-assisted partial nephrectomy in the management of clinical T1 renal masses: A systematic review and meta-analysis.</a> Medicine 97(45): e13102	- Study does not contain a relevant intervention
<a href="#">Yoshida, Kazuhiko, Oida, Nao, Kondo, Tsunenori et al. (2024) Surgical and functional outcomes of repeat robot-assisted laparoscopic partial nephrectomy compared with repeat open partial nephrectomy.</a> International journal of urology : official journal of the Japanese Urological Association 31(4): 355-361	- Exclude Review C. - Study included only patients T1-T2
<a href="#">You, Dalsan, Jeong, In Gab, Song, Cheryn et al. (2015) Analysis of pre-operative variables for identifying patients who might benefit from upfront cytoreductive nephrectomy for metastatic renal cell carcinoma in the targeted therapy era.</a> Japanese journal of clinical oncology 45(1): 96-102	- Data not reported in an extractable format
<a href="#">Youn, C.S., Park, J.M., Lee, J.Y. et al. (2013) Comparison of laparoscopic radiofrequency ablation and open partial nephrectomy in patients with a small renal mass.</a> Korean Journal of Urology 54(9): 603-608	- Primary study covered fully by an included systematic review
<a href="#">Yu, Jie, Liang, Ping, Yu, Xiao-ling et al. (2014) US-guided percutaneous microwave ablation versus open radical nephrectomy for small renal cell carcinoma: intermediate-term results.</a> Radiology 270(3): 880-7	- Non-OECD country
<a href="#">Yu, Kun, Liu, Meiping, Xie, Zhenguo et al. (2020) Comparison of efficacy and long-term</a>	- Non-OECD country

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Study	Reason
<a href="#">survival of laparoscopic radical nephrectomy with partial nephrectomy in the treatment of patients with early renal cell carcinoma Running title: laparoscopic radical nephrectomy.</a> Journal of B.U.ON. : official journal of the Balkan Union of Oncology 25(2): 1155-1160	
<a href="#">Zaid, Harras B, Parker, William P, Safdar, Nida S et al. (2017) Outcomes Following Complete Surgical Metastasectomy for Patients with Metastatic Renal Cell Carcinoma: A Systematic Review and Meta-Analysis.</a> The Journal of urology 197(1): 44-49	- Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Zaorsky, Nicholas G, Lehrer, Eric J, Kothari, Gargi et al. (2019) Stereotactic ablative radiation therapy for oligometastatic renal cell carcinoma (SABR ORCA): a meta-analysis of 28 studies.</a> European urology oncology 2(5): 515-523	- Exclude - wrong population - Study did not compare the interventions of interest
<a href="#">Zargar, Homayoun, Bhayani, Sam, Allaf, Mohamad E et al. (2014) Comparison of perioperative outcomes of robot-assisted partial nephrectomy and open partial nephrectomy in patients with a solitary kidney.</a> Journal of endourology 28(10): 1224-30	- Exclude - For Review C. Proportion of patients stage T3 < 90%
<a href="#">Zeng, Zhiqiang, Ge, Si, Li, Yunxiang et al. (2024) Perioperative and Oncological Outcomes of Partial Versus Radical Nephrectomy for Complex Renal Tumors (RENAL Score &gt;= 7): Systematic Review and Meta-Analysis.</a> Annals of surgical oncology 31(7): 4762-4772	- Systematic review used as source of primary studies
<a href="#">Zhang, Fan, Hu, Jiang-Sheng, Zhang, Kai-Yu et al. (2023) Perioperative, functional, and oncologic outcomes of laparoscopic partial nephrectomy versus open partial nephrectomy for complex renal tumors: a systematic review and meta-analysis.</a> Frontiers in oncology 13: 1283935	- Exclude - For Review C. Proportion of patients stage T3 < 90%
<a href="#">Zhang, M., Zhao, Z., Duan, X. et al. (2018) Partial versus radical nephrectomy for T1b-2N0M0 renal tumors: A propensity score matching study based on the SEER database.</a> PLoS ONE 13(2): e0193530	- SEER database overlap
<a href="#">Zhang, Y., Hu, J., Xie, Y. et al. (2022) Selection of Optimal Candidates for Cytoreductive Nephrectomy in Patients with Metastatic Clear Cell Renal Cell Carcinoma: A Predictive Model</a>	- Mixed population of SACT pre/post non-pharmacological regimens

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Study	Reason
<a href="#">Based on SEER Database.</a> Frontiers in Oncology 12: 814512	
<a href="#">Zhang, Yu, Bi, Hai, Yan, Ye et al. (2023) Comparative analysis of surgical and oncologic outcomes of robotic, laparoscopic and open radical nephrectomy with venous thrombectomy: a propensity-matched cohort study.</a> International journal of clinical oncology 28(1): 145-154	- Non-OECD country
<a href="#">Zhang, Yuanyuan, Schoenhals, Jonathan, Christie, Alana et al. (2019) Stereotactic Ablative Radiation Therapy (SAbR) Used to Defer Systemic Therapy in Oligometastatic Renal Cell Cancer.</a> International journal of radiation oncology, biology, physics 105(2): 367-375	- Not a relevant study design - Mixed population of SACT pre/post non-pharmacological regimens
<a href="#">Zhang, Yucong, Long, Gongwei, Shang, Haojie et al. (2021) Comparison of the oncological, perioperative and functional outcomes of partial nephrectomy versus radical nephrectomy for clinical T1b renal cell carcinoma: A systematic review and meta-analysis of retrospective studies.</a> Asian journal of urology 8(1): 117-125	- Systematic review used as source of primary studies
<a href="#">Zhang, Zhao, Wu, Hongliang, Yang, Tong et al. (2020) Metastatic renal cell carcinoma patients of T4 stage who are in status of N1 stage or older than 76 years cannot benefit from cytoreductive nephrectomy.</a> BMC cancer 20(1): 844	- Mixed population of SACT pre/post non-pharmacological regimens <i>No information regarding SACT in both arms</i>
<a href="#">Zhao, Kaidong, Kim, Eric H, Vetter, Joel M et al. (2020) Laparoscopic cytoreductive nephrectomy is associated with significantly improved survival compared with open cytoreductive nephrectomy or targeted therapy alone.</a> Molecular and clinical oncology 13(6): 71	- Exclude - Outcome was measured using a measure out of scope <i>OS reported in median months</i>
<a href="#">Zhao, Z., Wu, W., Duan, X. et al. (2019) The value of cytoreductive nephrectomy on the survival of metastatic renal carcinoma patients based on the number of site-specific metastases.</a> PLoS ONE 14(4): e0215861	- Mixed population of SACT pre/post non-pharmacological regimens <i>No information about the treatment received by non CN arm reported. The sequence of SACT reported is also not reported.</i>
<a href="#">Zhou, Minerva, Mills, Abigail, Noda, Christopher et al. (2018) SEER study of ablation versus partial nephrectomy in cT1A renal cell carcinoma.</a> Future oncology (London, England) 14(17): 17111-1719	- Secondary publication of an included study that does not provide any additional relevant information <i>SEER database - more fully covered in another included study</i>



Study	Reason
<a href="#">Zhuang, W, Chen, J, Li, Y et al. (2019) The effect of cytoreductive partial nephrectomy in elderly patients with metastatic renal cell carcinoma : a systematic review.</a> ResearchSquare	- Exclude - Outcome was measured using a measure out of scope
<a href="#">Zini, Laurent, Perrotte, Paul, Jeldres, Claudio et al. (2008) Nephrectomy improves the survival of patients with locally advanced renal cell carcinoma.</a> BJU international 102(11): 1610-4	- Comparator in study does not match that specified in protocol <i>Nephrectomy vs no surgery</i>

1

2

**Economic studies**

3

4

HE excluded at full text (n=2)

Study	Reason for exclusion
Health Improvement Scotland (2011) Evidence Note: Is radiofrequency ablation treatment a clinically and cost effective treatment to be offered to people with renal cancer in NHS Scotland? <a href="#">Is radiofrequency ablation treatment a clinically and cost effective treatment to be offered to people with renal cancer in NHSScotland? (york.ac.uk)</a>	-Based on a US health economics study with a quasi-societal perspective and US costs.
<a href="#">Iossa, Vincenzo, Pandolfo, Savio Domenico, Buonopane, Roberto et al. (2025) Robot-assisted partial nephrectomy vs. percutaneous cryoablation for T1a renal tumors: a single-center retrospective analysis of outcomes and costs.</a> International urology and nephrology 57(4): 1097-1104	- Exclude - cost analysis only, did not have a QoL outcome

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# 1 **Appendix K– Research recommendations – full details**

## 2 **K1.1 Research recommendation 1**

3 What is the clinical and cost effectiveness of metastasectomy before systemic anticancer  
4 therapy (SACT) or after SACT has been started compared to SACT alone for people with  
5 metastatic renal cell carcinoma who have had their primary mass removed?

### 6 **K1.1.1 Why this is important**

7 Metastasectomy is an option to treat metastases from RCC, particularly after the person has  
8 had a good response to systemic anti-cancer therapy (SACT). However, there is a lack of  
9 data about its effectiveness.

### 10 **K1.1.2 Rationale for research recommendation 1**

11 **Table 15: Rationale for research recommendation 1**

Importance to 'patients' or the population	Metastasectomy could be used to remove metastases after a good response to SACT, which could mean the person has no visible evidence of disease on imaging. This would be a meaningful milestone for many people
Relevance to NICE guidance	Metastasectomy has been considered in this guideline and there is a lack of data on effectiveness before or after SACT
Relevance to the NHS	The outcome would affect the types of non-pharmacological interventions for metastatic RCC provided by the NHS
National priorities	Low
Current evidence base	No evidence was identified about metastasectomy specifically before or after SACT
Equality considerations	None known

### 12 **K1.1.3 Modified PICO table**

13 **Table 16: Modified PICO table**

Population	Adults (18 years or over) with metastatic RCC who have had their primary lesion treated and who have only metastatic disease remaining
Intervention	<ul style="list-style-type: none"> <li>• Metastasectomy before SACT or</li> <li>• Metastasectomy after SACT has been started</li> </ul>
Comparator	Interventions compared with each other or with SACT alone
Outcome	Progression-free survival Overall survival Cancer-specific survival Adverse events Quality of life Duration of hospital stay Cost effectiveness

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Study design	Randomised controlled trials Comparative cohort studies
Timeframe	All
Additional information	Studies must present results separately for before and after SACT

## 1 **K1.2 Research recommendation 2**

2 What is the clinical and cost effectiveness of thermal ablation or external beam radiotherapy  
3 (excluding stereotactic ablative radiotherapy) after systemic anticancer therapy (SACT) has  
4 been started compared to SACT alone for treating metastases in people with metastatic  
5 renal cell carcinoma?

### 6 **K1.1.1 Why this is important**

7 Thermal ablation and external beam radiation therapy (EBRT) are both options to treat  
8 metastases from RCC under certain circumstances. However, there is a lack of data about  
9 their effectiveness. (SABR is not included because there are ongoing clinical trials looking at  
10 this.)

### 11 **K1.1.2 Rationale for research recommendation 2**

#### 12 **Table 17: Rationale for research recommendation 2**

Importance to 'patients' or the population	For people who are healthy enough to receive additional intervention once they have started SACT for metastases from RCC, thermal ablation or EBRT of metastases could further control and reduce disease.
Relevance to NICE guidance	These interventions have been considered in this guideline and there is a lack of data on effectiveness after SACT has been started.
Relevance to the NHS	The outcome would affect the types of non-pharmacological interventions for metastatic RCC provided by the NHS.
National priorities	Low
Current evidence base	No evidence was identified about these interventions after SACT has been started.
Equality considerations	None known

### 13 **K1.1.3 Modified PICO table**

#### 14 **Table 18: Modified PICO table**

Population	Adults (18 years or over) with metastatic RCC
Intervention	<ul style="list-style-type: none"> <li>• EBRT after SACT has been started or</li> <li>• Thermal ablation after SACT has been started</li> </ul>
Comparator	SACT alone
Outcome	Progression-free survival Overall survival

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	Cancer-specific survival Adverse events Quality of life Duration of hospital stay Cost effectiveness
Study design	Randomised controlled trials Comparative cohort studies
Timeframe	All
Additional information	None

### 1 **K1.3 Research recommendation 3**

2 What is the clinical and cost effectiveness of stereotactic ablative radiotherapy for treating  
3 the primary mass after systemic anticancer therapy has been started in people with locally  
4 advanced inoperable renal cell carcinoma?

#### 5 **K1.3.1 Why this is important?**

6  
7 Stereotactic ablative radiotherapy (SABR) has a potential role in locally advanced inoperable  
8 disease after SACT if there has been sufficient downstaging of the primary tumour to  
9 facilitate radiotherapy.

### 10 **K1.3.2 Rationale for research recommendation 3**

#### 11 **Table 19: Rationale for research recommendation**

Importance to 'patients' or the population	For people who are healthy enough to receive additional intervention once they have started SACT for locally advanced inoperable disease, SABR could further control and reduce disease after there has been downstaging of the tumour.
Relevance to NICE guidance	SABR have been considered in this guideline and there is a lack of data on effectiveness after SACT has been started.
Relevance to the NHS	The outcome would affect the types of non-pharmacological interventions for locally advanced inoperable RCC provided by the NHS.
National priorities	Low
Current evidence base	No evidence was identified for the use of SABR in locally advanced inoperable disease after SACT.
Equality considerations	None known

### 12 **K1.3.3 Modified PICO table**

#### 13 **Table 20: Modified PICO table**

Population	Adults (18 years or over) with locally advanced inoperable RCC
Intervention	SABR after SACT has been started
Comparator	SACT alone

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Outcome	Progression-free survival Overall survival Cancer-specific survival Adverse events Quality of life Duration of hospital stay Cost effectiveness
Study design	Randomised controlled trials Comparative cohort studies
Timeframe	All
Additional information	None

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