National Institute for Health and Care Excellence

Kidney cancer: diagnosis and management

[K] Evidence review for risk prediction tools for localised and locally advanced renal cell carcinoma

NICE guideline NG256

Evidence underpinning recommendations 1.9.1 to 1.9.9 and research recommendations in the NICE guideline

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FINAL

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1.1 Review question

In adults with suspected or confirmed non-metastatic renal cell carcinoma, which validated risk prediction models are most effective at predicting survival and recurrence?

1.1.1 Introduction

Multiple risk prediction tools have been developed to assess the prognosis of patients with non-metastatic renal cell carcinoma (RCC). These tools vary in the clinical, surgical and pathological factors used to predict prognosis and are important for counselling patients and guiding treatment decisions. Currently there is no national guideline in the UK that informs clinicians of the most appropriate models to use, leading to variation in practice and patient care. This review aims to identify which models best predict survival and disease progression in people with non-metastatic RCC of various subtypes. This evidence around risk tools and categories of risk will be used to inform recommendations around management and follow-up, which are covered by other sections of the guideline under development.

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria

Population	Adults (18 years or over) with suspected or confirmed localised or locally advanced renal cell carcinoma
Predictive tools	Validated risk prediction tools from the lists below. Validated models and scores may be augmented and further validated by additional individual factors. Post-first line treatment risk prediction tools to predict survival or recurrence outcomes: • GRANT • Karakiewicz • Kattan • Leibovich 2003 • Leibovich 2018 • Sorbellini • SSIGN • UISS • VENUSS • Zisman
Outcomes	• Progression free survival • Recurrence free survival • Disease-free survival, including cancer-free survival

	• Overall survival • Cancer specific survival
Study type	• Prospective and retrospective cohort studies, (specifically validation studies of models or derivation studies that also include independent validation data) • Systematic reviews of these studies
Subgroups	RCC subtypes, for example, clear cell RCC, papillary RCC.

For the full protocol see appendix A.

1.1.3 Methods and process

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

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

Methods and technical decisions specific to part one of this review looking at models to predict non-metastatic RCC are summarised below:

1. Post-treatment risk prediction models have been selected with committee input as the most established validated models of relevance to clinical practice.
2. Studies that include people with metastases were excluded, regardless of the proportion compared with non-metastatic population.
3. Of studies reporting outcomes for pathological TNM, we have prioritised data for the TNM 2016 version only as this is the most recent version and used in practice.
4. Studies that report a c-statistics without a 95% confidence interval or without data to calculate the 95% confidence interval have been excluded as it is not possible to meta-analyse these studies.
5. Where studies report both a c-statistic and AUC (area under the curve) for the same survival outcome, the c-statistic has been extracted as the preferred choice as this preserves the time to event element of the outcome.
6. Studies that only report an AUC for the risk prediction tools for survival outcomes have been excluded.
7. As per the protocol we have only extracted model validation results. We have therefore extracted HR data from univariate analyses only as multivariate analyses would have adjusted for more variables than the model of interest.
8. For risk of bias using the PROBAST tool we used the ratings from the included systematic review Usher-Smith et al. (2022) for the relevant included studies. The authors did not complete domain 4.6 so we also did not complete this domain for consistency. In addition, we did not complete domains 4.5, 4.8 and 4.9 which are for derivation studies only.
9. For the imprecision domain in GRADE for HR data, we used the line of no effect and a sample size of <500 as the two thresholds for downgrading.

10. Where data could not be pooled due to I^2>80%, we carried out GRADE as detailed in the methods chapter to produce a summary GRADE rating but reported the median [IQR] values in the summary GRADE tables.

1.1.3.1 Search methods

The searches for the effectiveness evidence were run on 16/07/2024 and re-run on 31/03/2025. The following databases were searched: Cochrane CENTRAL (Wiley), Cochrane CDSR (Wiley), Embase (Ovid), Epistemonikos (Epistemonikos), International Health Technology Assessment Database (INAHTA), Medline ALL (Ovid). Limits were applied to remove animal studies, conference abstracts, editorials, letters, news items and commentaries, as well as papers not published in the English language. Filters were used to limit to systematic review and prognostic studies.

Additional searches were carried out on 16/07/2024 and updated on 01/04/2025. The following databases were searched: Embase (Ovid), Epistemonikos (Epistemonikos), Medline ALL (Ovid) and Web of Science (Clarivate).

The searches for the cost effectiveness evidence were run on 18/07/2024 and re-run on 07/05/2025. The following databases were searched: Econlit (Ovid), Embase (Ovid), NHS EED (CRD York), HTA (CRD York), International Health Technology Assessment Database (INAHTA), Medline ALL (Ovid). Limits were applied to remove animal studies, conference abstracts, editorials, letters, news items and commentaries, as well as papers not published in the English language. Filters were used to limit to cost-effectiveness studies.

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

1.1.4 Prognostic evidence

1.1.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 12,041 references (see appendix B for the literature search strategy). This was a joint search that was done for reviews K and L (non-metastatic and metastatic populations).

These 12,930 references were screened at title and abstract level against the review protocol, with 12,525 excluded at this level. 10% of references were screened separately by two reviewers with 100% agreement.

The full texts of 405 articles were ordered for closer inspection. 68 of these studies (1 systematic review and 67 cohort study) were relevant for the non-metastatic population and met the criteria specified in the review protocol (appendix A). For a summary of the 68 non-metastatic population included studies see Table 4.

For studies where the population was people with clear cell RCC, no evidence was identified for the following models: GRANT, Karakiewicz, VENUSS, and Zisman. In studies where people had papillary RCC, no evidence was identified for the following models: Karakiewicz, Kattan, Sorbellini, SSIGN, and Zisman. For studies where people had chromophobe RCC, no evidence was identified for the following models: Karakiewicz, Kattan, Sorbellini, SSIGN, TNM 2016, UISS, VENUSS, and Zisman. Where studies reported on all RCC subtypes and

data could not be extracted separately by subtype, no evidence was identified for the following models: Leibovich 2018, TNM 2016, and VENUSS.

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

See section 1.1.14 References – included studies for the full references of the non-metastatic population included studies.

1.1.4.2 Excluded studies

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

1.1.5 Summary of studies included in the prognostic evidence

Risk prediction tool characteristics

Table 2 Summary of risk prediction tools for localised or locally advanced renal cell carcinoma
Table adapted from Usher-Smith et al. 2022

Risk model	Development population	Original outcome	Prediction timepoint	Risk factors included	Interpretation
GRANT	RCC	OS, RFS	5 years	1. Fuhrman grade 2. Age 3. Pathological nodal status 4. Pathological tumour size	Number of unfavourable risk factors is summed (0-4) Favourable risk group: score 0-1 Unfavourable risk group: score ≥2
Karakiewicz	RCC	CSS	1,2,5 and 10 years	1. T stage 2. N stage 3. M stage 4. Tumour size 5. Fuhrman grade 6. Symptom classification	Nomogram giving continuous quantification of risk
Kattan	RCC	RFS	5 years	1. Pathological tumour stage 2. Tumour size 3. Histology 4. Symptoms	Nomogram giving continuous quantification of risk
Leibovich 2003	ccRCC	RFS	5 years	1. Pathological T stage 2. Regional lymph node status 3. Tumour size 4. Nuclear grade 5. Histological tumour necrosis	Score range 0-11 Low risk: score 0-2 Intermediate risk: score 3-5

Risk model	Development population	Original outcome	Prediction timepoint	Risk factors included	Interpretation
					High risk: ≥6
Leibovich 2018	RCC (ccRCC, pRCC and chrRCC)	PFS, CSS	5, 10 and 15 years	**ccRCC** 1. Grade 2. Necrosis 3. Sarcomatoid differentiation 4. Tumour size 5. Perinephric or renal sinus fat invasion 6. Tumour thrombus 7. Extension beyond kidney 8. Nodal involvement **pRCC** 1. Fat invasion 2. Thrombus **chRCC** 1. Fat invasion 2. Sarcomatoid differentiation 3. Nodal involvement	Scoring ccRCC PFS: 0 to ≥15 ccRCC CSS: 0 to ≥18 No risk groups pRCC and chRCC PFS and CSS: Risk group 1 Risk group 2 Risk group 3
Sorbellini	ccRCC	RFS	5 years	1. 2002 TNM stage 2. Tumour size (cm) 3. Fuhrman grade 4. Necrosis 5. Vascular invasion	Nomogram giving continuous quantification of risk

Risk model	Development population	Original outcome	Prediction timepoint	Risk factors included	Interpretation
				6. Clinical presentation: a) incidental asymptomatic; b) locally symptomatic; c) systemically symptomatic	
SSIGN	ccRCC	CSS	5 years	1. T stage 2. N stage 3. M stage 4. Tumour size 5. Nuclear grade 6. Histological tumour necrosis	Score range 0-15 Increasing score associated with decreasing CSS
UISS	RCC	OS	5 years	1. 1997 TNM stage 2. Fuhrman grade 3. ECOG PS	Five survival stratification groups (higher group number associated with worse survival) Group I: TNM stage 1, Fuhrman Grade 1-2; PS 0 Group II: Any other TNM stage 1; TNM stage 2; TNM stage 3, any Fuhrman Grade, PS 0; TNM stage 3, Fuhrman Grade 1, PS ≥1 Group III: TNM stage 3, Fuhrman Grade 2-4, PS ≥1; TNM stage 4, Fuhrman Grade 1-2, PS 0 Group IV: TNM stage 3, Fuhrman Grade 3-4, PS 0; TN stage 4, Fuhrman Grade 1-2, PS 0 Group V: TNM stage 4, Fuhrman Grade 4, PS ≥1

Risk model	Development population	Original outcome	Prediction timepoint	Risk factors included	Interpretation
					Nomogram giving continuous quantification of risk
VENUSS	PRCC	Disease recurrence	5 years	1. Venous tumour thrombus 2. Nuclear grade 3. Tumour size 4. T stage 5. N stage	Score range 0-11 points Low risk: 0-2 points Intermediate risk: 3 – 5 points High risk: ≥ 6 points
Zisman	RCC (including ccRCC, pRCC and chRCC)	CCS	5 years	1. 1997 T classification 2. Fuhrman grade 3. ECOG PS	Low risk: pT1N0M0, Fuhrman Grade 1-2, PS 0 Intermediate risk: Any other N0M0 High risk: T3N0M0, Fuhrman Grade >1, PS ≥1; Any pT4N0M0

Abbreviations: ccRCC = clear cell renal cell cancer, chRCC = chromophobe renal cell cancer, CSS = cancer-specific survival, ECOG PS = Eastern Cooperative Oncology Group performance status, GRANT = Grade, Age, Nodes and Tumour, OS = overall survival, PFS = progression free survival, PRCC = papillary renal cell carcinoma, RCC = renal cell carcinoma, RFS = recurrence-free survival, SSIGN = Stage, Size, Grade and Necrosis, UICC = International Union Against Cancer, UISS = UCLA Integrated Staging System

Systematic review characteristics

Table 3 Systematic review (for full details of included primary studies, see Usher-Smith 2022)

Author (year)	Primary studies from Usher-Smith 2022, included in the NICE review	Population covered by systematic review	Risk model(s)	Outcomes predicted	Outcome measure	Risk of bias/Applicability of the systematic review
Usher-Smith (2022)	• An (2015) • Beisland (2015) • Buti (2019) • Capogrosso (2018) • Chen (2017) • Cindolo (2005) • Fu (2015) • Haddad (2017) • Han (2003) • Hupertan (2006) • Hutterer (2014) • Jensen (2009) • Klatte (2009) • Lee (2018) • Liu (2009) • Liu (2016) • Lucca (2015) • Morgan (2018) • Na (2016)	**Inclusion criteria:** • Peer-reviewed studies • reported a quantitative measure of the performance of one or more risk models patients after surgical resection for localised renal cell carcinoma • external validation studies • studies reporting performance of an existing model alongside the performance of that model plus additional prognostic markers. **Exclusion criteria:** Metastatic population	Karakiewicz Kattan Leibovich 2003 Sorbellini TNM UISS Zisman	Recurrence-free/disease-free survival Overall survival Cancer-specific survival	Model discrimination (C-stats)	Low Partially applicable

Author (year)	Primary studies from Usher-Smith 2022, included in the NICE review	Population covered by systematic review	Risk model(s)	Outcomes predicted	Outcome measure	Risk of bias/Applicability of the systematic review
	• Pichler (2011) • Rini (2015) • Seles (2017) • Sorbellini (2005) • Suzuki (2011) • Tan (2010) • Tan (2011) • Tsujino (2017b) • Tsujino (2019) • Utsumi (2011) • Vasudev (2019) • Viers (2014) • Wang (2016b) • Xia (2016) • Xiong (2017) • Zhang (2017) • Zhu (2019)					

See Appendix D – Prognostic evidence for full evidence tables

Primary study characteristics

Table 4 Summary of primary studies included in the prognostic evidence

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
An (2015) N=191 Retrospective cohort Follow-up time: 67 months	China	People who underwent radical nephrectomy, or nephron-sparing surgery. Clear cell renal cell carcinoma	Leibovich 2003	Recurrence-free/disease-free survival Overall survival	Model discrimination (C-stats)	High
Baykal (2025) N=197 Retrospective cohort Follow-up time: 49 months	Turkey	People who underwent radical nephrectomy due to renal tumour People with histopathological renal cell carcinoma	UISS	Overall survival	Hazard ratio	High
Beisland (2015) N=386 Retrospective cohort Follow-up time: 51.6 months	Norway	People who underwent radical or partial nephrectomy. Clear cell renal cell carcinoma	Leibovich 2003	Recurrence-free/disease-free survival	Model discrimination (C-stats) Hazard ratio	High
Buti (2019) N=73217 Follow-up time: 5 years	United States	People who underwent radical or partial nephrectomy. Clear cell and papillary renal cell carcinoma	GRANT	Overall survival	Model discrimination (C-stats)	High

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Capogrosso (2018) N=1630 Retrospective cohort Follow-up time: 60 months	United States	People who underwent radical or partial nephrectomy. Renal cell carcinoma	UISS	Recurrence-free/disease-free survival	Hazard ratio	High
Chen (2017) Retrospective cohort N=176 Follow-up time: 42.3 months	China	People who underwent radical or partial nephrectomy. Renal cell carcinoma	Leibovich 2003 SSIGN	Overall survival	Model discrimination (C-stats)	High
Cindolo (2005) Retrospective cohort N=2404 Follow-up time: 5 years	Italy, France, Austria	People who underwent radical or partial nephrectomy. Renal cell carcinoma	Kattan UISS	Cancer-specific survival Recurrence-free/disease-free survival Overall survival	Model discrimination (C-stats)	High
Correa (2019) Retrospective cohort N=1647	United States	People who underwent radical or partial nephrectomy. Renal cell carcinoma	Kattan Karakiewicz Leibovich 2003	Cancer-specific survival	Model discrimination (C-stats)	Unclear

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Follow-up time: 2.5 to 12 years (depending on model)			SSIGN UISS	Recurrence-free/disease-free survival Overall survival		
Cortellini (2020) Retrospective cohort N=134 Follow-up time: 96 months	Italy	People who underwent radical or partial nephrectomy. Renal cell carcinoma	UISS	Recurrence-free/disease-free survival	Hazard ratio Model discrimination (C-stats)	Unclear
Erdem (2022) Retrospective cohort N=980 Follow-up time: 48 months	7 tertiary institutions in Europe	People who underwent radical or partial nephrectomy. Papillary renal cell carcinoma	VENUSS	Local recurrence Recurrence-free/disease-free survival	Hazard ratio Model discrimination (C-stats)	Low
Flippot (2017) Retrospective cohort N=167 Follow-up time: 41 months	France	People who underwent radical or partial nephrectomy. Clear cell renal cell carcinoma	Leibovich 2003	Recurrence-free/disease-free survival	Hazard ratio	High
Fu (2015) Retrospective cohort	China	People who underwent radical or partial nephrectomy.	SSIGN UISS	Cancer-specific survival	Model discrimination (C-stats)	Unclear

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
N=180 Follow-up time:110 months		Clear cell renal cell carcinoma				
Fu (2016) Retrospective cohort N=472 Follow-up time: 73 months	China	People who underwent radical or partial nephrectomy. Clear cell renal cell carcinoma	Leibovich 2003	Recurrence-free/disease-free survival	Model discrimination (C-stats)	Unclear
Haddad (2017) Retrospective cohort N=367 Follow-up time: 63.5 months	United States	People who underwent radical or partial nephrectomy. Clear cell renal cell carcinoma	SSIGN	Recurrence-free/disease-free survival	Model discrimination (C-stats) Hazard ratio	High
Han (2003) Retrospective cohort N=177 NN N=399 MDA N=484 UCLA Follow-up time: 63 months NN 32 months MDA 33 months UCLA	The Netherlands and United States	People who underwent radical or partial nephrectomy with localised disease who had no evidence of nodal involvement or metastatic spread.	Zisman	Cancer-specific survival	Model discrimination (C-stats)	High
He (2020) Retrospective cohort	China	People with ccRCC	TNM 2016	Overall survival	Hazard ratio	Low

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
N=614 Follow-up time: Not reported						
Hu (2020) Retrospective cohort N=648 Follow-up time: 84 months	China	People with non-metastatic RCC who have had nephrectomy	SSIGN UISS	Overall survival Cancer-specific survival	Model discrimination (C-stats)	High
Huang (2017) Retrospective cohort N=268 Follow-up time: 38 months	China	People with non-metastatic ccRCC.	Leibovich 2003	Progression-free survival	Model discrimination (C-stats)	High
Hupertan (2006) N=565 Follow-up time: 60 months	France	People who had undergone surgery (open radical nephrectomy, partial nephrectomy, or *in situ* tumour resection after a subcostal or flank incision).	Kattan	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Hutterer (2014) N=678 Follow-up time: 44 months	Austria	People with non-metastatic RCC who underwent curative radical or partial nephrectomy.	Leibovich 2003	Cancer-specific survival	Model discrimination (C-stats)	High

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Hutterer (2019) N=382 Follow-up time: 7.8 years	Austria	People with clinically localised (N0M0) RCC who had undergone surgery.	SSIGN	Cancer-specific survival	Model discrimination (C-stats)	High
Ishiyama (2024) N=235 Follow-up time: 19.8 months	Japan	People with non-metastatic RCC who had undergone curative surgery, pT3 or higher staging, or pN1-2 lymph node involvement.	GRANT UISS	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Jensen (2009) N=121 Follow-up time: 124 months	Denmark	People with radical nephrectomy. People were excluded if they had non-clear cell histology or distant metastases or significant lymphadenopathy at diagnosis.	Leibovich 2003	Recurrence-free/disease-free survival	Model discrimination (C-stats) Event data	High
Kang (2020) N=442 Follow-up time: 58.7 months	China	People with ccRCC who had received complete resection of the tumour.	SSIGN	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Klatte (2009) N=170 Follow-up time: 7.1 years	United States	People who underwent radical or partial nephrectomy for sporadic, clinically localised (N0M0) ccRCC.	UISS	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Klatte (2019) N=556	United States	People with completely resected non-metastatic RCC, high risk for recurrence.	Leibovich 2018 UISS	Local recurrence	Model discrimination (C-stats)	Low

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Follow-up time: 53 months			VENUSS TNM not specified			
Kroeger (2022) N=240 Follow-up time: 43.4 months	United States	People with non-metastatic people localised ccRCC.	UISS	Recurrence-free/disease-free survival	Hazard ratio	High
Lee (2018) N=1,642 Follow-up time:39 months	United States	People who underwent partial or radical nephrectomy for clinically localised ccRCC.	Sorbellini	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Lee (2019) N=942 Follow-up time: 76 months clear cell, 69.5 months papillary	Singapore	Binephric people with sporadic, unilateral RCC treated with radical or partial nephrectomy.	Leibovich 2018	Progression-free survival Cancer-specific survival	Model discrimination (C-stats)	Moderate
Li (2024) N=364 Follow-up time: 49.6 months	China	People with histological subtype of ccRCC and classed as clinical stage I-III.	SSIGN UISS TNM 2016	Recurrence-free/disease-free survival	Model discrimination (C-stats) Hazard ratio	High
Liu (2016) N=263	China	People with non-metastatic ccRCC who underwent radical or partial nephrectomy.	SSIGN	Overall survival	Model discrimination (C-stats)	High

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Follow-up time: 120 months				Recurrence-free/disease-free survival		
Liu (2009) N=653 Follow-up time: 65 months	China	People who underwent radical or partial nephrectomy due to RCC.	Karakiewicz Kattan Sorbellini SSIGN UISS	Overall survival Cancer-specific survival Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Lucca (2015) N=430 Follow-up time: 40 months	Austria	People treated with radical or partial nephrectomy for clinically localised unilateral RCC.	SSIGN	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Morgan (2018) N=565 Follow-up time: 90.8 months	United States	People who underwent radical nephrectomy with localised pT1-T3 clear cell, papillary, or chromophobe RCC.	Karakiewicz	Cancer-specific survival	Model discrimination (C-stats)	High
Na (2016) N=162 Follow-up time: not reported	China	People who had radical nephrectomy with confirmed ccRCC who did not receive radiotherapy or chemotherapy before surgery and had no metastasis (M0).	SSIGN UISS TNM 2010	Overall survival	Model discrimination (C-stats)	High

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Nie (2023) N=799 Follow-up time: 53 months	China	People with pathologically confirmed localised ccRCC who had received surgery.	SSIGN UISS	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Oza (2022) N=1,669 Follow-up time: 7.3 months	147 centres in seven countries: United Kingdom, Australia, France, Belgium, the Netherlands, Spain, and Denmark	People with clear cell histology and intermediate (3-5) or high (≥6) Leibovich scores.	Leibovich 2003	Recurrence-free/disease-free survival	Model discrimination (C-stats) Hazard ratio	Moderate
Piccinelli (2023a) N=4,184 Follow-up time: 4.9 years	United States	People who had radical or partial nephrectomy and papillary RCC.	GRANT VENUSS	Cancer-specific survival	Hazard ratio	Low
Piccinelli (2023b) N=2,761 Follow-up time: 5 years	United States	People with non-metastatic chromophobe kidney cancer who had received radical or partial nephrectomy for unilateral RCC.	GRANT Leibovich 2018	Cancer-specific survival	Hazard ratio	Moderate
Pichler (2011) N=1,754 Median follow-up time: 82 months	Austria	People with RCC who underwent partial or radical nephrectomy.	Leibovich 2003	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Rini (2015) N=626 Median follow-up time: 5.5 years	France	People with ccRCC stage 1, 2 or 3 treated with nephrectomy alone.	Leibovich 2003	Recurrence-free/disease-free survival	Model discrimination (C-stats) Hazard ratio	High
Schmeusser (2024) N=2,295 Median follow-up time: 52 months	United States	People who had radical or partial nephrectomy with chromophobe, papillary and ccRCC who were non-metastatic at the time of surgery.	Leibovich 2018	Progression-free survival Cancer-specific survival	Hazard ratio	Low
Seles (2017) N=676 Follow-up time: 6.1 years	Austria	People with localised RCC who underwent open or laparoscopic curative nephron sparing surgery or radical nephrectomy.	Leibovich 2003	Recurrence-free/disease-free survival Cancer-specific survival	Model discrimination (C-stats) Hazard ratio	High
Shao (2020) N=652 Follow-up time: 6.1 years	Austria	People with localised RCC who underwent open or laparoscopic curative nephron sparing surgery or radical nephrectomy	Leibovich 2003 SSIGN UISS	Cancer specific survival Disease free survival Overall survival	Model discrimination (C-stats)	High
Sorbellini (2005) N=200 Follow-up time: 33 months	United States	People who had undergone single radical or partial nephrectomy for unilateral locally confined disease.	Sorbellini	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Suzuki (2011) N=211 Follow-up time: 81 months	Japan	People with ccRCC N0M0 tumour.	Kattan	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Tan (2010) N=355 Follow-up time: 56 months	Singapore	People with non-metastatic unilateral ccRCC who underwent nephrectomy.	Leibovich 2003 UISS	Overall survival Cancer-specific survival Recurrence-free/disease-free survival	Model discrimination (C-stats) Hazard ratio	Moderate
Tan (2011) N=390 Follow-up time: 5 years	Singapore	People who underwent nephrectomy for sporadic non-metastatic unilateral RCC.	Karakiewicz Kattan Leibovich 2003 Sorbellini	Recurrence-free/disease-free survival Overall survival Cancer-specific survival	Model discrimination (C-stats)	Moderate
Tsujino (2017a) N=268 Follow-up time: 60 months	Japan	People with RCC without metastasis who underwent nephrectomy.	SSIGN UISS	Recurrence-free/disease-free survival Overall survival	Hazard ratio	High
Tsujino (2017b) N=219 Follow-up time: 57 months	Japan	People who underwent nephrectomy with curative (for localised RCC) or non-curative (for cytoreduction to metastatic	SSIGN UISS	Overall survival Cancer-specific survival	Model discrimination (C-stats) Hazard ratio	High

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
		RCC) intent due to diagnosis of RCC.				
Tsujino (2019) N=699 Follow-up time: 73 months	Japan	People with RCC who underwent nephrectomy.	UISS	Recurrence-free/disease-free survival	Model discrimination (C-stats) Hazard ratio	High
Um (2020) N=120 Follow-up time: Not reported	Scotland	People with clear cell RCC TNM9 pathological stage pT1-3 disease who had extirpative surgery [presumed to mean either radical or partial nephrectomy]	Leibovich 2003	Recurrence	Sensitivity/ specificity	High
Utsumi (2011) N=217 Follow-up time: Not reported	Japan	People who underwent partial or radical nephrectomy for non-metastatic RCC.	Kattan	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Vasudev (2019) N=575 Follow-up time: 4.4 years contemporary cohort 10.7 years historical cohort	UK	People with newly diagnosed suspected RCC who had received no prior treatment.	Leibovich 2003	Recurrence-free/disease-free survival	Model discrimination (C-stats) Hazard ratio	High

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Viers (2014) N=827 Follow-up time: 9.3 years	United States	People treated with radical nephrectomy for sporadic, unilateral, non-cystic, M0 RCC.	SSIGN	Cancer-specific survival	Model discrimination (C-stats)	High
Wang (2021a) N=310 Follow-up time: 5 years	China	People with ccRCC who underwent nephron sparing surgery or radical nephrectomy.	SSIGN TNM not specified	Progression-free survival Overall survival	Model discrimination (C-stats) Hazard ratio	High
Wang (2021b) N=300 Follow-up time: Not specified	China	People with pathologically diagnosed ccRCC.	SSIGN TNM not specified	Progression-free survival Overall survival	Model discrimination (C-stats)	High
Wang (2016) N=268 Follow-up time: 89 months	China	People with non-metastatic ccRCC who underwent surgical treatment.	Leibovich 2003 UISS	Overall survival Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Wen (2023) N=612 Follow-up time: 73.71 months	China	People with localised ccRCC who underwent radical or partial nephrectomy.	SSIGN	Recurrence-free/disease-free survival	Model discrimination (C-stats)	Low
Xia (2016) N=290 Follow-up time: 99.03 months	China	People with pathologically proven ccRCC who received partial or radical nephrectomy.	Leibovich 2003 UISS	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Xiao (2021) N=146 Follow-up time: 19 months	China	People diagnosed with renal neoplasms and tumour thrombus receiving nephrectomy and thrombectomy. People with preoperative suspicious distant metastasis were excluded.	SSIGN	Overall survival Progression-free survival	Hazard ratio	High
Xiong (2017) N=286 Follow-up time:90.87 months	China	People with pathologically proved ccRCC, having received nephrectomy.	SSIGN	Recurrence-free/disease-free survival	Model discrimination (C-stats)	High
Xv (2024) N=707	China	People who underwent partial/radical nephrectomies and had histologically diagnosed ccRCC.	Leibovich 2003 UISS	Recurrence-free/disease-free survival	Model discrimination (C-stats)	Low
Yang (2022) N=866 Follow-up time: 50 months	China	People with a pathologically confirmed ccRCC after surgery.	SSIGN UISS	Recurrence-free/disease-free survival	Hazard ratio	Low
Zhang (2017) N=585 Follow-up time: 68 months training set, 67 months validation set	China	People with histopathological confirmed ccRCC who have undergone radical or partial nephrectomy with no previous anticancer therapy or history of malignancies.	SSIGN UISS	Recurrence-free/disease-free survival Overall survival	Model discrimination (C-stats)	Moderate

Study details	Setting/Location	Population	Risk model(s)	Outcomes predicted	Outcome measure	Overall risk of bias [applies to all outcomes unless specified]
Zhu (2021) N=640 Follow-up time: Not reported	China	People who were pathologically diagnosed with ccRCC.	SSIGN	Progression-free survival Overall survival	Model discrimination (C-stats) Hazard ratio	High
Zhu (2019) N=942 Follow-up time: 72 months	China	People with ccRCC who had undergone radical or partial nephrectomy. People with distant metastases were excluded.	Leibovich 2018	Recurrence-free/disease-free survival	Model discrimination (C-stats)	Low
Zhu (2024) N=2218 Follow-up time: 62 months	China	People with pathologically confirmed RCC who had received nephrectomy. People who had received anti-tumour therapy before surgery or had stage 4 disease were excluded.	SSIGN	Cancer-specific survival	Model discrimination (C-stats)	High

Abbreviations: ccRCC - clear cell renal cell carcinoma.

See appendix D for full evidence tables.

1.1.6 Summary of the prognostic evidence

For risk prediction models and tools, discrimination was assessed using concordance (c-statistics). C statistics range from 0.5 (no discriminative ability) to 1 (perfect discriminative ability to discriminate between patients with different outcomes). The interpretation of discriminative ability based on c-statistics is shown in Table 5.

Table 5 Interpretation of risk prediction model discriminative ability

C-statistic	Interpretation of discriminative ability
c-statistic <0.6	Very poor
0.6 ≤ c-statistic <0.7	Poor
0.7 ≤ c-statistic <0.8	Fair
0.8 ≤ c-statistic <0.9	Good
0.9 ≤ c-statistic < 1.0	Excellent

For studies reporting the ability of a risk prediction tool to stratify by risk as hazard ratios or risk ratio, the line of no effect was used as a clinical decision-threshold for all clinical outcomes. For these outcomes evidence statements are divided into 2 groups as follows:

- We state that the evidence showed increased risk of an outcome/event with a particular risk group stratified by the risk prediction tool where the 95% CI does not cross the line of no effect.
- It is not possible from the evidence to differentiate between risk groups if the 95% CI crosses the line of no effect.

Clear cell subtype

Table 6: Summary of findings for Kattan model in clear cell RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
1 [Suzuki 2011]	Disease-free survival	211	0.73 (0.72, 0.73)	Very low	Fair

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

Table 7: Summary of findings for Leibovich 2003 in clear cell RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
1 [Huang 2017]	Progression-free survival	268	0.76 (0.68, 0.83)	Very low	Fair
2 [Tan 2010, Hutterer 2014]	Cancer-specific survival	1033	0.79 (0.11, 0.99)	Very low	Fair
5 [An 2015, Chen 2017, Tan 2010, Wang 2016b, Zhang 2017]	Overall survival	1575	0.74 (0.64, 0.81)	Very low	Fair
15 [An 2015, Beisland 2015, Correa 2019, Fu 2016, Jensen 2009, Oza 2022, Pichler 2011, Rini 2015, Tan 2010, Wang 2016b, Xia 2016, Xv 2024 (testing), Xv 2024 (internal), Xv 2024 (external), Zhang 2017]	Recurrence-free survival/disease-free survival	5571	C-statistics not pooled due to high heterogeneity Median (IQR) 0.68 (0.64, 0.765)	Very low	Median: Poor

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

Table 8: Summary of findings for Leibovich 2003 in clear cell RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate(c-statistic)	Certainty	Interpretation
High risk vs low risk					
4 [Beisland 2015, Flippot 2017, Rini 2015, Tan 2010]	Disease-free survival	1270	HR 8.92 (4.45, 17.90)	Low	Risk of recurrence or death significantly higher in the high-risk group
1 [Jensen 2009]	Recurrence	69	RR 3.12 (1.51, 6.46)	Very low	Risk of recurrence significantly higher in the high-risk group
1 [Tan 2010]	Cancer-specific survival	189	HR 10.84 (4.00, 29.39)	Very low	Risk of cancer-specific mortality significantly higher in the high-risk group
1 [Tan 2010]	Overall survival	189	HR 5.17 (2.59, 10.32)	Very low	Risk of mortality significantly higher in the high-risk group
Intermediate risk vs low risk					
4 [Beisland 2015, Flippot 2017, Rini 2015, Tan 2010]	Disease-free survival	1414	HR 2.82 (1.96, 4.06)	Moderate	Risk of recurrence or death significantly higher in the intermediate-risk group
1 [Jensen 2009]	Recurrence	78	RR 2.00 (0.93, 4.28)	Very low	Could not differentiate
1 [Tan 2010]	Cancer-specific survival	303	HR 3.41 (1.30, 8.96)	Very low	Risk of cancer-specific mortality significantly higher in the intermediate-risk group
1 [Tan 2010]	Overall survival	303	HR 2.05 (1.09, 3.86)	Very low	Risk of mortality significantly higher in the intermediate-risk group
High risk vs intermediate risk					
2 [Flippot 2017, Oza 2022]	Disease-free survival	1612	HR 3.23 (2.13, 4.89)	Moderate	Risk of recurrence or death significantly higher in the high-risk group
1 [Jensen 2009]	Recurrence	95	RR 1.56 (1.10, 2.21)	Very low	Risk of recurrence significantly higher in the high-risk group

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

Table 9: Summary of findings for Leibovich 2018 in clear cell RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
1 [Lee 2019]	Progression-free survival	829	0.81 (0.77, 0.85)	Very low	Good
1 [Lee 2019]	Cancer-specific survival	829	0.83 (0.79, 0.87)	Very low	Good

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

Table 10: Summary of findings for Sorbellini in clear cell RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
2 [Lee 2018, Sorbellini 2005]	Recurrence-free survival	1842	0.81 (0.76, 0.86)	Very low	Good

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

Table 11: Summary of findings for SSIGN in clear cell RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
8 [Wang 2021 (training), Wang 2021 (validation), Wang 2021b (training), Wang 2021b (validation), Zhu 2021 (cohort 1), Zhu 2021 (cohort 2), Zhu 2021 (training), Zhu 2021 (validation)]	Progression-free survival	1250	0.68 (0.64, 0.71)	Very low	Poor

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
14 [Haddad 2017 (training), Haddad 2017 (validation), Kang 2020 (training), Kang 2020 (validation), Liu 2016, Li 2024, (training), Li 2024 (validation), Lucca 2015, Nie 2023 (training), Nie 2023 (test), Wen 2023 (training), Wen 2023 (validation), Xiong 2017, Zhang 2017]	Recurrence-free/disease-free survival	4148	0.73 (0.68, 0.76)	Very low	Fair
12 [Chen 2017, Liu 2016, Na 2016, Wang 2021 (Training), Wang 2021 (Validation), Wang 2021b (Training), Wang 2021b (Validation), Zhang 2017, Zhu 2021 (cohort 1), Zhu 2021 (cohort 2), Zhu 2021 (training), Zhu 2021 (validation)]	Overall survival	2436	0.71 (0.68, 0.74)	Very low	Fair
3 [Correa 2019, Fu 2015, Viers 2014]	Cancer-specific survival	2654	C-statistics not pooled due to high heterogeneity Median (IQR) 0.69 (0.67, 0.75)	Very low	Median: Poor

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

Table 12: Summary of findings for SSIGN in clear cell RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
High risk vs low risk					
2 [Haddad 2017, Yang 2022]	Disease-free survival	1233	HRs not pooled due to high heterogeneity Median (IQR) 8.34 (5.74, 10.95)	Moderate	Risk of recurrence or death significantly higher in the high-risk group
2 [Wang 2021b training, Wang 2021b validation]	Overall survival	300	HR 8.28 (4.33, 15.82)	Very low	Risk of mortality significantly higher in the high-risk group
2 [Wang 2021b training, Wang 2021b validation]	Progression-free survival	300	HR 16.83 (8.94, 31.69)	Very low	Risk of progression significantly higher in the high-risk group
Intermediate risk vs low risk					
1 [Yang 2022]	Recurrence-free survival	231	HR 4.71 (3.18, 6.97)	Low	Risk of recurrence significantly higher in the intermediate-risk group

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

Table 13: Summary of findings for TNM 2016 in clear cell RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (C-statistic)	Certainty	Interpretation of discriminative ability
4 [Wang 2021 (training), Wang 2021 (validation), Wang 2021b (training), Wang 2021b (validation)]	Progression-free survival	610	0.64 (0.63, 0.66)	Low	Poor
4 [Wang 2021 (training), Wang 2021 (validation), Wang 2021b (training), Wang 2021b (validation)]	Overall survival	610	0.68 (0.65, 0.71)	Very low	Poor

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

Table 14: Summary of findings for TNM model stages 3 vs 1-2, clear cell RCC subtypes (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
Stages 3 vs 1-2					
1 [Li 2024]	Disease-free survival	344	HR 2.55 (1.34, 4.86)	Very low	Risk of recurrence or death significantly higher for stage 3 disease
1 [He 2020]	Overall survival	Not reported	HR 3.72 (2.41, 5.75)	Low	Risk of mortality significantly higher for stage 3 disease

Table 15: Summary of findings for UISS in clear cell RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
12 [Klatte 2009, Li 2024 (training), Li 2024 (validation), Nie 2023 (training), Nie 2023 (test), Tan 2010, Wang 2016b, Xia 2016, Xv 2024 (testing), Xv 2024 (internal), Xv 2024 (external), Zhang 2017]	Disease-free survival	3538	C-statistics not pooled due to high heterogeneity Median (IQR) 0.70 (0.65, 0.75)	Very low	Median: Fair
4 [Na 2016, Tan 2010, Wang 2016b, Zhang 2017]	Overall survival	1370	0.69 (0.60, 0.77)	Very low	Poor
2 [Fu 2015, Tan 2010]	Cancer-specific survival	535	0.66 (0.59, 0.72)	Very low	Poor

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

Table 16: Summary of findings for UISS in clear cell RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
High risk vs low risk					
1 [Tan 2010]	Cancer-specific survival	154	HR 6.54 (2.10, 20.35)	Very low	Risk of cancer-specific mortality significantly higher in the high-risk group
3 [Kroeger 2022, Tan 2010b, Yang 2022]	Disease-free survival	677	HR 5.57 (3.69, 8.41)	Moderate	Risk of recurrence or death significantly higher in the high-risk group
1 [Tan 2010]	Overall survival	154	HR 4.28 (1.92, 9.55)	Very low	Risk of mortality significantly higher in the high-risk group
Intermediate risk vs low risk					
1 [Tan 2010]	Cancer-specific survival	308	HR 3.94 (1.39, 11.18)	Very low	Risk of cancer-specific mortality in the high-risk group
2 [Tan 2010, Yang 2022]	Disease-free survival	1103	HR 2.75 (1.93, 3.92)	High	Risk of recurrence or death significantly higher in the intermediate-risk group
1 [Tan 2010]	Overall survival	308	HR 2.63 (1.28, 5.39)	Very low	Risk of mortality significantly higher in the intermediate-risk group
1 [Kroeger 2022]	Disease-free survival	135	HR 1.96 (0.87, 4.40)	Very low	Could not differentiate

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

Papillary subtype

Table 17: Summary of findings for GRANT in papillary RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
1 [Piccinelli 2023a]	Cancer-specific survival	4184	Poor risk vs favourable risk HR 3.60 (2.89, 4.48)	Moderate	Risk of cancer-specific mortality higher in the poor risk group

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

Table 18: Summary of findings for Leibovich 2003 in papillary RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (C-statistic)	Certainty	Interpretation of discriminative ability
1 [Oza 2022]	Recurrence-free survival/disease free survival	128	0.63 (0.56, 0.69)	Very low	Poor

Table 19: Summary of findings for Leibovich 2003 in papillary RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
1 [Oza 2022]	Recurrence-free survival/disease free survival	128	High risk vs intermediate risk HR 2.61 (1.44, 4.72)	Very low	Risk of recurrence or death higher in the high-risk group

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

Table 20: Summary of findings for Leibovich 2018 in papillary RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
1 [Lee 2019]	Progression-free survival	113	0.72 (0.57, 0.83)	Very low	Fair
1 [Lee 2019]	Cancer-specific survival	113	0.74 (0.59, 0.85)	Very low	Fair
1 [Klatte 2019]	Recurrence-free survival/disease free survival	556	0.58 (0.52, 0.64)	Low	Very poor

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

Table 21: Summary of findings for Leibovich 2018 in papillary RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Quality	Interpretation
High risk vs low risk					
1 [Schmeusser 2023]	Cancer-specific survival	190	HR 9.16 (3.38, 24.82)	Low	Risk of cancer-specific mortality significantly higher in the high-risk group
1 [Schmeusser 2023, Black ethnicity]	Cancer-specific survival	88	HR 27.72 (4.96, 155.03)	Low	Risk of cancer-specific mortality significantly higher in the high-risk group
1 [Schmeusser 2023]	Progression-free survival	190	HR 11.22 (5.05, 24.96)	Low	Risk of progression significantly higher in the high-risk group
1 [Schmeusser 2023, Black ethnicity]	Progression-free survival	88	HR 10.72 (3.27, 35.18)	Low	Risk of progression significantly higher in the high-risk group
Intermediate risk vs low risk					
1 [Schmeusser 2023]	Cancer-specific survival	357	HR 1.94 (0.78, 4.81)	Very low	Could not differentiate
1 [Schmeusser 2023, Black ethnicity]	Cancer-specific survival	195		Very low	Could not differentiate

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Quality	Interpretation
			HR 3.65 (0.78, 17.05)		
1 [Schmeusser 2023]	Progression-free survival	357	HR 1.24 (0.55, 2.80)	Very low	Could not differentiate
1 [Schmeusser 2023, Black ethnicity]	Progression-free survival	195	HR 0.84 (0.31, 2.26)	Very low	Could not differentiate

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

Table 22: Summary of findings for TNM 2016 in papillary RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Quality	Interpretation of discriminative ability
1 [Klatte 2019]	Recurrence-free survival/disease free survival	556	0.60 (0.54, 0.66)	Low	Poor

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

Table 23: Summary of findings for UISS in papillary RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (C-statistic)	Quality	Interpretation of discriminative ability
1 [Klatte 2019]	Recurrence-free survival/disease free survival	556	0.62 (0.57, 0.68)	Low	Poor

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

Table 24: Summary of findings for VENUSS in papillary RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistics)	Quality	Interpretation of discriminative ability
2 [Erdem 2022, Klatte 2019]	Recurrence-free survival/disease free survival	1536	C-statistic not pooled due to high heterogeneity Median (IQR): 0.739 (0.702, 0.775)	Very low	Median: Fair

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

Table 25: Summary of findings for VENUSS in papillary RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Quality	Interpretation
High risk vs low risk					
1 [Piccinelli 2023a]	Cancer-specific survival	3180	HR 13.10 (9.91, 17.32)	Moderate	Risk of cancer-specific mortality significantly higher in the high-risk group
1 [Erdem 2022]	Recurrence-free survival/disease free survival	746	HR 17.90 (12.23, 26.20)	Moderate	Risk of recurrence or death significantly higher in the high-risk group
Intermediate risk vs low risk					
1 [Piccinelli 2023a]	Cancer-specific survival	3886	HR 2.70 (2.01, 3.62)	Moderate	Risk of cancer-specific mortality significantly higher in the intermediate-risk group
1 [Erdem 2022]	Recurrence-free survival/disease free survival	851	HR 2.91 (1.90, 4.46)	Moderate	Risk of recurrence or death significantly higher in the intermediate-risk group

High risk vs intermediate risk					
1 [Erdem 2022]	Recurrence-free survival/disease free survival	363	HR 6.07 (4.17, 8.83)	Moderate	Risk of recurrence or death significantly higher in the high-risk group

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

Chromophobe subtype

Table 26: Summary of findings for GRANT in chromophobe RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Quality	Interpretation
1 [Piccinelli 2023b]	Cancer-specific survival	2761	Poor risk vs favourable risk HR 3.00 (2.17, 4.15)	Low	Risk of cancer-specific mortality significantly higher in the poor-risk group

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

Table 27: Summary of findings for Leibovich 2003 in chromophobe RCC (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Quality	Interpretation of discriminative ability
1 [Oza 2022]	Recurrence-free survival/disease-free survival	96	0.65 (0.54, 0.75)	Very low	Poor

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

Table 28: Summary of findings for Leibovich 2003 in chromophobe RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
1 [Oza 2022]	Recurrence-free survival/disease-free survival	96	High risk vs intermediate risk HR 3.88 (1.56, 9.63)	Very low	Risk of recurrence or death significantly higher in the high-risk group

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

Table 29: Summary of findings for Leibovich 2018 in chromophobe RCC (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
High risk vs low risk					
2 [Piccinelli 2023b, Schmeusser 2023]	Cancer-specific survival	2560	HR 17.95 (11.32, 28.46)	High	Risk of cancer-specific mortality significantly higher in the high-risk group
1 [Schmeusser 2023]	Progression free survival	167	HR 45.35 (8.46, 243.18)	Low	Risk of progression significantly higher in the high-risk group
Intermediate risk vs low risk					
2 [Piccinelli 2023b, Schmeusser 2023]	Cancer-specific survival	2882	HR 3.49 (2.46, 4.95)	Moderate	Risk of cancer-specific mortality significantly higher in the intermediate-risk group
1 [Schmeusser 2023]	Progression free survival	174	HR 3.73 (0.47, 29.88)	Very low	Risk of progression significantly higher in the intermediate-risk group

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

All RCC subtypes

Table 30: Summary of findings for GRANT for all RCC subtypes (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
1 [Buti 2019]	Overall survival	73217	0.67 (0.66, 0.68)	Very low	Poor
2 [Cortellini 2020, Ishiyama 2024]	Recurrence-free survival/disease free survival	369	C-statistics not pooled due to high heterogeneity Median (IQR): 0.645 (0.618, 0.673)	Very low	Median: Poor

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

Table 31: Summary of findings for Karakiewicz in all RCC subtypes (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
4 [Correa 2019, Liu 2009, Morgan 2018, Tan 2011]	Cancer-specific survival	3346	C-statistic not pooled due to high heterogeneity Median (IQR): 0.795 (0.712, 0.840)	Very low	Median: Fair
2 [Liu 2009, Tan 2011]	Overall survival	1043	0.74 (0.70, 0.77)	Moderate	Fair
2 [Liu 2009, Tan 2011]	Recurrence-free survival/disease-free survival	1043	0.8 (0.77, 0.82)	Moderate	Good

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

Table 32: Summary of findings Kattan in all RCC subtypes (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
3 [Cindolo 2005, Liu 2009, Tan 2011]	Cancer-specific survival	3447	0.77 (0.75, 0.79)	Very low	Fair
3 [Cindolo 2005, Liu 2009, Tan 2011]	Overall survival	3447	0.71 (0.62, 0.79)	Very low	Fair
7 [Cindolo 2005, Correa 2019, Hupertan 2006, Liu 2009, Tan 2011, Utsumi 2011 CUH cohort, Utsumi 2011 CCC cohort]	Recurrence-free survival/disease-free survival	5876	C-statistic not pooled due to high heterogeneity Median (IQR) 0.73 0.676, 0.805)	Very low	Median: Fair

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

Table 33: Summary of findings to Leibovich 2003 in all RCC subtypes (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
2 [Shao 2020, Tan 2011]	Cancer-specific survival	1524	0.8 (0.76, 0.83)	Very low	Good
2 [Shao 2020, Tan 2011]	Overall survival	1524	0.77 (0.73, 0.81)	Very low	Fair
6 [Oza 2022, Shao 2020, Seles 2017, Tan 2011, Vasudev 2019 (his cohort), Vasudev 2019 (con cohort)]	Recurrence-free survival/disease-free survival	4220	C-statistic not pooled due to high heterogeneity Median (IQR) 0.754 (0.736, 0.793)	Very low	Median: Fair

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

Table 34: Summary of findings to Leibovich 2003 in all RCC subtypes (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
High risk vs low risk					
2 [Vasudev 2019 (his cohort), Vasudev 2019 (con cohort)]	Recurrence-free survival/disease-free survival	326	HR 19.14 (9.46, 38.75)	Very low	Risk of recurrence or death significantly higher in the high-risk group
Intermediate risk vs low risk					
2 [Vasudev 2019 (his cohort), Vasudev 2019 (con cohort)]	Recurrence-free survival/disease-free survival	459	HR 4.60 (2.26, 9.36)	Very low	Risk of recurrence or death significantly higher in the intermediate-risk group
High risk vs intermediate risk					
1 [Oza 2022]	Recurrence-free survival/disease-free survival	1669	HR 2.74 (2.29, 3.28)	Low	Risk of recurrence/disease significantly higher in the high-risk group

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

Table 35: Summary of findings for Sorbellini in all RCC subtypes (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
2 [Liu 2009, Tan 2011]	Cancer-specific survival	975	0.79 (0.75, 0.83)	Very low	Fair
2 [Liu 2009, Tan 2011]	Overall survival	975	0.74 (0.70, 0.78)	Low	Fair
2 [Liu 2009, Tan 2011]	Recurrence-free survival/disease-free survival	975	0.81 (0.78, 0.84)	Very low	Good

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

Table 36: Summary of findings for SSIGN in all RCC subtypes (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
2 [Liu 2009, Shao 2020]	Recurrence-free survival/disease-free survival	1855	0.79 (0.76, 0.82)	Very low	Fair
3 [Hu 2020, Liu 2009, Tsujino 2017b]	Overall survival	1520	C-statistic not pooled due to high heterogeneity Median (IQR) 0.83 (0.8, 0.838)	Very low	Median: Good
6 [Hu 2020, Hutterer 2019, Liu 2009, Zhu 2024 – external test, Zhu 2024 – training, Zhu 2024 – internal validation]	Cancer-specific survival	3901	C-statistic not pooled due to high heterogeneity Median (IQR) 0.81 (0.80, 0.83)	Very low	Median: Good

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

Table 37: Summary of findings for SSIGN in all RCC subtypes (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
High risk vs low risk					
1 [Tsujino 2017a]	Recurrence-free survival/disease-free survival	268	HR 4.09 (2.36, 7.10)	Very low	Risk of recurrence or death significantly higher in the high-risk group
1 [Tsujino 2017b]	Cancer-specific survival	219	HR 13.85 (4.97, 38.57)	Very low	Risk of cancer-specific mortality significantly higher in the high-risk group

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
2 [Tsujino 2017b, Xiao 2021b]	Overall survival	338	HR 4.55 (2.73, 7.58)	Very low	Risk of mortality significantly higher in the high-risk group
1 [Xiao 2021b]	Progression-free survival	70	HR 3.03 (1.23, 7.46)	Very low	Risk of progression significantly higher in the high-risk group
Intermediate risk vs low risk					
1 [Xiao 2021]	Overall survival	125	HR 1.45 (0.48, 4.42)	Very low	Could not differentiate
1 [Xiao 2021]	Progression-free survival	125	HR 1.83 (0.87, 3.85)	Very low	Could not differentiate

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

Table 38: Summary of findings for UISS in all RCC subtypes (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
5 [Cindolo 2005, Cortellini 2020, Ishiyama 2024, Liu 2009, Shao 2020]	Recurrence-free survival/disease-free survival	4628	C-statistic not pooled due to high heterogeneity Median (IQR): 0.653 (0.63, 0.67)	Very low	Median: Poor
5 [Cindolo 2005, Correa 2019, Hu 2020, Liu 2009, Tsujino 2017b]	Overall survival	5571	C-statistic not pooled due to high heterogeneity Median (IQR): 0.68 (0.64, 0.765)	Very low	Median: Poor
3 [Cindolo 2005, Hu 2020, Liu 2009]	Cancer-specific survival	3704	C-statistic not pooled due to high heterogeneity Median (IQR): 0.73 (0.69, 0.76)	Very low	Median: Fair

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

Table 39: Summary of findings for UISS in all RCC subtypes (hazard ratios)

Number of studies/cohorts	Outcome	Sample size	Effect estimate	Certainty	Interpretation
High risk vs low risk					
1 [Tsujino 2017b]	Cancer-specific survival	219	HR 18.20 (6.54, 50.64)	Very low	Risk of cancer-specific mortality significantly higher in the high-risk group
3 [Capogrosso 2018, Cortellini 2020, Tsujino 2019]	Recurrence-free survival/disease-free survival	1262	HR 2.42 (1.33, 4.42)	Low	Risk of recurrence or death significantly higher in the high-risk group
1 [Tsujino 2017a]	Overall survival	268	HR 4.39 (2.31, 8.33)	Very low	Risk of mortality significantly higher in the high-risk group
Intermediate risk vs low risk					
2 [Capogrosso 2018, Cortellini 2020]	Recurrence-free survival/disease-free survival	1443	HR 1.55 (0.94, 2.58)	Low	Risk of recurrence or death significantly higher in the intermediate-risk group
1 [Baykal 2025]	Overall survival	197	HR 2.84 (1.26, 6.41)	Very low	Risk of mortality significantly higher in the intermediate-risk group
High risk vs intermediate risk					
1 [Cortellini 2020]	Recurrence-free survival/disease-free survival	113	HR 0.99 (0.55, 1.78)	Very low	Could not differentiate
1 [Baykal 2025]	Overall survival	197	HR 4.64 (2.03, 10.61)	Very low	Risk of mortality significantly higher in the high-risk group

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

Table 40: Summary of findings for Zisman in all RCC subtypes (c-statistics)

Number of studies/cohorts	Outcome	Sample size	Effect estimate (C-statistic)	Certainty	Interpretation of discriminative ability
3 [Han 2003 (NN cohort), Han 2003 (MDA cohort), Han 2003 (UCLA cohort)]	Cancer-specific survival	1060	0.83 (0.80, 0.86)	Low	Good

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

1.1.7 Economic evidence

A literature search was conducted to identify published economic evaluations of relevance to the review questions on risk prediction models (evidence review K for risk prediction models for localised and locally advanced RCC, and evidence review L for risk prediction models for metastatic RCC), see appendix B for the search strategy. This search retrieved 787 studies, and none of these studies were considered relevant or applicable for either review question at title and abstract screening (see appendix G for economic evidence study selection).

1.1.7.1 Included studies

No studies were included for this evidence review.

1.1.7.2 Excluded studies

No studies were reviewed at full text and excluded.

1.1.8 Summary of included economic evidence

No economic evidence was identified for this review question.

1.1.9 Economic model

No original economic modelling was conducted for this review question.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

The committee agreed that the most clinically useful outcome that the risk tools could predict after surgery would be disease recurrence. They noted that disease recurrence was measured using recurrence-free survival or disease-free survival in the evidence. This outcome is important for both patients and clinicians as the ability to accurately predict the risk of recurrence could guide shared decisions around appropriate follow-up after surgery and who might benefit from adjuvant treatment. They also agreed that survival (measured as overall survival and cancer specific survival) would be of interest to clinicians in terms of management, as well as being important to the person who has been treated for RCC.

In order for the risk prediction tools to be useful for guiding management and follow up after surgery, the committee agreed that they need to be able to discriminate well between different risk groups; the committee therefore considered discrimination measures (c-statistics, sensitivity and specificity and likelihood ratios) to be particularly important. Sensitivity, specificity and likelihood ratios were the highest standard of evidence available as they involve evaluating the performance of a measure using a specified threshold, and link directly to decision making. However, in the absence of this type of data, c-statistics and hazard ratios (or odds ratios and risk ratios) were the key outcomes used to assess the performance of the risk prediction tools. These outcome measures provide an indication of classification accuracy, and the risk of an event associated with the classification.

1.1.12.2 The certainty of the evidence

Most of the evidence was judged to be low or very low certainty and was most frequently downgraded for risk of bias. Concerns that led to a judgment that there was a risk of bias included limited information provided by studies on the analysis, or inappropriate handling of missing data. Evidence was also downgraded for concerns around heterogeneity due to variation of results. For some of the outcomes across some of the tools, heterogeneity was significant (I^2 was more than 80%) and therefore it was not possible to pool the data. For these outcomes, the median point estimates were reported with the interquartile range. Evidence was also downgraded for concerns around imprecision, where the effect estimate crossed more than one classification accuracy category or sample size was smaller than 500 for HR or RR results.

The committee noted that the evidence for discrimination in this review was limited to outcomes reported using c-statistics as data to calculate sensitivity and specificity was not reported in the studies. They were aware of the limitations of the c-statistic, which looks at classification accuracy but places equal weight on false positives and false negatives. In comparison, if data is available to calculate sensitivity and specificity then the different decision thresholds can be set for both depending on whether it is more important to detect people who could be at high risk of recurrence (high sensitivity) or whether it is more important to minimise false positives (higher specificity). The committee noted that in practice the tools would be used to classify people into different risk groups to help determine which follow up strategy to use (see evidence review F on follow up for previously treated renal cell carcinoma) and to help identify patients at high-risk of recurrence, who may benefit from adjuvant therapy. They agreed that it would be worse to not identify people at higher risk of recurrence because if they are mistakenly classified as lower risk then they may have a shorter and less intense follow up schedule or not be offered adjuvant therapy, which may lead to worse outcomes for them. In the absence of sensitivity and specificity data, the

committee agreed that the c-statistic data could provide information to select a suitable tool to guide clinicians with treatment decisions and that a c-statistic of greater than 0.7 could indicate a useful test for prognosis. This corresponded to 'fair' in the classification of c-statistics that was used in this review. The committee agreed that this could be further supported with a larger risk of the outcome of interest, shown by the hazard ratio (HR), in more severe groups compared to less severe groups. They agreed that in practice this would be useful for guiding treatment options and follow-up schedule planning. No data was identified for the other outcome measures listed in the protocol.

1.1.12.3 Benefits and harms

Clear cell renal cell carcinoma

The committee discussed the evidence by subtype of renal cell carcinoma. They noted that most of the evidence was for the clear cell subtype as this is the most common subtype. The tools that were used for the clear cell subtype were Kattan, Leibovich 2003, Leibovich 2018, Sorbellini, SSIGN and UISS. In addition, many studies reported results from a mixed population of all subtypes but between 70% to 90% of the populations in these studies were of clear cell subtypes. Where this was the case, the committee agreed that the results could be considered alongside the evidence for clear cell only sub-populations. The tools that were used for mixed subtypes were GRANT, Karakiewicz, Kattan, Leibovich 2003, Sorbellini, SSIGN, UISS and Zisman. They noted that across all the outcomes taken together, the evidence did not show a single prognostic tool to be superior to others based on the c-statistics. As some tools were better at predicting one outcome over another, they therefore decided to consider the tools by outcome.

As discussed above, predicting recurrence (reported as recurrence-free survival or disease-free survival) is the most important use of these tools in clinical practice as this is used to guide the multidisciplinary team (MDT) discussions around follow up schedules and whether someone needs adjuvant treatment. The Leibovich 2003, SSIGN and UISS tools have been tested on many populations and the discriminative ability of these tools to predict recurrence was classified as 'fair' (c-statistic of greater than or equal to 0.7) apart from Leibovich 2003. The median c-statistic estimate for Leibovich 2003 was in the poor range for discriminative ability, with the interquartile range spanning across 2 classification categories (median 0.68, interquartile ranges of 0.64 to 0.77). The committee discussed the concerns with heterogeneity for this outcome which prevented meta-analysis of the data and noted that although the discriminative ability of the tool was poor in some cohorts, many cohorts reported fair to good discriminative ability. In addition, the c-statistics for recurrence-free survival/ disease-free survival for the mixed population (which was mainly people with clear cell RCC) had a 'fair' c-statistic. Taken together the committee agreed that Leibovich 2003 could be used to predict risk of recurrence in people with clear cell RCC.

The committee discussed the evidence on the risk of recurrence between the different risk groups, as reported by HR. There was evidence available for Leibovich 2003, SSIGN and UISS tools that showed that the groups identified as high risk according to the prognostic scores were more likely to have disease recurrence than those identified as intermediate or low risk. The committee agreed that this evidence supported the use of these risk prediction tools for predicting recurrence.

The committee also discussed the evidence for the Karakiewicz, Kattan and Sorbellini tools, and although the discriminative ability of these tools to predict recurrence was fair (Kattan) to good (Karakiewicz and Sorbellini), the committee noted that they had only been tested in a few populations other than those they were developed in. The GRANT score data could not

be pooled due to high heterogeneity. The median c-statistic indicated that its discriminative ability to predict recurrence was poor. There was no HR data reported for these risk prediction tools.

The committee looked at the risk factors included in the tools. They agreed that the choice of tool should not only be informed by the ability to predict outcomes, but also by the availability of information about the prognostic factors included in the model. The Leibovich 2003 and SSIGN scores could be calculated using information that was usually available on pathology reports. Some of the risk factors required to calculate scores for UISS, Karakiewicz, Kattan and Sorbellini were also available in pathology reports, but these tools also required other information (such as ECOG scale of performance status) that would need to be provided by clinical assessment. However, the committee agreed that the information required to use these tools will be available in practice. The committee noted that the Leibovich 2003 tool is commonly used in current practice and that it is easy to calculate, as the risk factors are readily available in the pathology report.

The committee agreed that overall, using a risk prediction tool to help predict the risk of recurrence would be beneficial to the MDT in terms of guiding decisions around follow up schedules and identifying who could benefit from adjuvant therapy. Taking the evidence above about the discriminative ability of the tools, the availability of data to calculate risk scores and the difference in risk between the high and low risk groups into account, they recommended that clinicians consider using the Leibovich 2003, SSIGN, UISS, Karakiewicz, Kattan or Sorbellini tools to predict risk of recurrence at 5 years.

The committee then discussed the evidence around the ability of the tools to predict survival outcomes (overall survival or cancer-specific survival). The discriminative ability of Leibovich 2003 to predict these outcomes was fair (for the clear cell specific population) to good (for cancer specific survival in the mixed population that mainly had clear cell RCC). The discriminative ability of Karakiewicz, Kattan and Sorbellini to predict these survival outcomes also ranged from fair to good, however the performance of these models had only been tested in a few external populations. Although the mixed population evidence suggested that SSIGN had good discriminative ability for both overall survival and cancer-specific survival, the evidence specific to the clear cell specific population suggested poor to fair discriminative ability for SSIGN and UISS.

Leibovich 2018 showed good discriminative ability for progression-free survival and cancer-specific survival in the clear cell population, however this was based on a single study. The committee noted that the Zisman model showed good discriminative ability for cancer specific survival. However, the data contributing to the evidence for the Zisman model was from a mixed population of people with RCC and did not specify the proportions of participants with each subtype of RCC, therefore the committee could not confidently say that the evidence on this model provided enough information on its discriminative ability for any particular subtype. In addition, the data was only from 2 studies.

The committee noted that predictions of the risk of overall survival and cancer specific survival would be unlikely to influence clinical decisions in terms of follow up or treatment options. Therefore, they only made recommendations around using risk prediction tools for predicting recurrence.

Papillary renal cell carcinoma

There was little evidence on risk prediction tools to predict recurrence (reported as recurrence-free survival or disease-free survival) in the papillary subtype of renal cell carcinoma to help inform decisions around follow up schedules and whether adjuvant treatment is suitable. The evidence for recurrence was limited to the Leibovich 2003, 2018

and UISS models, which showed very poor to poor discriminative ability and VENUSS which showed fair discriminative ability. They noted that the VENUSS model was specifically developed for prediction of the risk of papillary RCC recurrence, and that data was easily available from the pathology report for the risk factors included in the model. They agreed that the evidence supported the ability of the VENUSS score to predict the risk of recurrence (based on a median follow-up of 33 months) for people with papillary RCC based on c-statistic and HR data and made a consider recommendation to reflect this because it had only been externally validated in 2 populations.

The committee discussed the evidence for the prediction of risk of overall survival or cancer-specific survival in people with papillary RCC. As with recurrence, there was little evidence available. The only data for these outcomes came from Leibovich 2018 for cancer specific survival and this came from one external population. The committee agreed that although the average discriminative ability of the Leibovich 2018 was fair, there were concerns around imprecision as the classification accuracy spanned 3 categories, and the sample size was small. As with recommendations for people with clear cell RCC, the committee agreed that predictions around risk of overall survival and cancer-specific survival would be unlikely to influence clinical decision making; they therefore did not make any recommendations around using these risk prediction tools to predict overall survival or cancer-specific survival. As above, in cases where this tool is used to inform decision making the committee agreed that it would be important to share information about it with the person with papillary RCC to enable them to make an informed shared decision about their care.

Chromophobe

There was very little data for people with chromophobe RCC and this consisted of discriminative ability data for the Leibovich 2003 model only for recurrence (reported as recurrence-free survival or disease-free survival). The committee noted that it was current practice to use the Leibovich 2003, but also noted the challenge in that this model requires provision of a grade for chromophobe RCC, where currently there is no strictly recommended grading system for this tumour type. In addition, the evidence in this review showed that the performance of Leibovich 2003 was poor at predicting recurrence. The committee therefore agreed that it would not be appropriate to recommend the Leibovich 2003 tool to predict the risk of recurrence for people with chromophobe RCC.

Leibovich 2018 was not recommended because it does not predict recurrence-free survival, but instead predicts progression-free survival and cancer specific survival, which are broader than just recurrence. There were no discriminative c-statistics data for the Leibovich 2018 tool for people with chromophobe RCC However, the derivation study identified factors (fat invasion, sarcomatoid differentiation and nodal involvement) that were associated with a higher risk of progression and the committee agreed that these could also help identify people with a higher risk of recurrence. (See evidence review F on follow up for how the committee used these factors to make recommendations relating to follow up imaging.) The committee agreed that more evidence was required to guide clinical practice in this area and made a research recommendation to develop tools or identify biomarkers and factors to predict the risk of recurrence for people with non- clear cell RCC, which would include chromophobe RCC and other rare types of RCC.

1.1.12.4 Cost effectiveness and resource use

No published economic evidence was identified and original economic modelling was not prioritised for this review question.

The committee indicated that, in current practice, the information needed to calculate the recommended risk scores is already collected and reported in pathology reports, and it is not expected to incur further resources to calculate these risk scores. The use of risk prediction tools helps to provide follow-up and further care according to the individual's risk of recurrence, and this will lead to better outcomes and cost savings, and so their use is likely to be cost effective. Using these tools alongside clinical judgement is commonplace in current clinical practice, so these recommendations are expected to encourage standardisation of practice.

1.1.12.5 Other factors the committee took into account

The committee noted that most of the evidence in this review used external validation populations followed up for 5 years following surgery, therefore they agreed the recommendations that were supported by the evidence would be relevant to the risk of developing recurrence at 5 years for both the clear cell RCC and papillary RCC populations.

The committee made a number of overarching recommendations that apply to both the clear cell RCC and papillary RCC populations. They agreed that although prognostic models can be useful in stratifying people into risk groups for recurrence to help guide decisions around follow-up schedules and adjuvant treatment, the tools are not sufficiently accurate to be used in isolation. In addition, other factors such as co-morbidities, frailty, patient preferences and quality of life can affect risk, and these are not included in the recommended risk prediction tools. The committee also acknowledged that some groups of people with RCC are at a higher risk of recurrence than others, such as people with heritable RCC predisposition syndromes. They noted that the risk prediction tools in the evidence base have not been developed for or validated in these populations or in people with rarer forms of RCC and so there is more uncertainty about the accuracy of these tools in these populations. The committee therefore recommended that the risk prediction tools are not used in isolation and should be used alongside clinician judgement to inform decisions on management and follow-up.

The committee noted that the risk tools examined in this review were developed and validated using data from people who had undergone nephrectomy to remove the primary tumour, and most of the prognostic factors included in the prognostic models would be based on characteristics from a surgical specimen. The committee agreed that risk prediction tools could possibly be used where pathology information is only available from biopsy samples, for example, in people who have received thermal ablation or stereotactic ablative radiotherapy (SABR). However, they agreed that it was important to highlight that using pathology from biopsy samples is likely to be less reliable and accurate than surgical samples, and that this should be considered in the holistic assessment. No evidence was identified for risk prediction models for people who have not had surgery of the primary tumour, and the committee made a research recommendation to address the gap in the evidence. This was intended to promote the development of tools or identification of biomarkers and factors to predict the risk of recurrence for people who have had thermal ablation or SABR. The committee also made another research recommendation to cover prediction of the risk of progression, metastasis, or both of localised renal cell carcinoma (RCC) in people who are undergoing active surveillance because this group of people was also not covered by the existing risk prediction tools.

The committee highlighted that people may have more than one renal tumour, especially when they have a heritable RCC predisposition syndrome. In these cases, the committee recommended that the follow-up schedule is guided by risk score of the tumour with the highest risk of recurrence to ensure that people have adequate follow-up.

The committee were aware that in some cases technology appraisals (TAs) or NHS clinical commissioning criteria used specific risk prediction tools or scores such as TNM to help identify people who are eligible for adjuvant treatment with a particular drug. To future proof the guideline the committee recommended that where this happens the relevant tool should be used in addition to the recommended tools for clear cell RCC or papillary RCC.

The committee identified that there is some variation in practice around which data are routinely available in pathology reports, and that in some places the results of certain risk prediction tools reported in them. They also noted that some of the scores require additional clinical information before they can be calculated. To make it easier for the MDT to make faster follow up and treatment decisions the committee recommended that the pathology report contains all the pathology information needed to calculate the risk scores that have been chosen by the local MDTs. They also recommended that the pathology department should consider reporting these scores in the pathology report where possible.

The committee also agreed that it is important to record the risk score in the patient's clinical record before any decisions regarding management are made. They noted that this could improve transparency and facilitate shared decision making as it should prompt discussions about the results of the risk prediction tool with the patient.

The committee discussed what information about risk prediction tools and their uses are routinely shared with the person. They highlighted that there was variation in practice, with some people feeling that they are not receiving enough information around their risk of recurrence or survival and not understanding how the tools are used to help inform decisions about their follow up schedule and adjuvant treatment going forward. The committee agreed that it was important to share information about the type of risk prediction tool being used by name, what it is being used to predict and what the results mean for the individual so they can take part in shared decision making. They made a recommendation to reflect this.

The committee also highlighted the importance of clinicians being able to communicate information about risk to people effectively. They agreed that discussing the information about the risks of recurrence could be complicated and sensitive. They discussed the importance of understanding how best to communicate information for both patients and healthcare professionals. They were aware of existing NICE guidance on patient experience in the adult NHS services and shared decision making that can facilitate these discussions. The relevant sections are enabling patients to actively participate in their care in NICE's guideline on patient experience in adult NHS services, and communicating risks, benefits and consequences in NICE's guideline on shared decision making. Cross references to these guidelines are included in the Information section of the guideline and so were not repeated here.

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.9.1 to 1.9.9 and 3 research recommendations on risk prediction tools for people with localised renal cell carcinoma undergoing active surveillance; risk prediction tools for people with localised or locally advanced renal cell carcinoma having thermal ablation or stereotactic ablative radiotherapy; and risk prediction tools for people with localised or locally advanced chromophobe renal cell carcinoma.

1.1.14 References – included studies

1.1.14.1 Prognostic evidence

Systematic reviews

Usher-Smith, Juliet A, Li, Lanxin, Roberts, Lydia et al. (2022) Risk models for recurrence and survival after kidney cancer: a systematic review. BJU international 130(5): 562-579

Primary studies

An, Huimin, Xu, Le, Chang, Yuan et al. (2015) CXC chemokine receptor 2 is associated with postoperative recurrence and survival of patients with non-metastatic clear-cell renal cell carcinoma. European journal of cancer (Oxford, England : 1990) 51(14): 1953-61

Baykal, Serdar, Yilmaz, Hasan, Cinar, Naci Burak et al. (2025) The pan-immune-inflammation value: A novel independent predictive factor for overall survival in >=pT2a nonmetastatic renal cell carcinoma. Urologic oncology

Beisland, Christian, Gudbrandsdottir, Gigja, Reisaeter, Lars A R et al. (2015) Contemporary external validation of the Leibovich model for prediction of progression after radical surgery for clear cell renal cell carcinoma. Scandinavian journal of urology 49(3): 205-10

Buti, Sebastiano, Karakiewicz, Pierre I, Bersanelli, Melissa et al. (2019) Validation of the GRade, Age, Nodes and Tumor (GRANT) score within the Surveillance Epidemiology and End Results (SEER) database: A new tool to predict survival in surgically treated renal cell carcinoma patients. Scientific reports 9(1): 13218

Capogrosso, P., Larcher, A., Sjoberg, D.D. et al. (2018) Risk Based Surveillance after Surgical Treatment of Renal Cell Carcinoma. Journal of Urology 200(1): 61-67

Cindolo, Luca, Patard, Jean-Jacques, Chiodini, Paolo et al. (2005) Comparison of predictive accuracy of four prognostic models for nonmetastatic renal cell carcinoma after nephrectomy: a multicenter European study. Cancer 104(7): 1362-71

Correa, Andres F, Jegede, Opeyemi, Haas, Naomi B et al. (2019) Predicting Renal Cancer Recurrence: Defining Limitations of Existing Prognostic Models With Prospective Trial-Based Validation. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 37(23): 2062-2071

Cortellini, Alessio, Buti, Sebastiano, Bersanelli, Melissa et al. (2020) Predictive Ability for Disease-Free Survival of the GRade, Age, Nodes, and Tumor (GRANT) Score in Patients with Resected Renal Cell Carcinoma. Current urology 14(2): 98-104

Erdem, Selcuk, Capitanio, Umberto, Campi, Riccardo et al. (2022) External validation of the VENUSS prognostic model to predict recurrence after surgery in non-metastatic papillary renal cell carcinoma: A multi-institutional analysis. Urologic oncology 40(5): 198e9-198e17

Flippot, Ronan, Mouawad, Roger, Spano, Jean-Philippe et al. (2017) Expression of long non-coding RNA MFI2-AS1 is a strong predictor of recurrence in sporadic localized clear-cell renal cell carcinoma. Scientific reports 7(1): 8540

Fu, Qiang; Chang, Yuan; An, Huimin; Fu, Hangcheng; Zhu, Yu; Xu, Le; Zhang, Weijuan; Xu, Jiejie; (2015) Prognostic value of interleukin-6 and interleukin-6 receptor in organ-confined clear-cell renal cell carcinoma: a 5-year conditional cancer-specific survival analysis.; British journal of cancer; vol. 113 (no. 11); 1581-9

Fu, Qiang, Chang, Yuan, Zhou, Lin et al. (2016) Positive intratumoral chemokine (C-C motif) receptor 8 expression predicts high recurrence risk of post-operation clear-cell renal cell carcinoma patients. Oncotarget 7(7): 8413-21

Haddad, Ahmed Q, Luo, Jun-Hang, Krabbe, Laura-Maria et al. (2017) Prognostic value of tissue-based biomarker signature in clear cell renal cell carcinoma. BJU international 119(5): 741-747

Han, KR Bleumer, I Pantuck, AJ Kim, HL Dorey, FJ Janzen, NK Zisman, A Dinney, CP Wood, CG Swanson, DA Said, JW Figlin, RA Mulders, PFA Belldegrun, AS; (2003) Validation of an integrated staging system toward improved prognostication of patients with localized renal cell carcinoma in an international population; JOURNAL OF UROLOGY; vol. 170 (no. 6); 2221 – 2224

He, Z; Deng, T; Duan, X; Zeng, G; (2020) Profiles of overall survival-related gene expression-based risk signature and their prognostic implications in clear cell renal cell carcinoma.; Bioscience reports; vol. 40 (no. 9)

Hu, Xu, Yang, Zhi-Qiang, Dou, Wei-Chao et al. (2020) Validation of the Prognostic Value of Preoperative Albumin-to-Alkaline Phosphatase Ratio in Patients with Surgically Treated Non-Metastatic Renal Cell Carcinoma. OncoTargets and therapy 13: 8287-8297

Huang, H., Chen, S., Yu, W. et al. (2017) The association between renal sinus fat area and the progressionfree survival in Chinese non-metastatic clear-cell renal cell carcinoma patients. Oncotarget 8(39): 65481-65491

Hupertan, Vincent; Roupret, Morgan; Poisson, Jean-Francois; Chretien, Yves; Dufour, Bertrand; Thiounn, Nicolas; Mejean, Arnaud; (2006) Low predictive accuracy of the Kattan postoperative nomogram for renal cell carcinoma recurrence in a population of French patients.; Cancer; vol. 107 (no. 11); 2604-8

Hutterer, Georg C, Posch, Florian, Buser, Lorenz et al. (2019) BioScore (B7-H1, survivin, and Ki-67) does not predict cancer-specific mortality in surgically treated patients with renal cell carcinoma: An external validation study. Urologic oncology 37(7): 510-518

Hutterer, Georg C, Stoeckigt, Caroline, Stojakovic, Tatjana et al. (2014) Low preoperative lymphocyte-monocyte ratio (LMR) represents a potentially poor prognostic factor in nonmetastatic clear cell renal cell carcinoma. Urologic oncology 32(7): 1041-8

Ishiyama, Yudai, Kondo, Tsunenori, Yoshida, Kazuhiko et al. (2024) Prognostic Value of the Lung Immune Prognostic Index on Recurrence after Radical Surgery for High-Risk Renal Cell Carcinoma. Cancers 16(4)

Kang, Xiangpeng, Shi, Hongzhe, Wang, Dong et al. (2020) Combination of Hematology Indicators and Oncological Characteristics as a New Promising Prognostic Factor in Localized Clear Cell Renal Cell Carcinoma. Cancer management and research 12: 10023-10033

Klatte, T; Seligson, DB; LaRochelle, J; Shuch, B; Said, JW; Riggs, SB; Zomorodian, N; Kabbinavar, FF; Pantuck, AJ; Belldegrun, AS; (2009) Molecular signatures of localized clear cell renal cell carcinoma to predict disease-free survival after nephrectomy.; Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology; vol. 18 (no. 3); 894-900

Klatte, Tobias, Gallagher, Kevin M, Afferi, Luca et al. (2019) The VENUSS prognostic model to predict disease recurrence following surgery for non-metastatic papillary renal cell carcinoma: development and evaluation using the ASSURE prospective clinical trial cohort. BMC medicine 17(1): 182

Kroeger, Nils, Lebacle, Cedric, Hein, Justine et al. (2022) Pathological and genetic markers improve recurrence prognostication with the University of California Los Angeles Integrated Staging System for patients with clear cell renal cell carcinoma. European journal of cancer (Oxford, England : 1990) 168: 68-76

Lee, Byron H.; Feifer, Andrew; Feuerstein, Michael; Benfante, Nicole; Kou, Lei; Yu, Changhong; Kattan, Michael W.; Russo, Paul; (2018) Validation of a Postoperative Nomogram Predicting Recurrence in Patients with Conventional Clear Cell Renal Cell Carcinoma; European urology focus; vol. 4 (no. 1); 100-105

Lee, Han Jie, Lee, Alvin, Huang, Hong Hong et al. (2019) External validation of the updated Leibovich prognostic models for clear cell and papillary renal cell carcinoma in an Asian population. Urologic oncology 37(6): 356e9-356e18

Li, Xiaoxia, Zhang, Shaoting, Huang, Xiaolan et al. (2024) Development of a CT-assessed adiposity nomogram for predicting outcome in localized ccRCC. Abdominal radiology (New York)

Liu, Zheng, Lv, Jiaju, Ding, Kejia et al. (2009) Validation of the current prognostic models for nonmetastatic renal cell carcinoma after nephrectomy in Chinese population: a 15-year single center experience. International journal of urology : official journal of the Japanese Urological Association 16(3): 268-73

Liu, W.; Liu, Y.; Fu, Q.; Zhou, L.; Chang, Y.; Xu, L.; Zhang, W.; Xu, J.; (2016) Elevated expression of IFN-inducible CXCR3 ligands predicts poor prognosis in patients with non-metastatic clear-cell renal cell carcinoma; Oncotarget; vol. 7 (no. 12); 13976-13983

Lucca, Ilaria, de Martino, Michela, Hofbauer, Sebastian L et al. (2015) Comparison of the prognostic value of pretreatment measurements of systemic inflammatory response in patients undergoing curative resection of clear cell renal cell carcinoma. World journal of urology 33(12): 2045-52

Morgan, Todd M, Mehra, Rohit, Tiemeny, Placede et al. (2018) A Multigene Signature Based on Cell Cycle Proliferation Improves Prediction of Mortality Within 5 Yr of Radical Nephrectomy for Renal Cell Carcinoma. European urology 73(5): 763-769

Na, N., Si, T., Huang, Z. et al. (2016) High expression of HMGAGA2 predicts poor survival in patients with clear cell renal cell carcinoma. OncoTargets and Therapy 9: 7199-7205

Nie, Pei, Yang, Guangjie, Wang, Yanmei et al. (2023) A CT-based deep learning radiomics nomogram outperforms the existing prognostic models for outcome

prediction in clear cell renal cell carcinoma: a multicenter study. European radiology 33(12): 8858-8868

Oza, Bhavna, Eisen, Tim, Frangou, Eleni et al. (2022) External Validation of the 2003 Leibovich Prognostic Score in Patients Randomly Assigned to SORCE, an International Phase III Trial of Adjuvant Sorafenib in Renal Cell Cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 40(16): 1772-1782

Piccinelli, Mattia L, Tappero, Stefano, Cano Garcia, Cristina et al. (2023) Assessment of the VENUSS and GRANT Models for Individual Prediction of Cancer-specific Survival in Surgically Treated Nonmetastatic Papillary Renal Cell Carcinoma. European urology open science 53: 109-115

Piccinelli, Mattia Luca, Morra, Simone, Tappero, Stefano et al. (2023) Critical Appraisal of Leibovich 2018 and GRANT Models for Prediction of Cancer-Specific Survival in Non-Metastatic Chromophobe Renal Cell Carcinoma. Cancers 15(7)

Pichler, Martin, Hutterer, Georg C, Chromecki, Thomas F et al. (2011) External validation of the Leibovich prognosis score for nonmetastatic clear cell renal cell carcinoma at a single European center applying routine pathology. The Journal of urology 186(5): 1773-7

Rini, Brian, Goddard, Audrey, Knezevic, Dejan et al. (2015) A 16-gene assay to predict recurrence after surgery in localised renal cell carcinoma: development and validation studies. The Lancet. Oncology 16(6): 676-85

Schmeusser, Benjamin N, Patil, Dattatraya H, Nicaise, Edouard H et al. (2024) 2018 Leibovich prognostic model for renal cell carcinoma: Performance in a large population with special consideration of Black race. Cancer 130(3): 453-466

Seles, Maximilian, Posch, Florian, Pichler, Georg P et al. (2017) Blood Platelet Volume Represents a Novel Prognostic Factor in Patients with Nonmetastatic Renal Cell Carcinoma and Improves the Predictive Ability of Established Prognostic Scores. The Journal of urology 198(6): 1247-1252

Shao, Yanxiang, Xiong, Sanchao, Sun, Guangxi et al. (2020) Prognostic analysis of postoperative clinically nonmetastatic renal cell carcinoma. Cancer medicine 9(3): 959-970

Sorbellini, Maximiliano, Kattan, Michael W, Snyder, Mark E et al. (2005) A postoperative prognostic nomogram predicting recurrence for patients with conventional clear cell renal cell carcinoma. The Journal of urology 173(1): 48-51

Suzuki, Kazuya; Nishiyama, Tsutomu; Hara, Noboru; Akazawa, Kohei; Takahashi, Kota; (2011) Kattan postoperative nomogram for renal cell carcinoma: predictive accuracy in a Japanese population.; International journal of urology : official journal of the Japanese Urological Association; vol. 18 (no. 3); 194-9

Tan, Min-Han, Kanesvaran, Ravindran, Li, Huihua et al. (2010) Comparison of the UCLA Integrated Staging System and the Leibovich score in survival prediction for patients with nonmetastatic clear cell renal cell carcinoma. Urology 75(6): 1365-3

Tan, Min-Han, Li, Huihua, Choong, Caroline Victoria et al. (2011) The Karakiewicz nomogram is the most useful clinical predictor for survival outcomes in patients with localized renal cell carcinoma. Cancer 117(23): 5314-24

Tsujino, Takuya; Komura, Kazumasa; Ichihashi, Atsushi; Tsutsumi, Takeshi; Matsunaga, Tomohisa; Yoshikawa, Yuki; Maenosono, Ryoichi; Okita, Kyohei; Takai, Tomoaki; Oide, Rintaro; Minami, Koichiro; Uehara, Hirofumi; Taniguchi, Kohei; Hirano, Hajime; Nomi, Hayahito; Ibuki, Naokazu; Takahara, Kiyoshi; Inamoto, Teruo; Azuma, Haruhito; The combination of preoperative platelet count and neutrophil lymphocyte ratio as a prognostic indicator in localized renal cell carcinoma.; Oncotarget; 2017; vol. 8 (no. 66); 110311-110325

Tsujino, Takuya; Komura, Kazumasa; Matsunaga, Tomohisa; Yoshikawa, Yuki; Takai, Tomoaki; Uchimoto, Taizo; Saito, Kenkichi; Tanda, Naoki; Oide, Rintaro; Minami, Koichiro; Uehara, Hirofumi; Jeong, Seong Ho; Taniguchi, Kohei; Hirano, Hajime; Nomi, Hayahito; Ibuki, Naokazu; Takahara, Kiyoshi; Inamoto, Teruo; Azuma, Haruhito; Preoperative Measurement of the Modified Glasgow Prognostic Score Predicts Patient Survival in Non-Metastatic Renal Cell Carcinoma Prior to Nephrectomy; Annals of surgical oncology; 2017; vol. 24 (no. 9); 2787-2793

Tsujino, Takuya; Komura, Kazumasa; Hashimoto, Takeshi; Muraoka, Ryu; Satake, Naoya; Matsunaga, Tomohisa; Tsutsumi, Takeshi; Yoshikawa, Yuki; Takai, Tomoaki; Minami, Koichiro; Uehara, Hirofumi; Hirano, Hajime; Nomi, Hayahito; Ibuki, Naokazu; Takahara, Kiyoshi; Inamoto, Teruo; Ohno, Yoshio; Azuma, Haruhito; C-reactive protein-albumin ratio as a prognostic factor in renal cell carcinoma - A data from multi-institutional study in Japan.; Urologic oncology; 2019; vol. 37 (no. 11); 812e1-812e8

Um, In Hwa, Scott-Hayward, Lindesay, Mackenzie, Monique et al. (2020) Computerized Image Analysis of Tumor Cell Nuclear Morphology Can Improve Patient Selection for Clinical Trials in Localized Clear Cell Renal Cell Carcinoma. Journal of pathology informatics 11: 35

Utsumi, Takanobu; Ueda, Takeshi; Fukasawa, Satoshi; Komaru, Atsushi; Sazuka, Tomokazu; Kawamura, Koji; Imamoto, Takashi; Nihei, Naoki; Suzuki, Hiroyoshi; Ichikawa, Tomohiko; Prognostic models for renal cell carcinoma recurrence: external validation in a Japanese population.; International journal of urology : official journal of the Japanese Urological Association; 2011; vol. 18 (no. 9); 667-671

Vasudev, Naveen S, Hutchinson, Michelle, Trainor, Sebastian et al. (2020) UK Multicenter Prospective Evaluation of the Leibovich Score in Localized Renal Cell Carcinoma: Performance has Altered Over Time. Urology 136: 162-168

Viers, Boyd R.; Thompson, Robert Houston; Boorjian, Stephen A.; Lohse, Christine M.; Leibovich, Bradley C.; Tollefson, Matthew K.; Preoperative neutrophil-lymphocyte ratio predicts death among patients with localized clear cell renal carcinoma undergoing nephrectomy; Urologic oncology; 2014; vol. 32 (no. 8); 1277-1284

Wang, Chao, Dong, Kegin, Wang, Yuning et al. (2021) Integrating HECW1 expression into the clinical indicators exhibits high accuracy in assessing the prognosis of patients with clear cell renal cell carcinoma. BMC cancer 21(1): 890

Wang, Chao, Hong, TianYu, Wang, Yuning et al. (2021) Combining UBR5 and CD163+ tumor-associated macrophages better predicts prognosis of clear cell renal cell carcinoma patients. Cancer immunology, immunotherapy : CII 70(10): 2925-2935

Wen, Hongzhuang; Zhang, Yong; Yang, Zhan; Zhai, Zhao; Han, Zhenwei; Wang, Hu; Wang, Mingshuai; Shi, Hongzhe; Chen, Xi; Wahafu, Wasilijiang; Guan, Kaopeng; Wang, Xiaolu; The LMR-SSIGN-MAPS model predicts disease-free survival in

patients with localized clear cell renal cell carcinoma.; Wideochirurgia i inne techniki maloinwazyjne = Videosurgery and other miniinvasive techniques; 2023; vol. 18 (no. 2); 313-327

Xia, Yu; Liu, Li; Bai, Qi; Wang, Jiajun; Xi, Wei; Qu, Yang; Xiong, Ying; Long, Qilai; Xu, Jiejie; Guo, Jianming; Dectin-1 predicts adverse postoperative prognosis of patients with clear cell renal cell carcinoma.; Scientific reports; 2016; vol. 6; 32657

Xiao, Ruotao, Xu, Chuxiao, He, Wei et al. (2021) Preoperative anaemia and thrombocytosis predict adverse prognosis in non-metastatic renal cell carcinoma with tumour thrombus. BMC urology 21(1): 31

Xv, Yingjie, Wei, Zongjie, Jiang, Qing et al. (2024) Three-Dimensional (3D) deep learning model complements existing models for preoperative disease-free survival prediction (DFS) in localized clear cell renal cell carcinoma (ccRCC): A multicenter retrospective cohort study. International journal of surgery (London, England)

Yang, Guangjie, Nie, Pei, Yan, Lei et al. (2022) The radiomics-based tumor heterogeneity adds incremental value to the existing prognostic models for predicting outcome in localized clear cell renal cell carcinoma: a multicenter study. European journal of nuclear medicine and molecular imaging 49(8): 2949-2959

Zhang, Haijian, Liu, Yidong, Xie, Huyang et al. (2017) Beta-1,4-galactosyltransferase II predicts poor prognosis of patients with non-metastatic clear-cell renal cell carcinoma. Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine 39(2): 1010428317691417

Zhu, D., Shi, X., Gao, S. et al. (2021) RNF43 is a novel tumor-suppressor and prognostic indicator in clear cell renal cell carcinoma. Oncology Research 29(3): 159-174

Zhu, Yan, Zhao, Yao-Rui, Yang, Xian-Fa et al. (2019) Postoperative prognostic model for patients with clear cell renal cell carcinoma in a Chinese population. International journal of urology : official journal of the Japanese Urological Association 26(6): 624-629

Zhu, Pingyi, Dai, Chenchen, Xiong, Ying et al. (2024) Tumor contour irregularity on preoperative CT predicts prognosis in renal cell carcinoma: a multi-institutional study. EClinicalMedicine 75: 102775

1.1.14.2 Economic

No evidence was identified.

Appendices

Appendix A – Review protocols

Prognostic review protocol (protocol for reviews K and L)

ID	Field	Content
1.	Review title	Prognostic models to predict survival and/ or recurrence in adults with suspected or confirmed renal cell carcinoma (RCC).
2.	Review question	In adults with suspected or confirmed renal cell carcinoma, which validated prognostic models are most effective at predicting survival and/or recurrence?
3.	Objective	To evaluate and compare the ability of validated prognostic models to predict survival and/or recurrence in adults with suspected or confirmed RCC to help inform decisions about management options.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos For the economics review the following databases will be searched: • Embase • MEDLINE • Medline in Process • Medline EPub Ahead of Print • Econlit • HTA (legacy records) • NHS EED (legacy records) • INAHTA Searches will be restricted by: • Date limitations: None • English language • Human studies • Abstracts, conference presentations and theses will be excluded The full search strategies will be published in the final review.
5.	Condition or domain being studied	Suspected or confirmed renal cell carcinoma
6.	Population	• Adults (18 years or over) with suspected or confirmed RCC Suspected RCC refers to cases where there are diagnostic findings on CT or MRI suggestive of RCC but where a definitive diagnosis has not yet been made. Confirmed RCC refers to definitive diagnosis according to the clinical or pathological TNM staging and WHO subtyping classification,

		through histopathological examination of tissue samples obtained from biopsy or surgery.

7.	Predictor (Predictive prognostic model or score)	Validated prognostic models from the lists below. Validated models and scores may be augmented and further validated by additional individual factors.
		
		Localised or locally advanced RCC
		Post-first line treatment prognostic models to predict survival or recurrence outcomes:
		• GRANT
		• Karakiewicz
		• Kattan
		• Leibovich 2003
		• Leibovich 2018
		• Sorbellini
		• SSIGN
		• UISS
		• VENUSS
		• Zisman
		
		Prognostic models as above augmented with one or more additional scores (scores of interest are listed in review 2cii and below). Studies will be included if there is subsequent validation of the augmented model.
		
		For comparison (not a prognostic model):
		2016 version of the TNM classification (based on pathology post-surgery TNM and for prognostic assessment of survival outcomes, not initial classification and staging. Does not include clinical TNM, which is used before surgery.)
		
		Metastatic RCC pre- and post-first line treatment prognostic models:
		• IMDC
		• Meet-URO
		• MSKCC
		Prognostic models augmented with one or more additional scores. Scores of interest are listed in protocol 2cii on risk scores and below)
		
		• Exclusion: Molecular and radiomic factors will not be included for prognostic assessment at any stage because there are no known fully validated scores or models in these areas, they are not used in clinical practice routinely and the evidence base remains investigational.
		
		Scores of interest:
		• Clinical performance status (for predicting surgical and survival outcomes):
		  ○ ECOG
		
		• Patient factors (for predicting surgical and survival outcomes:
		  • Charlson comorbidity index
		  • Clinical frailty scale

8.	Types of study to be included	The following types of studies will be included in the review, restricted to those reporting: • Prospective and retrospective cohort studies, (specifically validation studies of models or derivation studies that also include independent validation data) • Systematic reviews of these studies Where good quality systematic reviews are identified, these may be used completely or as a source of references, depending on applicability. A recent systematic review (search date 12/12/2019) has been identified which will be considered for use in the analysis of post-treatment prognostic models, with a supplementary search for additional subsequent studies: Usher-Smith JA, Li L, Roberts L, Harrison H, Rossi SH, Sharp SJ, Coupland C, Hippisley-Cox J, Griffin SJ, Klatte T, Stewart GD. Risk models for recurrence and survival after kidney cancer: a systematic review. BJU Int. 2022 Nov;130(5):562-579.
9.	Other exclusion criteria	• Abstracts, conference presentations and theses • Non-human studies • Non-English language studies • Model derivation studies that do not contain any validation data.
10.	Context	There is currently no national guideline in the UK on the diagnosis and treatment of kidney cancer and audit data indicates variation in the clinical practice within NHS. Stakeholders identified this gap and NICE was commissioned to develop a guideline on kidney cancer by NHSE. Prognostic factors play a crucial role in the initial assessment of a patient's prognosis, in counselling patients, guiding treatment decisions, informing individualised surveillance protocols and in the design and recruitment of clinical trials. Therefore, this review aims to evaluate and compare the accuracy of individual or combined prognostic factors expressed as validated models or scores in adults with suspected or confirmed RCC to predict survival and recurrence outcomes. This information will help inform suitable management options.
11.	Outcomes to be predicted	**Outcomes predicted by prognostic models at the non-metastatic post-treatment stage:** • Progression free survival • Recurrence free survival • Disease-free survival, including cancer-free survival Some studies may report disease-free survival as recurrence free survival, local recurrence, or distant metastases. These will be extracted as proxy outcomes where survival data is not reported in the studies. • Overall survival • Cancer specific survival **Outcomes predicted by prognostic models at metastatic pre- and post-treatment stages:** • Overall survival • Progression free survival

12.	Outcome measures	For each outcome, prognostic accuracy measures will be reported where available, for example: • Odds ratios/hazard ratios/ risk ratios • Model fit statistics (for example R^2, Brier score) • Discrimination (for example C statistic, area under ROC curve, sensitivity and specificity and likelihood ratios). • Calibration (for example calibration slope) Where OR/RR and c-statistic data is reported at multiple time points then data will be pooled across studies for the timepoint closest to that in the model derivation paper/ time the model is used to predict outcomes for in practice (we expect that these will be the same). We will also extract data for the latest timepoint available and analyse this separately.
13.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow.
14.	Risk of bias (quality) assessment	Risk of bias of individual studies will be assessed using the preferred checklist as described in Developing NICE guidelines: the manual: PROBAST checklist for prognostic studies ROBIS for systematic reviews of prediction models
15.	Strategy for data synthesis	Where possible, meta-analyses will be conducted to combine the results of studies for each outcome. Hazard ratio and odds ratio outcome measures Where appropriate, hazard ratios will be pooled using the generic inverse-variance method. Adjusted odds ratios, hazard ratios and risk ratios from multivariate models will only be pooled if the same set of factors are used across multiple studies and if the same thresholds to measure factors were used across studies. Fixed- and random-effects models (der Simonian and Laird) will be fitted for all outcomes, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models will be deemed to be inappropriate if one or both of the following conditions are met: • Significant between-study heterogeneity in methodology, population, predictors, or comparator was identified by the reviewer in advance of data analysis. • The presence of significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$. Prognostic test accuracy outcome measures Where five or more studies were available that reported data in a 2x2 format (or that could be manipulated to derive this information) a bivariate model will be fitted using the mada package in R v3.4.0, which accounts for the correlations between positive and negative

		likelihood ratios, and between sensitivities and specificities. Where sufficient data is not available (2-4 studies), separate independent pooling will be performed for positive likelihood ratios, negative likelihood ratios, sensitivity and specificity.
		
		Meta-analysis of c-statistics will be considered when the same prognostic models have been evaluated across multiple studies. Meta-analyses of c statistics will be carried out using the metamisc package in R v4.2.3, which confines the analysis results to between 0 and 1 matching the limited range of values that c-statistics can take.
		
		A modified version of GRADE will be used to assess the quality of the outcomes. All outcomes in this review which come from validated cohort studies and systematic reviews will be rated as high quality initially and downgraded from this point.
		
		GRADE will be carried out at the level of likelihood ratios with LR+ being downgraded for imprecision if the 95%CI cross 1 or 2. For LR- the results will be downgraded if the 95% CI crosses 0.5 or 1. For c-statistics the result will be downgraded once for imprecision if the 95% CI crosses 2 categories of test classification accuracy (see thresholds below) and twice if it crosses 3 or more categories.
		
		Decision making thresholds for HR/OR data
		To assess imprecision, where there are no defined minimally important differences (MIDs) we will set the MID as the line of no effect for all outcomes (1.0 for dichotomous outcomes and 0 for continuous outcomes). (The second downgrade for imprecision will be based on sample size.)
		
		Decision making thresholds for prediction test accuracy data
		We will use the thresholds from Evidence Based Emergency Medicine; Part 5 Receiver Operating Curve and Area under the Curve to classify the c-statistics. According to this AUC can be interpreted as follows: 90 -100 = excellent; 80 - 90 = good; 70 - 80 = fair; 60 - 70 = poor; 50 - 60 = fail.
		
		Decision making thresholds (for likelihood ratios [LR])
		• For positive likelihood ratios:
		  • Potentially useful model LR ≥ 2.0 (with higher better)
		  • Not a useful model 1 < LR < 2.0
		
		• For negative likelihood ratios:
		  • Useful model LR ≤ 0.5 (lower better)
		  • Not a useful model 0.5 < LR ≤ 1.0

16.	Analysis of sub-groups	RCC subtypes, for example, clear cell RCC, papillary RCC.
17.	Type and method of review	X Intervention Diagnostic Prognostic Qualitative Epidemiologic Service Delivery Other (please specify)

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<tr><td>Preliminary searches</td><td></td><td>X</td></tr>
<tr><td>Piloting of the study selection process</td><td></td><td>X</td></tr>
<tr><td>Formal screening of search results against eligibility criteria</td><td></td><td>X</td></tr>
<tr><td>Data extraction</td><td></td><td>X</td></tr>
<tr><td>Risk of bias (quality) assessment</td><td></td><td>X</td></tr>
<tr><td>Data analysis</td><td></td><td>X</td></tr>
<tr><td>23.</td><td>Named contact</td><td colspan="3">5a. Named contact
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5e Organisational affiliation of the review
National Institute for Health and Care Excellence (NICE) and Guideline Development Team.</td></tr>
<tr><td>24.</td><td>Review team members</td><td colspan="3">From the Guideline Development Team:
Steve Sharp, Technical adviser
Marie Harrisingh, Technical adviser
Sarah Boyce, Senior technical analyst
Fernando Zanghelini, Technical analyst
Olivia Crane, Technical analyst
Lindsay Claxton, Health economics adviser
Hannah Tebbs, Senior Health economist
Yuanyuan Zhang, Health economist
Amy Finnegan, Senior Information specialist</td></tr>
<tr><td>25.</td><td>Funding sources/sponsor</td><td colspan="3">This systematic review is being completed by the Guideline Development Team which receives funding from NICE.</td></tr>
<tr><td>26.</td><td>Conflicts of interest</td><td colspan="3">All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be 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</td></tr>
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		declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: Kidney Cancer (GID-NG10398).
28.	Other registration details	None
29.	Reference/URL for published protocol	None
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
31.	Keywords	Renal cell carcinoma, prognosis, prognostic scores
32.	Details of existing review of same topic by same authors	Not applicable
33.	Current review status	X Ongoing Completed but not published Completed and published Completed, published and being updated Discontinued
34.	Additional information	None
35.	Details of final publication	www.nice.org.uk

Economic review protocol

ID	Field	Content
1.	Review title	K: Cost effectiveness of prognostic models to predict survival and/ or recurrence in adults with suspected or confirmed localised or locally advanced renal cell carcinoma L: Cost effectiveness of prognostic models to predict survival and/ or recurrence in adults with suspected or confirmed metastatic renal cell carcinoma
2.	Objective	To identify economic studies for the review of prognostic models to predict survival and/or recurrence in adults with suspected or confirmed RCC

3.	Inclusion criteria	• Populations, interventions and comparators as specified in the prognostic review protocol. • Relevant comparative economic study design: cost–utility analysis • Decision analytic model-based or within-trial economic analyses • OECD countries (except USA) • Healthcare and personal social services cost perspective • Studies published from 2010 – this cut off has been applied to restrict the review to more recent studies which will have more applicable resource use and costs High-quality studies in line with the NICE reference case (recent UK NHS/PSS cost-utility analyses using the QALY as the measure of outcome) are the most applicable to NICE decision making.
4.	Exclusion criteria	• Conference posters or abstract only studies – these do not provide sufficient information for quality assessment. • Studies published before 2010 – this cut off has been applied to restrict the review to more recent studies which will have more applicable resource use and costs • Studies from non-OECD countries or the USA – these are considered unlikely to be applicable to the UK NHS setting due to substantial differences in healthcare delivery and unit costs. • Non-comparative economic analyses including cost-of-illness studies. • Letters, editorials or commentaries, study protocols or reviews of economic evaluations (recent reviews will be ordered and the bibliographies will be checked for relevant individual economic studies, which will then be ordered and checked for eligibility). • Non-English language papers. • Studies considering exclusively intervention costs, e.g. medicine acquisition costs, without considering wider healthcare costs associated with the management of RCC. • Studies only focussing on productivity losses or gains.
5.	Search strategy	An economic study search will be undertaken using question-specific terms and an economic study filter. For search details see appendix B below. The following databases will be searched: • MEDLINE All, Ovid • Embase, Ovid • International HTA database, International Network of Agencies for Health Technology Assessment (INAHTA) • EconLit • EED and HTA (legacy records)
6.	Review strategy	• Studies meeting the inclusion and exclusion criteria will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist in appendix H of Developing NICE guidelines: the manual. • The NICE economic evaluation checklist assesses:

		○ Applicability to the NICE guideline decision making context with consideration of the NICE reference case relevant to the guideline. Recent UK studies that use the NICE reference case methods are the most applicable when considering cost effectiveness. ○ Methodological limitations. • The aim is to present the best available economic evidence to inform committee decision-making in the context of the guideline, the current UK NHS setting and NICE methods. Therefore, the health economist may not present all studies that meet inclusion criteria. If recent high quality, UK cost-utility analyses are available for a question, it is often not deemed informative to present studies that are less applicable or lower quality such as older UK analyses or analyses from other countries. A similar principle is deemed to apply more generally when considering applicability and methodological limitations. Some specific examples are given below: ○ If multiple versions of a model are available for the UK and other countries it is usually reasonable to only present the UK version. ○ If multiple versions of the same UK model are available, it is usually reasonable to present only the most recent. ○ If there has been a NICE MTA or guideline model that informs current NHS practice it is usually reasonable not to present older studies, unless they address a different subpopulation or other specific issue. ○ If a UK model that includes all interventions in the decision space is available it may be reasonable not to present studies that only include individual or fewer interventions, if the analysis is sufficiently applicable and of good methodological quality. • Quality and relevance of effectiveness data used in the economic analysis: the more closely the clinical effectiveness data used in the economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. • Hierarchy of economic evaluation evidence based on quality assessment ○ 'Directly applicable' and 'Minor limitations' (only recent UK CUAs can get this rating). Usually presented and used in decision-making. ○ Directly or partially applicable combined with minor or potentially serious limitations (other than 1). Discretion over whether these are presented and used in decision-making, depending on the availability of more relevant evidence. ○ 'Not applicable' or 'Very serious limitations'. Typically not presented and not used in decision-making. The health economist will make a decision based on the relative applicability and quality of the available evidence for each question, in discussion with the guideline committee if required. All decisions will be transparently reported in the evidence report. Studies that are presented to the committee and used in decision-making when formulating recommendations will be included in the summary tables and will have an evidence extraction. Other studies may not be presented to the committee in detail but will be listed, with the reason for not being presented to the committee and thus not used in decision-making being provided. Committee members can review and query the decision not to present studies with the health economist and will be provided with full details of these studies where requested.

Appendix B – Literature search strategies

Background and development

Search design and peer review

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

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

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

Review management

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

Prior work

The search maintained the same condition set as the combined search used for reviews A, B, C, H1 and H2 (review A: surgical interventions for localised RCC, review B: non-surgical interventions for localised RCC, review C: nephrectomy or stereotactic ablative radiotherapy for locally advanced RCC, reviews H1 and H2: non-pharmacological management of advanced RCC).

Nephrectomy was added to the population set for review K (current review) and review L as the question aimed to also include prognostic models that assessed surgical outcomes.

An exploratory search was performed prior to the search for review K (current review) and review L. The exploratory search looked for the names of validated prognostic models. The validated models that passed the question’s inclusion criteria were included in the second set of the search strategy.

The analysts identified 3 test papers prior to the search being developed.

Search limits and other restrictions

Formats

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

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

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

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

Date limits

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

Search filters and classifiers

Clinical searches

Systematic reviews filters:

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

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

Prognostic study filter (sensitive):

Wilczynski, N and Haynes, R. (2004) Developing optimal search strategies for detecting clinically sound prognostic studies in MEDLINE: an analytic survey. BMC Medicine 2

Cost effectiveness searches

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

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

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

Key decisions

10 references, not retrieved by the search, were manually added to the main search results. 2 of the references were identified as being relevant by the committee and 8 of the references were identified through systematic reviews captured by the search. The references that were manually added to the search results were not captured by the search as they did not mention model (intervention) terms or were filtered out of the results by the study filters.

Additional searches were carried out for this topic. A broader search was carried out as the same time as the main search on 16th July 2024. The search looked for any relevant prognostic studies, it was not limited to systematic review or cohort studies. The search was run in Medline ALL (Ovid), Embase (Ovid) and Epistemonikos (Epistemonikos). The main search results were excluded from the strategy using BOOLEAN NOT. The search results were added to a separate EPPI database from the main search results. The results were spot checked for relevancy.

On the 24th September 2024 backwards citations searching was carried out in Web of Science (WoS) across 35 papers after sifting the database searches carried out in July; 26 of the references were identified in forest plots and 9 were missing from the main search. Only those references that could be accessed through the NICE subscription to WOS were added to the search results. Duplicates were removed from the marked list in WOS before downloading the results.

Clinical searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	16/07/2024	Wiley	Issue 7 of 12, July 2024	93
Cochrane Database of Systematic Reviews (CDSR)	16/07/2024	Wiley	Issue 7 of 12, July 2024	0
Embase	16/07/2024	Ovid	1974 to 2024 July 15	2574
Epistemonikos	16/07/2024	Epistemonikos	N/A	190
International Health Technology Assessment Database (INAHTA)	16/07/2024	https://database.inahta.org/	N/A	11
MEDLINE ALL	16/07/2024	Ovid	1946 to July 15, 2024	989

Additional search methods

Databases	Date searched	No. of results downloaded
Medline	16/07/2024	989
Embase	16/07/2024	4151
Epistemonikos	16/07/2024	1507
WoS	24/09/2024	724

Search strategy history

Database name: Cochrane CENTRAL and CDSR

Searches	
#1	MeSH descriptor: [Kidney Neoplasms] explode all trees 1975
#2	MeSH descriptor: [Nephrectomy] explode all trees 585
#3	(Kidney* NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or 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 1427
#4	(collecting-duct* NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)):ti,ab 14
#5	(renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*):ti,ab 3866

Searches
#6 (Kidney* NEAR/2 (Transitional-cell* or cell or urothelial* or duct or advanc*) NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)):ti,ab 69
#7 (nephron* NEAR/2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)):ti,ab 128
#8 nephrectom*:ti,ab 1941
#9 {or #1-#8} 6414
#10 (UISS or karakiewicz or Kattan or leibovich or VENUSS or SSIGN or IMDC or Heng or Sorbellini* or Zisman* or Meet-URO or nephrometry):ti,ab 392
#11 ("UCLA integrated staging system" or "Preoperative Aspects and Dimensions Used for an Anatomical Classification"):ti,ab 6
#12 (("International Metastatic Renal Cell Carcinoma Database Consortium" or "grade age nodes and tumour" or "grade age nodes and tumor" or "Memorial Sloan-Kettering Cancer Center") NEAR/5 (grade* or index* or class* or scale* or model* or score* or scoring*)):ti,ab 6
#13 ((MSKCC or TNM or PADUA or Centrality-index or C-index or GRANT or SPARE) NEAR/3 (classification* or system* or score* or scoring* or staging* or model*)):ti,ab 1094
#14 (("tumour node metastasis" or "tumor node metastasis" or "tumour node metastases" or "tumor node metastases" or "tumour nodes metastases" or "tumor nodes metastases" or "tumour nodes metastasis" or "tumor nodes metastasis") near/5 (classification* or system* or score* or scoring* or staging*)):ti,ab 0
#15 ((ECOG or "Eastern Cooperative Oncology Group" or Karnofsky or ASA or "American Society of Anesthesiologists" or Charlson-comorbidity or clinical-frail* or clinically-frail* or MSKCC or TNM or PADUA or Centrality-index or C-index or WHO or World-health-organisation* or ISUP or "International Society of Urological Pathology" or Fuhrman) NEAR/3 (grade* or index* or class* or scale* or model* or score* or scoring*)):ti,ab 29964
#16 {or #10-#15} 30655
#17 #9 and #16 591
#18 MeSH descriptor: [Incidence] this term only 14390
#19 MeSH descriptor: [Mortality] explode all trees 18908
#20 MeSH descriptor: [Follow-Up Studies] this term only 74910
#21 (prognos* or predict* or course*):ti,ab,kw 240578
#22 {or #18-#21} 316167
#23 #17 and #22 226
#24 #17 and #22 in Cochrane Reviews 0
#25 "conference":pt or (clinicaltrials or trialsearch):so 765632
#26 #23 NOT #25 in Trials 93

Database name: Embase

Searches
1 exp kidney tumor/ or exp nephrectomy/ (216748)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or 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. (26798)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (752)

Searches
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (108685)
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (1229)
6 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (4946)
7 nephrectom*.ti,ab. (64450)
8 or/1-7 (252846)
9 (UISS or karakiewicz or Kattan or leibovich or VENUSS or SSIGN or IMDC or Heng or Sorbellini* or Zisman* or Meet-URO or nephrometry).ti,ab. (5037)
10 ("UCLA integrated staging system" or "Preoperative Aspects and Dimensions Used for an Anatomical Classification").ti,ab. (81)
11 (("International Metastatic Renal Cell Carcinoma Database Consortium" or "grade age nodes and tumo?r" or "Memorial Sloan-Kettering Cancer Center") adj5 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (534)
12 ((MSKCC or TNM or PADUA or Centrality-index or C-index or GRANT or SPARE) adj3 (classification* or system* or score* or scoring* or staging* or model*)).ti,ab. (22950)
13 ("tumo?r node* metastas*" adj5 (classification* or system* or score* or scoring* or staging*)).ti,ab. (2748)
14 ((ECOG or "Eastern Cooperative Oncology Group" or Karnofsky or ASA or "American Society of Anesthesiologists" or Charlson-comorbidity or clinical*-frail* or MSKCC or TNM or PADUA or Centrality-index or C-index or WHO or World-health-organisation* or ISUP or "International Society of Urological Pathology" or Fuhrman) adj3 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (185750)
15 or/9-14 (200434)
16 8 and 15 (11887)
17 incidence.sh. (618107)
18 exp mortality/ (1454260)
19 follow-up studies.sh. (107)
20 prognos:.tw. (1276643)
21 predict:.tw. (2948385)
22 course:.tw. (1028156)
23 or/17-22 (6207241)
24 Cohort analysis/ or cohort.tw. or validat*.tw. (2770940)
25 (MEDLINE or pubmed).tw. (453291)
26 exp systematic review/ or systematic review.tw. (563805)
27 meta-analysis/ (321939)
28 intervention$.ti. (285171)
29 or/24-28 (3711136)
30 16 and 23 and 29 (2628)
31 nonhuman/ not human/ (5484164)
32 30 not 31 (2612)
33 limit 32 to english language (2576)
34 ("clinical conference" or congress* or overall* or consensus*).pt. or (conference* or proceeding*).jn. or (conference* not (video* or conference-call* or case* or charter* or declaration* or treaty* or treaties)).ti. (279084)
35 33 not 34 (2574)

Searches
36 16 and 23 (6993)
37 nonhuman/ not human/ (5484164)
38 36 not 37 (6971)
39 limit 38 to english language (6731)
40 ("clinical conference" or congress* or overall* or consensus*).pt. or (conference* or proceeding*).jn. or (conference* not (video* or conference-call* or case* or charter* or declaration* or treaty* or treaties)).ti. (279084)
41 39 not 40 (6725)
42 41 not 35 (4151)

Database name: Epistemonikos

Searches
(title:((Kidney* AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma* OR 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* OR "collecting duct*") AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma* OR stage-4)) OR (renal-cell* OR "renal cell*" OR RCC OR ccRCC OR Renal-mass* OR "Renal mass*" OR renal-tumor* OR renal-tumour* OR "renal tumor*" OR "renal tumour*" OR grawitz-tumor* OR grawitz-tumour* OR "grawitz tumor*" OR "grawitz tumour*" OR hypernephroma* OR nephrocarcinoma*) OR (Kidney* AND (Transitional-cell* OR "Transitional cell*" OR cell OR urothelial* OR duct OR advanc*) AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*)) OR (nephron* AND (surg* OR remov* OR partial* OR procedur* OR treat* OR operat* OR spar* OR preserv*)) OR (nephrectom*)) OR abstract:((Kidney* AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma* OR 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* OR "collecting duct*") AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma* OR stage-4)) OR (renal-cell* OR "renal cell*" OR RCC OR ccRCC OR Renal-mass* OR "Renal mass*" OR renal-tumor* OR renal-tumour* OR "renal tumor*" OR "renal tumour*" OR grawitz-tumor* OR grawitz-tumour* OR "grawitz tumor*" OR "grawitz tumour*" OR hypernephroma* OR nephrocarcinoma*) OR (Kidney* AND (Transitional-cell* OR "Transitional cell*" OR cell OR urothelial* OR duct OR advanc*) AND (cancer* OR carcinoma* OR carcinosarcoma* OR adenocarcino* OR neoplas* OR tumor* OR tumour* OR mass OR metastat* OR malignan* OR sarcoma* OR parenchyma*)) OR (nephron* AND (surg* OR remov* OR partial* OR procedur* OR treat* OR operat* OR spar* OR preserv*)) OR (nephrectom*))) AND (title:((UISS OR karakiewicz OR Kattan OR leibovich OR VENUSS OR SSIGN OR IMDC OR Heng OR Sorbellini* OR Zisman* OR Meet-URO OR "Meet URO" OR nephrometry) OR ("UCLA integrated staging system" OR "Preoperative Aspects AND Dimensions Used for an Anatomical Classification") OR (("International Metastatic Renal Cell Carcinoma Database Consortium" OR "grade age nodes AND tumor" OR "grade age nodes AND tumour" OR "Memorial Sloan-Kettering Cancer Center") AND (grade* OR index* OR class* OR scale* OR model* OR score* OR scoring*)) OR ((MSKCC OR TNM OR PADUA OR Centrality-index OR C-index OR "C index" OR GRANT OR SPARE) AND (classification* OR system* OR score* OR scoring* OR staging* OR model*)) OR (("tumour node metastasis" OR "tumor node metastasis" OR "tumour node metastases" OR "tumor node metastases" OR "tumour nodes metastases" OR "tumor nodes metastases" OR "tumour nodes metastasis" OR "tumor nodes metastasis") AND (classification* OR system* OR score* OR scoring* OR staging*)) OR ((ECOG OR "Eastern Cooperative Oncology Group" OR Karnofsky OR ASA OR "American Society of Anesthesiologists" OR Charlson-comorbidity OR clinical-frail* OR

Searches
clinically-frail* OR MSKCC OR TNM OR PADUA OR Centrality-index OR C-index OR WHO OR World-health-organisation* OR "World health organisation" OR ISUP OR "International Society of Urological Pathology" OR Fuhrman) AND (grade* OR index* OR class* OR scale* OR model* OR score* OR scoring*))) OR abstract:((UISS OR karakiewicz OR Kattan OR leibovich OR VENUSS OR SSIGN OR IMDC OR Heng OR Sorbellini* OR Zisman* OR Meet-URO OR "Meet URO" OR nephrometry) OR ("UCLA integrated staging system" OR "Preoperative Aspects AND Dimensions Used for an Anatomical Classification") OR (("International Metastatic Renal Cell Carcinoma Database Consortium" OR "grade age nodes AND tumor" OR "grade age nodes AND tumour" OR "Memorial Sloan-Kettering Cancer Center") AND (grade* OR index* OR class* OR scale* OR model* OR score* OR scoring*)) OR ((MSKCC OR TNM OR PADUA OR Centrality-index OR C-index OR "C index" OR GRANT OR SPARE) AND (classification* OR system* OR score* OR scoring* OR staging* OR model*)) OR (("tumour node metastasis" OR "tumor node metastasis" OR "tumour node metastases" OR "tumor node metastases" OR "tumour nodes metastases" OR "tumor nodes metastases" OR "tumour nodes metastasis" OR "tumor nodes metastasis") AND (classification* OR system* OR score* OR scoring* OR staging*)) OR ((ECOG OR "Eastern Cooperative Oncology Group" OR Karnofsky OR ASA OR "American Society of Anesthesiologists" OR Charlson-comorbidity OR clinical-frail* OR clinically-frail* OR MSKCC OR TNM OR PADUA OR Centrality-index OR C-index OR WHO OR World-health-organisation* OR "World health organisation" OR ISUP OR "International Society of Urological Pathology" OR Fuhrman) AND (grade* OR index* OR class* OR scale* OR model* OR score* OR scoring*)))) AND (title:(Incidence* OR mortality* OR prognos* OR predict* OR course* OR "follow up study" OR "follow-up study" OR "follow up studies" OR "follow-up studies") OR abstract:(Incidence* OR mortality* OR prognos* OR predict* OR course* OR "follow up study" OR "follow-up study" OR "follow up studies" OR "follow-up studies"))

Database name: INAHTA

Searches
#1 (Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or 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* OR "collecting duct*") AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or "renal cell*" or RCC or ccRCC or Renal-mass* or "Renal mass*" or renal-tumor* or renal-tumour* or "renal tumor*" or "renal tumour*" or grawitz-tumor* or grawitz-tumour* or "grawitz tumor*" or "grawitz tumour*" or hypernephroma* or nephrocarcinoma*)) OR (Kidney* AND (Transitional-cell* or "Transitional cell*" or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*)) OR (nephron* AND (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)) AND (nephrectom*) 153 #2 (UISS or karakiewicz or Kattan or leibovich or VENUSS or SSIGN or IMDC or Heng or Sorbellini* or Zisman* or Meet-URO or "Meet URO" or nephrometry) OR ("UCLA integrated staging system" or "Preoperative Aspects and Dimensions Used for an Anatomical Classification") OR (("International Metastatic Renal Cell Carcinoma Database Consortium" or "grade age nodes and tumor" or "grade age nodes and tumour" or "Memorial Sloan-Kettering Cancer Center") AND (grade* or index* or class* or scale* or model* or score* or scoring*)) OR ((MSKCC or TNM or PADUA or Centrality-index or C-index OR "C index" or GRANT or SPARE) AND (classification* or system* or score* or scoring* or staging* or model*)) OR (("tumour node metastasis" or "tumor node metastasis" or "tumour node metastases" or "tumor node metastases" or "tumour nodes metastases" or "tumor nodes metastases" or "tumour nodes metastasis" or "tumor nodes metastasis") AND (classification* or system* or score* or scoring* or staging*)) OR ((ECOG or "Eastern

Searches
Cooperative Oncology Group" or Karnofsky or ASA or "American Society of Anesthesiologists" or Charlson-comorbidity or clinical-frail* or clinically-frail* or MSKCC or TNM or PADUA or Centrality-index or C-index or WHO or World-health-organisation* or "World health organisation" or ISUP or "International Society of Urological Pathology" or Fuhrman) AND (grade* or index* or class* or scale* or model* or score* or scoring*)) 1100 #3 #1 AND #2 11

Database name: Medline ALL

Searches
1 exp Kidney Neoplasms/ or exp nephrectomy/ (109945)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or 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. (17733)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (503)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (72591)
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (855)
6 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (2714)
7 nephrectom*.ti,ab. (41402)
8 or/1-7 (154034)
9 (UISS or karakiewicz or Kattan or leibovich or VENUSS or SSIGN or IMDC or Heng or Sorbellini* or Zisman* or Meet-URO or nephrometry).ti,ab. (2074)
10 ("UCLA integrated staging system" or "Preoperative Aspects and Dimensions Used for an Anatomical Classification").ti,ab. (56)
11 (("International Metastatic Renal Cell Carcinoma Database Consortium" or "grade age nodes and tumo?r" or "Memorial Sloan-Kettering Cancer Center") adj5 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (357)
12 ((MSKCC or TNM or PADUA or Centrality-index or C-index or GRANT or SPARE) adj3 (classification* or system* or score* or scoring* or staging* or model*)).ti,ab. (14276)
13 ("tumo?r node* metastas*" adj5 (classification* or system* or score* or scoring* or staging*)).ti,ab. (2500)
14 ((ECOG or "Eastern Cooperative Oncology Group" or Karnofsky or ASA or "American Society of Anesthesiologists" or Charlson-comorbidity or clinical*-frail* or MSKCC or TNM or PADUA or Centrality-index or C-index or WHO or World-health-organisation* or ISUP or "International Society of Urological Pathology" or Fuhrman) adj3 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (105881)
15 or/9-14 (114642)
16 8 and 15 (5125)
17 incidence.sh. (309064)
18 exp mortality/ (429835)
19 follow-up studies.sh. (700226)
20 prognos:.tw. (853921)
21 predict:.tw. (2203246)

Searches
22 course:.tw. (733615)
23 or/17-22 (4465499)
24 exp Cohort Studies/ or cohort.tw. or validat*.tw. (3676032)
25 (MEDLINE or pubmed).tw. (366550)
26 systematic review.tw. (308367)
27 systematic review.pt. (266180)
28 meta-analysis.pt. (204095)
29 intervention$.ti. (217527)
30 or/24-29 (4318796)
31 16 and 23 and 30 (2231)
32 animals/ not humans/ (5206081)
33 31 not 32 (2229)
34 limit 33 to english language (2125)
35 limit 34 to (letter or historical article or comment or editorial or news or case reports) (19)
36 34 not 35 (2106)
37 ("clinical conference" or congress* or overall* or consensus*).pt. or (conference* or proceeding*).jn. or (conference* not (video* or conference-call* or case* or charter* or declaration* or treaty* or treaties)).ti. (388945)
38 36 not 37 (2104)
39 16 and 23 (3370)
40 animals/ not humans/ (5206081)
41 39 not 40 (3368)
42 limit 41 to english language (3190)
43 limit 42 to (letter or historical article or comment or editorial or news or case reports) (92)
44 42 not 43 (3098)
45 ("clinical conference" or congress* or overall* or consensus*).pt. or (conference* or proceeding*).jn. or (conference* not (video* or conference-call* or case* or charter* or declaration* or treaty* or treaties)).ti. (388945)
46 44 not 45 (3093)
47 46 not 36 (989)

Cost-effectiveness searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	18/07/2024	OVID	1886 to July 10, 2024	0
EED	18/07/2024	CRD	N/A	0
Embase	18/07/2024	Ovid	1974 to 2024 July 17	688
HTA	18/07/2024	CRD	N/A	1
INAHTA	18/07/2024	INAHTA	N/A	11
MEDLINE ALL	18/07/2024	Ovid	1946 to July 17, 2024	265

Search strategy history

Database name: Econlit

Searches
1 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or 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. (8)
2 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (0)
3 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (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 tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (0)
5 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (0)
6 nephrectom*.ti,ab. (0)
7 or/1-6 (30)
8 (UISS or karakiewicz or Kattan or leibovich or VENUSS or SSIGN or IMDC or Heng or Sorbellini* or Zisman* or Meet-URO or nephrometry).ti,ab. (28)
9 ("UCLA integrated staging system" or "Preoperative Aspects and Dimensions Used for an Anatomical Classification").ti,ab. (0)
10 (("International Metastatic Renal Cell Carcinoma Database Consortium" or "grade age nodes and tumo?r" or "Memorial Sloan-Kettering Cancer Center") adj5 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (1)
11 ((MSKCC or TNM or PADUA or Centrality-index or C-index or GRANT or SPARE) adj3 (classification* or system* or score* or scoring* or staging* or model*)).ti,ab. (189)
12 ("tumo?r node* metastas*" adj5 (classification* or system* or score* or scoring* or staging*)).ti,ab. (0)

Searches
13 ((ECOG or "Eastern Cooperative Oncology Group" or Karnofsky or ASA or "American Society of Anesthesiologists" or Charlson-comorbidity or clinical*-frail* or MSKCC or TNM or PADUA or Centrality-index or C-index or WHO or World-health-organisation* or ISUP or "International Society of Urological Pathology" or Fuhrman) adj3 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (1018)
14 or/8-13 (1235)
15 7 and 14 (0)

Database name: EED and HTA

Searches

Line	Search	Hits
1	MESH DESCRIPTOR Kidney Neoplasms EXPLODE ALL TREES	201
2	MESH DESCRIPTOR Nephrectomy EXPLODE ALL TREES	95
3	(Kidney* NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?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))	194
4	(collecting-duct* NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4))	1
5	(renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*)	204
6	(Kidney* NEAR2 (Transitional-cell* or cell or urothelial* or duct or advanc*) NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*))	3
7	(nephron* NEAR2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*))	9
8	nephrectom*	139
9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	342
10	(UISS or karakiewicz or Kattan or leibovich or VENUSS or SSIGN or IMDC or Heng or Sorbellini* or Zisman* or Meet-URO or nephrometry)	34
11	"UCLA integrated staging system" or "Dimensions Used for an Anatomical Classification"	0
12	("International Metastatic Renal Cell Carcinoma Database Consortium" or "grade age nodes" or "Memorial Sloan-Kettering Cancer Center") NEAR5 (grade* or index* or class* or scale* or model* or score* or scoring*)	1
13	((MSKCC or TNM or PADUA or Centrality-index or C-index or GRANT or SPARE) NEAR3 (classification* or system* or score* or scoring* or staging* or model*))	27
14	(("tumour node metastasis" or "tumor node metastasis" or "tumour node metastases" or "tumor node metastases" or "tumour nodes metastases" or "tumor nodes metastases" or "tumour nodes metastasis" or "tumor nodes metastasis") near5 (classification* or system* or score* or scoring* or staging*))	6
15	((ECOG or "Eastern Cooperative Oncology Group" or Karnofsky or ASA or "American Society of Anesthesiologists" or Charlson-comorbidity or clinical-frail* or clinically-frail* or MSKCC or TNM or PADUA or Centrality-index or C-index or WHO or World-health-organisation* or ISUP or "International Society of Urological Pathology" or Fuhrman) NEAR3 (grade* or index* or class* or scale* or model* or score* or scoring*))	313
16	#10 OR #11 OR #12 OR #13 OR #14 OR #15	366
17	#9 AND #16	15
18	MESH DESCRIPTOR Incidence	1373
19	MESH DESCRIPTOR Mortality EXPLODE ALL TREES	2099
20	MESH DESCRIPTOR Follow-Up Studies	2032
21	(prognos* or predict* or course*)	8966
22	#18 OR #19 OR #20 OR #21	13139
23	#17 AND #22	6
24	(#23) IN NHSEED	0
25	(#23) IN HTA	1

Database name: Embase

Searches
1 exp kidney tumor/ or exp nephrectomy/ (216789)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or 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. (26808)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (752)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (108713)
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (1229)
6 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (4946)
7 nephrectom*.ti,ab. (64461)
8 or/1-7 (252893)
9 (UISS or karakiewicz or Kattan or leibovich or VENUSS or SSIGN or IMDC or Heng or Sorbellini* or Zisman* or Meet-URO or nephrometry).ti,ab. (5040)
10 ("UCLA integrated staging system" or "Preoperative Aspects and Dimensions Used for an Anatomical Classification").ti,ab. (81)
11 (("International Metastatic Renal Cell Carcinoma Database Consortium" or "grade age nodes and tumo?r" or "Memorial Sloan-Kettering Cancer Center") adj5 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (534)
12 ((MSKCC or TNM or PADUA or Centrality-index or C-index or GRANT or SPARE) adj3 (classification* or system* or score* or scoring* or staging* or model*)).ti,ab. (22957)
13 ("tumo?r node* metastas*" adj5 (classification* or system* or score* or scoring* or staging*)).ti,ab. (2749)
14 ((ECOG or "Eastern Cooperative Oncology Group" or Karnofsky or ASA or "American Society of Anesthesiologists" or Charlson-comorbidity or clinical*-frail* or MSKCC or TNM or PADUA or Centrality-index or C-index or WHO or World-health-organisation* or ISUP or "International Society of Urological Pathology" or Fuhrman) adj3 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (185802)
15 or/9-14 (200493)
16 8 and 15 (11890)
17 incidence.sh. (618367)
18 exp mortality/ (1454641)
19 follow-up studies.sh. (107)
20 prognos:.tw. (1277114)
21 predict:.tw. (2949422)
22 course:.tw. (1028312)
23 or/17-22 (6209156)
24 16 and 23 (6994)
25 nonhuman/ not human/ (5485460)
26 24 not 25 (6972)
27 limit 26 to english language (6732)
28 27 not (letter or editorial).pt. (6710)
29 exp Health Economics/ (1083212)

Searches
30 exp "Health Care Cost"/ (355582)
31 exp Pharmacoeconomics/ (244320)
32 Monte Carlo Method/ (54181)
33 Decision Tree/ (25166)
34 econom$.tw. (530905)
35 cba.tw. (14606)
36 cea.tw. (43369)
37 cua.tw. (1987)
38 markov$.tw. (42273)
39 (monte adj carlo).tw. (64709)
40 (decision adj3 (tree$ or analys$)).tw. (43496)
41 (cost or costs or costing$ or costly or costed).tw. (1056833)
42 (price$ or pricing$).tw. (77523)
43 budget$.tw. (49784)
44 expenditure$.tw. (95221)
45 (value adj3 (money or monetary)).tw. (4531)
46 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (9949)
47 or/29-46 (2386194)
48 "Quality of Life"/ (674998)
49 Quality Adjusted Life Year/ (37922)
50 Quality of Life Index/ (3301)
51 Short Form 36/ (42364)
52 Health Status/ (158972)
53 quality of life.tw. (635402)
54 quality adjusted life.tw. (28264)
55 (qaly$ or qald$ or qale$ or qtime$).tw. (28723)
56 disability adjusted life.tw. (7415)
57 daly$.tw. (7121)
58 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (51877)
59 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (3112)
60 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (12830)
61 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (73)
62 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (543)
63 (euroqol or euro qol or eq5d or eq 5d).tw. (32912)
64 (qol or hql or hqol or hrqol).tw. (140391)
65 (hye or hyes).tw. (193)
66 health$ year$ equivalent$.tw. (41)
67 utilit$.tw. (402088)
68 (hui or hui1 or hui2 or hui3).tw. (3363)
69 disutili$.tw. (1375)
70 rosser.tw. (144)

Searches	
71	quality of wellbeing.tw. (79)
72	quality of well-being.tw. (591)
73	qwb.tw. (276)
74	willingness to pay.tw. (14111)
75	standard gamble$.tw. (1219)
76	time trade off.tw. (2162)
77	time tradeoff.tw. (323)
78	tto.tw. (2364)
79	or/48-78 (1389661)
80	47 or 79 (3554361)
81	28 and 80 (688)

Database name: INAHTA

Searches
#1 (Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or 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* OR "collecting duct*") AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or "renal cell*" or RCC or ccRCC or Renal-mass* or "Renal mass*" or renal-tumor* or renal-tumour* or "renal tumor*" or "renal tumour*" or grawitz-tumor* or grawitz-tumour* or "grawitz tumor*" or "grawitz tumour*" or hypernephroma* or nephrocarcinoma*)) OR (Kidney* AND (Transitional-cell* or "Transitional cell*" or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*)) OR (nephron* AND (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)) AND (nephrectom*) 153 #2 (UISS or karakiewicz or Kattan or leibovich or VENUSS or SSIGN or IMDC or Heng or Sorbellini* or Zisman* or Meet-URO or "Meet URO" or nephrometry) OR ("UCLA integrated staging system" or "Preoperative Aspects and Dimensions Used for an Anatomical Classification") OR (("International Metastatic Renal Cell Carcinoma Database Consortium" or "grade age nodes and tumor" or "grade age nodes and tumour" or "Memorial Sloan-Kettering Cancer Center") AND (grade* or index* or class* or scale* or model* or score* or scoring*)) OR ((MSKCC or TNM or PADUA or Centrality-index or C-index OR "C index" or GRANT or SPARE) AND (classification* or system* or score* or scoring* or staging* or model*)) OR (("tumour node metastasis" or "tumor node metastasis" or "tumour node metastases" or "tumor node metastases" or "tumour nodes metastases" or "tumor nodes metastases" or "tumour nodes metastasis" or "tumor nodes metastasis") AND (classification* or system* or score* or scoring* or staging*)) OR ((ECOG or "Eastern Cooperative Oncology Group" or Karnofsky or ASA or "American Society of Anesthesiologists" or Charlson-comorbidity or clinical-frail* or clinically-frail* or MSKCC or TNM or PADUA or Centrality-index or C-index or WHO or World-health-organisation* or "World health organisation" or ISUP or "International Society of Urological Pathology" or Fuhrman) AND (grade* or index* or class* or scale* or model* or score* or scoring*)) 1100 #3 #1 AND #2 11

Database name: Medline ALL

Searches	
1	exp Kidney Neoplasms/ or exp nephrectomy/ (109936)

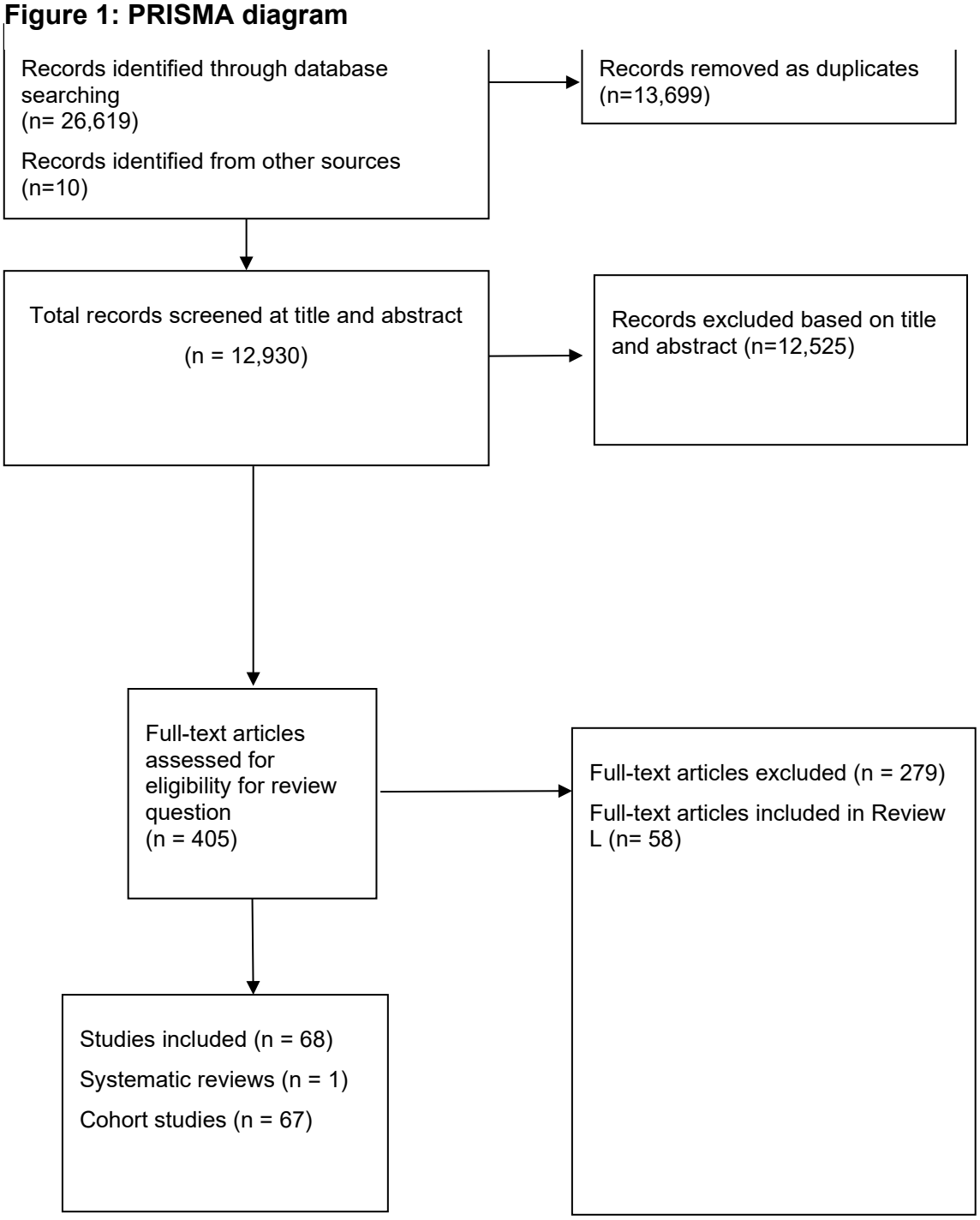
Searches
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (17737)
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (502)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (72591)
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (855)
6 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (2711)
7 nephrectom*.ti,ab. (41398)
8 or/1-7 (154033)
9 (UISS or karakiewicz or Kattan or leibovich or VENUSS or SSIGN or IMDC or Heng or Sorbellini* or Zisman* or Meet-URO or nephrometry).ti,ab. (2071)
10 ("UCLA integrated staging system" or "Preoperative Aspects and Dimensions Used for an Anatomical Classification").ti,ab. (56)
11 (("International Metastatic Renal Cell Carcinoma Database Consortium" or "grade age nodes and tumo?r" or "Memorial Sloan-Kettering Cancer Center") adj5 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (356)
12 ((MSKCC or TNM or PADUA or Centrality-index or C-index or GRANT or SPARE) adj3 (classification* or system* or score* or scoring* or staging* or model*)).ti,ab. (14282)
13 ("tumo?r node* metastas*" adj5 (classification* or system* or score* or scoring* or staging*)).ti,ab. (2501)
14 ((ECOG or "Eastern Cooperative Oncology Group" or Karnofsky or ASA or "American Society of Anesthesiologists" or Charlson-comorbidity or clinical*-frail* or MSKCC or TNM or PADUA or Centrality-index or C-index or WHO or World-health-organisation* or ISUP or "International Society of Urological Pathology" or Fuhrman) adj3 (grade* or index* or class* or scale* or model* or score* or scoring*)).ti,ab. (105869)
15 or/9-14 (114632)
16 8 and 15 (5123)
17 incidence.sh. (309038)
18 exp mortality/ (429831)
19 follow-up studies.sh. (700181)
20 prognos:.tw. (853881)
21 predict:.tw. (2203330)
22 course:.tw. (733589)
23 or/17-22 (4465429)
24 16 and 23 (3373)
25 animals/ not humans/ (5206131)
26 24 not 25 (3371)
27 limit 26 to english language (3193)
28 limit 27 to (letter or historical article or comment or editorial or news or case reports) (92)
29 27 not 28 (3101)
30 Economics/ (27537)

Searches
31 exp "Costs and Cost Analysis"/ (271763)
32 Economics, Dental/ (1922)
33 exp Economics, Hospital/ (25902)
34 exp Economics, Medical/ (14440)
35 Economics, Nursing/ (4013)
36 Economics, Pharmaceutical/ (3141)
37 Budgets/ (11831)
38 exp Models, Economic/ (16414)
39 Markov Chains/ (16286)
40 Monte Carlo Method/ (33069)
41 Decision Trees/ (12271)
42 econom$.tw. (439037)
43 cba.tw. (11416)
44 cea.tw. (28063)
45 cua.tw. (1510)
46 markov$.tw. (33575)
47 (monte adj carlo).tw. (61974)
48 (decision adj3 (tree$ or analys$)).tw. (32918)
49 (cost or costs or costing$ or costly or costed).tw. (797355)
50 (price$ or pricing$).tw. (56942)
51 budget$.tw. (37769)
52 expenditure$.tw. (72169)
53 (value adj3 (money or monetary)).tw. (3390)
54 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (4644)
55 or/30-54 (1528988)
56 "Quality of Life"/ (290886)
57 quality of life.tw. (406896)
58 "Value of Life"/ (5827)
59 Quality-Adjusted Life Years/ (16590)
60 quality adjusted life.tw. (18598)
61 (qaly$ or qald$ or qale$ or qtime$).tw. (15565)
62 disability adjusted life.tw. (6190)
63 daly$.tw. (5560)
64 Health Status Indicators/ (24132)
65 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (31978)
66 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2782)
67 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (8114)
68 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (42)
69 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (467)
70 (euroqol or euro qol or eq5d or eq 5d).tw. (18396)
71 (qol or hql or hqol or hrqol).tw. (79365)

Searches	
72	(hye or hyes).tw. (77)
73	health$ year$ equivalent$.tw. (40)
74	utilit$.tw. (288878)
75	(hui or hui1 or hui2 or hui3).tw. (2103)
76	disutili$.tw. (687)
77	rosser.tw. (111)
78	quality of wellbeing.tw. (52)
79	quality of well-being.tw. (511)
80	qwb.tw. (219)
81	willingness to pay.tw. (9444)
82	standard gamble$.tw. (919)
83	time trade off.tw. (1451)
84	time tradeoff.tw. (268)
85	tto.tw. (1484)
86	or/56-85 (805571)
87	55 or 86 (2222501)
88	29 and 87 (265)

Appendix C – Prognostic evidence study selection

Figure 1: PRISMA diagram



Appendix D – Prognostic evidence

An, 2015

Bibliographic Reference	An, Huimin; Xu, Le; Chang, Yuan; Zhu, Yu; Yang, Yuanfeng; Chen, Lian; Lin, Zongming; Xu, Jiejie; CXC chemokine receptor 2 is associated with postoperative recurrence and survival of patients with non-metastatic clear-cell renal cell carcinoma.; European journal of cancer (Oxford, England : 1990); 2015; vol. 51 (no. 14); 1953-61

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2003 to 2008
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• Patients who underwent radical nephrectomy or nephron-sparing surgery • no history of anti-cancer therapy • no history of other malignant tumours • histopathological proven clear cell renal cell carcinoma (ccRCC).
Exclusion criteria	• Metastatic disease (N1 or M1 tumours)
Selection of cohort	Single centre
Number of participants	N=191
Length of follow-up	67 months (range: 12–74 months)
Follow-up schedule	Physical examinations, laboratory tests, chest imaging, abdominal ultrasound or CT scans were performed biannually for the first 5 years, and then annually after.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Overall survival
Source of funding	Not industry funded
Additional comments	Survival curves were established using the Kaplan–Meier method. The significance of difference between the curves was analysed with the log-rank test. The Cox proportional hazards regression model was used to perform univariate analyses.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 191)
% Female Sample size	n = 52 ; % = 26.9
Age Mean (SD)	55.2 (11.6)
T1 Sample size	n = 138 ; % = 72.3
T2 Sample size	n = 19 ; % = 9.9
T3 Sample size	n = 32 ; % = 16.8
T4 Sample size	n = 2 ; % = 1

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (High risk of bias for *analysis as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Baykal, 2025

Bibliographic Reference	Baykal, Serdar; Yilmaz, Hasan; Cinar, Naci Burak; Akdas, Enes Malik; Baynal, Enes Abdullah; Teke, Kerem; Dillioglugil, Ozdal; The pan-immune-inflammation value: A novel independent predictive factor for overall survival in >=pT2a nonmetastatic renal cell carcinoma.; Urologic oncology; 2025

Study Characteristics

Study design	Retrospective cohort study
Study location	Turkey

Study dates	2008 to 2022
Prognostic model(s)	UISS
Inclusion criteria	• People who underwent radical nephrectomy due to renal tumour • People with histopathological RCC
Exclusion criteria	• People with non-RCC kidney carcinoma, urothelial carcinoma, cystic nephroma, angiomyolipoma, liposarcoma, polycystic kidney disease, multiple myeloma, cystic hydatid disease, perioperative deaths • Missing variables and/or follow-up information • Metastatic disease before nephrectomy
Selection of cohort	Single centre
Number of participants	n=197
Length of follow-up	Median follow-up time: 49 months (IQR 19 to 94.5)
Follow-up schedule	Follow-up at 1 month after surgery then every 3 months for the first year, every 6 months for the second year, and annually thereafter.
Outcome(s) of interest	Overall survival
Outcome(s) of interest	Overall survival Hazard ratios
Source of funding	None
Additional comments	None

Study arms
UISS - low risk (N = NR)

UISS - intermediate risk (N = NR)

UISS - high risk (N = NR)

Population characteristics
Study-level characteristics

Characteristic	**Study (N = 197)**
% Female Sample size	n = 68 ; % = 33.5
Age Median (IQR)	59 (51 to 66)
RCC subtypes Sample size	n = NA ; % = NA
RCC subtypes - Clear cell	n = 134 ; % = 68

Characteristic	Study (N = 197)
Sample size	
RCC subtypes - Papillary Sample size	n = 33 ; % = 16.7
RCC subtypes - Chromophobe Sample size	n = 21 ; % = 10.8
RCC subtypes - Other Sample size	n = 9 ; % = 4.5
TNM classification Sample size	n = NA ; % = NA
TNM classification - pT2 Sample size	n = 107 ; % = 54.3
TNM classification - pT3 Sample size	n = 89 ; % = 45.1
TNM classification - pT4 Sample size	n = 1 ; % = 0.6
TNM classification - pN0 Sample size	n = 186 ; % = 94.4
TNM classification - pN1 Sample size	n = 11 ; % = 5.6

Outcomes

Time-to-event outcomes

Outcome	UISS - intermediate risk vs UISS - low risk, N2 = NR, N1 = NR	UISS - high risk vs UISS - intermediate risk, N2 = NR, N1 = NR
Overall survival Hazard ratio/95% CI	2.84 (1.26 to 6.41)	4.64 (2.03 to 10.62)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(Did not report discrimination and calibration)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Beisland, 2015

Bibliographic Reference	Beisland, Christian; Gudbrandsdottir, Gigja; Reisaeter, Lars A R; Bostad, Leif; Wentzel-Larsen, Tore; Hjelle, Karin M; Contemporary external validation of the Leibovich model for prediction of progression after radical surgery for clear cell renal cell

carcinoma.; Scandinavian journal of urology; 2015; vol. 49 (no. 3); 205-10

Study Characteristics

Study design	Retrospective cohort study
Study location	Norway
Study dates	1997 to 2013
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• Primary-treated sporadic unilateral clear cell renal cell carcinoma (CCRCC). • Operated on at Haukeland University Hospital • Partial or radical nephrectomy
Exclusion criteria	• Bilateral synchronous tumours • inheritable forms of renal cell carcinoma including hereditary papillary • with von Hippel-Lindau and tuberous sclerosis syndromes • with Wilms tumour • prior or concurrent distant metastases • age < 18 years at surgery • denied access to medical records for research.
Selection of cohort	Single centre
Number of participants	N=386
Length of follow-up	51.6 ± 42.6 months (mean ± SD)
Follow-up schedule	Clinical examination, blood tests and chest x-ray performed every 6 months for 5 years. Nephrectomy patients with intermediate and high-risk tumours had routine abdominal CT for follow-up. Chest CT was used based on individual evaluation.
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not industry funded

Additional comments	To validate the discriminative ability of the model, the c-index was used. The discriminative ability was further tested by evaluating the hazard ratios over the risk groups in a Cox model.

Study arms
Leibovich 2003 low risk (N = 223)

Leibovich 2003 intermediate risk (N = 95)

Leibovich 2003 high risk (N = 65)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 386)
% Female Sample size	n = 145 ; % = 37.6
Age Mean (SE)	63.3 (12.1)
Radical nephrectomy No of events	n = 251 ; % = 65
N1 Sample size	n = 25 ; % = 6.5
N2 Sample size	n = 202 ; % = 52.3
N3 Sample size	n = 100 ; % = 25.9
N4 Sample size	n = 56 ; % = 14.5

Outcomes
Recurrence free survival

Outcome	Leibovich 2003 intermediate risk vs Leibovich 2003 low risk, N2 = 95, N1 = 223	Leibovich 2003 high risk vs Leibovich 2003 low risk, N2 = 65, N1 = 223
Recurrence free survival Hazard ratio/95% CI	5.29 (2.33 to 12.01)	21.56 (9.99 to 46.52)

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*high risk of bias for outcome or its determination assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Buti, 2019

Bibliographic Reference	Buti, Sebastiano; Karakiewicz, Pierre I; Bersanelli, Melissa; Capitanio, Umberto; Tian, Zhe; Cortellini, Alessio; Taguchi, Satoru; Briganti, Alberto; Montorsi, Francesco; Leonardi, Francesco; Bandini, Marco; Validation of the GRade, Age, Nodes and Tumor (GRANT) score within the Surveillance Epidemiology and End Results (SEER) database: A new tool to predict survival in surgically treated renal cell carcinoma patients.; Scientific reports; 2019; vol. 9 (no. 1); 13218

Study Characteristics

Study design	Retrospective cohort study
Study location	United States
Study dates	2001 to 2015
Prognostic model(s)	GRANT
Inclusion criteria	• Histologically confirmed non-metastatic (M0 at diagnosis) renal cell carcinoma (RCC) stage pT1-4, N any • death certificate only • the histological subtypes included were clear cell RCC and papillary RC • 18 years or older • treated with partial or radical nephrectomy.
Exclusion criteria	• Autopsy cases • patient with bilateral tumours • unknown tumour grade • unknown lymph node status • unknown T classification • unknown age • unknown follow-up data.

Selection of cohort	Database or clinical registry (Surveillance, Epidemiology, and End Results (SEER) database)
Number of participants	N=73217
Length of follow-up	5 years
Follow-up schedule	Not reported
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	Not industry funded
Additional comments	Kaplan-Meier used to plot overall survival. The validation of the GRANT score was investigated through the development of a Cox-based model.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 73217)
% Female Sample size	n = 26464 ; % = 36.1
Age Range	53 to 70
Partial nephrectomy No of events	n = 25115 ; % = 34.3
Radical nephrectomy No of events	n = 48102 ; % = 65.7
Clear cell Sample size	n = 60900 ; % = 83.2
Papillary Sample size	n = 12317 ; % = 16.8

Characteristic	Study (N = 73217)
T stage T1-2-3a Sample size	n = 71819 ; % = 98.1
T stage T3b-3c-4 Sample size	n = 1398 ; % = 1.9
N stage 0-X Sample size	n = 72139 ; % = 98.5
N stage 1 Sample size	n = 1078 ; % = 1.5

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*high risk of bias around analysis and unclear risk of bias around outcome or its determination as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Capogrosso, 2018

Bibliographic Reference	Capogrosso, P.; Larcher, A.; Sjoberg, D.D.; Vertosick, E.A.; Cianflone, F.; Dell'Oglio, P.; Carenzi, C.; Salonia, A.; Vickers, A.J.; Montorsi, F.; Bertini, R.; Capitanio, U.; Risk Based Surveillance after Surgical Treatment of Renal Cell Carcinoma; Journal of Urology; 2018; vol. 200 (no. 1); 61-67

Study Characteristics

Study design	Retrospective cohort study
Study location	United States
Study dates	1995 to 2016
Prognostic model(s)	UISS

Inclusion criteria	• Patients with renal cell carcinoma (RCC) who had a partial or radical nephrectomy • histology-proven malignant disease • free from metastases at preoperative staging.
Exclusion criteria	• Missing clinical or pathological data.
Selection of cohort	Single centre
Number of participants	N=1630
Length of follow-up	3, 6 and 12 months, and 60 months
Follow-up schedule	Total-body CT scans performed at 3 to 6 months and at 12 months after surgery over the first year, and annually thereafter. Additional evaluations were performed throughout the follow-up period if the patient's symptoms raised clinical suspicion of relapse. Patients who did not experience relapse were censored at the date of last follow-up.
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Local recurrence
Source of funding	Not industry funded
Additional comments	A Cox regression analysis tested the accuracy of the two models in patients who were recurrence-free five years after surgery. The cumulative incidence of recurrence after five years according to the UISS risk categories was calculated and graphically displayed with Kaplan-Meier analysis

Study arms
UISS, low risk (N = 320)

UISS, intermediate risk (N = 1018)

UISS, high risk (N = 265)

Population characteristics
Study-level characteristics

Characteristic	**Study (N = 1630)**
Age Median (IQR)	62 (52 to 70)

Characteristic	Study (N = 1630)
Radical nephrectomy No of events	n = 854 ; % = 52
Partial nephrectomy No of events	n = 776 ; % = 48
Clear cell Sample size	n = 1273 ; % = 78
Papillary type 1 Sample size	n = 137 ; % = 8.4
Papillary type 2 Sample size	n = 113 ; % = 6.9
Chromophobe Sample size	n = 107 ; % = 6.6
N0/Nx Sample size	n = 1571 ; % = 96.3
N1 Sample size	n = 59 ; % = 3.6
t1 Sample size	n = 1107 ; % = 68
t2 Sample size	n = 163 ; % = 10
t3 Sample size	n = 342 ; % = 21
t4 Sample size	n = 18 ; % = 1.1

Outcomes
UISS

Outcome	UISS, intermediate risk vs UISS, low risk, N2 = 1018, N1 = 320	UISS, high risk vs UISS, low risk, N2 = 265, N1 = 320
local recurrence	1.65 (0.79 to 3.44)	2.27 (0.76 to 6.81)

Outcome	UISS, intermediate risk vs UISS, low risk, N2 = 1018, N1 = 320	UISS, high risk vs UISS, low risk, N2 = 265, N1 = 320
Hazard ratio/95% CI		

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias around analysis and unclear risk of bias around selection of participants and outcome or its determination as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Chen, 2017

Bibliographic Reference	Chen, Zhen; Shao, Yingjie; Yao, Hongwei; Zhuang, Qianfeng; Wang, Kun; Xing, Zhaoyu; Xu, Xianlin; He, Xiaozhou; Xu, Renfang; Preoperative albumin to globulin ratio predicts survival in clear cell renal cell carcinoma patients.; Oncotarget; 2017; vol. 8 (no. 29); 48291-48302

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	Validation cohort: May 2012 to December 2013
Prognostic model(s)	Leibovich 2003 SSIGN
Inclusion criteria	Patients with RCC who underwent radical or partial nephrectomy
Exclusion criteria	• Patients with a history of anti-tumour therapy and other concurrent tumours • Other acute or chronic concurrent non-cancer diseases (including liver disease, inflammation, and infection)

	• Concurrent distant metastasis • Patients lost to follow-up
Selection of cohort	Single centre
Number of participants	Validation cohort: n=176
Length of follow-up	Validation cohort: median follow-up 42.3 months (range 3 to 50)
Follow-up schedule	Postoperative follow-ups occurred every six months for the first three years and annually thereafter for locally advanced CCRCC patients. For localized CCRCC patients, follow-up imaging was performed twice in the first year and annually thereafter.
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	National Science Foundation of Jiangsu Province
Additional comments	C-indices were derived from the validation cohort.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 176)
% Female Sample size	n = 61 ; % = 34.7
Age - 60 years or younger Sample size	n = 105 ; % = 59.7
Age - older than 60 years Sample size	n = 71 ; % = 40.3
RCC subtypes Sample size	n = 176 ; % = 100
TNM classification - T stage - 1 Sample size	n = 144 ; % = 81.8
TNM classification - T stage - 2 Sample size	n = 18 ; % = 10.2
TNM classification - T stage - 3 Sample size	n = 14 ; % = 8

Characteristic	Study (N = 176)
TNM classification - N stage 0 Sample size	n = 174 ; % = 98.9
TNM classification - N stage 1 Sample size	n = 2 ; % = 1.1

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for outcome or its determination and analysis as assessed by Usher-Smith 2022)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Cindolo, 2005

Bibliographic Reference	Cindolo, Luca; Patard, Jean-Jacques; Chiodini, Paolo; Schips, Luigi; Ficarra, Vincenzo; Tostain, Jacques; de La Taille, Alexandre; Altieri, Vincenzo; Lobel, Bernard; Zigeuner, Richard E; Artibani, Walter; Guille, Francois; Abbou, Claude C; Salzano, Luigi; Gallo, Ciro; Comparison of predictive accuracy of four prognostic models for nonmetastatic renal cell carcinoma after nephrectomy: a multicenter European study.; Cancer; 2005; vol. 104 (no. 7); 1362-71

Study Characteristics

Study design	Retrospective cohort study
Study location	Italy, France and Austria
Study dates	1984 to 2002
Prognostic model(s)	Kattan UISS
Inclusion criteria	• Patients who underwent surgery for renal cell carcinoma (RCC).
Exclusion criteria	• Patients with distant metastasis (M+) • histologically confirmed lymph node-positive (N+) • large tumours (pT4) • benign disease • bilateral disease • carcinoma of the Bellini ducts • unclassified histology

	• those who died of surgical complications in the first month after nephrectomy • follow-up <1 month.
Selection of cohort	Multicentre
Number of participants	N=2404
Length of follow-up	5 years
Follow-up schedule	Not reported
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Overall survival Cancer-specific survival
Source of funding	Not industry funded
Additional comments	Survival curves were estimated by the product-limit method of Kaplan–Meier and compared by the log-rank statistic. The discriminating ability of the prognostic models was assessed using receiver operating characteristic (ROC) curves. The area under the ROC curves was calculated using a modified version for censored data of the c-index.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 2404)
% Female Sample size	% = 35.5
Age Custom value	62 (10 to 91)
Radical No of events	n = 89.9

Characteristic	Study (N = 2404)
Partial No of events	n = 10.1
Chromophobe Sample size	% = 3.5
Papillary Sample size	% = 9.6
Clear cell Sample size	% = 86.9
TNM 1 Sample size	% = 58.5
TNM 2 Sample size	% = 12.2
TNM 3a Sample size	% = 13.5
TNM 3b/c Sample size	% = 15.8

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias due to outcome or its determination and analysis as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Correa, 2019

Bibliographic Reference	Correa, Andres F; Jegede, Opeyemi; Haas, Naomi B; Flaherty, Keith T; Pins, Michael R; Messing, Edward M; Manola, Judith; Wood, Christopher G; Kane, Christopher J; Jewett, Michael A S; Dutcher, Janice P; DiPaola, Robert S; Carducci, Michael A; Uzzo, Robert G; Predicting Renal Cancer Recurrence: Defining Limitations of Existing Prognostic Models With Prospective Trial-Based Validation.; Journal of clinical oncology : official journal of the American Society of Clinical Oncology; 2019; vol. 37 (no. 23); 2062-2071

Study Characteristics

Study design	Retrospective cohort study
Study location	USA
Study dates	2010 to 2017
Prognostic model(s)	Karakiewicz Kattan Leibovich 2003 SSIGN UISS
Inclusion criteria	• Clear cell and non–clear cell RCC • intermediate or high risk RCC per modified UISS (pT1b and G3-4; pT2/pT3/pT4; N1).
Exclusion criteria	• Metastatic • central pathology unavailable • collecting duct histology • mixed histology.
Selection of cohort	Database or clinical registry ASSURE cohort
Number of participants	N=1647
Length of follow-up	Median follow-up, years UISS: 2.5 SSIGN: 9.7 Leibovich 2003: 5.4 Kattan: 3.3 Karakiewicz: 12
Follow-up schedule	Patients were assessed every 18 weeks by computed tomography or magnetic resonance imaging scans for recurrence during the first year. Then using scans and laboratory and clinical assessments every 6 months for another year, then once per year until disease recurrence or through 10 years.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Overall survival

	Cancer-specific survival
Source of funding	Authors received research funding from: Novartis, Sanofi Argos Therapeutics, Pfizer Bristol-Myers Squibb (Inst), Pfizer (Inst), AstraZeneca (Inst), Gilead Sciences (Inst), EMD Serono (Inst), eFFECTOR Therapeutics (Inst)
Additional comments	Discrimination was measured using the C-index. Model calibration was assessed by using calibration plots depicting predicted versus observed 5-year recurrence-free survival probabilities.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 1647)
% Female Sample size	n = 532 ; % = 32.3
Age Mean (SD)	55.9 (10.7)
TNM classification - pT1a Sample size	n = 10 ; % = 0.6
TNM classification - pT1b Sample size	n = 145 ; % = 8.8
TNM classification - pT2a Sample size	n = 219 ; % = 13.4
TNM classification - pT2b Sample size	n = 158 ; % = 9.6
TNM classification - pT3a Sample size	n = 1064 ; % = 64.8
TNM classification - pT3b Sample size	n = 25 ; % = 1.5
TNM classification - pT3c Sample size	n = 6 ; % = 0.4
TNM classification - pT4 Sample size	n = 14 ; % = 0.9

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate (*No information around loss to follow-up*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Cortellini, 2020

Bibliographic Reference	Cortellini, Alessio; Buti, Sebastiano; Bersanelli, Melissa; Cannita, Katia; Pinterpe, Giada; Venditti, Olga; Verna, Lucilla; Porzio, Giampiero; Natoli, Clara; Tinari, Nicola; Cindolo, Luca; Di Clemente, Luigi; Grassadonia, Antonino; De Tursi, Michele; Ficorella, Corrado; Predictive Ability for Disease-Free Survival of the GRade, Age, Nodes, and Tumor (GRANT) Score in Patients with Resected Renal Cell Carcinoma.; Current urology; 2020; vol. 14 (no. 2); 98-104

Study Characteristics

Study design	Retrospective cohort study
Study location	Italy
Study dates	1998-2018
Prognostic model(s)	GRANT UISS
Inclusion criteria	• Histologically confirmed diagnosis of renal cell carcinoma (RCC) • aged at least 18 years old • partial or radical nephrectomy.
Exclusion criteria	Not specified
Selection of cohort	Multicentre
Number of participants	N=134
Length of follow-up	Median 96 months (range 1.7–287.1 months)
Follow-up schedule	Patients were monitored with haematological and radiological examinations as indicated by physician’s choice, or at least every 6 months.
Outcome(s) of interest	Recurrence-free/disease-free survival

Source of funding	Supported by the Consorzio Interuniversitario Nazionale per la Bio-Oncologia (CINBO).
Additional comments	Median disease-free survival (DFS) and median overall survival (OS) were computed with Kaplan-Meier survival analysis, and the log-rank test was used to compare the median DFS among different risk subgroups by GRANT and UISS scores, and to evaluate hazard ratios (HRs) for each comparison.

Study arms
UISS low risk (N = 21)

UISS intermediate risk (N = 84)

UISS high risk (N = 29)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 134)
% Female Sample size	n = 41 ; % = 30.6
Age Custom value	Median 59 (range 29-84)
Clear cell Sample size	n = 105 ; % = 78.4
Papillary/chromophobe Sample size	n = 15 ; % = 11.2
Others Sample size	n = 14 ; % = 10.4
T1-3a Sample size	n = 105 ; % = 78.4
T3b-4 Sample size	n = 29 ; % = 21.6

Outcomes
UISS disease-free survival

Outcome	UISS intermediate risk vs UISS low risk, N2 = 84, N1 = 21	UISS high risk vs UISS low risk, N2 = 29, N1 = 21	UISS high risk vs UISS intermediate risk, N2 = 29, N1 = 84
Disease-free survival Hazard ratio/95% CI	0.68 (0.34 to 1.38)	0.68 (0.34 to 1.38)	0.99 (0.55 to 1.77)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate (No specific description of whether all enrolled participants were analysed, however there is some indication that censoring was performed. No measure of calibration was reported.)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Erdem, 2022

Bibliographic Reference	Erdem, Selcuk; Capitanio, Umberto; Campi, Riccardo; Mir, Maria Carme; Roussel, Eduard; Pavan, Nicola; Kara, Onder; Klatte, Tobias; Kriegmair, Maximilian C; Degirmenci, Enes; Aydin, Resat; Minervini, Andrea; Serni, Sergio; Berni, Alessandro; Rebez, Giacomo; Ozcan, Faruk; External validation of the VENUSS prognostic model to predict recurrence after surgery in non-metastatic papillary renal cell carcinoma: A multi-institutional analysis.; Urologic oncology; 2022; vol. 40 (no. 5); 198e9-198e17

Study Characteristics

Study design	Retrospective cohort study
Study location	7 tertiary institutions in Europe.
Study dates	1987-2020
Prognostic model(s)	VENUSS
Inclusion criteria	• Sporadic, unilateral, non-metastatic and histopathological proven papillary renal cell carcinoma (papRCC).
Exclusion criteria	• Without accurate postoperative follow-up data.

Selection of cohort	Multicentre
Number of participants	N=980
Length of follow-up	Median: 48 months (IQR 23-88)
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Local recurrence
Source of funding	Not reported
Additional comments	Univariate Cox Regression was performed to determine the association of VENUSS score and VENUSS risk groups with disease-recurrence (reported as a hazard ratio with 95% CI). Discrimination of disease-recurrence was assessed using the concordance index (reported with 95% CI).

Study arms
VENUSS low risk (0-2) (N = 617)

VENUSS intermediate risk (3-5) (N = 234)

VENUSS high risk (6-11) (N = 129)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 980)
% Female Sample size	n = 171 ; % = 17.4
Age Median (IQR)	64 (55 to 70)
Partial nephrectomy Sample size	n = 611 ; % = 62.3
Radical nephrectomy Sample size	n = 369 ; % = 37.7
Papillary type 1 Sample size	n = 471 ; % = 48.1
Papillary type 2 Sample size	n = 320 ; % = 32.7

Characteristic	Study (N = 980)
Papillary mixed Sample size	n = 4 ; % = 0.4
Papillary unknown subtype Sample size	n = 185 ; % = 18.9
pT1 Sample size	n = 675 ; % = 68.9
pT2 Sample size	n = 108 ; % = 11.1
pT3 Sample size	n = 187 ; % = 19.1
pT4 Sample size	n = 9 ; % = 0.9

Outcomes
Disease-recurrence

Outcome	VENUSS intermediate risk (3-5) vs VENUSS low risk (0-2), N2 = 234, N1 = 617	VENUSS high risk (6-11) vs VENUSS low risk (0-2), N2 = 129, N1 = 617	VENUSS high risk (6-11) vs VENUSS intermediate risk (3-5), N2 = 129, N1 = 234
Disease-recurrence Hazard ratio/95% CI	2.91 (1.9 to 4.46)	17.9 (12.25 to 26.25)	6.07 (4.17 to 8.83)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Flippot, 2017

Bibliographic Reference	Flippot, Ronan; Mouawad, Roger; Spano, Jean-Philippe; Roupret, Morgan; Comperat, Eva; Bitker, Marc-Olivier; Parra, Jerome; Vaessen, Christophe; Allanic, Frederick; Manach, Quentin; Tannir, Nizar M; Khayat, David; Su, Xiaoping; Malouf, Gabriel G; Expression of long non-coding RNA MFI2-AS1 is a strong predictor of recurrence in sporadic localized clear-cell renal cell carcinoma.; Scientific reports; 2017; vol. 7 (no. 1); 8540

Study Characteristics

Study design	Retrospective cohort study
Study location	France
Study dates	Not reported - if the dates match the discovery cohort (not extracted as no relevant outcomes reported for that cohort) then August 2005 to January 2016.
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• available fresh frozen tumour samples from stages I, II and III clear cell renal cell carcinoma • nephrectomy status: not reported for validation cohort. Discovery cohort (not extracted, see above) had partial or radical nephrectomy. Unclear whether this criteria was applied for the validation cohort.
Exclusion criteria	• Patients withTFE3 or TFEB translocations and hereditary cancers were excluded because the natural history and oncogenic alterations might differ from those associated with sporadic ccRCC • insufficient RNA yield • Follow up less than 3 months
Selection of cohort	Single centre (Pitié-Salpêtrière Hospital)
Number of participants	N=167
Length of follow-up	Median 41 months (range 3-122)
Follow-up schedule	Follow up for each patient was not standardised, but patients were monitored according to the standard of care, which included receiving a CT scan every 3–6 months
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Recurrence-free/disease-free survival
Source of funding	"Fondation Avec" (charity) provided laboratory equipment funding and research grants.
Additional comments	Disease free survival was defined as the time from initial surgery to first relapse, identified by physical examination, biopsy or imaging.

	DFS was censored at the last FU or death in patients without documented recurrence. Leibovich classification stratifies patients with low (0–2), intermediate (3–5) or high (>5) recurrence risk. This study also analysed between patients with Leibovich scores <5 and those with scores ≥5 to account for intermediate-risk patients with aggressive features and comply with current adjuvant trials. This study also reports a discovery cohort. No results from this cohort are relevant to this review. Statistical analysis: correlation between Leibovich scores and DFS was estimated by the Kaplan-Meier model (univariate analysis). C-statistics were determined but not presented with confidence intervals so not extracted.

Study arms
Leibovich 2003 low risk (N = 107)

Leibovich 2003 intermediate risk (N = 40)

Leibovich 2003 high risk (N = 20)

Leibovich 2003 <5 points (N = 135)

Leibovich 2003 ≥5 points (N = 32)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 167)
% Female No of events	n = 56 ; % = 34
Age Custom value	median 63, range 31-90
TNM stage 1-2 No of events	n = 144 ; % = 86
TNM stage 3-4 No of events	n = 23 ; % = 14

Outcomes
Disease-free survival

Outcome	Leibovich 2003 intermediate risk vs Leibovich 2003 low risk, N2 = 40, N1 = 107	Leibovich 2003 high risk vs Leibovich 2003 low risk, N2 = 20, N1 = 107	Leibovich 2003 high risk vs Leibovich 2003 intermediate risk, N2 = 20, N1 = 40	Leibovich 2003 ≥5 points vs Leibovich 2003 <5 points, N2 = 32, N1 = 135
Disease-free survival Univariate analysis Hazard ratio/95% CI	1.99 (0.8 to 4.93)	7.29 (1.63 to 32.58)	3.33 (1.11 to 9.99)	4.11 (1.52 to 11.1)

Disease-free survival - Polarity - Lower values are better

Critical appraisal PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis and unclear risk of bias for selection of participants: Participants with incomplete data were excluded, potentially leading to biased predictor-outcome associations and predictive performance. No measures of calibration reported. Inclusion and exclusion criteria not fully reported.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Fu, 2015

Bibliographic Reference	Fu, Qiang; Chang, Yuan; An, Huimin; Fu, Hangcheng; Zhu, Yu; Xu, Le; Zhang, Weijuan; Xu, Jiejie; Prognostic value of interleukin-6 and interleukin-6 receptor in organ-confined clear-cell renal cell carcinoma: a 5-year conditional cancer-specific survival analysis.; British journal of cancer; 2015; vol. 113 (no. 11); 1581-9

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2001-2004
Prognostic model(s)	SSIGN UISS

Inclusion criteria	• Pathologically proven renal cell carcinoma • clear cell
Exclusion criteria	• Deficient follow-up • unreached clinical records • poor tumour sample preservation for TNM • unqualified HR section • suspicious death (died within 1 month after surgery) • extensive necrosis • inadequate control staining or ambiguous marker staining • unexpected therapy (treated with cytokine; merely open biopsy) • metastasis.
Selection of cohort	Single centre
Number of participants	N=180
Length of follow-up	Median (IQR): 110 (82–117) months
Follow-up schedule	All patients had routine examination every 5–6 months during the first 5 years and annually thereafter.
Outcome(s) of interest	Cancer-specific survival
Source of funding	Grants from National Basic Research Program of China, National Natural Science Foundation of China, Program for New Century Excellent Talents in University (NCET-13-0146), and Shanghai Rising-Star Program
Additional comments	CSS was assessed and graphically illustrated using Kaplan–Meier or life-table method, and log-rank test was used for comparing different scoring categories. The concordance index (C index) was used to assess the predictive accuracy of different models.

Population characteristics
Study-level characteristics

Characteristic	**Study (N = 180)**
% Female Sample size	n = 61 ; % = 33.9
Age Median (IQR)	58 (50 to 68)
Nephrectomy status - Partial nephrectomy Sample size	n = 32 ; % = 17.8
Nephrectomy status - Radical nephrectomy	n = 148 ; % = 82.2

Characteristic	Study (N = 180)
Sample size	
TNM classification - pT1 Sample size	n = 117 ; % = 65
TNM classification - pT2 Sample size	n = 21 ; % = 11.7
TNM classification - pT3 Sample size	n = 41 ; % = 22.8
TNM classification - pT4 Sample size	n = 1 ; % = 0.5

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate (*assessed by Usher-Smith 2022 as low risk. Downgraded as there was not enough information to judge whether there was a measure of calibration*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Fu, 2016

Bibliographic Reference	Fu, Qiang; Chang, Yuan; Zhou, Lin; An, Huimin; Zhu, Yu; Xu, Le; Zhang, Weijuan; Xu, Jiejie; Positive intratumoral chemokine (C-C motif) receptor 8 expression predicts high recurrence risk of post-operation clear-cell renal cell carcinoma patients.; Oncotarget; 2016; vol. 7 (no. 7); 8413-21

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2008 to 2009
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• histopathological-proven clear cell RCC • received partial- or radical- nephrectomy between Jan 7, 2008 and Dec 23, 2009 • had available specimen of tumor mass

Exclusion criteria	• people with T4 stage • people with M1 metastatic • cases with tissue which failed to stain
Number of participants	N=472
Length of follow-up	Median for patients alive at last follow-up: 73 months (IQR 72-74).
Follow-up schedule	All patients were examined routinely every 5-6 months during the first 5 years of follow-up and annually thereafter.
Outcome(s) of interest	Model discrimination (C-stats)
Source of funding	National Basic Research Program of China National Natural Science Foundation of China Program for New Century Excellent Talents in University Shanghai Rising-Star Program
Additional comments	Leibovich 2003 c index for recurrence free survival extracted. The Leibovich recurrence risk scores of all 472 patients were calculated and divided into three risk groups: low risk (score 0-2; n = 260, 55.1%), intermediate risk (score 3-5; n = 164, 34.7%), high risk (score≥6; n = 48, 10.2%). The concordance index (C index) and Akaike's Information Criteria (AIC) were used to assess the predictive accuracy and sufficiency of different models. To reduce overfit bias and internally validate the predictive accuracy estimates, multivariable models and C index calculations were subjected to 1000 bootstrap resamples.

Population characteristics
Study-level characteristics

Characteristic	**Study (N = 472)**
% Female No of events	n = 137 ; % = 29
Age Median (IQR)	55 (46 to 63)
Had partial nephrectomy No of events	n = 227 ; % = 48.1
Had radical nephrectomy No of events	n = 245 ; % = 51.9

Characteristic	Study (N = 472)
TNM classification: pT1 No of events	n = 330 ; % = 69.9
TNM classification: pT2 No of events	n = 33 ; % = 7
TNM classification: pT3 No of events	n = 109 ; % = 23.1

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate *(Unclear risk of bias for analysis: unclear whether all enrolled participants were included in the analysis, and whether missing data was handled appropriately.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Haddad, 2017

Bibliographic Reference	Haddad, Ahmed Q; Luo, Jun-Hang; Krabbe, Laura-Maria; Darwish, Oussama; Gayed, Bishoy; Youssef, Ramy; Kapur, Payal; Rakheja, Dinesh; Lotan, Yair; Sagalowsky, Arthur; Margulis, Vitaly; Prognostic value of tissue-based biomarker signature in clear cell renal cell carcinoma.; BJU international; 2017; vol. 119 (no. 5); 741-747

Study Characteristics

Study design	Retrospective cohort study
Study location	United States
Study dates	1997 to 2010
Prognostic model(s)	SSIGN
Inclusion criteria	• Partial or radical nephrectomy • clear cell renal cell carcinoma • non-metastatic.
Exclusion criteria	• No complete immunostaining for the markers evaluated in the study.

FINAL

Selection of cohort	Single centre
Number of participants	N= 367 overall cohort n=183 training cohort n=184 validation cohort
Length of follow-up	Median 63.5 months (IQR 24.0 to 85.3)
Follow-up schedule	Physical examination, serum chemistry, liver function tests, chest radiography and abdominal US or CT scan performed every 3 months for the first year and semi-annually after.
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Recurrence-free/disease-free survival
Source of funding	No funding
Additional comments	Survival probabilities were determined by Kaplan–Meier analysis. Cox regression was used to evaluate the association of the final risk classifier and SSIGN score with RFS.

Study arms
SSIGN, score 0-5, overall cohort (N = 309)

SSIGN,>5, overall cohort (N = 58)

Population characteristics
Study-level characteristics

Characteristic	**Study (N =)**
% female, training set Sample size	n = 75 ; % = 41
% female, validation set Sample size	n = 76 ; % = 41.3
Age, training set Median (IQR)	56 (27 to 85)
Age, validation set Median (IQR)	59 (17 to 85)

Characteristic	Study (N =)
Radical nephrectomy, training set Sample size	n = 107 ; % = 58.5
Partial nephrectomy, training set Sample size	n = 76 ; % = 41.5
Radical nephrectomy, validation set Sample size	n = 97 ; % = 52.7
Partial nephrectomy, training set Sample size	n = 87 ; % = 47.3
PT1a, training set No of events	n = 81 ; % = 44.3
pT1b, training set No of events	n = 43 ; % = 23.5
pT2, training set No of events	n = 16 ; % = 8.7
pT3a, training set No of events	n = 12 ; % = 6.6
pT3b, training set No of events	n = 30 ; % = 16.4
pT3c, training set No of events	n = 1 ; % = 0.5
pT4, training set No of events	n = 0 ; % = 0
pT1a, validation set No of events	n = 100 ; % = 54.3
pT1b, validation set No of events	n = 37 ; % = 20.1
pT2, validation set No of events	n = 14 ; % = 7.6
pT3a, validation set No of events	n = 11 ; % = 6

Characteristic	Study (N =)
pT3b, validation set No of events	n = 20 ; % = 10.9
pT3c, validation set No of events	n = 0 ; % = 0
pT4, validation set No of events	n = 2 ; % = 1.1

Outcomes

Recurrence-free survival

Outcome	SSIGN,>5, overall cohort vs SSIGN, score 0-5, overall cohort, N2 = 58, N1 = 309
Recurrence-free survival Hazard ratio/95% CI	3.13 (1.69 to 5.78)

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Han, 2003

Bibliographic Reference	Han, KR Bleumer, I Pantuck, AJ Kim, HL Dorey, FJ Janzen, NK Zisman, A Dinney, CP Wood, CG Swanson, DA Said, JW Figlin, RA Mulders, PFA Belldegrun, AS; Validation of an integrated staging system toward improved prognostication of patients with localized renal cell carcinoma in an international population; JOURNAL OF UROLOGY; 2003; vol. 170 (no. 6); 2221 - 2224

Study Characteristics

Study design	Retrospective cohort study
Study location	The Netherlands and the US
Study dates	NN: 1990 to 2001; MDA: 1987 to 2000; UCLA: 1989 to 2001
Prognostic model(s)	Zisman

Inclusion criteria	People who underwent radical or partial nephrectomy with localized disease who had no evidence of nodal involvement or metastatic spread.
Exclusion criteria	Not reported
Selection of cohort	Multicentre
Number of participants	NN: N=177; MDA: N=399; UCLA: N=484
Length of follow-up	NN: median 63 months; MDA: median 32 months; UCLA: median 33 months
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Cancer-specific survival Described as disease-specific survival
Source of funding	Not reported
Additional comments	None

Study arms
NN (N = 177)
University Medical Center Nijmegen, Netherlands

MDA (N = 399)
MD Anderson, US

UCLA (N = 484)
University of California, Los Angeles

Population characteristics
Arm-level characteristics

Characteristic	NN (N = 177)	MDA (N = 399)	UCLA (N = 484)
% Female Converted from number of males Sample size	n = 56 ; % = 32	n = 134 ; % = 34	n = 175 ; % = 36
Age Mean (SD)	59.6 (*NR*)	58.1 (*NR*)	61.5 (*NR*)
TNM classification - T1 Sample size	n = 58 ; % = 33	n = 157 ; % = 39	n = 272 ; % = 56

Characteristic	NN (N = 177)	MDA (N = 399)	UCLA (N = 484)
TNM classification - T2 Sample size	n = 32 ; % = 18	n = 89 ; % = 23	n = 69 ; % = 14
TNM classification - T3 Sample size	n = 83 ; % = 47	n = 153 ; % = 38	n = 138 ; % = 29
TNM classification - T4 Sample size	n = 4 ; % = 2	n = 0 ; % = 0	n = 5 ; % = 1

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(The paper did not report a measure of calibration. There was also a lack of clarity around follow-up, and how many people had the outcome.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

He, 2020

Bibliographic Reference	He, Z; Deng, T; Duan, X; Zeng, G; Profiles of overall survival-related gene expression-based risk signature and their prognostic implications in clear cell renal cell carcinoma.; Bioscience reports; 2020; vol. 40 (no. 9)

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	December 2019
Prognostic model(s)	TNM 2016
Inclusion criteria	Patients with ccRCC Patients with Fragments Per Kilobase per Million (FPKM) expression
Exclusion criteria	Patients with lack survival information
Selection of cohort	Multicentre
Number of participants	Total N = 614

	Training cohort N = 265 Validation cohort N = 265 ICGC cohort N = 84
Length of follow-up	Not reported
Outcome(s) of interest	Overall survival
Source of funding	This work was supported by the National Natural Science Foundation of China [grant numbers 1670643, 81870483, 81802821]; the Collaborative Innovation Project of Guangzhou Education Bureau [grant number 1201620011]; the Guangzhou Science Technology and Innovation Commission [grant number 201704020193]; and the Science and Technology Planning Project of Guangdong Province [grant number 2017B030314108].
Additional comments	To identify independent prognostic factors to OS, parameters including age, gender, TNM stage, history of prior malignancy, and the aforesaid risk score were included in univariate and multivariate Cox regression analyses in the training set.

Study arms
Training TCGA cohort (N = 265)

Validation TGCA cohort (N = 265)

ICGC cohort (N = 84)

Stage I/II (N = 322)

Stage III/IV (N = 205)

Population characteristics
Arm-level characteristics

Characteristic	Training TCGA cohort (N = 265)	Validation TGCA cohort (N = 265)	ICGC cohort (N = 84)
% Female No of events	n = 99 ; % = 37.36	n = 87 ; % = 32.83	n = 9 ; % = 10.71
Age Mean (SD)	60.72 (12.84)	60.4 (11.41)	60.86 (9.68)
TNM classification - Stage I No of events	n = 133 ; % = 50.19	n = 132 ; % = 49.81	n = 48 ; % = 57.14

Characteristic	Training TCGA cohort (N = 265)	Validation TGCA cohort (N = 265)	ICGC cohort (N = 84)
TNM classification - Stage II No of events	n = 28 ; % = 10.57	n = 29 ; % = 10.94	n = 12 ; % = 14.29
TNM classification - Stage III No of events	n = 61 ; % = 23.02	n = 62 ; % = 23.4	n = 15 ; % = 17.86
TNM classification - Stage IV No of events	n = 43 ; % = 16.22	n = 39 ; % = 14.72	n = 9 ; % = 10.71
TNM classification - Not available No of events	n = 0 ; % = 0	n = 3 ; % = 1.13	n = 0 ; % = 0

Outcomes
Survival

Outcome	Stage III/IV vs Stage I/II, N2 = 205, N1 = 322
Overall survival Hazard ratio/95% CI	3.72 (2.41 to 5.75)

Overall survival - Polarity - Higher values are better

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Hu, 2020

Bibliographic Reference	Hu, Xu; Yang, Zhi-Qiang; Dou, Wei-Chao; Shao, Yan-Xiang; Wang, Yao-Hui; Lia, Thongher; Li, Xiang; Validation of the Prognostic Value of Preoperative Albumin-to-Alkaline Phosphatase Ratio in Patients with Surgically Treated Non-Metastatic Renal Cell Carcinoma.; OncoTargets and therapy; 2020; vol. 13; 8287-8297

Study Characteristics

Study design	Retrospective cohort study

Study location	China
Study dates	January 2010 to December 2013
Prognostic model(s)	SSIGN UISS
Inclusion criteria	• Non-metastatic renal cell carcinoma • Have had nephrectomy
Exclusion criteria	• Incomplete clinicopathological information • Bilateral / multiple RCC • with diseases that might influence albumin or alkaline phosphatase (e.g. bone diseases, liver diseases, active infection) • Pathological N+ or distant metastases • Without available follow-up data
Selection of cohort	Single centre (University West China Hospital)
Number of participants	N=648
Length of follow-up	Median: 84 months. No further information reported.
Outcome(s) of interest	Model discrimination (C-stats) Overall survival Cancer-specific survival
Source of funding	No conflicts of interest.
Additional comments	Discrimination evaluated using the concordance index (C-index) - no further information reported. All patients were regularly followed up every 3 months for the first 2 years, every 6 months for 3–5 years, and then once a year afterward.

Population characteristics
Study-level characteristics

Characteristic	**Study (N = 648)**
% Female No of events	n = 254 ; % = 39.2
Age Mean (SD)	54.84 (12.64)

Characteristic	Study (N = 648)
Radical nephrectomy No of events	n = 437 ; % = 67.44
Partial nephrectomy No of events	n = 211 ; % = 32.56
Clear cell RCC No of events	n = 545 ; % = 84.1
Non-clear cell RCC No of events	n = 103 ; % = 15.9
Pathological T1 No of events	n = 522 ; % = 80.56
Pathological T2 No of events	n = 55 ; % = 8.49
Pathological T3 No of events	n = 63 ; % = 9.72
Pathological T4 No of events	n = 8 ; % = 1.23

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: Participants with incomplete data were excluded, potentially leading to biased predictor-outcome associations and predictive performance.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Huang, 2017

Bibliographic Reference	Huang, H.; Chen, S.; Yu, W.; Ye, Z.; Li, W.; Xing, J.; Wu, X.; The association between renal sinus fat area and the progressionfree survival in Chinese non-metastatic clear-cell renal cell carcinoma patients; Oncotarget; 2017; vol. 8 (no. 39); 65481-65491

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	December 2009 and December 2015
Prognostic model(s)	Leibovich 2003
Inclusion criteria	Patients with non-metastatic clear cell renal cell carcinoma
Exclusion criteria	Patients were excluded from the analyses if (1) they were operated in our centre but had received CT scans in other hospitals before operation and therefore digital CT images were not available for analysis; (2) they did not undergo operation (partial or radical nephrectomy) as the main treatment; and (3) they had surgery elsewhere.
Selection of cohort	Single centre
Number of participants	N = 268 Low renal sinus fat area N = 134 High renal sinus fat area N = 134
Length of follow-up	Median: 38 months
Follow-up schedule	Not reported
Covariates adjusted for in the multivariable regression modelling	Fuhrman and WHO/ISUP grading systems were analysed by univariable and multivariable Cox regression models.
Outcome(s) of interest	Model discrimination (C-stats) Progression-free survival
Source of funding	None
Additional comments	Survival curves were plotted by the Kaplan-Meier method and assessed by the Log-rank test. Subsequently, Cox regression analysis was performed to identify potential prognostic factors for survival. All the independent predictive factors were organized into a prognostic nomogram. The Harrell's concordance index (c-index) was determined for the Leibovich score system and the new nomogram to assess prognostic accuracy

Study arms

Low renal sinus fat area (N = 134)

High renal sinus fat area (N = 134)

Population characteristics

Arm-level characteristics

Characteristic	Low renal sinus fat area (N = 134)	High renal sinus fat area (N = 134)
% Female No of events	n = 46 ; % = 34.3	n = 42 ; % = 31.3
Less than 60 No of events	n = 91 ; % = 67.9	n = 83 ; % = 64.9
60 or greater No of events	n = 43 ; % = 32.1	n = 51 ; % = 38.1
stage I No of events	n = 87 ; % = 64.9	n = 113 ; % = 84.3
Stage II No of events	n = 24 ; % = 17.9	n = 11 ; % = 8.2
Stage III No of events	n = 23 ; % = 17.2	n = 10 ; % = 7.5

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis and unclear risk of bias for outcome or is determination.*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Hupertan, 2006

Bibliographic Reference	Hupertan, Vincent; Roupret, Morgan; Poisson, Jean-Francois; Chretien, Yves; Dufour, Bertrand; Thiounn, Nicolas; Mejean, Arnaud; Low predictive accuracy of the Kattan postoperative nomogram for renal cell carcinoma recurrence in a population of French patients.; Cancer; 2006; vol. 107 (no. 11); 2604-8

Study Characteristics

Study design	Retrospective cohort study

Study location	France
Study dates	1985 to 2000
Prognostic model(s)	Kattan
Inclusion criteria	• Had undergone surgery (open radical nephrectomy, partial nephrectomy, or in situ tumor resection after a subcostal or flank incision).
Exclusion criteria	• Performance status >3 and/or metastatic disease at diagnosis • a large tumour (pT4) • bilateral synchronous disease (ie, Von Hippel Lindau) • preoperative lymph node invasion • benign disease of final pathological exam • collect duct carcinoma • tumour with unclassified histology • chronic renal insufficiency • solitary kidney • lost to follow-up.
Selection of cohort	Single centre
Number of participants	N=565
Length of follow-up	Median 60 months
Follow-up schedule	Annual abdominal US and CT abdomen
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not reported
Additional comments	Relations between all predictor variables included in the Kattan nomogram and survival were evaluated by Cox proportional hazards regression analysis.

Population characteristics
Study-level characteristics

Characteristic	**Study (N = 656)**
% Female Sample size	n = 163 ; % = 28.9
Age Median (IQR)	62 (*empty data* to *empty data*)

Characteristic	Study (N = 656)
Nephrectomy status - Radical Sample size	n = 477 ; % = 84.4
Nephrectomy status - Tumorectomy Sample size	n = 60 ; % = 10.6
Nephrectomy status - Nephron-sparing Sample size	n = 28 ; % = 5
RCC subtypes - Clear cell Sample size	n = 470 ; % = 83.2
RCC subtypes - Papillary Sample size	n = 74 ; % = 13.1
RCC subtypes - Chromophobe Sample size	n = 21 ; % = 3.7
TNM classification - TNM 1 Sample size	n = 363 ; % = 64.2
TNM classification - TNM 2 Sample size	n = 118 ; % = 20.9
TNM classification - TNM 3a Sample size	n = 40 ; % = 7.1
TNM classification - TNM 3b/c Sample size	n = 44 ; % = 7.8

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Hutterer, 2019

Bibliographic Reference	Hutterer, Georg C; Posch, Florian; Buser, Lorenz; Zigeuner, Richard; Morshauser, Laura; Otto, Wolfgang; Wild, Peter J; Burger, Maximilian; May, Matthias; Pichler, Martin; Brookman-May, Sabine

D; BioScore (B7-H1, survivin, and Ki-67) does not predict cancer-specific mortality in surgically treated patients with renal cell carcinoma: An external validation study.; Urologic oncology; 2019; vol. 37 (no. 7); 510-518

Study Characteristics

Study design	Retrospective cohort study
Study location	Austria
Study dates	1999 to 2004
Prognostic model(s)	SSIGN
Inclusion criteria	• Clinically localised (N0M0) renal cell carcinoma • Had undergone surgery between 1999 and 2004 at a single centre
Exclusion criteria	• Missing follow-up information / tissue specimens
Selection of cohort	Single centre ("academic tertiary centre")
Number of participants	N=382
Length of follow-up	7.8 years (6.3, 9.9) (Median, IQR)
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Cancer-specific survival
Source of funding	No funding received
Additional comments	C index quantified with Harrell's concordance index. Cancer-specific survival was analysed with Kaplan-Meier estimators and compared between 2 or more groups with the log-rank test. Hazards of death-from-RCC were modelled with uni- and multivariable Cox proportional hazards models. Hazard ratio is from a univariate analysis.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 382)
% Female No of events	n = 150 ; % = 39
Age Median (IQR)	64 (57 to 71)
Clear cell RCC No of events	n = 277 ; % = 73
Papillary RCC No of events	n = 87 ; % = 23
Chromophobe RCC No of events	n = 18 ; % = 5
TNM pT3b-pT4 No of events	n = 14 ; % = 4

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: Participants with incomplete data were excluded, potentially leading to biased predictor-outcome associations and predictive performance. No measure of calibration presented.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Hutterer, 2014

Bibliographic Reference	Hutterer, Georg C; Stoeckigt, Caroline; Stojakovic, Tatjana; Jesche, Johanna; Eberhard, Katharina; Pummer, Karl; Zigeuner, Richard; Pichler, Martin; Low preoperative lymphocyte-monocyte ratio (LMR) represents a potentially poor prognostic factor in nonmetastatic clear cell renal cell carcinoma.; Urologic oncology; 2014; vol. 32 (no. 7); 1041-8

Study Characteristics

Study design	Retrospective cohort study

Study location	Austria
Study dates	2000 and 2010
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• Participants with non-metastatic clear cell renal cell carcinoma (RCC) who underwent curative radical or partial nephrectomy.
Exclusion criteria	Not specified
Selection of cohort	Single centre
Number of participants	N=678
Length of follow-up	Mean 44 (range to 130) months
Follow-up schedule	Follow-up evaluations were carried out every 6 months for the first 5 years, and then annually after for locally advanced tumours. For organ confined cancers, imaging was performed 2 times in the first year after surgery, and then annually.
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Cancer-specific survival
Source of funding	Not reported
Additional comments	Patients' clinical endpoints were calculated using the Kaplan-Meier method and compared using the log-rank test. The Harrell concordance index(c-index) was used for assessment of the prognostic accuracy of the model in multivariate analyses.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 678)
% Female Sample size	n = 273 ; % = 40.3

Characteristic	Study (N = 678)
Age Mean (SD)	63.8 (11.97)
T1a Sample size	n = 334 ; % = 49.3
T1b Sample size	n = 117 ; % = 17.2
T2a Sample size	n = 32 ; % = 4.7
T2b Sample size	n = 5 ; % = 0.7
T3a Sample size	n = 170 ; % = 25.1
T3b Sample size	n = 16 ; % = 2.4
T3c Sample size	n = 2 ; % = 0.3
T4 Sample size	n = 2 ; % = 0.3

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for outcome and its determination and analysis as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Ishiyama, 2024

Bibliographic Reference	Ishiyama, Yudai; Kondo, Tsunenori; Yoshida, Kazuhiko; Iizuka, Junpei; Takagi, Toshio; Prognostic Value of the Lung Immune Prognostic Index on Recurrence after Radical Surgery for High-Risk Renal Cell Carcinoma.; Cancers; 2024; vol. 16 (no. 4)

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	January 2004 to August 2021
Prognostic model(s)	GRANT UISS
Inclusion criteria	• Nonmetastatic renal cell carcinoma • Had undergone curative surgery • pT3 or higher staging, or pN1-2 lymph node involvement confirmed by histopathology
Exclusion criteria	• Inadequate laboratory data • Incomplete follow up • For patients who had enlarged regional lymph nodes in the pre-surgical imaging, only those with their nodes subsequently completely resected were included.
Selection of cohort	Multicentre (Two tertiary care centres affiliated with Tokyo Women's Medical University)
Number of participants	N=235
Length of follow-up	19.8 months (5.9, 48.3) (median, IQR)
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	No funding received.
Additional comments	Harrell’s concordance index (C-index) was used to assess the discrimination of the UISS and GRANT scores. These were compared to a new model which is not included in the protocol for this review.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 235)
% Female No of events	n = 69 ; % = 29.4
Age Median (IQR)	67 (61 to 73)
Clear cell RCC No of events	n = 202 ; % = 86
Non-clear cell RCC No of events	n = 33 ; % = 14
Pathological T stage: T1/T2 No of events	n = 62 ; % = 26.4
Pathological T stage: T3a No of events	n = 101 ; % = 43
Pathological T stage: T3b No of events	n = 47 ; % = 20
Pathological T stage: T3c No of events	n = 20 ; % = 8.5
Pathological T stage: T4 No of events	n = 5 ; % = 2.1

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: Participants with incomplete data were excluded, potentially leading to biased predictor-outcome associations and predictive performance. No calibration results presented.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Jensen, 2009

Bibliographic Reference	Jensen, Hanne Krogh; Donskov, Frede; Marcussen, Niels; Nordsmark, Marianne; Lundbeck, Finn; von der Maase, Hans; Presence of intratumoral neutrophils is an independent prognostic factor in localized renal cell carcinoma.; Journal of clinical oncology : official journal of the American Society of Clinical Oncology; 2009; vol. 27 (no. 28); 4709-17

Study Characteristics

Study design	Retrospective cohort study
Study location	Denmark
Study dates	Between 1992 and 2001
Prognostic model(s)	Leibovich 2003
Inclusion criteria	Patients with radical nephrectomy
Exclusion criteria	• non–clear cell histology • distant metastases or significant lymphadenopathy at diagnosis • recurrence of previous RCC • previous interleukin-2 treatment, other synchronic cancers, perioperative mortality, renal transplantation, and lack of tumour tissue
Selection of cohort	Single centre
Number of participants	N=121
Length of follow-up	Median 124 months (74 to 194) for patients who were alive at the end of the study
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Aarhus University Hospital Research Initiative; Max and Inger Wørzner Foundation; Frits, Georg, and Marie Cecilie Glud Foundation; and Aarhus Radium Center Research Foundation.
Additional comments	The paper describes that "the low-risk population had a lower RFS than expected, which may be due to selection of patients with large tumours and other comorbidities who were referred to the specialized university hospital. Thus, the distribution according to stage was skewed toward locally advanced tumours."

Study arms

Leibovich 2003, low risk (N = 26)

Leibovich 2003, intermediate risk (N = 52)

Leibovich 2003, high risk (N = 43)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 121)
% Female Sample size	n = 47 ; % = 39
Age Range	19 to 82
Age Median (IQR)	61 (*NR* to *NR*)
Nephrectomy status - Radical nephrectomy Sample size	n = 121 ; % = 100
RCC subtypes - Clear cell Sample size	n = 121 ; % = 100
TNM classification - 2002 TNM stage I Sample size	n = 50 ; % = 41
TNM classification - 2002 TNM stage II Sample size	n = 16 ; % = 13
TNM classification - 2002 TNM stage III Sample size	n = 51 ; % = 42
TNM classification - 2002 TNM stage IV Sample size	n = 4 ; % = 3

Outcomes

Arm-based data

Outcome	Leibovich 2003, low risk, Follow-up, N = 26	Leibovich 2003, intermediate risk, Follow-up, N = 52	Leibovich 2003, high risk, Follow-up, N = 43
Recurrence-free survival	n = 6 ; % = 23.1	n = 24 ; % = 46.2	n = 31 ; % = 72.1

Outcome	Leibovich 2003, low risk, Follow-up, N = 26	Leibovich 2003, intermediate risk, Follow-up, N = 52	Leibovich 2003, high risk, Follow-up, N = 43
No of events			

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(The follow-up schedule was not reported, so it was unclear whether all participants had similar follow-up. The paper did not report a measure of calibration. Staging was done retrospectively on the basis of pathology reports and patient files, and it was unclear whether this was done without knowledge of the outcome.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Kang, 2020

Bibliographic Reference	Kang, Xiangpeng; Shi, Hongzhe; Wang, Dong; Xiao, Zejun; Tian, Jun; Bi, Xingang; Jiang, Weixing; Li, Changling; Ma, Jianhui; Zheng, Shan; Sun, Yueping; Shou, Jianzhong; Combination of Hematology Indicators and Oncological Characteristics as a New Promising Prognostic Factor in Localized Clear Cell Renal Cell Carcinoma.; Cancer management and research; 2020; vol. 12; 10023-10033

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	March 2013 to March 2015
Prognostic model(s)	SSIGN
Inclusion criteria	• No primary cancer of any other organs before nephrectomy • No chronic inflammatory allergic disease • No history of taking anticoagulants such as for cardiovascular or cerebrovascular thrombosis • Exact pathological diagnosis of clear cell renal cell carcinoma (ccRCC) • Complete resection of the tumour, which was defined as a negative incisal margin • Complete clinicopathological characteristics and follow-up data • No evidence of extrarenal metastasis.

Exclusion criteria	Not reported
Selection of cohort	Single centre (Cancer Institute and Hospital of the Chinese Academy of Medical Sciences [CAMS])
Number of participants	Training cohort: N=221 Validation cohort: N=221
Length of follow-up	58.7 months (51.7, 65.1) (median, range)
Outcome(s) of interest	Model discrimination (C-stats)
Source of funding	• Chinese Academy of Medical Sciences (CAMS) Initiative for Innovative Medicine • Beijing hope run special fund of cancer foundation of China • Chinese Academy of Medical Sciences (CAMS) Initiative for Innovative Medicine
Additional comments	The dataset was split into training and validation cohorts with repeated random sampling until there was no significant difference between the two cohorts with respect to all variables. The prognostic accuracy of the SSIGN risk model using Harrell's concordance index (C-index). The authors also reported on a new model which is not included in the protocol for this review. Characteristics are for all participants overall (N=442)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 442)
% Female No of events	n = 127 ; % = 28.7
Under 60 years old No of events	n = 314 ; % = 71
60 and older No of events	n = 128 ; % = 29
TNM stage 1-2 No of events	n = 390 ; % = 88.2

Characteristic	Study (N = 442)
TNM stage 3 No of events	n = 52 ; % = 11.8

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: Participants with incomplete data were excluded, potentially leading to biased predictor-outcome associations and predictive performance.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Klatte, 2009

Bibliographic Reference	Klatte, T; Seligson, DB; LaRochelle, J; Shuch, B; Said, JW; Riggs, SB; Zomorodian, N; Kabbinavar, FF; Pantuck, AJ; Belldegrun, AS; Molecular signatures of localized clear cell renal cell carcinoma to predict disease-free survival after nephrectomy.; Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology; 2009; vol. 18 (no. 3); 894-900

Study Characteristics

Study design	Retrospective cohort study
Study location	The US
Study dates	Between 1989 and 2000
Prognostic model(s)	UISS
Inclusion criteria	Patients who underwent radical or partial nephrectomy for sporadic, clinically localised (N0M0) clear cell RCC
Exclusion criteria	Not reported
Selection of cohort	Single centre
Number of participants	N=170
Length of follow-up	Median follow-up 7.1 years (range 0.6 to 16.9 years)

Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not reported
Additional comments	None

Population characteristics
Study-level characteristics

Characteristic	**Study (N = 170)**
% Female Sample size	n = 62 ; % = 36
Age Range	27 to 89
Age Median (IQR)	64 (*NR* to *NR*)
Nephrectomy status - Radical Sample size	n = 124 ; % = 72.9
Nephrectomy status - Partial Sample size	n = 46 ; % = 27.1
RCC subtypes - Clear cell Sample size	n = 170 ; % = 100
TNM classification - T1 Sample size	n = 94 ; % = 55
TNM classification - T2 Sample size	n = 18 ; % = 11
TNM classification - T3 Sample size	n = 54 ; % = 32
TNM classification - T4 Sample size	n = 4 ; % = 2

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Klatte, 2019

Bibliographic Reference	Klatte, Tobias; Gallagher, Kevin M; Afferi, Luca; Volpe, Alessandro; Kroeger, Nils; Ribback, Silvia; McNeill, Alan; Riddick, Antony C P; Armitage, James N; 'Aho, Tevita F; Eisen, Tim; Fife, Kate; Bex, Axel; Pantuck, Allan J; Stewart, Grant D; The VENUSS prognostic model to predict disease recurrence following surgery for non-metastatic papillary renal cell carcinoma: development and evaluation using the ASSURE prospective clinical trial cohort.; BMC medicine; 2019; vol. 17 (no. 1); 182

Study Characteristics

Study design	Retrospective cohort study
Study location	USA
Prognostic model(s)	Leibovich 2018 UISS VENUSS TNM not specified
Inclusion criteria	• Completely resected non-metastatic renal cell carcinoma (RCC) • high risk for recurrence.
Exclusion criteria	Not specified but same as exclusion criteria applied to participants entering the RCT where data is from.
Selection of cohort	Database or clinical registry ASSURE
Number of participants	N=556
Length of follow-up	Median: 53 months (SE = 3 months)

Follow-up schedule	Assessed every 18 weeks by computed tomography or magnetic resonance imaging scans for recurrence during the first year. Then using scan, laboratory and clinical assessments every 6 months for another year, then once per year until disease recurrence or through 10 years.
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Local recurrence
Source of funding	No funding received.
Additional comments	Fine and Gray's competing-risk regression was used to model the data. Potential predictors of recurrence were analysed by univariable and multivariable models. Calibration plots to compare predicted probabilities at 5 years to the observed frequencies.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 556)
% Female Sample size	n = 145 ; % = 26.1
Age Median (IQR)	63 (54 to 70)
RCC subtypes - Papillary type 1 Sample size	n = 227 ; % = 46
RCC subtypes - Papillary type 2 Sample size	n = 266 ; % = 54
TNM classification - TNM 1 Sample size	n = 369 ; % = 66.4
TNM classification - TNM 2 Sample size	n = 60 ; % = 10.8
TNM classification - TNM 3 Sample size	n = 125 ; % = 22.5
TNM classification - TNM 4	n = 2 ; % = 0.4

Characteristic	Study (N = 556)
Sample size	

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Kroeger, 2022

Bibliographic Reference Kroeger, Nils; Lebacle, Cedric; Hein, Justine; Rao, P N; Nejati, Reza; Wei, Shuanzeng; Burchardt, Martin; Drakaki, Alexandra; Strother, Marshall; Kutikov, Alexander; Uzzo, Robert; Pantuck, Allan J; Pathological and genetic markers improve recurrence prognostication with the University of California Los Angeles Integrated Staging System for patients with clear cell renal cell carcinoma.; European journal of cancer (Oxford, England : 1990); 2022; vol. 168; 68-76

Study Characteristics

Study design	Retrospective cohort study
Study location	United States
Study dates	January 1989 to April 2007
Prognostic model(s)	UISS
Inclusion criteria	• Localised clear cell renal cell carcinoma • Non-metastatic patients
Exclusion criteria	Not reported
Selection of cohort	Database or clinical registry (UCLA cytogenetics RCC database)
Number of participants	N=240
Length of follow-up	43.4 months (54.1 months) (median, standard deviation)
Covariates adjusted for in the multivariable regression modelling	Not reported

Outcome(s) of interest	Recurrence-free/disease-free survival
Source of funding	None received.
Additional comments	Survival estimates were done with Kaplan Meier method and associations with survival times were assessed with univariable and multivariable Cox regression analyses. Univariable results extracted.

Study arms
SSIGN low risk (N = 105)

SSIGN intermediate risk (N = 114)

SSIGN high risk (N = 21)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 240)
% Female No of events	n = 79 ; % = 33
Age Mean (SD)	60 (12.28)
T stage: T1 No of events	n = 154 ; % = 64
T stage: T2 No of events	n = 29 ; % = 12
T stage: T3 No of events	n = 57 ; % = 24
T stage: T4 No of events	n = 0 ; % = 0

Outcomes
Recurrence

Outcome	SSIGN low risk vs SSIGN high risk, N2 = 105, N1 = 21	SSIGN intermediate risk vs SSIGN high risk, N2 = 114, N1 = 21
Recurrence-free survival Hazard ratio/95% CI	0.21 (0.08 to 0.54)	0.51 (0.23 to 1.16)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: No information on how missing data was dealt with. No calibration outcomes reported.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Lee, 2018

Bibliographic Reference	Lee, Byron H.; Feifer, Andrew; Feuerstein, Michael; Benfante, Nicole; Kou, Lei; Yu, Changhong; Kattan, Michael W.; Russo, Paul; Validation of a Postoperative Nomogram Predicting Recurrence in Patients with Conventional Clear Cell Renal Cell Carcinoma; European urology focus; 2018; vol. 4 (no. 1); 100-105

Study Characteristics

Study design	Retrospective cohort study
Study location	The US
Study dates	Between 1990 and 2009
Prognostic model(s)	Sorbellini
Inclusion criteria	Patients who underwent partial or radical nephrectomy for clinically localized clear cell RCC
Exclusion criteria	• Patients with bilateral renal masses and familial RCC syndromes such as von Hippel-Lindau disease • Patients with T3c and T4 tumours as well as those with sarcomatoid elements
Number of participants	N=1642
Length of follow-up	Median follow-up 39 months (IQR: 14-79 months)
Follow-up schedule	Patients were followed with chest radiograph and renal/retroperitoneal ultrasound or cross-sectional imaging every 3–6 months, depending on pathologic stage and grade. In general, patients with greater than pathological T2 disease or Fuhrman grade 3-4 underwent more intense follow-up.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival

Source of funding	National Cancer Institute/National Institutes of Health (NIH); Kirschstein National Research Service Award Institutional Research Training Grant
Additional comments	The paper reported c-index for the validation cohort and combined validation and Sorbellini 2005 cohort.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 1642)
Nephrectomy status - Radical Sample size	n = 829 ; % = 50
Nephrectomy status - Partial Sample size	n = 813 ; % = 50
RCC subtypes - Clear cell Sample size	n = 1642 ; % = 100
TNM classification - T1a Sample size	n = 817 ; % = 49.8
TNM classification - T1b Sample size	n = 349 ; % = 21.3
TNM classification - T2 Sample size	n = 102 ; % = 6.2
TNM classification - T3a Sample size	n = 235 ; % = 14.3
TNM classification - T3b Sample size	n = 139 ; % = 8.5
TNM classification - Not available Sample size	n = 0 ; % = 0

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for outcome or its determinants and unclear risk of bias for analysis as assessed by Usher-Smith 2022.)*

Section	Question	Answer
Overall Risk of bias and Applicability	Concerns for applicability	Low

Lee, 2019

Bibliographic Reference	Lee, Han Jie; Lee, Alvin; Huang, Hong Hong; Lau, Weber Kam On; External validation of the updated Leibovich prognostic models for clear cell and papillary renal cell carcinoma in an Asian population.; Urologic oncology; 2019; vol. 37 (no. 6); 356e9-356e18

Study Characteristics

Study design	Retrospective cohort study
Study location	Singapore
Study dates	1999 to 2015
Prognostic model(s)	Leibovich 2018
Inclusion criteria	• Binephric patients with sporadic, unilateral renal cell carcinoma (RCC) • treated with radical or partial nephrectomy during study dates.
Exclusion criteria	• Bilateral synchronous tumours • genetic causes of renal cell carcinoma including von Hippel-Lindau syndrome • presence of metastases (regional/nonregional lymph node involvement or distant metastases) • incomplete medical records • other histological RCC including collecting duct RCC, acquired cystic disease associated RCC, mixed clear cell/papillary RCC and other rare types.
Selection of cohort	Single centre
Number of participants	N total=942 Clear cell N=829 Papillary N=113
Length of follow-up	Clear cell RCC: median 76 (42-117) months Papillary RCC: median 69.5 (33-115) months
Follow-up schedule	Not reported

Outcome(s) of interest	Model discrimination (C-stats) Progression-free survival Cancer-specific survival
Source of funding	No funding received
Additional comments	For clear cell RCC, scores were calculated without pooling the cases into risk groups. For papillary RCC, scores were calculated for risk groups 1/2/3. Discrimination and calibration was assessed for the Leibovich score.

Study arms
Clear cell (N = 829)

Papillary (N = 113)

Population characteristics
Arm-level characteristics

Characteristic	Clear cell (N = 829)	Papillary (N = 113)
% Female Sample size	n = 300 ; % = 36	n = 34 ; % = 30
Age Custom value	Median (range): 58 (50-67)	Median (range): 61 (52-68)
Open radical nephrectomy Sample size	n = 192 ; % = 23	n = 29 ; % = 26
Open partial nephrectomy Sample size	n = 123 ; % = 15	n = 16 ; % = 14
Laparoscopic radical nephrectomy Sample size	n = 387 ; % = 47	n = 51 ; % = 45
Laparoscopic partial nephrectomy Sample size	n = 127 ; % = 15	n = 17 ; % = 15
pT1a Sample size	n = 374 ; % = 45	n = 46 ; % = 41
pT1b Sample size	n = 189 ; % = 23	n = 23 ; % = 20

Characteristic	Clear cell (N = 829)	Papillary (N = 113)
pT2a Sample size	n = 62 ; % = 7	n = 13 ; % = 12
pT2b Sample size	n = 24 ; % = 3	n = 11 ; % = 10
pT3a Sample size	n = 156 ; % = 19	n = 44 ; % = 7
pT3b Sample size	n = 11 ; % = 1	n = 2 ; % = 2
pT3c Sample size	n = 4 ; % = 1	n = 0 ; % = 0
pT4 Sample size	n = 9 ; % = 1	n = 1 ; % = 1

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate (*Unclear whether all enrolled participants were included in the analysis*.)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Li, 2024

Bibliographic Reference	Li, Xiaoxia; Zhang, Shaoting; Huang, Xiaolan; Lin, Dengqiang; Zhou, Jianjun; Development of a CT-assessed adiposity nomogram for predicting outcome in localized ccRCC.; Abdominal radiology (New York); 2024

Study Characteristics

Study design	Retrospective cohort study
Study dates	January 2015 to December 2018
Prognostic model(s)	SSIGN UISS TNM 2016

Inclusion criteria	• Underwent preoperative CT scan • Histological subtype of clear cell RCC and were classed as clinical stage I–III • Complete clinical data and follow up information
Exclusion criteria	• Compromised CT image quality • Previous preoperative or postoperative therapy (e.g. targeted therapy, immunotherapy) • No complete image and clinical information
Selection of cohort	Single centre (Shanghai hospital)
Number of participants	N=364
Length of follow-up	49.55 months (39.05, 62.60) (median, IQR)
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Scientific Research Project of Fujian for Youth
Additional comments	To identify independent outcome predictors for ccRCC patients, both univariable and multivariable Cox regression analyses were performed. DeLong's test was conducted to examine the area under the receiver operating characteristic curve, evaluating the diagnostic performance of each model. TNM staging follows the guidelines outlined in the "Cancer Staging Manual, eighth edition" by the American Joint Committee on Cancer (2016). The participants were divided into a training set and a testing (validation) set for the paper's new model. Results are reported from both sets. Study characteristics are for participants overall.

Study arms
TNM stage 1-2 (N = 140)

TNM stage 3 (N = 24)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 364)
% Female No of events	n = 133 ; % = 36.5
Age Median (IQR)	59 (51 to 66)
Radical nephrectomy No of events	n = 214 ; % = 58.79
Partial nephrectomy No of events	n = 150 ; % = 41.21
TNM stage 1 No of events	n = 306 ; % = 84.1
TNM stage 2 No of events	n = 34 ; % = 9.34
TNM stage 3 No of events	n = 24 ; % = 6.59

Outcomes
Disease-free survival

Outcome	TNM stage 3 vs TNM stage 1-2, N2 = 340, N1 = 24
Disease-free survival Hazard ratio/95% CI	2.55 (1.78 to 6.48)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: Fewer than 50 events, incomplete follow up data or clinicopathological information is exclusion criteria.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Liu, 2009

Bibliographic Reference	Liu, Zheng; Lv, Jiaju; Ding, Kejia; Fu, Qiang; Cao, Qingwei; Wang, Facheng; Validation of the current prognostic models for nonmetastatic renal cell carcinoma after nephrectomy in Chinese population: a 15-year single center experience.; International journal of urology : official journal of the Japanese Urological Association; 2009; vol. 16 (no. 3); 268-73

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	1993 to 2004
Prognostic model(s)	Karakiewicz Kattan Sorbellini SSIGN UISS
Inclusion criteria	• patients who underwent radical or partial nephrectomy due to renal cell carcinoma
Exclusion criteria	• Distant metastases • lymph node invasion before or at the time of surgery • large tumours (pT4) • bilateral disease • tumour with unclassified histology or Fuhrman grade • chronic renal insufficiency • lost to follow-up.
Selection of cohort	Single centre
Number of participants	N=653
Length of follow-up	Median 65 months, range 13 to 198 months
Follow-up schedule	After surgery patient were followed up annually with abdominal ultrasonography and abdominal computed tomography.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Overall survival

	Cancer-specific survival
Source of funding	Not reported
Additional comments	Survival curves were performed using the Kaplan–Meier method and compared using the log–rank test.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 653)
% Female Sample size	n = 209 ; % = 32
Age Median (IQR)	61 (19 to 94)
Radical Sample size	n = 544 ; % = 83.3
Partial Sample size	n = 109 ; % = 16.7
Clear cell Sample size	n = 529 ; % = 81
Papillary Sample size	n = 97 ; % = 14.9
Chromophobe Sample size	n = 27 ; % = 4.1
TNM 1 Sample size	n = 366 ; % = 56
TNM 2 Sample size	n = 152 ; % = 23.3
TNM 3a Sample size	n = 80 ; % = 12.3
TNM 3b/c Sample size	n = 55 ; % = 8.4

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis as judged by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Liu, 2016

Bibliographic Reference	Liu, W.; Liu, Y.; Fu, Q.; Zhou, L.; Chang, Y.; Xu, L.; Zhang, W.; Xu, J.; Elevated expression of IFN-inducible CXCR3 ligands predicts poor prognosis in patients with non-metastatic clear-cell renal cell carcinoma; Oncotarget; 2016; vol. 7 (no. 12); 13976-13983

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2001 to 2004
Prognostic model(s)	SSIGN
Inclusion criteria	Non-metastatic ccRCC patients who underwent radical or partial nephrectomy.
Exclusion criteria	The patients with larger necrotic and haemorrhagic area hampering the obtaining of representative area in sample or receiving preoperative neoadjuvant therapy were excluded.
Selection of cohort	Single centre
Number of participants	N=263
Length of follow-up	120 months
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Overall survival
Source of funding	National Basic Research Program of China, National Natural Science Foundation of China, Program for New Century Excellent Talents in University, and Shanghai Rising-Star Program
Additional comments	Meanwhile, OS and RFS were estimated by Kaplan-Meier method and analysed by log-rank test. The paper also reported hazard ratios for SSIGN, however, this was not dichotomised so could not be used.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 263)
% Female Sample size	n = 79 ; % = 30
Age Mean (SD)	56.7 (*NR*)
Age Median (IQR)	56 (48 to 67)
RCC subtypes Sample size	n = 263 ; % = 100
TNM classification - pT1 Sample size	n = 169 ; % = 64.3
TNM classification - pT2 Sample size	n = 33 ; % = 12.5
TNM classification - pT3 Sample size	n = 61 ; % = 12.9

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(There was an unclear risk of bias for outcome or its determination and analysis as reported by Usher-Smith 2022. The paper did not report a measure of calibration, and therefore was assessed as high risk of bias for this review.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Lucca, 2015

Bibliographic Reference	Lucca, Ilaria; de Martino, Michela; Hofbauer, Sebastian L; Zamani, Nura; Shariat, Shahrokh F; Klatte, Tobias; Comparison of the prognostic value of pretreatment measurements of systemic inflammatory response in patients undergoing curative resection of clear cell renal cell carcinoma.; World journal of urology; 2015; vol. 33 (no. 12); 2045-52

Study Characteristics

Study design	Retrospective cohort study
Study location	Austria
Study dates	2002 to 2014
Prognostic model(s)	SSIGN
Inclusion criteria	• Patients treated with radical or partial nephrectomy for clinically localised unilateral renal cell carcinoma (RCC)
Exclusion criteria	• Cell types other than clear cell • relevant comorbidities affected systemic inflammatory response markers • patients with missing data on at least one of the relevant preoperative laboratory parameters within 1 month prior to surgery.
Selection of cohort	Single centre
Number of participants	N=430
Length of follow-up	Median 40 months (IQR 17-73)
Follow-up schedule	Follow-up as recommendations in guidelines - not specified further
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	TK is supported by funds of the Oesterreichische Nationalbank
Additional comments	Univariable and multivariable estimates were obtained from Cox models as hazard ratios and 95% confidence intervals. Discrimination of Cox models was assessed with Harrell's concordance index.

Population characteristics

Study-level characteristics

Characteristic	**Study (N = 430)**
% Female Sample size	n = 173 ; % = 40.2
Age Median (IQR)	65.5 (57 to 73)
pT1-2	n = 346 ; % = 80.5

Characteristic	Study (N = 430)
Sample size	
pT3-4 Sample size	n = 84 ; % = 19.5

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Morgan, 2018

Bibliographic Reference	Morgan, Todd M; Mehra, Rohit; Tiemeny, Placede; Wolf, J Stuart; Wu, Shulin; Sangale, Zaina; Brawer, Michael; Stone, Steven; Wu, Chin-Lee; Feldman, Adam S; A Multigene Signature Based on Cell Cycle Proliferation Improves Prediction of Mortality Within 5 Yr of Radical Nephrectomy for Renal Cell Carcinoma.; European urology; 2018; vol. 73 (no. 5); 763-769

Study Characteristics

Study design	Retrospective cohort study
Study location	USA
Study dates	2000-2009
Prognostic model(s)	Karakiewicz
Inclusion criteria	• Patients who underwent radical nephrectomy. • Localised pT1-T3 clear cell, papillary, or chromophobe renal cell carcinoma. • 37 or more days of follow-up.
Exclusion criteria	• Received neoadjuvant therapy. • Bilateral, sarcomatoid, collecting duct, node-positive tumours. • Any clinical evidence of metastatic disease.
Selection of cohort	Multicentre
Number of participants	N=565

Length of follow-up	Median: 90.8 months (IQR 51.8 to 119.2 months)
Follow-up schedule	Not reported.
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Cancer-specific survival
Source of funding	NCCN Foundation Young Investigator Award. Department of Defense Physician Research Training Award, the Prostate Cancer Foundation and the A. Alfred Taubman Medical Research Institute. Cycle cell proliferation (CCP) testing was provided by Myriad Genetics, Inc.
Additional comments	Discrimination of the Karakiewicz and combined R-CCP scores were established according to the Harrell's concordance index (c-index), and decision-curve analysis was used to assess clinical net benefit.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 565)
% Female Sample size	n = 194 ; % = 34
Age less than or equal to 50 Sample size	n = 113 ; % = 20
Age 51-60 Sample size	n = 150 ; % = 27
Age 61-70 Sample size	n = 165 ; % = 29
Age 71-80 Sample size	n = 105 ; % = 19
Age: 80+ Sample size	n = 32 ; % = 6
Clear cell Sample size	n = 456 ; % = 81

Characteristic	Study (N = 565)
Papillary Sample size	n = 62 ; % = 11
Chromophobe Sample size	n = 47 ; % = 8
T1 Sample size	n = 328 ; % = 58
T2 Sample size	n = 74 ; % = 13
T3 Sample size	n = 136 ; % = 29

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis and unclear risk of bias for outcome or its determination ass assess by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Na, 2016

Bibliographic Reference	Na, N.; Si, T.; Huang, Z.; Miao, B.; Hong, L.; Li, H.; Qiu, J.; High expression of HMGAGA2 predicts poor survival in patients with clear cell renal cell carcinoma; OncoTargets and Therapy; 2016; vol. 9; 7199-7205

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2003 to 2004
Prognostic model(s)	SSIGN UISS TNM 2010

Inclusion criteria	• Radical nephrectomy by open surgery or laparoscopy • confirmed clear cell renal cell carcinoma by postoperative histopathology • no radiotherapy or chemotherapy before surgery • no metastasis (M0).
Exclusion criteria	• Patients who died from postoperative complications.
Selection of cohort	Multicentre
Number of participants	N=162
Length of follow-up	Not reported
Follow-up schedule	Not reported
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	Not industry funded
Additional comments	Kaplan–Meier survival analysis was used to assess the overall survival. Cox proportional hazard models were generated for multivariate analyses.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 162)
% Female Sample size	n = 58 ; % = 37.7
Age Mean (SD)	52.6 (10.6)
T1 Sample size	n = 42 ; % = 25.9
T2 Sample size	n = 72 ; % = 44.4

Characteristic	Study (N = 162)
T3 Sample size	n = 41 ; % = 25.3
T4 Sample size	n = 7 ; % = 4.3
Nx-N0 Sample size	n = 133 ; % = 82.1
N1 Sample size	n = 29 ; % = 17.9

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Nie, 2023

Bibliographic Reference	Nie, Pei; Yang, Guangjie; Wang, Yanmei; Xu, Yuchao; Yan, Lei; Zhang, Mingxin; Zhao, Lianzi; Wang, Ning; Zhao, Xia; Li, Xianjun; Cheng, Nan; Wang, Yicong; Chen, Chengcheng; Wang, Nan; Duan, Shaofeng; Wang, Ximing; Wang, Zhenguang; A CT-based deep learning radiomics nomogram outperforms the existing prognostic models for outcome prediction in clear cell renal cell carcinoma: a multicenter study.; European radiology; 2023; vol. 33 (no. 12); 8858-8868

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	May 2011 to June 2019
Prognostic model(s)	SSIGN UISS
Inclusion criteria	• Pathologically confirmed localised clear cell renal cell carcinoma

	• After surgery
Exclusion criteria	• Insufficient image quality • Anti-tumour therapy before surgery
Selection of cohort	Multicentre (Training cohort: 6 hospitals; Test cohort: 3 different hospitals)
Number of participants	Training cohort: N=558 Test cohort: N=241
Length of follow-up	Median 53 months (range 1-118)
Follow-up schedule	Patients were postoperatively followed up every 6-12 months for the first 2 years and then annually. Follow-up information from medical records included physical exams, tumour biomarkers, and imaging findings (CT, PET/CT, ultrasound or MRI).
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Postdoctoral Science Foundation of China and the National Natural Science Foundation of China.
Additional comments	Survival analysis. Harrel's concordance index used to evaluate predictive accuracy of the models.

Study arms
Training cohort (N = 558)

Test cohort (N = 241)

Population characteristics
Arm-level characteristics

Characteristic	Training cohort (N = 558)	Test cohort (N = 241)
% Female No of events	n = 189 ; % = 33.9	n = 79 ; % = 32.8
Age: Recurrent Median (IQR)	60.5 (53 to 67)	63 (52.9 to 67)
Age: Non-recurrent Median (IQR)	57 (48 to 64)	55 (48 to 62)
TNM classification: stage 1 No of events	n = 285 ; % = 51.1	n = 124 ; % = 51.5

Characteristic	Training cohort (N = 558)	Test cohort (N = 241)
TNM classification: stage 2 No of events	n = 163 ; % = 29.2	n = 66 ; % = 27.4
TNM classification: stage 3 No of events	n = 55 ; % = 10	n = 23 ; % = 9.5
TNM classification: stage 4 No of events	n = 55 ; % = 10	n = 28 ; % = 11.6

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: Participants with incomplete data were excluded, potentially leading to biased predictor-outcome associations and predictive performance.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Oza, 2022

Bibliographic Reference	Oza, Bhavna; Eisen, Tim; Frangou, Eleni; Stewart, Grant D; Bex, Axel; Ritchie, Alastair W S; Kaplan, Rick; Smith, Benjamin; Davis, Ian D; Stockler, Martin R; Albiges, Laurence; Escudier, Bernard; Larkin, James; Joniau, Steven; Hancock, Barry; Hermann, Gregers G; Bellmunt, Joaquim; Parmar, Mahesh K B; Royston, Patrick; Meade, Angela; External Validation of the 2003 Leibovich Prognostic Score in Patients Randomly Assigned to SORCE, an International Phase III Trial of Adjuvant Sorafenib in Renal Cell Cancer.; Journal of clinical oncology : official journal of the American Society of Clinical Oncology; 2022; vol. 40 (no. 16); 1772-1782

Study Characteristics

Study design	Prospective cohort study
Study location	147 centres in seven countries: United Kingdom, Australia, France, Belgium, the Netherlands, Spain, and Denmark
Study dates	July 2007 to April 2013
Prognostic model(s)	Leibovich 2003
Inclusion criteria	patients with intermediate (3-5) or high (≥ 6) Leibovich scores

Exclusion criteria	Non–clear cell histology
Selection of cohort	Multicentre (SORCE cohort (a phase 3 trial in RCC))
Number of participants	Clear cell RCC N=1,445 Papillary RCC N = 128 Chromophobe N = 96 Main results are presented for clear cell RCC only. Secondary analysis results are presented for non-clear cell, papillary only and chromophobe only.
Length of follow-up	Median follow-up - Years (IQR): 7.3 (6.1-8.4)
Follow-up schedule	Not reported
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not reported
Additional comments	Survival analysis allowing for late entry was used. Missing surgery dates were estimated by random selection from the distribution of observed data. Discrimination was assessed graphically by observing the degree of separation between the Kaplan-Meier curves and by the hazard ratio (HR) between intermediate-risk and high-risk Leibovich risk groups in each cohort. Discrimination quantified with Harrell's c-index.

Study arms
Non–clear cell RCC (N = 266)

Papillary RCC (N = 128)

Chromophobe RCC (N = 96)

High risk (N = 669)

Intermediate risk (N = 776)

Population characteristics
Study-level characteristics

Characteristic	Study (N =)
Clear cell No of events	n = 1445 ; % = 84
Papillary No of events	n = 128 ; % = 7
Chromophobe No of events	n = 96 ; % = 6
Collecting duct No of events	n = 4 ; % = 1
Other No of events	n = 38 ; % = 2
pT1a No of events	n = 7 ; % = 1
pT1b No of events	n = 197 ; % = 12
pT2 No of events	n = 400 ; % = 23
pT3a-4 No of events	n = 1107 ; % = 65

Outcomes
Survival

Outcome	Intermediate risk vs High risk, N2 = 776, N1 = 669
Metastasis-free survival - whole cohort Hazard ratio/95% CI	2.74 (2.29 to 3.28)
Metastasis-free survival - Non–clear cell Hazard ratio/95% CI	3.21 (2.05 to 5.03)

Outcome	Intermediate risk vs High risk, N2 = 776, N1 = 669
Metastasis-free survival - Papillary Hazard ratio/95% CI	2.61 (1.44 to 4.7)
Metastasis-free survival - Chromophobe Hazard ratio/95% CI	3.88 (1.56 to 9.61)

Metastasis-free survival - whole cohort - Polarity - Higher values are better

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate (*Unclear risk of bias for analysis as there is no information on the number of events for the outcome assessed and missing data.*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Piccinelli, 2023a

Bibliographic Reference	Piccinelli, Mattia L; Tappero, Stefano; Cano Garcia, Cristina; Barletta, Francesco; Incesu, Reha-Baris; Morra, Simone; Scheipner, Lukas; Tian, Zhe; Luzzago, Stefano; Mistretta, Francesco A; Ferro, Matteo; Saad, Fred; Shariat, Shahrokh F; Ahyai, Sascha; Longo, Nicola; Tilki, Derya; Briganti, Alberto; Chun, Felix K H; Terrone, Carlo; de Cobelli, Ottavio; Musi, Gennaro; Karakiewicz, Pierre I; Assessment of the VENUSS and GRANT Models for Individual Prediction of Cancer-specific Survival in Surgically Treated Nonmetastatic Papillary Renal Cell Carcinoma.; European urology open science; 2023; vol. 53; 109-115

Study Characteristics

Study design	Retrospective cohort study
Study location	USA
Study dates	2004-2019
Prognostic model(s)	GRANT VENUSS
Inclusion criteria	• Aged 18 or over • radial or partial nephrectomy

	• only patients who fulfilled criteria that were subsequently used to generate the VENUSS and GRANT risk categories.
Exclusion criteria	• Non-papillary subtypes.
Selection of cohort	Database or clinical registry Surveillance Epidemiology, and End Results (SEER) database
Number of participants	N=4184
Length of follow-up	Median (IQR): 4.9 years (2.1-8.8)
Follow-up schedule	Not reported
Outcome(s) of interest	Cancer-specific survival
Source of funding	Not industry funded
Additional comments	GRANT or VENUSS risk categories were applied and the regression coefficient quantified for the risk groups relative to low risk. Accuracy was generated for the cross-validation model-derived probability for every subject and was quantified using Heagerty's concordance index. Predicted 5-year cancer specific survivals were plotted against the actual observed and calibration plots generated.

Study arms
VENUSS low-risk (N = 2882)

VENUSS intermediate-risk (N = 1004)

VENUSS high-risk (N = 298)

GRANT favourable risk (N = 3144)

GRANT unfavourable risk (N = 1040)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 4184)
% Female Sample size	n = 1021 ; % = 24
Age Median (IQR)	62 (55 to 69)
Nephrectomy status - Partial	n = 2142 ; % = 51

Characteristic	Study (N = 4184)
Sample size	
TNM classification - T1 Sample size	n = 3263 ; % = 78
TNM classification - T2 Sample size	n = 504 ; % = 12
TNM classification - T3 Sample size	n = 384 ; % = 9.2
TNM classification - T4 Sample size	n = 33 ; % = 0.8

Outcomes
VENUSS

Outcome	VENUSS intermediate-risk vs VENUSS low-risk, N2 = 1004, N1 = 2882	VENUSS high-risk vs VENUSS low-risk, N2 = 298, N1 = 2882
Cancer-specific survival Hazard ratio/95% CI	2.7 (2 to 3.6)	13.1 (9.9 to 17.3)

GRANT

Outcome	GRANT unfavourable risk vs GRANT favourable risk, N2 = 1040, N1 = 3144
Cancer-specific survival Hazard ratio/95% CI	3.6 (2.9 to 4.5)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Piccinelli, 2023b

Bibliographic Reference	Piccinelli, Mattia Luca; Morra, Simone; Tappero, Stefano; Cano Garcia, Cristina; Barletta, Francesco; Incesu, Reha-Baris; Scheipner, Lukas; Baudo, Andrea; Tian, Zhe; Luzzago, Stefano; Mistretta, Francesco Alessandro; Ferro, Matteo; Saad, Fred;

Shariat, Shahrokh F; Carmignani, Luca; Ahyai, Sascha; Tilki, Derya; Briganti, Alberto; Chun, Felix K H; Terrone, Carlo; Longo, Nicola; de Cobelli, Ottavio; Musi, Gennaro; Karakiewicz, Pierre I; Critical Appraisal of Leibovich 2018 and GRANT Models for Prediction of Cancer-Specific Survival in Non-Metastatic Chromophobe Renal Cell Carcinoma.; Cancers; 2023; vol. 15 (no. 7)

Study Characteristics

Study design	Retrospective cohort study
Study location	USA
Study dates	2000-2019
Prognostic model(s)	GRANT Leibovich 2018
Inclusion criteria	• Aged 18 or over • non-metastatic chromophobe kidney cancer • radical or partial nephrectomy for unilateral renal cell carcinoma (RCC) • complete data for age at diagnosis, T stage, N stage, grade, tumour size and sarcomatoid differentiation.
Exclusion criteria	Not specified
Selection of cohort	Database or clinical registry Surveillance, Epidemiology, and End Results (SEER) database
Number of participants	N=2761 Study also reports an external validation cohort however this information has not been extracted as the Hazard ratios extracted are for the development cohort.
Length of follow-up	5 years
Follow-up schedule	Not reported
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Cancer-specific survival

Source of funding	No funding received
Additional comments	Leibovich 2018 and GRANT risk categories were applied to the cohort and quantified the regression coefficients for the prediction of cancer-specific mortality (CSM). Univariable Cox regression models tested time to CSM.

Study arms
Leibovich 2018 risk group 1 (N = 2340)

Leibovich 2018 risk group 2 (N = 368)

Leibovich 2018 risk group 3 (N = 53)

GRANT favourable (N = 2251)

GRANT unfavourable (N = 510)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 2761)
% Female Sample size	n = 1181 ; % = 43
Age Median (IQR)	59 (49 to 68)
Nephrectomy status - Radical Sample size	n = 1772 ; % = 64
Nephrectomy status - Partial Sample size	n = 989 ; % = 36
TNM classification - T1 Sample size	n = 1722 ; % = 62
TNM classification - T2 Sample size	n = 491 ; % = 18
TNM classification - T3 Sample size	n = 503 ; % = 18
TNM classification - T4 Sample size	n = 45 ; % = 2

Outcomes

Outcome	Leibovich 2018 risk group 2 vs Leibovich 2018 risk group 1, , N2 = 368, N1 = 2340	Leibovich 2018 risk group 3 vs Leibovich 2018 risk group 1, , N2 = 53, N1 = 2340
Cancer-specific mortality Hazard ratio/95% CI	3.3 (2.3 to 4.7)	17 (10.6 to 27.5)

GRANT

Outcome	GRANT unfavourable vs GRANT favourable, , N2 = 510, N1 = 2251
Cancer specific-mortality Hazard ratio/95% CI	3 (2.2 to 4.2)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate (*Unclear risk of bias for analysis as there is not enough information on the number of participants with the outcome.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Pichler, 2011

Bibliographic Reference	Pichler, Martin; Hutterer, Georg C; Chromecki, Thomas F; Jesche, Johanna; Kampel-Kettner, Karin; Rehak, Peter; Pummer, Karl; Zigeuner, Richard; External validation of the Leibovich prognosis score for nonmetastatic clear cell renal cell carcinoma at a single European center applying routine pathology.; The Journal of urology; 2011; vol. 186 (no. 5); 1773-7

Study Characteristics

Study design	Retrospective cohort study
Study location	Austria
Study dates	1984 to 2006
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• Patients with renal cell carcinoma (RCC) who underwent partial or radical nephrectomy.

Exclusion criteria	• Nonclear cell histology • metastatic disease at diagnosis • bilateral tumours • younger than 18 years old at diagnosis.
Selection of cohort	Single centre
Number of participants	N=1754
Length of follow-up	Median follow-up: 82 months (IQR 39 to 142 months)
Follow-up schedule	Follow-up evaluations were performed every 6 months for the first 5 years and then annually thereafter for locally advanced tumours.
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Recurrence-free/disease-free survival
Source of funding	Not reported
Additional comments	Metastasis-free survival was assessed using the Kaplan-Meier method. Univariate and multivariate Cox proportional hazards models were fit to determine statistically significantly parameters associated with distant metastasis. The concordance index described by Harrell et al was used to assess the multivariate prognostic ability of the model.

Population characteristics
Study-level characteristics

Characteristic	**Study (N =)**
Age Mean (SD)	62.6 (11.2)

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	**Question**	**Answer**
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022.)*

Section	Question	Answer
Overall Risk of bias and Applicability	Concerns for applicability	Low

Rini, 2015

Bibliographic Reference	Rini, Brian; Goddard, Audrey; Knezevic, Dejan; Maddala, Tara; Zhou, Ming; Aydin, Hakan; Campbell, Steven; Elson, Paul; Koscielny, Serge; Lopatin, Margarita; Svedman, Christer; Martini, Jean-Francois; Williams, J Andrew; Verkarre, Virginie; Radulescu, Camelia; Neuzillet, Yann; Hemmerle, Isabelle; Timsit, Marc Olivier; Tsiatis, Athanasios C; Bonham, Michael; Lebret, Thierry; Mejean, Arnaud; Escudier, Bernard; A 16-gene assay to predict recurrence after surgery in localised renal cell carcinoma: development and validation studies.; The Lancet. Oncology; 2015; vol. 16 (no. 6); 676-85

Study Characteristics

Study design	Retrospective cohort study
Study location	France
Study dates	1995 to 2007
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• Clear cell renal cell carcinoma • stage 1, 2 or 3 • treated with nephrectomy alone • available fixed tumour tissue.
Exclusion criteria	• Neoadjuvant or adjuvant systemic therapy • synchronous or metachronous bilateral renal cell carcinoma • history of inherited von Hippel-Lindau disease • insufficient RNA for RT-PCR analysis • inadequate RNA quality measured by standard methods • patients with recurrence within 6 months of surgery in absence of adequate imaging at the time of surgery or during the 6 months following surgery.
Selection of cohort	Multicentre
Number of participants	N=626
Length of follow-up	Median 5.5 years (IQR 3.5 to 7.9)
Follow-up schedule	Not reported

Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Funded by Genomic Health Inc and Pfizer Inc.
Additional comments	Cox proportional hazards regression models stratified by stage (stage I vs stage II–III) were used to assess time-to-event endpoints.

Study arms
Leibovich 2003, low risk (N = 1)

Leibovich 2003, intermediate risk (N = 1)

Leibovich 2003, high risk (N = 1)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 626)
% Female Sample size	n = 183 ; % = 29
Age Mean (SD)	61.4 (12)
Radical nephrectomy Sample size	n = 399 ; % = 64

Outcomes
Recurrence-free survival

Outcome	Leibovich 2003, high risk vs Leibovich 2003, low risk, N2 = , N1 =	Leibovich 2003, intermediate risk vs Leibovich 2003, low risk, N2 = , N1 =
Recurrence-free interval Hazard ratio/95% CI	4.31 (1.66 to 11.2)	3.08 (1.35 to 7.05)

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Schmeusser, 2024

Bibliographic Reference Schmeusser, Benjamin N; Patil, Dattatraya H; Nicaise, Edouard H; Armas-Phan, Manuel; Nabavizadeh, Reza; Narayan, Vikram M; Joshi, Shreyas S; Ogan, Kenneth; Osunkoya, Adeboye O; Bilen, Mehmet A; Master, Viraj A; 2018 Leibovich prognostic model for renal cell carcinoma: Performance in a large population with special consideration of Black race.; Cancer; 2024; vol. 130 (no. 3); 453-466

Study Characteristics

Study design	Retrospective cohort study
Study location	USA
Study dates	2000-2022
Prognostic model(s)	Leibovich 2018
Inclusion criteria	• Informed consent • first radical or partial nephrectomy • chromophobe, papillary and clear cell renal cell carcinomas • nephrectomy performed in the year 2000 or later • non-metastatic at the time of surgery • no missing critical demographic, clinical, pathological, or surgical variables (as specified in original Leibovich 2018 paper).
Exclusion criteria	Not specified
Selection of cohort	Database or clinical registry A renal cell carcinoma institutional database
Number of participants	N=2295
Length of follow-up	Median 52 months (IQR, 38.5–79.0 months)
Follow-up schedule	Regular follow-up which included chest and cross-sectional abdominal imaging, blood samples, and physical examinations according to standard-of-care guidelines or appropriate physician discretion for patients after surgical treatment of RCC.

Outcome(s) of interest	Progression-free survival Cancer-specific survival
Source of funding	John Robinson Family Foundation, the Christopher Churchill Foundation, and the Cox Immunology Fund.
Additional comments	Hazard ratios (HRs) were fit with Cox proportional models for 2018 Leibovich scores in the respective histologic cohorts. To determine the performance of each respective histologic 2018 Leibovich model, area under the curve (AUC) analysis and calibration plots were constructed.

Study arms
Papillary RCC (N = 402)

Chromophobe RCC (N = 177)

Papillary risk score 1 (N = 153)

Papillary risk score 2 (N = 204)

Papillary risk score 3 (N = 37)

Chromophobe risk score 1 (N = 164)

Chromophobe risk score 2 (N = 10)

Chromophobe risk score 3 (N = 3)

Population characteristics
Arm-level characteristics

Characteristic	Papillary RCC (N = 402)	Chromophobe RCC (N = 177)
% Female Sample size	n = 105 ; % = 26.1	n = 74 ; % = 41.8
Age Median (IQR)	61 (52 to 68)	58 (48 to 67)
Nephrectomy status - Partial, laparoscopic-assisted Sample size	n = 108 ; % = 26.9	n = 45 ; % = 25.4

Characteristic	Papillary RCC (N = 402)	Chromophobe RCC (N = 177)
Nephrectomy status - Radical, laparoscopic-assisted Sample size	n = 146 ; % = 36.3	n = 60 ; % = 33.9
Nephrectomy status - Partial, open Sample size	n = 73 ; % = 18.2	n = 36 ; % = 20.3
Nephrectomy status - Radical, open Sample size	n = 75 ; % = 18.7	n = 36 ; % = 20.3
TNM classification - T1a Sample size	n = 184 ; % = 45.8	n = 70 ; % = 39.5
TNM classification - T1b Sample size	n = 119 ; % = 29.6	n = 38 ; % = 21.5
TNM classification - T2a Sample size	n = 38 ; % = 9.5	n = 13 ; % = 7.3
TNM classification - T2b Sample size	n = 18 ; % = 4.5	n = 14 ; % = 7.9
TNM classification - T3a Sample size	n = 29 ; % = 7.2	n = 36 ; % = 20.3
TNM classification - T3b Sample size	n = 8 ; % = 2	n = 1 ; % = 0.6
TNM classification - T3c Sample size	n = 4 ; % = 1	n = 1 ; % = 0.6
TNM classification - T4 Sample size	n = 2 ; % = 0.5	n = 4 ; % = 2.3

Outcomes

Papillary renal cell carcinoma

Outcome	Papillary risk score 2 vs Papillary risk score 1, N2 = 204, N1 = 153	Papillary risk score 3 vs Papillary risk score 1, N2 = 37, N1 = 153
Progression free survival Hazard ratio/95% CI	1.24 (0.55 to 2.8)	11.22 (5.05 to 24.96)
Cancer specific survival Hazard ratio/95% CI	1.94 (0.78 to 4.81)	9.16 (3.38 to 24.82)

Chromophobe renal cell carcinoma

Outcome	Chromophobe risk score 2 vs Chromophobe risk score 1, N2 = 10, N1 = 164	Chromophobe risk score 3 vs Chromophobe risk score 1, N2 = 3, N1 = 164
Progression free survival Hazard ratio/95% CI	3.73 (0.47 to 29.88)	45.35 (8.46 to 243.18)
Cancer specific survival Hazard ratio/95% CI	12.28 (2.22 to 67.85)	39.13 (6.44 to 237.68)

Black ethnicity

Outcome	Papillary risk score 2 vs Papillary risk score 1, N2 = 121, N1 = 74	Papillary risk score 3 vs Papillary risk score 1, N2 = 14, N1 = 74
Progression free survival Hazard ratio/95% CI	0.84 (0.31 to 2.26)	10.72 (3.27 to 35.18)
Cancer specific survival Hazard ratio/95% CI	3.65 (0.78 to 17.05)	27.72 (4.96 to 155.03)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Seles, 2017

Bibliographic Reference	Seles, Maximilian; Posch, Florian; Pichler, Georg P; Gary, Thomas; Pummer, Karl; Zigeuner, Richard; Hutterer, Georg C; Pichler, Martin; Blood Platelet Volume Represents a Novel Prognostic Factor in Patients with Nonmetastatic Renal Cell Carcinoma and Improves the Predictive Ability of Established Prognostic Scores.; The Journal of urology; 2017; vol. 198 (no. 6); 1247-1252

Study Characteristics

Study design	Retrospective cohort study
Study location	Austria
Study dates	2005-2013
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• Localised renal cell carcinoma (RCC) • open or laparoscopic curative nephron sparing surgery or radical nephrectomy.
Exclusion criteria	• Missing data
Selection of cohort	Single centre
Number of participants	N=676
Length of follow-up	Median of 6.1 years (range 1 day to 11.3 years)
Follow-up schedule	Not specified
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Cancer-specific survival
Source of funding	Austrian Society of Urology and Andrology fund and a Oesterreichische Nationalbank fund
Additional comments	Uni- and multivariable modelling of time-to-event was performed with Cox proportional hazards models for the death-from-any cause endpoint and with Fine & Gray proportional sub-distribution hazards model for all other endpoints.

Study arms
Leibovich 2003 high risk (N = 171)

Leibovich 2003 moderate risk (N = 195)

Leibovich 2003 low risk (N = 286)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 652)
% Female Sample size	n = 253 ; % = 38.8
Age Median (IQR)	65.6 (56.5 to 73.4)
Nephrectomy status - Partial Sample size	n = 314 ; % = 48.2
RCC subtypes - Non–clear cell Sample size	n = 121 ; % = 18.6
TNM classification - pT1a + pT1b Sample size	n = 467 ; % = 71.6
TNM classification - pT2a + pT2b Sample size	n = 44 ; % = 6.8
TNM classification - pT3a-c Sample size	n = 141 ; % = 21.6

Outcomes
Leibovich 2003

Outcome	Leibovich 2003 moderate risk vs Leibovich 2003 low risk, N2 = 195, N1 = 286	Leibovich 2003 high risk vs Leibovich 2003 low risk, N2 = 171, N1 = 286
Recurrence-free Hazard ratio/95% CI	3.97 (1.57 to 10.03)	15.24 (6.58 to 35.29)
Cancer-specific survival	5.85 (0.65 to 52.26)	46 (6.34 to 333.63)

Outcome	Leibovich 2003 moderate risk vs Leibovich 2003 low risk, N2 = 195, N1 = 286	Leibovich 2003 high risk vs Leibovich 2003 low risk, N2 = 171, N1 = 286
Hazard ratio/95% CI		

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Shao, 2020

Bibliographic Reference	Shao, Yanxiang; Xiong, Sanchao; Sun, Guangxi; Dou, Weichao; Hu, Xu; Yang, Weixiao; Lia, Thongher; Deng, Shi; Wei, Qiang; Zeng, Hao; Li, Xiang; Prognostic analysis of postoperative clinically nonmetastatic renal cell carcinoma.; Cancer medicine; 2020; vol. 9 (no. 3); 959-970

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	1999 to 2012
Prognostic model(s)	Leibovich 2003 SSIGN UISS
Inclusion criteria	• Non-metastatic patients who underwent radical nephrectomy or partial nephrectomy
Exclusion criteria	• Bilateral renal neoplasms • ECOG score >1 • those not willing to provide information regarding their disease.
Selection of cohort	Single centre
Number of participants	N=1202

Length of follow-up	Median: 63.02 months (IQR 47.2 - 83.4)
Follow-up schedule	Chest and abdominal computerized tomography (CT) performed 3 months after surgery. Abdominal ultrasound or CT performed twice annually for the first 5 years, and once annually thereafter. Chest X-rays performed annually. All patients received a telephone call follow-up every year.
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats)
Source of funding	National Natural Science Foundation of China
Additional comments	Univariate and multivariate Cox regression analyses were performed to determine the clinicopathological parameters associated with survival. Patients were stratified using the SSIGN, Leibovich, and UISS scores. The predictive ability of these models was evaluated using the concordance index (c-index).

Population characteristics
Study-level characteristics

Characteristic	Study (N = 1202)
% Female Sample size	n = 452 ; % = 37.6
Age - over 50 Sample size	n = 755 ; % = 62.8
Age - less than or equal to 50 Sample size	n = 447 ; % = 37.2
RCC subtypes - Clear cell Sample size	n = 1066 ; % = 88.7
RCC subtypes - Papillary Sample size	n = 43 ; % = 3.6
RCC subtypes - Chromophobe Sample size	n = 51 ; % = 4.2
RCC subtypes - Other Sample size	n = 42 ; % = 3.5

Characteristic	Study (N = 1202)
TNM classification - pT1 Sample size	n = 921 ; % = 76.6
TNM classification - pT2 Sample size	n = 149 ; % = 12.4
TNM classification - pT3 Sample size	n = 89 ; % = 7.4
TNM classification - pT4 Sample size	n = 43 ; % = 3.6

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: No calibration measures reported and no information on number of participants with the outcome)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Sorbellini, 2005

Bibliographic Reference	Sorbellini, Maximiliano; Kattan, Michael W; Snyder, Mark E; Reuter, Victor; Motzer, Robert; Goetzl, Manlio; McKiernan, James; Russo, Paul; A postoperative prognostic nomogram predicting recurrence for patients with conventional clear cell renal cell carcinoma.; The Journal of urology; 2005; vol. 173 (no. 1); 48-51

Study Characteristics

Study design	Retrospective cohort study
Study location	United States
Study dates	1989 to 2002 (dates for development cohort, but dates for validation cohort not reported)
Prognostic model(s)	Sorbellini
Inclusion criteria	• Patients who had undergone single nephrectomy for unilateral locally confined disease • radical or partial nephrectomy.

Exclusion criteria	• Patients with von Hippel-Lindau disease • hereditary papillary renal cell carcinoma (RCC) • bilateral renal masses • stage pT4 and pT3c • distant metastases • metastatic regional lymph nodes.
Selection of cohort	Single centre
Number of participants	N=200
Length of follow-up	Median 33 months, maximum 149 months
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not reported
Additional comments	Progression-free probability was estimated using the Kaplan-Meier method. Multivariate analysis was performed with Cox proportional hazards regression. A nomogram was constructed for freedom from recurrence with the information obtained from the Cox proportional hazards regression model.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 200)
pT1a Sample size	n = 76 ; % = 38
pT1b Sample size	n = 34 ; % = 17
pT2 Sample size	n = 10 ; % = 5
pT3a Sample size	n = 42 ; % = 21
pT3b Sample size	n = 38 ; % = 19

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Suzuki, 2011

Bibliographic Reference	Suzuki, Kazuya; Nishiyama, Tsutomu; Hara, Noboru; Akazawa, Kohei; Takahashi, Kota; Kattan postoperative nomogram for renal cell carcinoma: predictive accuracy in a Japanese population.; International journal of urology : official journal of the Japanese Urological Association; 2011; vol. 18 (no. 3); 194-9

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	1991 to 2004
Prognostic model(s)	Kattan
Inclusion criteria	• Clear cell renal cell carcinoma • N0M0 tumour
Exclusion criteria	Not specified
Selection of cohort	Single centre
Number of participants	N=211
Length of follow-up	Median 81 months (range: 4–208).
Follow-up schedule	Clinical examination, laboratory tests, chest–abdominal CT every 6 months during the first 5 years, and yearly thereafter.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not reported
Additional comments	A scatterplot was used to compare the probability of remaining free of RCC at 5 years as estimated by the Kattan nomogram and as given by the Cox proportional hazards analysis. The predictive accuracy of

	the nomogram was evaluated using c-index. The 95% confidence intervals (95%CI) of the c-index were calculated by bootstrapping.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 211)
% Female Sample size	n = 59 ; % = 28
Age Median (IQR)	59.1 (*NR* to *NR*)
Nephrectomy status - Radical Sample size	n = 173 ; % = 82
Nephrectomy status - Nephron-sparing Sample size	n = 38 ; % = 18
TNM classification - T1 Sample size	n = 140 ; % = 66.4
TNM classification - T2 Sample size	n = 26 ; % = 12.3
TNM classification - T3a Sample size	n = 24 ; % = 11.4
TNM classification - T3b-c Sample size	n = 21 ; % = 9.9

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Tan, 2010

Bibliographic Reference	Tan, Min-Han; Kanesvaran, Ravindran; Li, Huihua; Tan, Hwei Ling; Tan, Puay Hoon; Wong, Chin Fong; Chia, Kee Seng; Teh, Bin Tean; Yuen, John; Chong, Tsung Wen; Comparison of the UCLA Integrated Staging System and the Leibovich score in survival

prediction for patients with nonmetastatic clear cell renal cell carcinoma.; Urology; 2010; vol. 75 (no. 6); 1365-3

Study Characteristics

Study design	Retrospective cohort study
Study location	Singapore
Study dates	1990 to 2006
Prognostic model(s)	Leibovich 2003 UISS
Inclusion criteria	• Non-metastatic unilateral clear call renal cell carcinoma (RCC) who underwent nephrectomies.
Exclusion criteria	• Metastatic disease • regional or non-regional lymph nodes.
Selection of cohort	Single centre
Number of participants	N=355
Length of follow-up	Median 56 months
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Overall survival Cancer-specific survival
Source of funding	Not reported
Additional comments	

Study arms
Leibovich, low risk (N = 137)

Leibovich, intermediate risk (N = 166)

Leibovich, high risk (N = 52)

UISS, low risk (N = 107)

UISS, intermediate risk (N = 201)

UISS, high risk (N = 47)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 355)
% Female Sample size	n = 127 ; % = 35.8
Age Mean (SD)	57 (12.4)
pT1a Sample size	n = 96 ; % = 27
pT1b Sample size	n = 82 ; % = 23.1
pT2 Sample size	n = 76 ; % = 21.4
pT3a Sample size	n = 57 ; % = 16.1
pT3b Sample size	n = 39 ; % = 11
pT3c Sample size	n = 1 ; % = 0.3
pT4 Sample size	n = 4 ; % = 1.1

Outcomes
Leibovich

Outcome	Leibovich, intermediate risk vs Leibovich, low risk, N2 = 166, N1 = 137	Leibovich, high risk vs Leibovich, low risk, N2 = 52, N1 = 137
Overall survival Hazard ratio/95% CI	2.05 (1.09 to 3.86)	5.17 (2.59 to 10.32)

Outcome	Leibovich, intermediate risk vs Leibovich, low risk, N2 = 166, N1 = 137	Leibovich, high risk vs Leibovich, low risk, N2 = 52, N1 = 137
Cancer-specific survival Hazard ratio/95% CI	3.41 (1.3 to 8.97)	10.84 (4 to 29.41)
Disease-free survival Hazard ratio/95% CI	2.32 (1.34 to 4.02)	7.74 (4.32 to 13.87)

UIS

Outcome	UISS, intermediate risk vs UISS, low risk, N2 = 201, N1 = 107	UISS, high risk vs UISS, low risk, N2 = 47, N1 = 107
Overall survival Hazard ratio/95% CI	2.63 (1.28 to 5.38)	4.28 (1.92 to 9.55)
Cancer-specific survival Hazard ratio/95% CI	3.94 (1.39 to 11.19)	6.54 (2.1 to 20.34)
Disease-free survival Hazard ratio/95% CI	2.72 (1.5 to 4.95)	5.17 (2.64 to 10.12)

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate – overall survival and recurrence-free survival *(Unclear risk of bias for outcome or its determination and analysis as assessed by Usher-Smith 2022)* High – cancer-specific survival *(High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Tan, 2011

Bibliographic Reference	Tan, Min-Han; Li, Huihua; Choong, Caroline Victoria; Chia, Kee Seng; Toh, Chee Keong; Tang, Tiffany; Tan, Puay Hoon; Wong, Chin Fong; Lau, Weber; Cheng, Christopher; The Karakiewicz nomogram is the most useful clinical predictor for survival outcomes in patients with localized renal cell carcinoma.; Cancer; 2011; vol. 117 (no. 23); 5314-24

Study Characteristics

Study design	Retrospective cohort study
Study location	Singapore
Study dates	1990 to 2006
Prognostic model(s)	Karakiewicz Kattan Leibovich 2003 Sorbellini
Inclusion criteria	• Patients who underwent nephrectomy for sporadic non-metastatic unilateral renal cell carcinoma (RCC)
Exclusion criteria	• Subtypes other than clear cell, papillary or chromophobe renal cell carcinoma • large tumours - pT4 • Eastern Cooperative Oncology Group (ECOG) >1.
Selection of cohort	Single centre
Number of participants	Cohort: N=390 N=390 Kattan and Karakiewicz N=322 Sorbellini N=322 Leibovich
Length of follow-up	5 years
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival

	Overall survival Cancer-specific survival
Source of funding	Not industry funded
Additional comments	Outcomes were estimated by the Kaplan-Meier approach, and Cox regression was used to evaluate the effects of covariates.

Population characteristics
Study-level characteristics

Characteristic	**Study (N = 390)**
% Female Sample size	n = 134 ; % = 34
Age Median (range) Custom value	57 (16 to 91)
Radical nephrectomy Sample size	n = 355 ; % = 91
Partial nephrectomy Sample size	n = 34 ; % = 9
Unknown nephrectomy Sample size	n = 1 ; % = 0
Clear cell Sample size	n = 334 ; % = 86
Papillary Sample size	n = 44 ; % = 11
Chromophobe Sample size	n = 12 ; % = 3
TNM 1 Sample size	n = 214 ; % = 55
TNM 2 Sample size	n = 65 ; % = 17
TNM 3a Sample size	n = 69 ; % = 18

Characteristic	Study (N = 390)
TNM 3 b/c Sample size	n = 42 ; % = 11

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate (*Unclear risk of bias for analysis and outcome or its determination as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Tsujino, 2017a

Bibliographic Reference	Tsujino, Takuya; Komura, Kazumasa; Ichihashi, Atsushi; Tsutsumi, Takeshi; Matsunaga, Tomohisa; Yoshikawa, Yuki; Maenosono, Ryoichi; Okita, Kyohei; Takai, Tomoaki; Oide, Rintaro; Minami, Koichiro; Uehara, Hirofumi; Taniguchi, Kohei; Hirano, Hajime; Nomi, Hayahito; Ibuki, Naokazu; Takahara, Kiyoshi; Inamoto, Teruo; Azuma, Haruhito; The combination of preoperative platelet count and neutrophil lymphocyte ratio as a prognostic indicator in localized renal cell carcinoma.; Oncotarget; 2017; vol. 8 (no. 66); 110311-110325

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	2002 to 2015
Prognostic model(s)	SSIGN UISS
Inclusion criteria	RCC patients who underwent nephrectomy
Exclusion criteria	• Patients with metastasis at the time of nephrectomy • Patients with missing clinicopathological information
Selection of cohort	Single centre Osaka Medical College Hospital
Number of participants	N=268

Length of follow-up	60 months median
Follow-up schedule	Follow-up CT and chest X-ray every 3 months in the first year and every 6 months thereafter
Outcome(s) of interest	Recurrence-free/disease-free survival Overall survival
Source of funding	Not reported
Additional comments	A Kaplan-Meier analysis was carried out to estimate survival free ratio, and log-rank test was performed to compare the difference between assigned patient groups. For the extracted univariate analysis, Cox proportional-hazard regression models were used to estimate crude hazard ratios (HR).

Study arms
UISS, low risk (N = 164)

UISS, intermediate-high risk (N = 104)

SSIGN, 0-2 (N = 222)

SSIGN, >=3 (N = 46)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 268)
% Female Sample size	n = 82 ; % = 30.6
Age Mean (SD)	64 (11.3)
RCC subtypes - Clear Sample size	n = 241 ; % = 89.9
RCC subtypes - Papillary Sample size	n = 12 ; % = 4.5
RCC subtypes - Chromophobe Sample size	n = 9 ; % = 3.4
RCC subtypes - Others Sample size	n = 6 ; % = 2.2
TNM classification - T classification I-II	n = 236 ; % = 88.1

Characteristic	Study (N = 268)
Sample size	
TNM classification - T classification III-IV Sample size	n = 32 ; % = 11.9

Outcomes

Study timepoints

- Median 60 months

UISS

Outcome	UISS, low risk vs UISS, intermediate-high risk, Median 60 months, N2 = , N1 =
Recurrence-free survival Hazard ratio/95% CI	3.17 (1.83 to 5.64)
Overall survival Hazard ratio/95% CI	4.39 (2.39 to 8.61)

SSIGN

Outcome	SSIGN, 0-2 vs SSIGN, >=3, Median 60 months, N2 = , N1 =
Recurrence-free survival Hazard ratio/95% CI	4.09 (2.34 to 7.05)
Overall survival Hazard ratio/95% CI	4.28 (2.42 to 7.56)

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis as assessed by Usher-Smith 2022.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Tsujino, 2017b

Bibliographic Reference	Tsujino, Takuya; Komura, Kazumasa; Matsunaga, Tomohisa; Yoshikawa, Yuki; Takai, Tomoaki; Uchimoto, Taizo; Saito, Kenkichi; Tanda, Naoki; Oide, Rintaro; Minami, Koichiro; Uehara, Hirofumi; Jeong, Seong Ho; Taniguchi, Kohei; Hirano, Hajime; Nomi, Hayahito; Ibuki, Naokazu; Takahara, Kiyoshi; Inamoto, Teruo; Azuma, Haruhito; Preoperative Measurement of the Modified Glasgow Prognostic Score Predicts Patient Survival in Non-Metastatic Renal Cell Carcinoma Prior to Nephrectomy; Annals of surgical oncology; 2017; vol. 24 (no. 9); 2787-2793

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	2005 to 2015
Prognostic model(s)	SSIGN UISS
Inclusion criteria	Patients who underwent nephrectomy with curative (for localised RCC) or non-curative (for cytoreduction to metastatic RCC) intent due to diagnosis of RCC.
Exclusion criteria	Patients who did not undergo nephrectomy or had missing clinicopathological information.
Selection of cohort	Single centre
Number of participants	N=219
Length of follow-up	Median follow-up 57 months
Follow-up schedule	After discharge, follow-up CT and chest X-ray were performed every 3 months in the first year to detect any findings suspicious of disease progression. Thereafter, patients were followed-up every 6 months.
Outcome(s) of interest	Model discrimination (C-stats) Overall survival Overall survival Hazard ratio reported, however, due to overlap, data from Tsujino 2017a will be used instead Cancer-specific survival Hazard ratio
Source of funding	Not reported

Additional comments	A Kaplan–Meier analysis was carried out to estimate the survival-free ratio, and the log-rank test was performed to compare the difference between assigned patient groups. On univariate analysis, Cox proportional hazard regression models were used to estimate crude hazard ratios (HRs). The Harrell's concordance index (C-index) was determined to compare the predictive value of each scoring model systems.

Study arms
UISS, low risk (N = 161)
Patients without metastasis at baseline

UISS, intermediate-high (N = 34)
Patients without metastasis at baseline

SSIGN, 0-2 (N = 156)
Patients without metastasis at baseline

SSIGN, <=3 (N = 39)
Patients without metastasis at baseline

Population characteristics
Study-level characteristics

Characteristic	Study (N = 195)
% Female Patients without metastasis at baseline Sample size	n = 58 ; % = 29.7
Age Mean (SD)	65.1 (10.8)
RCC subtypes - Clear Sample size	n = 179 ; % = 91.8
RCC subtypes - Papillary Sample size	n = 10 ; % = 5.1
RCC subtypes - Chromophobe Sample size	n = 5 ; % = 2.6
RCC subtypes - Others Sample size	n = 1 ; % = 0.5
TNM classification - T classification I-II Sample size	n = 171 ; % = 87.7
TNM classification - T classification III-IV	n = 24 ; % = 12.3

FINAL

Characteristic	Study (N = 195)
Sample size	

Outcomes
Study timepoints

- median 57 months

Contrast data

Outcome	UISS, intermediate-high vs UISS, low risk, median 57 months, N2 = , N1 =	SSIGN, <=3 vs SSIGN, 0-2, median 57 months, N2 = , N1 =
Cancer-specific survival Hazard ratio/95% CI	18.2 (7.17 to 55.5)	13.85 (5.45 to 42.27)

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis as assessed by Usher-Smith 2022.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Tsujino, 2019

Bibliographic Reference	Tsujino, Takuya; Komura, Kazumasa; Hashimoto, Takeshi; Muraoka, Ryu; Satake, Naoya; Matsunaga, Tomohisa; Tsutsumi, Takeshi; Yoshikawa, Yuki; Takai, Tomoaki; Minami, Koichiro; Uehara, Hirofumi; Hirano, Hajime; Nomi, Hayahito; Ibuki, Naokazu; Takahara, Kiyoshi; Inamoto, Teruo; Ohno, Yoshio; Azuma, Haruhito; C-reactive protein-albumin ratio as a prognostic factor in renal cell carcinoma - A data from multi-institutional study in Japan.; Urologic oncology; 2019; vol. 37 (no. 11); 812e1-812e8

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	1990 to 2015
Prognostic model(s)	UISS

Inclusion criteria	Patients with RCC who underwent nephrectomy
Exclusion criteria	• Patients who did not undergo nephrectomy • Patients missing any clinicopathological information • Patients with insufficient follow-up (less than 12 months)
Selection of cohort	Multicentre
Number of participants	N=699
Length of follow-up	Median follow-up time of 73 months
Follow-up schedule	Follow-up CT and Chest X-ray were performed to detect any findings suspected to disease progression every three months in the first 2 year. Thereafter, patients were followed up every 6 months.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Hazard ratio extracted for people with no metastasis at time of nephrectomy
Source of funding	Not reported
Additional comments	RFS was calculated from the date of surgery to the date of disease recurrence or metastasis or the last follow-up in M0 RCC patients who underwent nephrectomy. A Kaplan-Meier analysis was carried out to estimate survival free ratio, and log-rank test was performed to compare the difference between assigned patient groups. On univariate analysis, Cox proportional-hazard regression models were used to estimate crude hazard ratios (HR).

Study arms
UISS, low risk (N = 394)
Patients without metastasis at baseline

UISS, intermediate-high risk (N = 233)
Patients without metastasis at baseline

Population characteristics
Study-level characteristics

Characteristic	Study (N = 627)
% Female All characteristics for patients without metastasis at baseline Sample size	n = 176 ; % = 28.1
Age Mean (SD)	61.7 (11.9)

Characteristic	Study (N = 627)
Nephrectomy status - Radical Sample size	n = 522 ; % = 83.3
Nephrectomy status - Partial Sample size	n = 105 ; % = 16.7
RCC subtypes - Clear Sample size	n = 562 ; % = 89.6
RCC subtypes - Papillary Sample size	n = 229 ; % = 36.5
RCC subtypes - Chromophobe Sample size	n = 16 ; % = 2.6
RCC subtypes - Others Sample size	n = 20 ; % = 3.2
TNM classification - T classification 1-2 Sample size	n = 540 ; % = 86.1
TNM classification - T classification 3-4 Sample size	n = 87 ; % = 13.9
TNM classification - N classification 0 Sample size	n = 611 ; % = 97.4
TNM classification - N classification 1 Sample size	n = 16 ; % = 2.6

Outcomes

Study timepoints

- Median 73 months

Hazard ratios - patients without metastasis at baseline

Outcome	UISS, intermediate-high risk vs UISS, low risk, Median 73 months, N2 = , N1 =
Recurrence-free survival Hazard ratio/95% CI	3.48 (2.47 to 4.94)

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis as assessed by Usher-Smith 2022.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Um, 2020

Bibliographic Reference Um, In Hwa; Scott-Hayward, Lindesay; Mackenzie, Monique; Tan, Puay Hoon; Kanesvaran, Ravindran; Choudhury, Yukti; Caie, Peter D; Tan, Min-Han; O'Donnell, Marie; Leung, Steve; Stewart, Grant D; Harrison, David J; Computerized Image Analysis of Tumor Cell Nuclear Morphology Can Improve Patient Selection for Clinical Trials in Localized Clear Cell Renal Cell Carcinoma.; Journal of pathology informatics; 2020; vol. 11; 35

Study Characteristics

Study design	Retrospective cohort study
Study location	Scotland
Study dates	Scotland: 2007 to 2010
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• clear cell renal cell carcinoma • TNM9 pathological stage pT1-3 disease • having had extirpative surgery (presumed to mean either radical or partial nephrectomy) between 2007 and 2010)
Exclusion criteria	None reported
Selection of cohort	Database or clinical registry (Scottish Collaboration on Translational Research into Renal Cell Carcinoma [SCOTRRCC])
Number of participants	N=120
Length of follow-up	Length of follow up not reported
Follow-up schedule	Not reported
Covariates adjusted for in the multivariable regression modelling	Not reported

Outcome(s) of interest	Sensitivity/specificity
Source of funding	Laboratory Medicine R&D Fund and iCAIRD
Additional comments	The primary clinical end point was disease recurrence-free status. If the patient had a disease recurrence by imaging or a biopsy either locally or remotely at the time of data collection, it was deemed to be a recurrence; otherwise, the patient was censored as non-recurrence. C index was reported but not extracted because confidence intervals were not available.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 120)
% Female No of events	n = 56 ; % = 47
Age Custom value	Median 65, range 31-90
TNM stage 1 No of events	n = 54 ; % = 45
TNM stage 2 No of events	n = 14 ; % = 12
TNM stage 3 No of events	n = 52 ; % = 43

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: No calibration outcomes reported. Unclear reporting about missing data and whether these participants were assumed to have no recurrence.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Usher-Smith, 2022

Bibliographic Reference	Usher-Smith, Juliet A; Li, Lanxin; Roberts, Lydia; Harrison, Hannah; Rossi, Sabrina H; Sharp, Stephen J; Coupland, Carol;

Hippisley-Cox, Julia; Griffin, Simon J; Klatte, Tobias; Stewart, Grant D; Risk models for recurrence and survival after kidney cancer: a systematic review.; BJU international; 2022; vol. 130 (no. 5); 562-579

Study Characteristics

Study design	Systematic review
Study details	Dates searched 1 January 2000 to 12 December 2019 Databases searched Medline, EMBASE and Cochrane Library Sources of funding Various support of authors by Cancer Research UK; NHS in the East of England through the Clinical Academic Reserve; Renal Cancer Research Fund; the Mark Foundation for Cancer Research, National Institute of Health Research (NIHR) Cambridge Biomedical Research Centre.
Inclusion criteria	• Peer-reviewed studies • reported a quantitative measure of the performance of one or more risk models including a combination of 2 or more risk factors to predict at least one of the outcomes of interest • patients after surgical resection for localised renal cell carcinoma • external validation studies • studies reporting performance of an existing model alongside the performance of that model plus additional prognostic markers.
Outcome(s)	• Recurrence-free survival (metastasis-free survival; local recurrence-free survival; progression to metastatic disease; recurrence of disease) • Cancer-specific survival • Overall survival
Number of studies included in the systematic review	• Studies where it was not possible to separate patients with localised disease from metastatic disease • studies only including specific groups (for example those with high-grade disease)
Studies from the systematic review that	• An 2015 • Beisland 2014 • Buti 2019 • Capogrosso 2018

are relevant for use in the current review	• Chen 2017 • Cindolo 2005 • Fu 2015 • Haddad 2017 • Han 2003 • Hupertan 2006 • Hutterer 2014 • Jensen 2009 • Klatte 2009 • Lee 2018 • Liu 2009 • Liu 2016 • Lucca 2015 • Morgan 2018 • Na 2016 • Pichler 2011 • Rini 2015 • Seles 2017 • Sorbellini 2005 • Suzuki 2011 • Tan 2010 • Tan 2011 • Tsujino 2017 • Tsujino 2019 • Utsumi 2011 • Vasudev 2020 • Verine 2018 • Viers 2014 • Wang 2016 • Xia 2016 • Xiong 2017 • Zhang 2017 • Zhu 2019
Studies from the systematic review that are not relevant for use in the current review	• Bai 2015 • Bezan 2015 • Brookman-Amissah 2009 • Brooks 2014 • Chang 2015 • Chang 2016 • Fu 2015b • Jeong 2017 • Liu 2014 • Liu 2015 • May 2009 • Morshaeuser 2018 • Niu 2016 • Pan 2015 • Pichler 2012 • Pichler 2013 • Qu 2016 • Sekar 2017 • Sim 2012

	• Song 2019 • Tsujino 2018 • Verine 2018 • Wei 2019 • Wu 2015 • Xia 2017 • Xu 2015 • Xu 2017 • Yang 2015 • Yang 2016 • Zhu 2015 • Zhu 2017
Additional comments	None

Critical appraisal - ROBIS checklist

Section	Question	Answer
Overall study ratings	Overall risk of bias	Low *(Overall low risk of bias: no concerns about study eligibility criteria. methods used to identify and select studies, or collecting data and appraising studies. Some concerns about robustness of data due to a lack of sensitivity analysis or further testing of results.)*
Overall study ratings	Applicability as a source of data	Partially applicable *(This systematic review covers a discrete subsection of the review protocol: it presents c index results for clear cell carcinoma only. It does not include locally advanced cancer, other histological subtypes, and does not fully present other outcomes from the protocol (for example, area under the ROC curve, hazard ratios).)*

Utsumi, 2011

Bibliographic Reference	Utsumi, Takanobu; Ueda, Takeshi; Fukasawa, Satoshi; Komaru, Atsushi; Sazuka, Tomokazu; Kawamura, Koji; Imamoto, Takashi; Nihei, Naoki; Suzuki, Hiroyoshi; Ichikawa, Tomohiko; Prognostic models for renal cell carcinoma recurrence: external validation in a Japanese population.; International journal of urology : official journal of the Japanese Urological Association; 2011; vol. 18 (no. 9); 667-671

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	Between 1990 and 2005
Prognostic model(s)	Kattan

Inclusion criteria	Patients who underwent partial or radical nephrectomy for non-metastatic RCC
Exclusion criteria	Patients with large tumour (T4), bilateral disease, tumour with unclassified histology, chronic renal insufficiency or lost to follow up.
Selection of cohort	Multicentre
Number of participants	N=217
Length of follow-up	Not reported
Follow-up schedule	A follow up of the patients was basically carried out every 3 months. Radiological tests were carried out in accordance with the protocols of each institution.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not reported
Additional comments	None

Study arms
CUH cohort (N = 152)

CCC cohort (N = 65)

Population characteristics
Arm-level characteristics

Characteristic	CUH cohort (N = 152)	CCC cohort (N = 65)
% Female Sample size	n = 38 ; % = 25	n = 18 ; % = 27.7
Age Range	31 to 79	26 to 81
Age Median (IQR)	58 (IQR not reported)	61 (IQR not reported)
Nephrectomy status - Radical Sample size	n = 142 ; % = 93.4	n = 64 ; % = 98.5
Nephrectomy status - Partial Sample size	n = 10 ; % = 6.6	n = 1 ; % = 1.5

Characteristic	CUH cohort (N = 152)	CCC cohort (N = 65)
RCC subtypes - Clear cell Sample size	n = 143 ; % = 94.1	n = 58 ; % = 89.2
RCC subtypes - Papillary Sample size	n = 5 ; % = 3.3	n = 5 ; % = 7.7
RCC subtypes - Chromophobe Sample size	n = 4 ; % = 2.6	n = 2 ; % = 3.1
TNM classification - 1997 TNM classification 1 Sample size	n = 117 ; % = 77	n = 35 ; % = 53.9
TNM classification - 1997 TNM classification 2 Sample size	n = 11 ; % = 7.2	n = 8 ; % = 12.2
TNM classification - 1997 TNM classification 3a Sample size	n = 8 ; % = 5.3	n = 12 ; % = 18.5
TNM classification - 1997 TNM classification 3b/c Sample size	n = 16 ; % = 10.5	n = 10 ; % = 15.4

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Vasudev, 2020

Bibliographic Reference	Vasudev, Naveen S; Hutchinson, Michelle; Trainor, Sebastian; Ferguson, Roisean; Bhattarai, Selina; Adeyoju, Adebanji; Cartledge, Jon; Kimuli, Michael; Datta, Shibendra; Hanbury, Damian; Hrouda, David; Oades, Grenville; Patel, Poulam; Soomro, Naeem; Stewart, Grant D; Sullivan, Mark; Webster, Jeff; Messenger, Michael; Selby, Peter J; Banks, Rosamonde E; UK Multicenter Prospective Evaluation of the Leibovich Score in

Localized Renal Cell Carcinoma: Performance has Altered Over Time.; Urology; 2020; vol. 136; 162-168

Study Characteristics

Study design	Prospective cohort study
Study location	UK
Study dates	1998 to 2006 - historic cohort 2011 to 2014 - contemporary cohort
Prognostic model(s)	Leibovich 2003
Inclusion criteria	• Patients with newly diagnosed suspected renal cell carcinoma • all stages • all histologic types • no prior treatment.
Exclusion criteria	• Known familial renal cell carcinoma • renal cancer acquired following and/or during renal replacement therapy • those and high risk or known HIV • hepatitis B/C or other blood-borne infectious disease.
Selection of cohort	Single centre (historic cohort) Multicentre (contemporary cohort)
Number of participants	N= 384 contemporary cohort N=191 historical cohort
Length of follow-up	Contemporary cohort: Median 4.4 years (IQR 3.4, 5.2) Historical cohort: Median 10.7 years (IQR 7.87, 12.71)
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not industry funded
Additional comments	Cox proportional hazard models with Leibovich risk group as the predictor were used to estimate hazard ratios and c-index to assess discrimination.

	The Kaplan-Meier method was used to estimate and visualize metastasis-free survival to assess calibration.

Study arms
Contemporary cohort, low risk (N = 150)

Contemporary cohort, intermediate risk (N = 163)

Contemporary cohort, high risk (N = 71)

Historic cohort, low risk (N = 60)

Historic cohort, intermediate risk (N = 86)

Historic cohort, high risk (N = 45)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 575)
% Female, contemporary cohort Sample size	n = 132 ; % = 34
% Female, historic cohort Sample size	n = 81 ; % = 42
Age, contemporary cohort median, range Custom value	63 (29 to 92)
Age, historic cohort median, range Custom value	64 (29 to 86)
Partial nephrectomy, contemporary cohort Sample size	n = 100 ; % = 26
Radical nephrectomy, contemporary cohort Sample size	n = 284 ; % = 74
Missing nephrectomy status, contemporary cohort Sample size	n = 0 ; % = 0
Partial nephrectomy, historic cohort Sample size	n = 12 ; % = 6
Radical nephrectomy, historic cohort	n = 178 ; % = 93

Characteristic	Study (N = 575)
Sample size	
Missing nephrectomy status, historic cohort Sample size	n = 1 ; % = 1
T1a, contemporary cohort Sample size	n = 126 ; % = 33
T1b, contemporary cohort Sample size	n = 102 ; % = 27
T2, contemporary cohort Sample size	n = 42 ; % = 11
T3, contemporary cohort Sample size	n = 114 ; % = 29
T1a, historic cohort Sample size	n = 45 ; % = 24
T1b, historic cohort Sample size	n = 48 ; % = 25
T2, historic cohort Sample size	n = 16 ; % = 8
T3, historic cohort Sample size	n = 82 ; % = 43

Outcomes
Leibovich, contemporary cohort

Outcome	Contemporary cohort, intermediate risk vs Contemporary cohort, low risk, N2 = 163, N1 = 150	Contemporary cohort, high risk vs Contemporary cohort, low risk, N2 = 71, N1 = 150
Disease-free survival Hazard ratio/95% CI	5.11 (1.77 to 14.8)	23.4 (8.3 to 66)

Leibovich, historic cohort

Outcome	Historic cohort, intermediate risk vs Historic cohort, low risk, N2 = 86, N1 = 60	Historic cohort, high risk vs Historic cohort, low risk, N2 = 45, N1 = 60
Disease-free survival Hazard ratio/95% CI	4.22 (1.62 to 11)	16.1 (6.16 to 42.2)

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis and unclear risk of bias for outcome or its determination as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Viers, 2014

Bibliographic Reference	Viers, Boyd R.; Thompson, Robert Houston; Boorjian, Stephen A.; Lohse, Christine M.; Leibovich, Bradley C.; Tollefson, Matthew K.; Preoperative neutrophil-lymphocyte ratio predicts death among patients with localized clear cell renal carcinoma undergoing nephrectomy; Urologic oncology; 2014; vol. 32 (no. 8); 1277-1284

Study Characteristics

Study design	Retrospective cohort study
Study location	The US
Study dates	Between 1995 and 2008
Prognostic model(s)	SSIGN
Inclusion criteria	Patients treated with radical nephrectomy for sporadic, unilateral, non-cystic, M0 ccRCC
Exclusion criteria	Not reported
Selection of cohort	Database or clinical registry
Number of participants	N=827
Length of follow-up	Median 9.3 years (IQR: 6.3 to 12.8)

Follow-up schedule	At Mayo clinic, follow-up follow-up was generally done quarterly for the first 2 years, semi-annually for the next 2 years, and annually there after for patients without evidence of recurrent disease. For patients followed up elsewhere, the Nephrectomy Registry monitored outcomes annually.
Outcome(s) of interest	Model discrimination (C-stats) Cancer-specific survival
Source of funding	Not reported
Additional comments	None

Population characteristics
Study-level characteristics

Characteristic	Study (N = 827)
% Female Sample size	n = 292 ; % = 35
Age Median (IQR)	65 (56 to 73)
Nephrectomy status - Open radical Sample size	n = 716 ; % = 87
Nephrectomy status - Laparoscopic radical Sample size	n = 111 ; % = 13
RCC subtypes Sample size	n = 827 ; % = 100
TNM classification - 2009 Primary tumour classification - pT1a Sample size	n = 136 ; % = 16
TNM classification - 2009 Primary tumour classification - pT1b Sample size	n = 206 ; % = 25
TNM classification - 2009 Primary tumour classification - pT2a Sample size	n = 105 ; % = 13
TNM classification - 2009 Primary tumour classification - pT2b Sample size	n = 47 ; % = 6

Characteristic	Study (N = 827)
TNM classification - 2009 Primary tumour classification - pT3a Sample size	n = 223 ; % = 27
TNM classification - 2009 Primary tumour classification - pT3b Sample size	n = 78 ; % = 9
TNM classification - 2009 Primary tumour classification - pT3c Sample size	n = 15 ; % = 2
TNM classification - 2009 Primary tumour classification - pT4 Sample size	n = 15 ; % = 2
TNM classification - pNx Sample size	n = 520 ; % = 63
TNM classification - pN0 Sample size	n = 252 ; % = 30
TNM classification - pN1 Sample size	n = 55 ; % = 7

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(Unclear risk of bias for analysis as assessed by Usher-Smith 2022. However, no measure of calibration was reported for the model of interest, and therefore a high risk of bias was assigned for this review)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Wang, 2016

Bibliographic Reference	Wang, Zewei; Xie, Huyang; Zhou, Lin; Liu, Zheng; Fu, Hangcheng; Zhu, Yu; Xu, Le; Xu, Jiejie; CCL2/CCR2 axis is associated with postoperative survival and recurrence of patients with non-metastatic clear-cell renal cell carcinoma; Oncotarget; 2016; vol. 7 (no. 32); 51525-51534

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	Between 2001 and 2004
Prognostic model(s)	Leibovich 2003 UISS
Inclusion criteria	Patients with non-metastatic ccRCC who underwent surgical treatment
Exclusion criteria	Not reported
Selection of cohort	Single centre
Number of participants	N=268
Length of follow-up	Median follow-up 89 months (range: 12 to 120 months)
Follow-up schedule	After surgery, patients accepted physical examination, laboratory diagnosis, chest imaging, abdominal CT scans or ultrasound twice a year for the first two years and annually thereafter.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Overall survival
Source of funding	National Key Projects for Infectious Diseases of China, National Natural Science Foundation of China, Program for New Century Excellent Talents in University
Additional comments	None

Population characteristics

Study-level characteristics

Characteristic	**Study (N = 268)**
% Female Sample size	n = 80 ; % = 70.1
Age Range	48 to 67
Age Median (IQR)	56 (*NR* to *NR*)

Characteristic	Study (N = 268)
RCC subtypes Sample size	n = 268 ; % = 100
TNM classification - T1a Sample size	n = 96 ; % = 35.8
TNM classification - T1b Sample size	n = 74 ; % = 27.6
TNM classification - T2 Sample size	n = 34 ; % = 12.7
TNM classification - T3 + T4 Sample size	n = 64 ; % = 23.9

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(Unclear risk of bias for analysis as assessed by Usher-Smith 2022. Because calibration measures were not reported for the model of interest the risk of bias was judged as high in this review)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Wang, 2021a

Bibliographic Reference	Wang, Chao; Hong, TianYu; Wang, Yuning; Peng, Guang; Yu, Yongwei; Zhang, Jing; Zhuo, Dong; Zheng, Jingcun; Ma, Xiaojing; Cui, Xingang; Combining UBR5 and CD163+ tumor-associated macrophages better predicts prognosis of clear cell renal cell carcinoma patients.; Cancer immunology, immunotherapy : CII; 2021; vol. 70 (no. 10); 2925-2935

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2010 to 2014

Prognostic model(s)	SSIGN TNM not specified
Inclusion criteria	• People who underwent nephron sparing surgery or radical nephrectomy • Clear cell renal cell carcinoma
Exclusion criteria	Not reported
Selection of cohort	Single centre (Changhai Hospital)
Number of participants	N=310
Length of follow-up	Outcomes estimated at 5 years - no further information reported
Follow-up schedule	Not reported
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Model discrimination (C-stats)
Source of funding	Various national science foundations and funds.
Additional comments	Prognostic accuracy of the models was indicated by Harrell's concordance index. Study is primarily concerned with additional prognostic markers and compares these to TNM and SSIGN. TNM version is unspecified - due to date of publication it is assumed TNM 2016 is used.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 310)
% Female No of events	n = 87 ; % = 28.1
Age under 60 No of events	n = 185 ; % = 59.7
Age 60 and over No of events	n = 125 ; % = 40.3

Characteristic	Study (N = 310)
TNM stage 1-2 No of events	n = 270 ; % = 92.3
TNM stage 3 No of events	n = 40 ; % = 12.9

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(High risk of bias for analysis: no information about missing information, including whether participants with missing information were included in the study / analysis or not. No calibration results.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Wang, 2021b

Bibliographic Reference	Wang, Chao; Dong, Keqin; Wang, Yuning; Peng, Guang; Song, Xu; Yu, Yongwei; Shen, Pei; Cui, Xingang; Integrating HECW1 expression into the clinical indicators exhibits high accuracy in assessing the prognosis of patients with clear cell renal cell carcinoma.; BMC cancer; 2021; vol. 21 (no. 1); 890

Study Characteristics

Study design	Retrospective cohort study
Study location	China`
Study dates	2012-2014
Prognostic model(s)	SSIGN TNM not specified
Inclusion criteria	• Patients with pathologically diagnosed clear cell renal cell carcinoma (ccRCC).
Exclusion criteria	Not reported
Selection of cohort	Single centre
Number of participants	N=300

Length of follow-up	Not specified
Follow-up schedule	Not specified
Outcome(s) of interest	Model discrimination (C-stats) Progression-free survival Overall survival
Source of funding	Funding from various research projects in China. Not industry funded.
Additional comments	Survival curves were plotted using Kaplan-Meier analysis and compared via log-rank test. Prognostic accuracy of prognostic indicators was indicated by Harrell's concordance index using 'rms' package(c-index). Study reports results for participants in 3:2 randomisation ratio and 1:1 randomisation ratio. Only results for 1:1 have been extracted to avoid double counting.

Study arms
Training cohort (N = 150)

Validation cohort (N = 150)

SSIGN 1-4 (N = 281)

SSIGN >=5 (N = 19)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 300)
Nephrectomy status - Partial nephrectomy Sample size	n = 174
Nephrectomy status - Radical nephrectomy Sample size	n = 126

Arm-level characteristics

Characteristic	Training cohort (N = 150)	Validation cohort (N = 150)
% Female Sample size	n = 40 ; % = 26.7	n = 45 ; % = 30
Age 60 or over Sample size	n = 69 ; % = 46	n = 49 ; % = 32.7
TNM stage 1-2 Sample size	n = 108 ; % = 72	n = 120 ; % = 80
TNM stage 3-4 Sample size	n = 14 ; % = 9.3	n = 20 ; % = 13.3

Outcomes

Training cohort

Outcome	SSIGN >=5 vs SSIGN 1-4, N2 = 11, N1 = 139
Overall survival Hazard ratio/95% CI	9.24 (3.88 to 21.98)
Progression-free survival Hazard ratio/95% CI	17.91 (8.06 to 39.8)

Validation cohort

Outcome	SSIGN >=5 vs SSIGN 1-4, N2 = 8, N1 = 142
Overall survival Hazard ratio/95% CI	7.22 (2.73 to 19.14)
Progression-free survival Hazard ratio/95% CI	15.16 (5.37 to 42.77)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for outcome and its determination and analysis*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Wen, 2023

Bibliographic Reference	Wen, Hongzhuang; Zhang, Yong; Yang, Zhan; Zhai, Zhao; Han, Zhenwei; Wang, Hu; Wang, Mingshuai; Shi, Hongzhe; Chen, Xi; Wahafu, Wasilijiang; Guan, Kaopeng; Wang, Xiaolu; The LMR-SSIGN-MAPS model predicts disease-free survival in patients with localized clear cell renal cell carcinoma.; Wideochirurgia i inne techniki maloinwazyjne = Videosurgery and other miniinvasive techniques; 2023; vol. 18 (no. 2); 313-327

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2010 to 2015
Prognostic model(s)	SSIGN
Inclusion criteria	• Definitive pathological diagnosis and complete resection of tumour with negative margins • complete preoperative medical information or follow-up data • available preoperative MAPS measurements with computerized tomography (CT) or magnetic resonance imaging (MRI) scan.
Exclusion criteria	• Any solid tumours before surgery • history of using statins for hyperlipidaemia • thyroid disease, liver or kidney dysfunction • bilateral or multiple ccRCC • previous kidney surgery or kidney injury • signs of extrarenal metastases and preoperative adjuvant therapy.
Selection of cohort	Single centre
Number of participants	N=612 Training cohort: n=414 Validation cohort: n=198
Length of follow-up	Mean, (SD): 73.71 (28.49) months
Follow-up schedule	Physical examination, routine haematological index, and imaging such as CT or MRI were performed every 3–6 months 2 years after surgery and annually thereafter.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival

Source of funding	Not reported
Additional comments	The LASSO Cox regression was conducted to determine the DFS-related variables to develop predictive models for feature selection of high-dimensional variables and multicollinearity among variables.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 612)
% Female Sample size	n = 180 ; % = 29.4
Age - Less than 60 Sample size	n = 439 ; % = 71.7
Nephrectomy status - Partial Sample size	n = 220 ; % = 35.9
Nephrectomy status - Radical Sample size	n = 392 ; % = 64.1
TNM classification - T1 Sample size	n = 486 ; % = 79.4
TNM classification - T2 Sample size	n = 17 ; % = 2.8
TNM classification - T3 Sample size	n = 109 ; % = 17.8

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Xia, 2016

Bibliographic Reference	Xia, Yu; Liu, Li; Bai, Qi; Wang, Jiajun; Xi, Wei; Qu, Yang; Xiong, Ying; Long, Qilai; Xu, Jiejie; Guo, Jianming; Dectin-1 predicts adverse postoperative prognosis of patients with clear cell renal cell carcinoma.; Scientific reports; 2016; vol. 6; 32657

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	Jan 2005 to 2007
Prognostic model(s)	Leibovich 2003 Described as SSIGN localized (Leibovich) - reported in Usher-Smith as Leibovich 2003 UISS
Inclusion criteria	• Pathologically proven ccRCC • Received partial or radical nephrectomy • Available Formalin Fixed Paraffin Embedded (FFPE) specimen of tumour mass (≥ 1cm3).
Exclusion criteria	Those who had other former malignant tumour, perioperative mortalities, histories of adjuvant or neoadjuvant targeted therapies and patients with mixed type renal cancer, bilateral renal cancer and FFPE samples necrosis area >80%.
Selection of cohort	Single centre
Number of participants	N=290
Length of follow-up	Median follow-up time 99.03 months (range 2.63–120.47)
Follow-up schedule	The follow-up interval was three months during the first 5 years and annually thereafter.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	National Key Projects for Infectious Diseases of China, National Natural Science Foundation of China, Program for New Century Excellent Talents in University and Science and Technology Commission of Shanghai Municipality
Additional comments	The paper also reported c-indices for OS, however, these were not extracted as they included patients with preoperative metastases.

Population characteristics

Study-level characteristics

Characteristic	**Study (N = 290)**
% Female Baseline characteristics include patients with distant metastasis Sample size	n = 91 ; % = 34.4

Characteristic	Study (N = 290)
Age - less than or equal to 55 years Sample size	n = 143 ; % = 49.3
Age - greater than 55 years Sample size	n = 147 ; % = 50.7
RCC subtypes Sample size	n = 290 ; % = 100
RCC subtypes - Clear cell Sample size	n = 290 ; % = 100
TNM classification - TNM stage I Sample size	n = 177 ; % = 61
TNM classification - TNM stage II Sample size	n = 23 ; % = 7.9
TNM classification - TNM stage I-II Sample size	n = 70 ; % = 24.1
TNM classification - TNM stage IV Sample size	n = 20 ; % = 6.9

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*Low risk of bias assessed by Usher-Smith 2022. However, as a measure of calibration was not provided for the model of interest, this was assessed as high risk in this review*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Xiao, 2021

Bibliographic Reference	Xiao, Ruotao; Xu, Chuxiao; He, Wei; Liu, Lei; Zhang, Hongxian; Liu, Cheng; Ma, Lulin; Preoperative anaemia and thrombocytosis predict adverse prognosis in non-metastatic renal cell carcinoma with tumour thrombus.; BMC urology; 2021; vol. 21 (no. 1); 31

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2014 to 2019
Prognostic model(s)	SSIGN
Inclusion criteria	• Diagnosed with renal neoplasms and tumour thrombus • receiving nephrectomy and thrombectomy.
Exclusion criteria	• Non-renal cell carcinoma • preoperative suspicious distant metastasis • bilateral or recurrent tumour • combined with haematological disease or gastrointestinal disease • past history of splenectomy.
Selection of cohort	Single centre
Number of participants	N=146
Length of follow-up	139 (95.2 %) patients were followed up for a median of 19 months (IQR 8–32). 28 (19.2 %) patients died with the mean overall survival (OS) of 46.82 months (median OS was not reached).
Follow-up schedule	Patients were recommended to a follow-up every 3 months for the first years, every 6 months for the next 2 years, and then yearly. Laboratory examination, X-ray, ultrasound scan or abdominal CT were performed at follow-up visits.
Outcome(s) of interest	Progression-free survival Overall survival
Source of funding	No funding received.
Additional comments	The OS and progression-free survival (PFS) were estimated using the Kaplan–Meier curves and survival differences were compared using the log-rank test.

Study arms

SSIGN low-risk (score 2-4) (N = 49)

SSIGN intermediate-risk (score 5-7) (N = 76)

SSIGN high-risk (score 8-11) (N = 21)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 146)
% Female Sample size	n = 33 ; % = 22.6
Age Median (IQR)	60 (54 to 66.25)
Clear cell Sample size	n = 124 ; % = 84.9
Non–clear cell Sample size	n = 22 ; % = 15.1

Outcomes

Outcome	SSIGN intermediate-risk (score 5-7) vs SSIGN low-risk (score 2-4), N2 = 76, N1 = 49	SSIGN high-risk (score 8-11) vs SSIGN low-risk (score 2-4), N2 = 21, N1 = 49
Overall survival Hazard ratio/95% CI	1.45 (0.45 to 4.19)	5.85 (1.84 to 18.6)
Progression-free survival Hazard ratio/95% CI	1.83 (0.87 to 3.86)	3.03 (1.23 to 7.44)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(No information on number with the outcome, or information on any missing data. There was also no measure of calibration reported.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Xiong, 2017

Bibliographic Reference	Xiong, Ying; Liu, Li; Xia, Yu; Wang, Jiajun; Xi, Wei; Bai, Qi; Qu, Yang; Xu, Jiejie; Guo, Jianming; Low CCL17 expression

associates with unfavorable postoperative prognosis of patients with clear cell renal cell carcinoma.; BMC cancer; 2017; vol. 17 (no. 1); 117

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	Jan 2005 to June 2007
Prognostic model(s)	SSIGN
Inclusion criteria	Patients with pathologically proved ccRCC, having received nephrectomy and having available Formalin Fixed Paraffin Embedded (FFPE) specimen of tumor mass (≥1 cm3).
Exclusion criteria	Patients who had other former malignant tumours, perioperative mortalities, histories of adjuvant or neo-adjuvant therapies including targeted therapies, mixed type renal cancer or bilateral renal cancer were excluded. Samples with over 80% necrotic or haemorrhagic area were also excluded.
Selection of cohort	Single centre
Number of participants	N=286
Length of follow-up	Median follow-up time was 90.87 months (range 2.63 to 120.47)
Follow-up schedule	Recurrence was confirmed by imaging, biopsy or physical examination. Patients were followed up every 3 months during the first 5 years after operation and once a year thereafter.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	National Natural Science Foundation of China, Program for New Century Excellent Talents in University, Shanghai Municipal Natural Science Foundation and Zhongshan Hospital Science Foundation
Additional comments	The paper reported c-indices for RFS for UISS, however, these were not extracted due to overlap with Xia 2016. The paper also reported c-indices for OS, however, these were not extracted as the OS analyses included patients with pre-operational metastasis.

Population characteristics
Study-level characteristics

Characteristic	Study (N = 286)
% Female Sample size	n = 87 ; % = 30.4

Characteristic	Study (N = 286)
Age Mean (SD)	55.37 (13.24)
RCC subtypes - Clear cell Sample size	n = 286 ; % = 100
TNM classification - pT1 Sample size	n = 181 ; % = 63.3
TNM classification - pT2 Sample size	n = 26 ; % = 9.1
TNM classification - pT3 Sample size	n = 75 ; % = 26.2
TNM classification - pT4 Sample size	n = 4 ; % = 1.4
TNM classification - pNx Sample size	n = 240 ; % = 83.9
TNM classification - pN0 Sample size	n = 44 ; % = 15.4
TNM classification - pN1 Sample size	n = 2 ; % = 0.7

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(Assessed as low risk by Usher-Smith 2022. However, because a calibration measure was not reported for the model of interest, the review was judged as high risk for this review.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Xv, 2024

Bibliographic Reference	Xv, Yingjie; Wei, Zongjie; Jiang, Qing; Zhang, Xuan; Chen, Yong; Xiao, Bangxin; Yin, Siwen; Xia, Zongyu; Qiu, Ming; Li, Yang; Tan, Hao; Xiao, Mingzhao; Three-Dimensional (3D) deep learning

model complements existing models for preoperative disease-free survival prediction (DFS) in localized clear cell renal cell carcinoma (ccRCC): A multicenter retrospective cohort study.; International journal of surgery (London, England); 2024

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	Patients were enrolled during two time periods: (1) At Center 1, Center 2, and Center 3, recruitment occurred between December 2013 and March 2020; (2) At Center 4, Center 5, and Center 6, recruitment took place between June 2013 and December 2016.
Prognostic model(s)	Leibovich 2003 UISS
Inclusion criteria	Patients who underwent partial/radical nephrectomies and histologically diagnosed as ccRCC
Exclusion criteria	Patients with incomplete clinic-pathological data; lack of preoperative contrast-enhanced CT images or the image quality was unsuitable for analysis; who received pre-surgery neoadjuvant or adjuvant therapies; with multiple renal tumours or/and had synchronous metastasis
Selection of cohort	Multicentre
Number of participants	N = 707 Training set N = 364 Internal testing set N = 156 External testing set N = 187
Length of follow-up	Follow-up all participants (months) = 57.8 (40.6-83.3) Training set = 54.0 (39.6- 66.9) Internal testing set = 58.2 (29.9-85.9) External testing = 79.9 (54.4-96.9)
Covariates adjusted for in the multivariable regression modelling	Pathological grade, age, sex, pathological necrosis, tumour laterality, surgical procedure, tumour size, ECOG-PS, pT stage, pN status, TNM stage, UISS risk and SSIGN risk

Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not reported
Additional comments	The DFS predictive performances of models were assessed by the Harrell's consistency index (C-index) and time-dependent receiver operating characteristic (ROC) curve analysis. The DFS differences between the stratified groups and subgroups split by pathological grade, age, sex, pathological necrosis, tumour laterality, surgical procedure, tumour size, ECOG-PS, pT stage, pN status, TNM stage, UISS risk and SSIGN risk were further explored by the Univariate Cox analysis and Kaplan-Meier survival analysis with log-rank test. The calibration curve analysis was performed to determine the consistency between nomogram predicted and observed DFS probability.

Study arms
Training set (N = 364)

Internal testing set (N = 156)

External testing set (N = 187)

Population characteristics
Study-level characteristics

Characteristic	Study (N = 707)
% Female Sample size	n = 255 ; % = 36.1
Age - <60 Sample size	n = 355 ; % = 50.2
Nephrectomy status - Partial nephrectomy Sample size	n = 353 ; % = 49.9
Nephrectomy status - Radical nephrectomy Sample size	n = 354 ; % = 50.1
TNM classification - TNM 1 Sample size	n = 539 ; % = 76.2
TNM classification - TNM 2 Sample size	n = 68 ; % = 9.6
TNM classification - TNM 3 Sample size	n = 100 ; % = 14.2

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Yang, 2022

Bibliographic Reference	Yang, Guangjie; Nie, Pei; Yan, Lei; Zhang, Mingxin; Wang, Yangyang; Zhao, Lianzi; Li, Mingyao; Xie, Fei; Xie, Haizhu; Li, Xianjun; Xiang, Fawei; Wang, Nan; Cheng, Nan; Zhao, Xia; Wang, Ning; Wang, Yicong; Chen, Chengcheng; Yun, Canhua; Cui, Jingjing; Duan, Shaofeng; Zhang, Ran; Hao, Dapeng; Wang, Ximing; Wang, Zhenguang; Niu, Haitao; The radiomics-based tumor heterogeneity adds incremental value to the existing prognostic models for predicting outcome in localized clear cell renal cell carcinoma: a multicenter study.; European journal of nuclear medicine and molecular imaging; 2022; vol. 49 (no. 8); 2949-2959

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	Not reported
Prognostic model(s)	SSIGN UISS
Inclusion criteria	• Patients with a pathologically confirmed clear cell renal cell carcinoma (ccRCC) after surgery • patients who had a contrast-CT scan less than 15 days before surgery • favourable image quality for analysis • complete follow-up data.
Exclusion criteria	• Synchronous metastasis • other malignancies • received anti-tumour therapy before surgery.
Selection of cohort	Multicentre
Number of participants	N=866
Length of follow-up	Median: 50 months (range 1-118)

Follow-up schedule	Patients were followed up every 6-12 months for the first 2 years and then annually. Follow-up data was collected from medical records including physical examinations and images.
Covariates adjusted for in the multivariable regression modelling	Not reported
Outcome(s) of interest	Recurrence-free/disease-free survival
Source of funding	Postdoctoral Science Foundation of China
Additional comments	Univariate Cox regression analysis, Cox regression analysis, calibration plots, survival analysis and C-index, were performed with R statistical software.

Study arms
UISS low-risk (N = 353)

UISS intermediate-risk (N = 469)

UISS high-risk (N = 44)

SSIGN low-risk (N = 635)

SSIGN intermediate-risk (N = 188)

SSIGN high-risk (N = 43)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 866)
% Female Sample size	n = 293
Age - for non-recurrence Custom value	Median 56.5 (range 18-84)
Age - recurrence Custom value	Median 62 (range 28-87)
TNM classification - pT1 Sample size	n = 695
TNM classification - pT2	n = 84

FINAL

Characteristic	Study (N = 866)
Sample size	
TNM classification - pT3a Sample size	n = 42
TNM classification - pT3b Sample size	n = 42
TNM classification - pT3c Sample size	n = 1
TNM classification - pT4 Sample size	n = 2

Outcomes
UISS

Outcome	UISS intermediate-risk vs UISS low-risk, N2 = 469, N1 = 353	UISS high-risk vs UISS low-risk, N2 = 44, N1 = 353
Recurrence-free survival Hazard ratio/95% CI	2.77 (1.79 to 4.3)	6.33 (3.39 to 11.83)

SSIGN

Outcome	SSIGN intermediate-risk vs SSIGN low-risk, N2 = 188, N1 = 635	SSIGN high-risk vs SSIGN low-risk, N2 = 43, N1 = 635
Recurrence-free survival Hazard ratio/95% CI	4.71 (3.18 to 6.97)	13.55 (8.41 to 21.84)

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Zhang, 2017

Bibliographic Reference	Zhang, Haijian; Liu, Yidong; Xie, Huyang; Fu, Qiang; Liu, Zheng; Zhu, Yu; Xu, Le; Zhang, Weijuan; Yang, Yuanfeng; Xu, Jiejie; Beta-1,4-galactosyltransferase II predicts poor prognosis of patients with

non-metastatic clear-cell renal cell carcinoma.; Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine; 2017; vol. 39 (no. 2); 1010428317691417

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2008-2009
Prognostic model(s)	Leibovich not specified SSIGN UISS
Inclusion criteria	• No history of previous anticancer therapy • no history of other malignancies • radical or partial nephrectomy • histopathological confirmed ccRCC.
Exclusion criteria	• Mixed type of primary renal cancer as confirmed by histopathology • tumours with necrosis >80%, • death within the first month of surgery due to surgical complications • N1 or M1 tumours/ metastatic disease.
Selection of cohort	Single centre
Number of participants	N=585
Length of follow-up	Training set: Median 68 months (range: 39–74 months) Validation set: 67 months (range: 40–74 months)
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival Overall survival
Source of funding	Not industry funded
Additional comments	Student’s t-test or χ2-test, Kaplan–Meier survival curves, univariate and multivariate Cox analysis were performed.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 585)
% Female Sample size	n = 94 ; % = 32.08
Age Mean (SD)	55.6 (12.54)
T1 Sample size	n = 211 ; % = 72.01
T2 Sample size	n = 20 ; % = 6.82
T3 Sample size	n = 57 ; % = 19.45
T4 Sample size	n = 5 ; % = 1.71

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	Moderate (*Unclear risk of bias for outcome or its determination and analysis as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Zhu, 2019

Bibliographic Reference	Zhu, Yan; Zhao, Yao-Rui; Yang, Xian-Fa; Wei, Mao-Ti; Niu, Yuan-Jie; Chang, Ji-Wu; Wang, Ai-Xiang; Liang, Xuan; Postoperative prognostic model for patients with clear cell renal cell carcinoma in a Chinese population.; International journal of urology : official journal of the Japanese Urological Association; 2019; vol. 26 (no. 6); 624-629

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2006 to 2013

Prognostic model(s)	Leibovich 2018
Inclusion criteria	• Clear cell renal cell carcinoma • radical or partial nephrectomy.
Exclusion criteria	• Distant metastases • bilateral renal masses before or at the time or surgery • hereditary renal cell carcinoma • von Hippel-Lindau disease • those lost to follow-up.
Selection of cohort	Single centre
Number of participants	N=942
Length of follow-up	Median 72 months (range 1 to 143 months)
Follow-up schedule	Clinical and radiological assessments (chest and abdominal CT) every 3 months for first 2 years after surgery, then every 6 months until 4 years, then every year thereafter.
Outcome(s) of interest	Model discrimination (C-stats) Recurrence-free/disease-free survival
Source of funding	Not reported
Additional comments	None

Population characteristics
Study-level characteristics

Characteristic	Study (N = 942)
% Female Sample size	n = 266 ; % = 28.2
Less than 57 years old Sample size	n = 468 ; % = 49.7
57 years old or over Sample size	n = 474 ; % = 50.3
Radical nephrectomy Sample size	n = 816 ; % = 86.6
Partial nephrectomy Sample size	n = 126 ; % = 13.4

Characteristic	Study (N = 942)
TNM pt3 + pt4 Sample size	n = 80 ; % = 8.5

Critical appraisal - PROBAST tool (assessment by Usher-Smith 2022 used) – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis as assessed by Usher-Smith 2022*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Zhu, 2021

Bibliographic Reference	Zhu, D.; Shi, X.; Gao, S.; Yue, C.; Zhang, L.; Bai, Y.; Wang, Q.; Okada, A.; Yasui, T.; Wang, C.; Cui, X.; Zuo, L.; RNF43 is a novel tumor-suppressor and prognostic indicator in clear cell renal cell carcinoma; Oncology Research; 2021; vol. 29 (no. 3); 159-174

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	Between 2010 and 2014
Prognostic model(s)	SSIGN
Inclusion criteria	Patients who were pathologically diagnosed with ccRCC
Exclusion criteria	Not reported
Selection of cohort	Multicentre
Number of participants	Total N = 640 Cohort 1 N = 193 Cohort 2 N = 127 Training cohort N = 160 Validation cohort N = 160
Length of follow-up	Not reported

Covariates adjusted for in the multivariable regression modelling	Survival curves were depicted using the Kaplan-Meier method and analysed by the log-rank test. Variables with p < 0.1 in univariate analysis were included in multivariate Cox proportional hazards analysis. The prognostic accuracy was assessed by Harrell's concordance index (c-index).
Outcome(s) of interest	Progression-free survival Overall survival
Source of funding	This work was supported by the Top-Level Clinical Discipline Project of Shanghai Pudong (PWYgf2018-03), National Natural Science Foundation of China (Nos. 81773154, 81902565, 81772747, 81974391), Shanghai Natural Science Foundation (No. 20ZR1449600), Pudong New Area Science and Technology Development Fund Special Fund for People's Livelihood Research (Medical and Health) (PKJ2019-Y19), Young Scientists Foundation of Changzhou No. 2 People's Hospital (2019K008), Changzhou Sci & Tech Program (CJ20190100), and the Program of Shanghai Academic/Technology Research Leader (No. 19XD1405100).
Additional comments	Univariable analysis of RNF43, YAP expression classifier and clinical characteristics such as age (<60 y vs. ≥60 y), Gender (Male vs. Female), WHO/ISUP Grading (1-2 vs. 3-4), TNM stage (1–2 vs. 3–4), and SSIGN (1–4 vs. ≥5)

Study arms
Cohort 1 (N = 193)

Cohort 2 (N = 127)

Training cohort (N = 160)

Validation cohort (N = 160)

TNM I-II (Cohort 1) (N = 158)

TNM III-IV (Cohort 1) (N = 35)

TNM I-II (Cohort 2) (N = 118)

TNM III-IV (Cohort 2) (N = 9)

Population characteristics
Arm-level characteristics

Characteristic	Cohort 1 (N = 193)	Cohort 2 (N = 127)	Training cohort (N = 160)	Validation cohort (N = 160)
% Female No of events	n = 64 ; % = 33.2	n = 30 ; % = 23.6	n = 46 ; % = 28.8	n = 48 ; % = 30

Characteristic	Cohort 1 (N = 193)	Cohort 2 (N = 127)	Training cohort (N = 160)	Validation cohort (N = 160)
TNM classification - TNM stage I-II No of events	n = 158 ; % = 81.9	n = 118 ; % = 92.9	n = 144 ; % = 90	n = 132 ; % = 82.5
TNM classification - TNM stage III-IV No of events	n = 35 ; % = 18.1	n = 9 ; % = 7.1	n = 16 ; % = 10	n = 28 ; % = 17.5

Outcomes
Survival

Outcome	TNM III-IV (Cohort 1) vs TNM I-II (Cohort 1), N2 = 35, N1 = 158	TNM III-IV (Cohort 2) vs TNM I-II (Cohort 2), N2 = 9, N1 = 118
Overal survival Hazard ratio/95% CI	11.95 (5.47 to 26.11)	20.74 (7.17 to 59.98)
Progression free survival Hazard ratio/95% CI	11.79 (5.4 to 25.74)	24.44 (8.37 to 71.36)

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

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High (*High risk of bias for analysis*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Zhu, 2024

Bibliographic Reference	Zhu, Pingyi; Dai, Chenchen; Xiong, Ying; Qu, Jianyi; Wang, Ruiting; Yao, Linpeng; Zhang, Feng; Hou, Jun; Zeng, Mengsu; Guo, Jianming; Wang, Shuo; Chen, Feng; Zhou, Jianjun; Tumor contour irregularity on preoperative CT predicts prognosis in renal

cell carcinoma: a multi-institutional study.; EClinicalMedicine; 2024; vol. 75; 102775

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	Training set and Internal validation set: 2009 to 2019 External test set: 2016 to 2017 and 2017 to 2023
Prognostic model(s)	SSIGN
Inclusion criteria	People with pathologically confirmed RCC who received nephrectomy: • Complete clinic-pathologic and follow-up data • Pre-treatment CT imaging
Exclusion criteria	• Poor image quality • Anti-tumour therapy before surgery • Other history of malignancy • Stage 4
Selection of cohort	Single centre Multicentre
Number of participants	Training set n=1185 Internal validation set n=297 External test set n=736
Length of follow-up	Median follow-up 62 months (range 6 to 154)
Follow-up schedule	Follow-up ever 6 to 12 months for the first 2 years post-surgery followed by annual check-ups.
Covariates adjusted for in the multivariable regression modelling	NA
Outcome(s) of interest	Model discrimination (C-stats)
Source of funding	National Natural Science Foundation of China; Shanghai Municipal Health Commission; China National Key R&D Program; Science and Technology Commission of Shanghai Municipality
Additional comments	N/A

Study arms

Zhongshan cohort (N = 1482)

Participants made up the Testing and Internal validation sets

Zhejiang cohort (N = 433)
Participants included in the External test cohort

Xiamen cohort (N = 126)
Participants included in the External test cohort

TCIA (N = 177)
Participants included in the External test cohort

Population characteristics
Arm-level characteristics

Characteristic	Zhongshan cohort (N = 1482)	Zhejiang cohort (N = 433)	Xiamen cohort (N = 126)	TCIA (N = 177)
% Female Sample size	n = 512 ; % = 34.5	n = 145 ; % = 33.5	n = 41 ; % = 32.5	n = 59 ; % = 33.3
Age Median (IQR)	58 (50 to 65)	56 (48 to 64)	56 (45 to 67)	59 (50 to 70)
Nephrectomy status Sample size	n = NA ; % = NA	n = NA ; % = NA	n = NA ; % = NA	n = NA ; % = NA
Nephrectomy status - Partial nephrectomy Sample size	n = 553 ; % = 37.3	n = 289 ; % = 66.7	n = 69 ; % = 54.8	n = 65 ; % = 35.7
Nephrectomy status - Radical nephrectomy Sample size	n = 929 ; % = 62.7	n = 144 ; % = 33.3	n = 57 ; % = 45.2	n = 112 ; % = 63.3
RCC subtypes Sample size	n = NA ; % = NA	n = NA ; % = NA	n = NA ; % = NA	n = NA ; % = NA
RCC subtypes - Clear cell Sample size	n = 1179 ; % = 79.6	n = 344 ; % = 79.5	n = 93 ; % = 73.8	n = 152 ; % = 85.9
RCC subtypes - Papillary Sample size	n = 118 ; % = 8	n = 19 ; % = 4.4	n = 9 ; % = 7.1	n = 16 ; % = 9
RCC subtypes - Chromophobe Sample size	n = 89 ; % = 6	n = 30 ; % = 6.9	n = 6 ; % = 4.8	n = 9 ; % = 5.1
RCC subtypes - Other malignant Sample size	n = 96 ; % = 6.4	n = 40 ; % = 9.2	n = 18 ; % = 14.3	n = 0 ; % = 0
TNM classification Sample size	n = NA ; % = NA	n = NA ; % = NA	n = NA ; % = NA	n = NA ; % = NA
TNM classification - T-stage I Sample size	n = 1243 ; % = 83.9	n = 372 ; % = 85.9	n = 107 ; % = 84.9	n = 109 ; % = 61.6

Characteristic	Zhongshan cohort (N = 1482)	Zhejiang cohort (N = 433)	Xiamen cohort (N = 126)	TCIA (N = 177)
TNM classification - T-stage II Sample size	n = 105 ; % = 7.1	n = 34 ; % = 8.1	n = 10 ; % = 8	n = 20 ; % = 11.3
TNM classification - T-stage III Sample size	n = 134 ; % = 9	n = 26 ; % = 6	n = 9 ; % = 7.1	n = 48 ; % = 27.1

Critical appraisal - PROBAST tool – applies to all outcomes unless otherwise specified

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(No information around the number of outcomes and no measure of calibration.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Appendix E – Forest plots

Clear cell subtype

GRANT

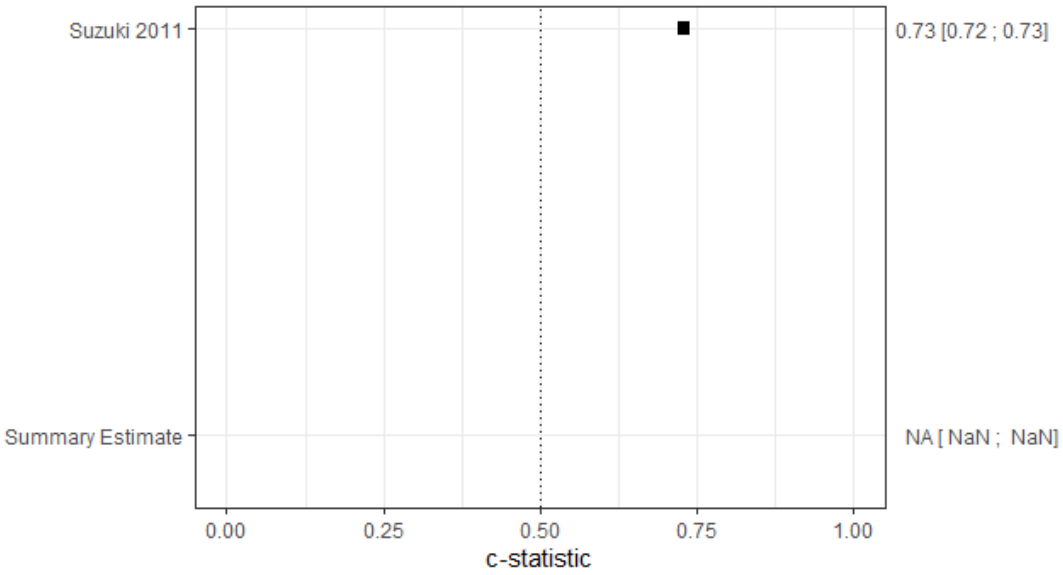
No evidence identified for this model.

Karakiewicz

No evidence identified for this model.

Kattan

Figure 2: Kattan: recurrence-free survival/disease-free survival - c-statistic, clear cell



Leibovich 2003

Figure 3: Leibovich 2003: progression-free survival - c-statistic, clear cell subtype

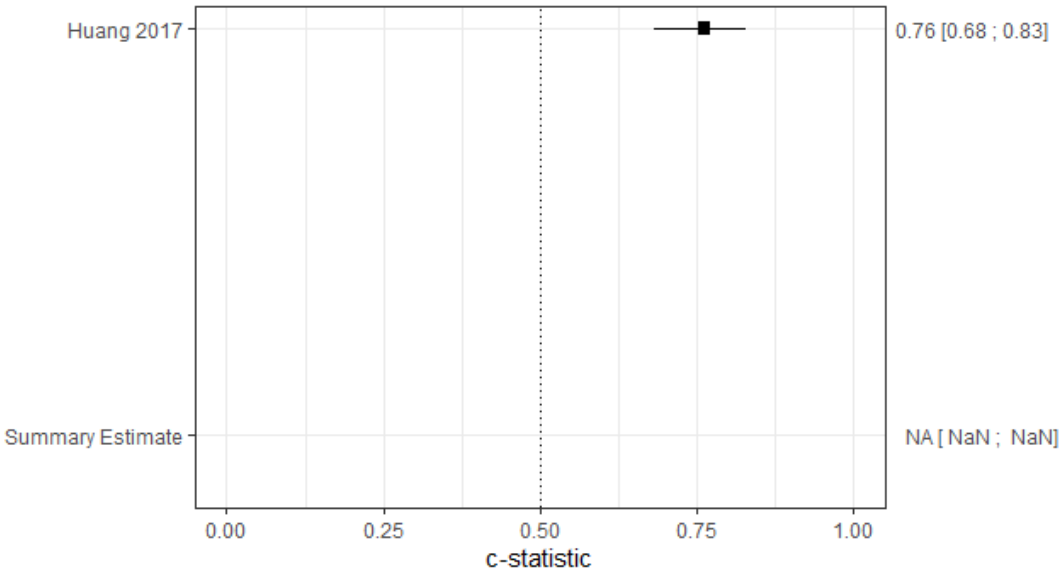
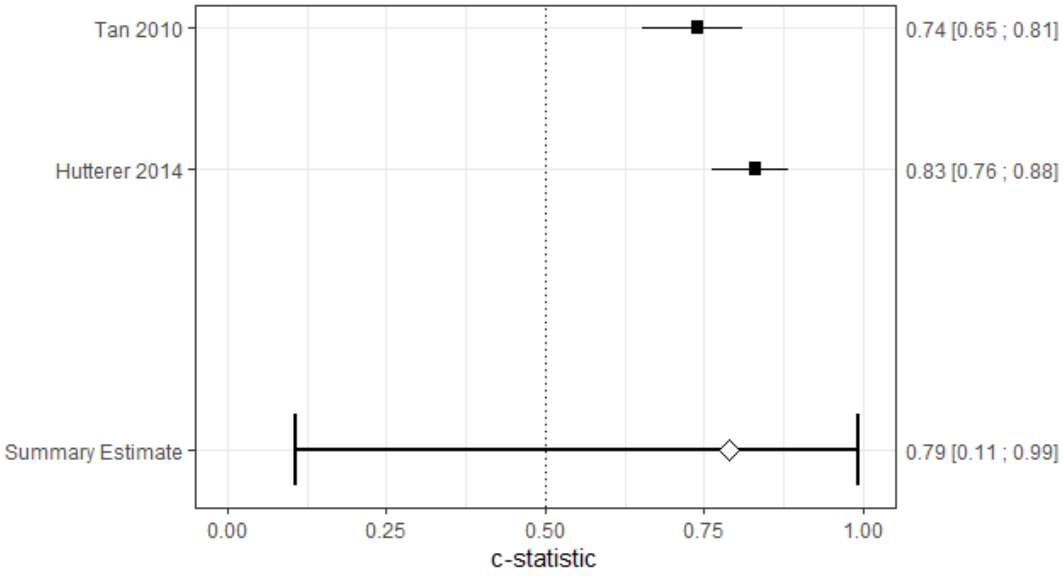
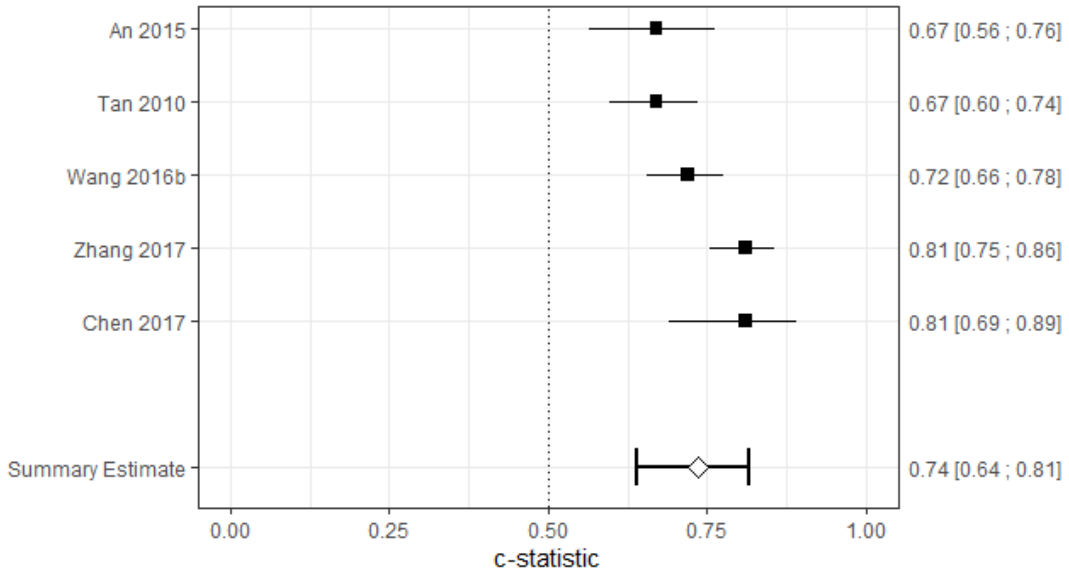


Figure 4: Leibovich 2003: cancer-specific survival - c-statistic, clear cell subtype, RE



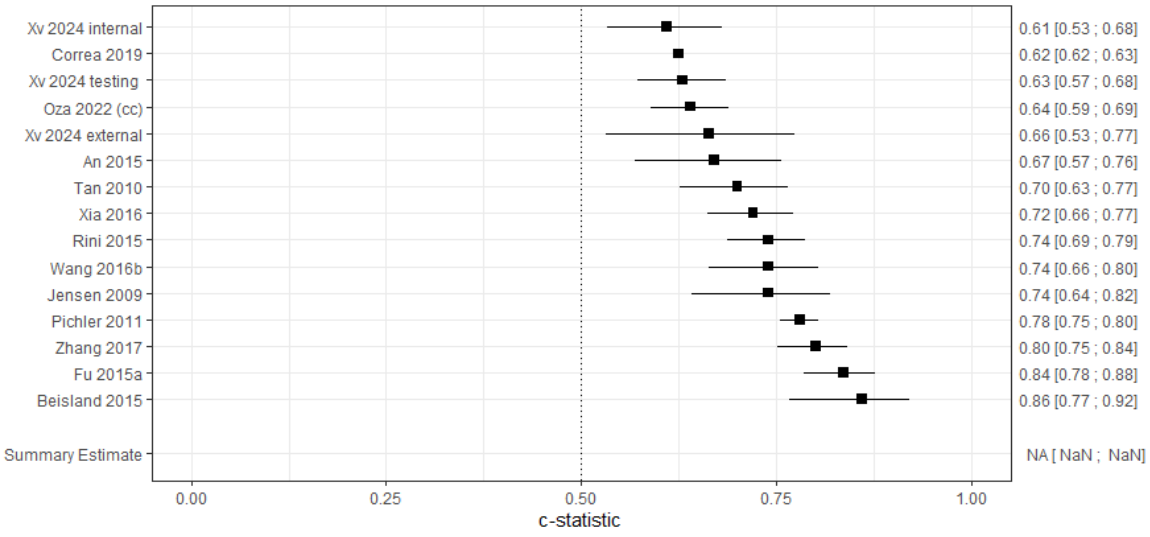
I^2 = 67.86%

Figure 5: Leibovich 2003: overall survival - c-statistic, clear cell, RE



I^2 = 73.90%

Figure 6: Leibovich 2003 recurrence-free survival/disease-free survival for clear cell RCC



Evidence could not be pooled as I^2 was above 80%.

Figure 7:Leibovich 2003: Disease-free survival - Hazard ratio for high risk vs low risk, clear cell RCC

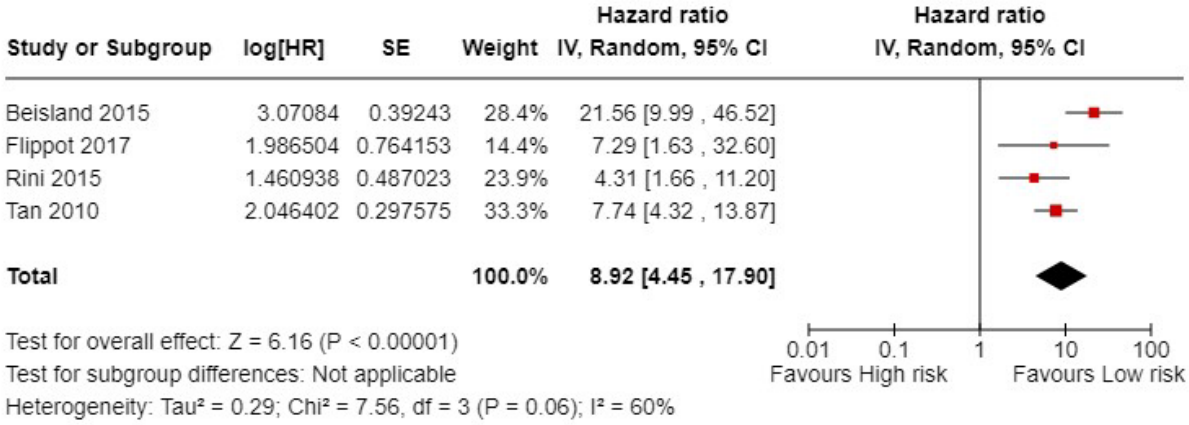


Figure 8: Leibovich 2003: Local recurrence - Hazard ratio for high risk vs low risk, clear cell RCC

Figure 9: Leibovich 2003: Cancer-specific survival - Hazard ratio for high risk vs low risk, clear cell RCC

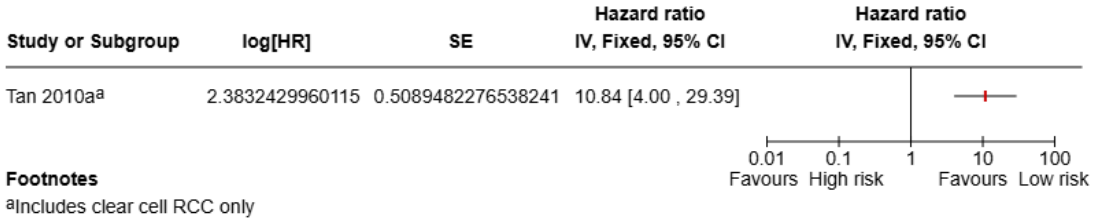


Figure 10: Overall survival - Hazard ratio for high risk vs low risk, clear cell RCC

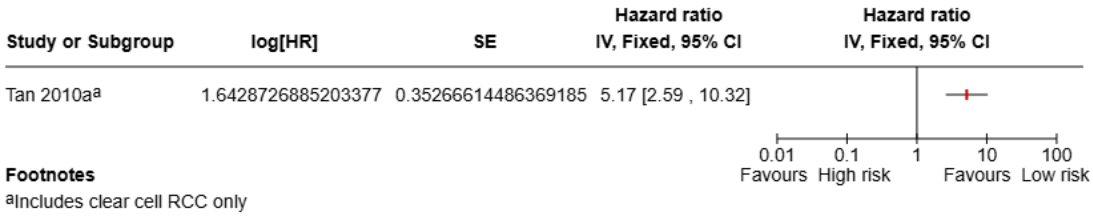


Figure 11: Leibovich 2003: Disease-free survival - Hazard ratio for intermediate risk vs low risk, clear cell RCC

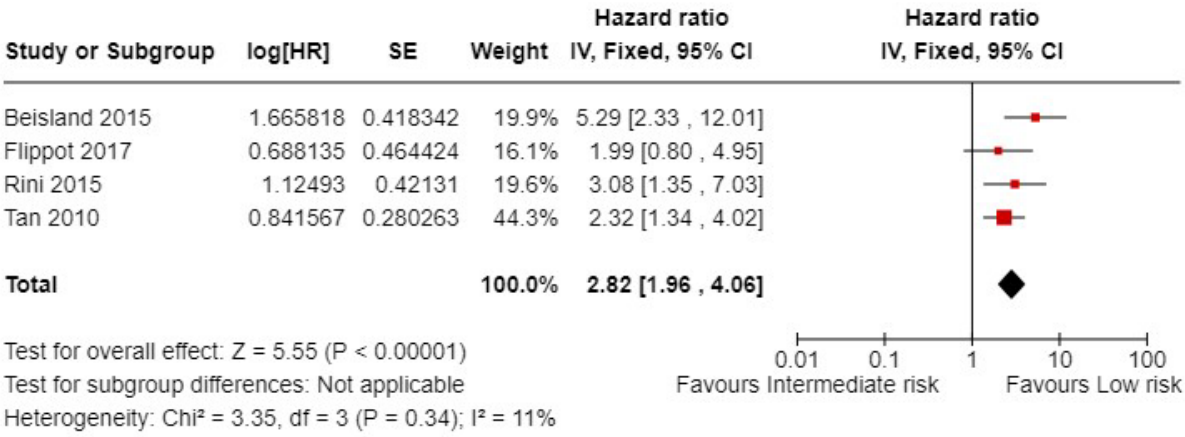


Figure 12: Leibovich 2003: Local recurrence - Risk ratio for intermediate risk vs low risk, clear cell RCC

Figure 13: Leibovich 2003: Cancer-specific survival - Hazard ratio for intermediate risk vs low risk, clear cell RCC

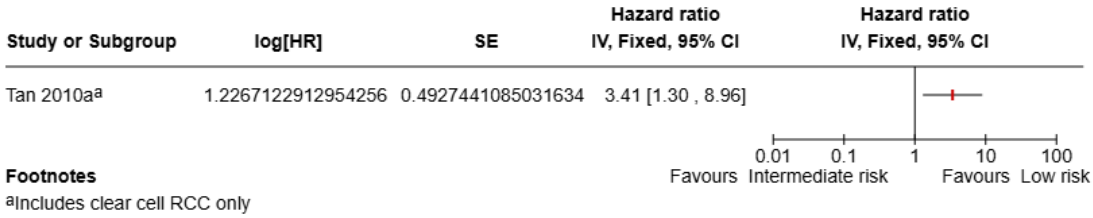


Figure 14: Overall survival - Hazard ratio for intermediate risk vs low risk, clear cell RCC

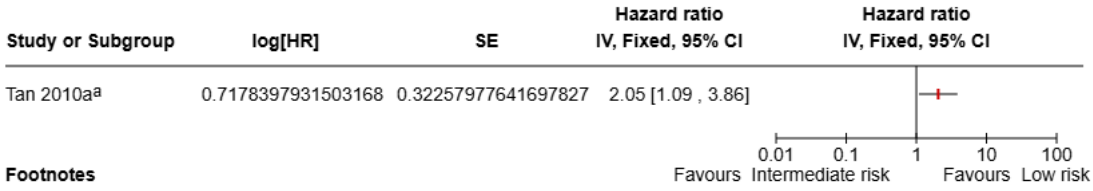


Figure 15: Leibovich 2003: Disease-free survival - Hazard ratio for high risk vs intermediate risk, clear cell RCC

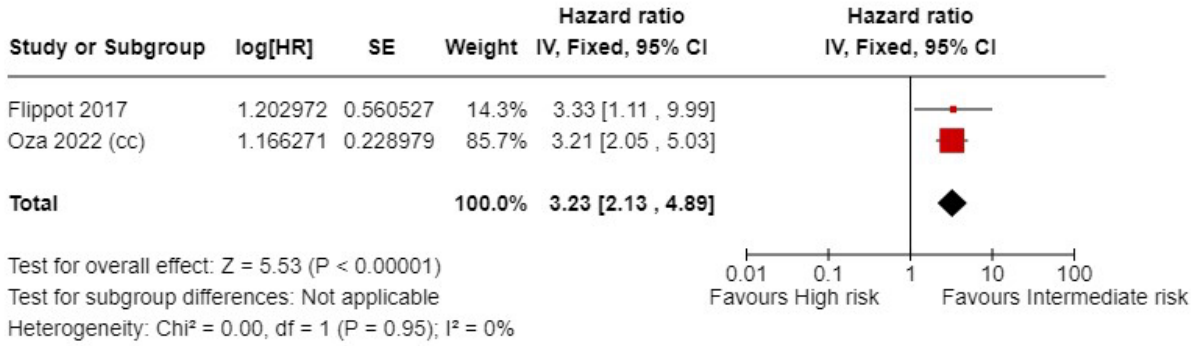
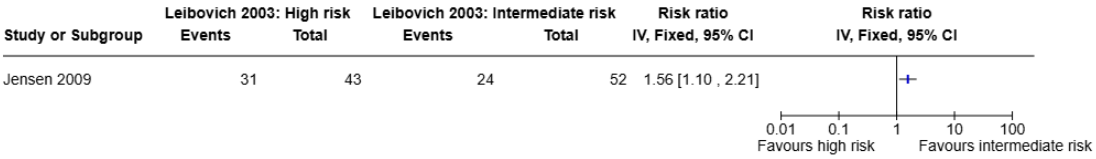


Figure 16: Leibovich 2003: Local recurrence - Risk ratio for high risk vs intermediate risk, clear cell RCC



Leibovich 2018

Figure 17: Leibovich 2018: progression-free survival - c-statistic, clear cell subtype

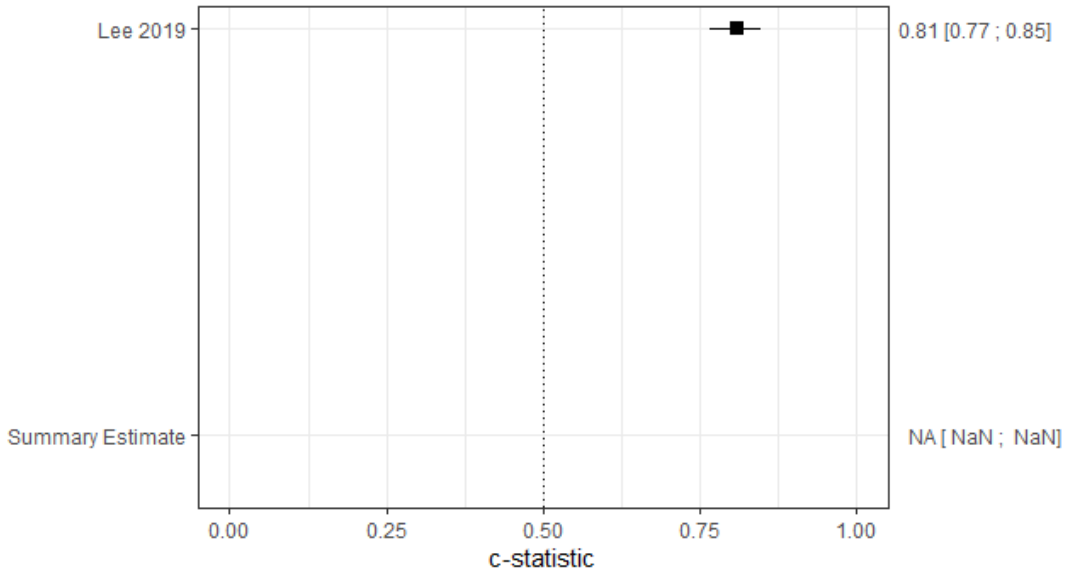
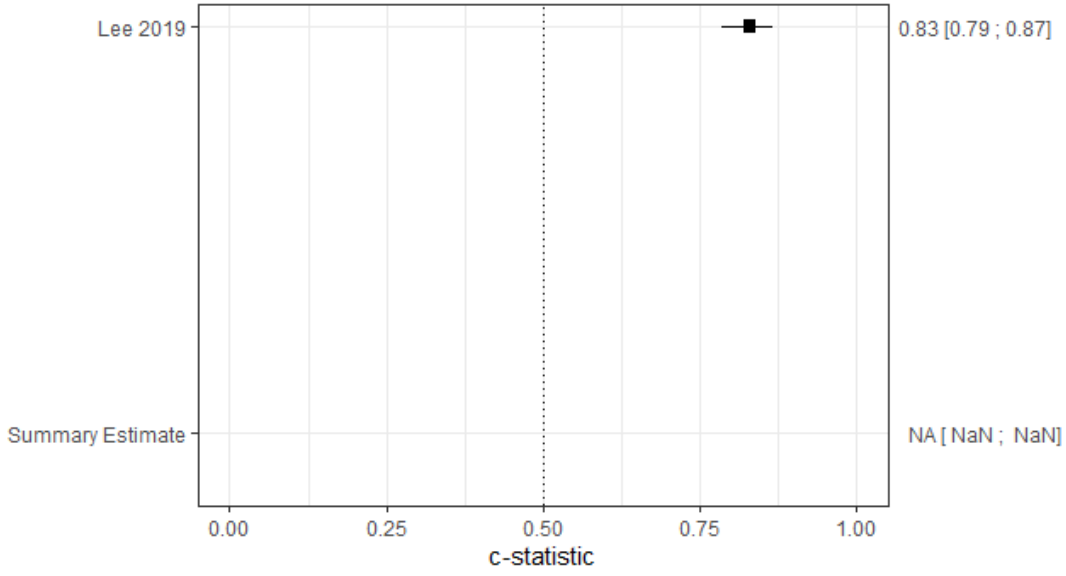
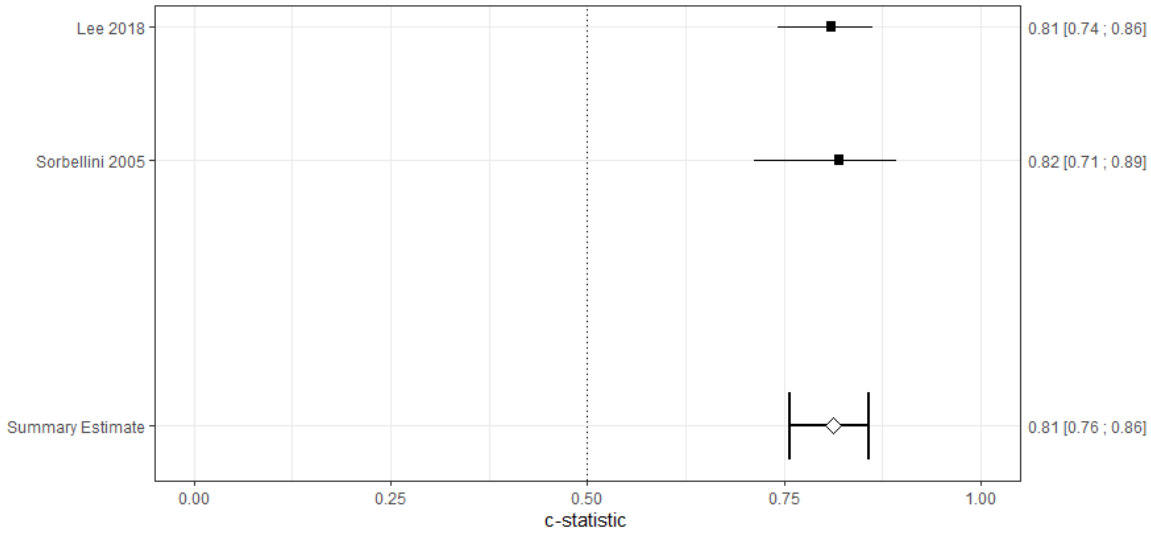


Figure 18: Leibovich 2018: cancer-specific survival - c-statistic, clear cell



Sorbellini

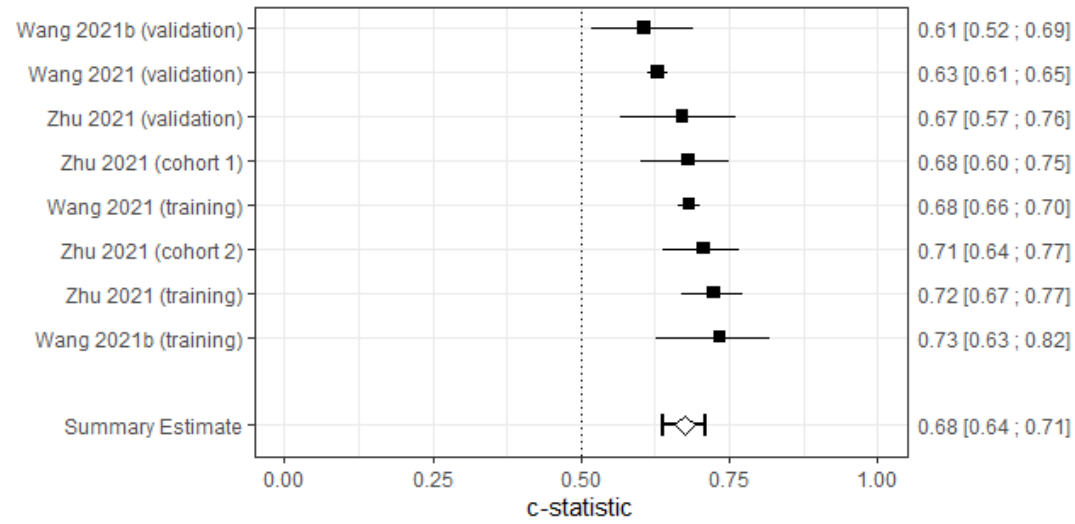
Figure 19: Sorbellini: recurrence-free survival/disease-free survival - c-statistic, clear cell subtype, FE



I^2 = 0.00%

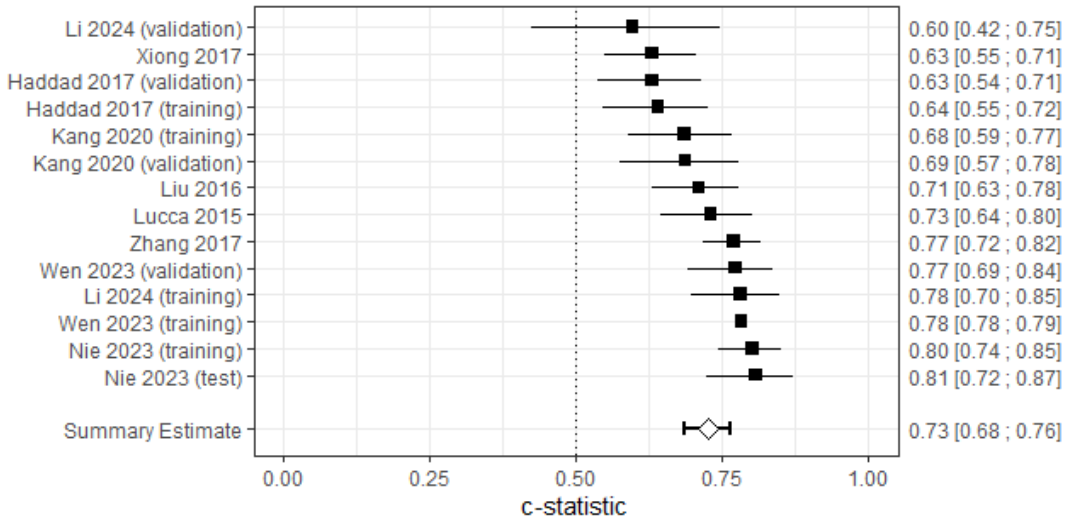
SSIGN

Figure 20: SSIGN: progression-free survival, clear cell subtype - c-statistic, RE



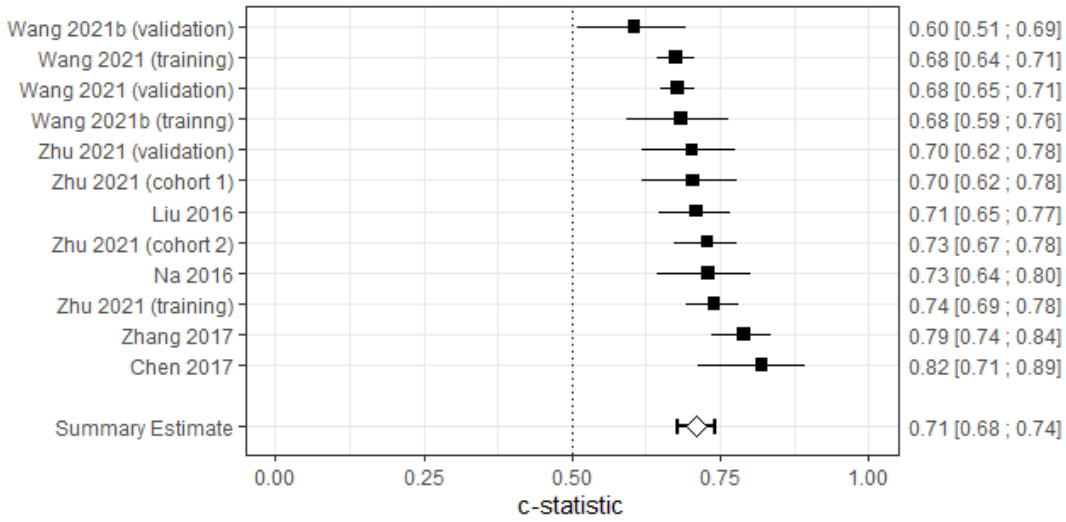
I^2 = 74.92%

Figure 21: SSIGN: recurrence-free survival/disease-free survival - c-statistic, clear cell subtype, RE



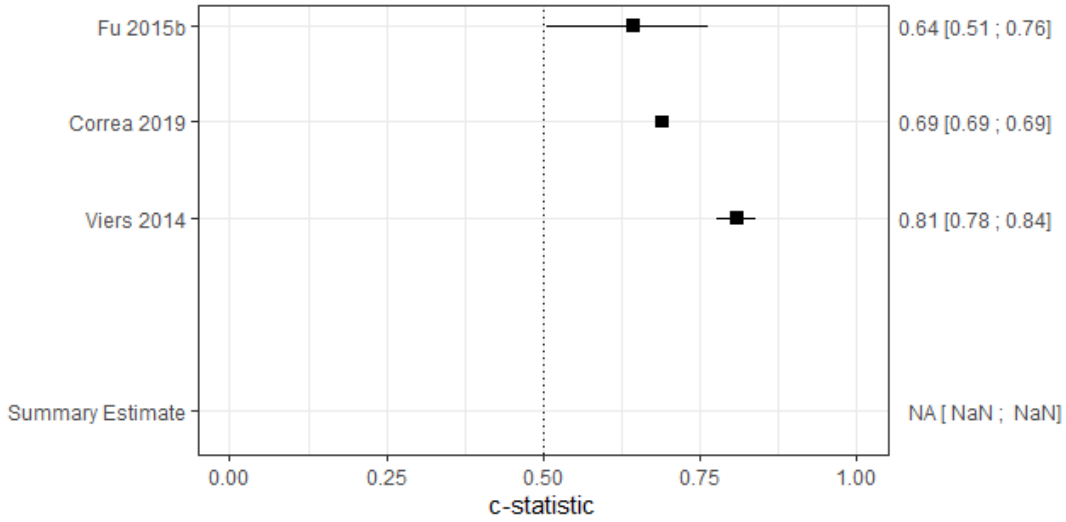
I^2 = 75.19%

Figure 22: SSIGN: overall survival - c-statistic, clear cell subtype, RE



I^2 = 65.48%

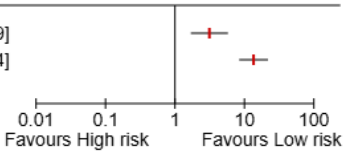
Figure 23: SSIGN: cancer-specific survival, clear cell subtype - c-statistic



Evidence could not be pooled as I^2 was above 80%

Figure 24: SSIGN: Disease-free survival - Hazard ratio for high risk vs low risk, clear cell RCC

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Random, 95% CI
Haddad 2017[a]	1.1410330045520618	0.3136984056934506	3.13 [1.69 , 5.79]
Yang 2022[b]	2.6063865473257097	0.2434538810082405	13.55 [8.41 , 21.84]



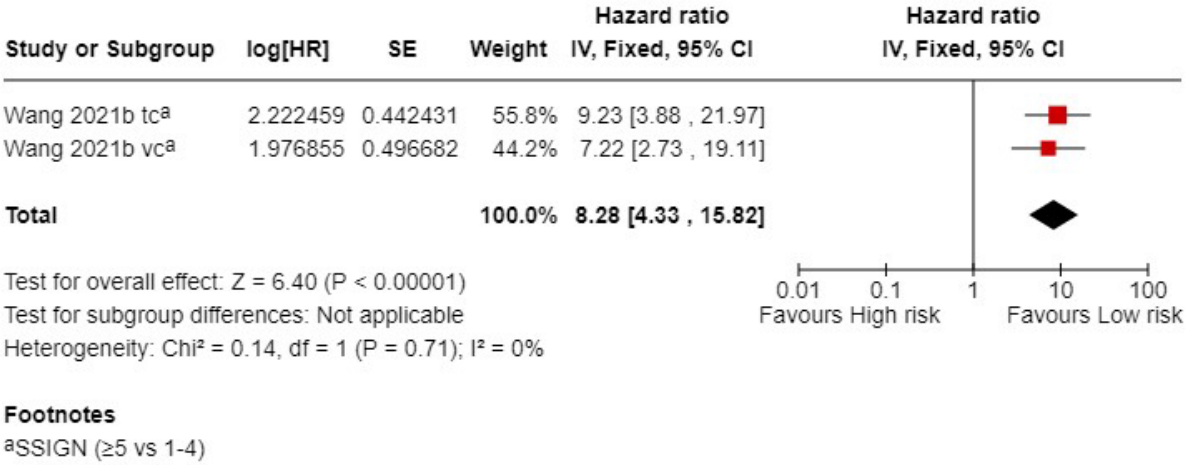
Footnotes

[a]SSIGN score 0-5 vs >5

[b]SSIGN risk groups reported as high-risk vs low risk and intermediate risk vs low risk. No score reported

Evidence could not be pooled as I^2 was above 80%

Figure 25: SSIGN: Overall survival - Hazard ratio for high risk vs low risk, clear cell RCC [Zhu 2021 removed]

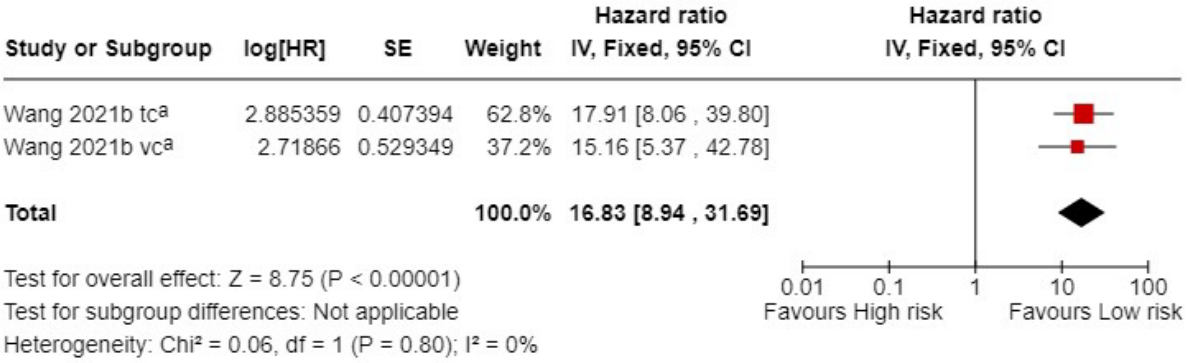


Footnotes

[a]SSIGN (≥5 vs 1-4)

Data from Zhu 2021 were removed as the reported hazard ratios favoured the high-risk subgroup. Including the data from Zhu 2021 introduced a high degree of heterogeneity, and it was judged likely that there was an error in the reporting of the results in this study.

Figure 26: SSIGN: Progression-free survival - Hazard ratio for high risk vs low risk, clear cell RCC [Zhu 2021 removed]

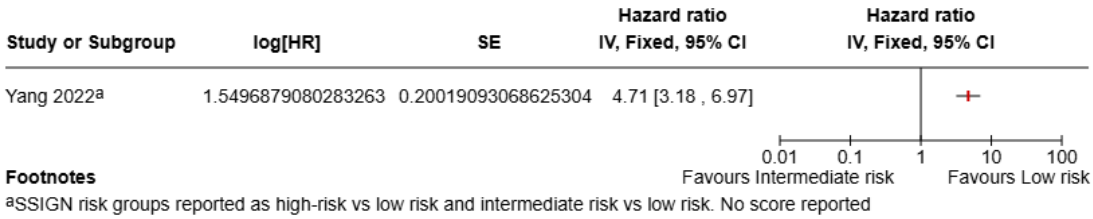


Footnotes

[a](SSIGN ≥5 vs 1-4)

Data from Zhu 2021 were removed as the reported hazard ratios favoured the high-risk subgroup. Including the data from Zhu 2021 introduced a high degree of heterogeneity, and it was judged likely that there was an error in the reporting of the results in this study.

Figure 27: SSIGN: Recurrence-free survival - Hazard ratio for intermediate risk vs low risk, clear cell RCC

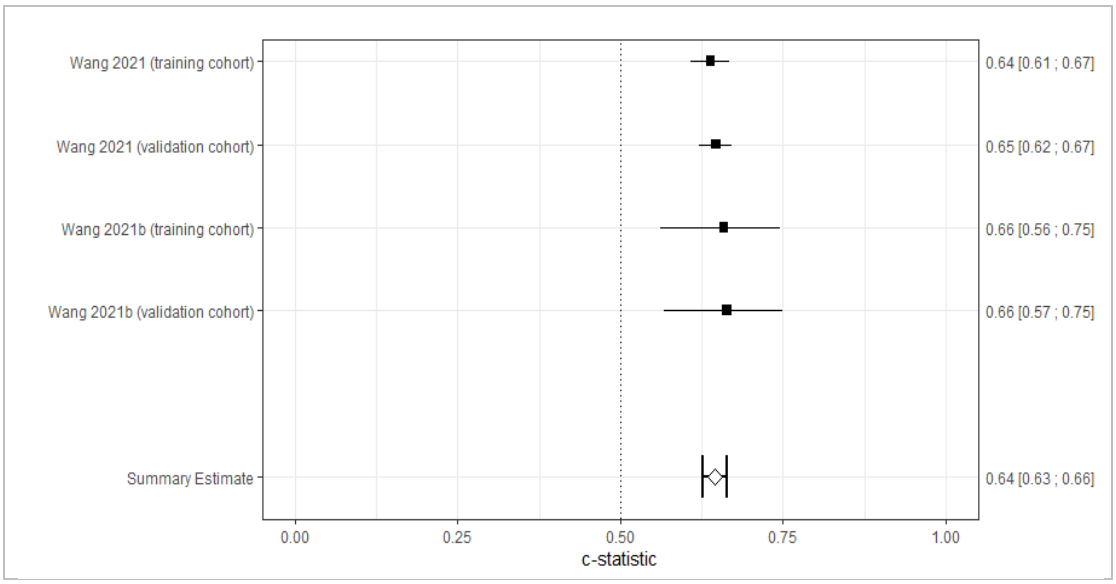


Footnotes

[a]SSIGN risk groups reported as high-risk vs low risk and intermediate risk vs low risk. No score reported

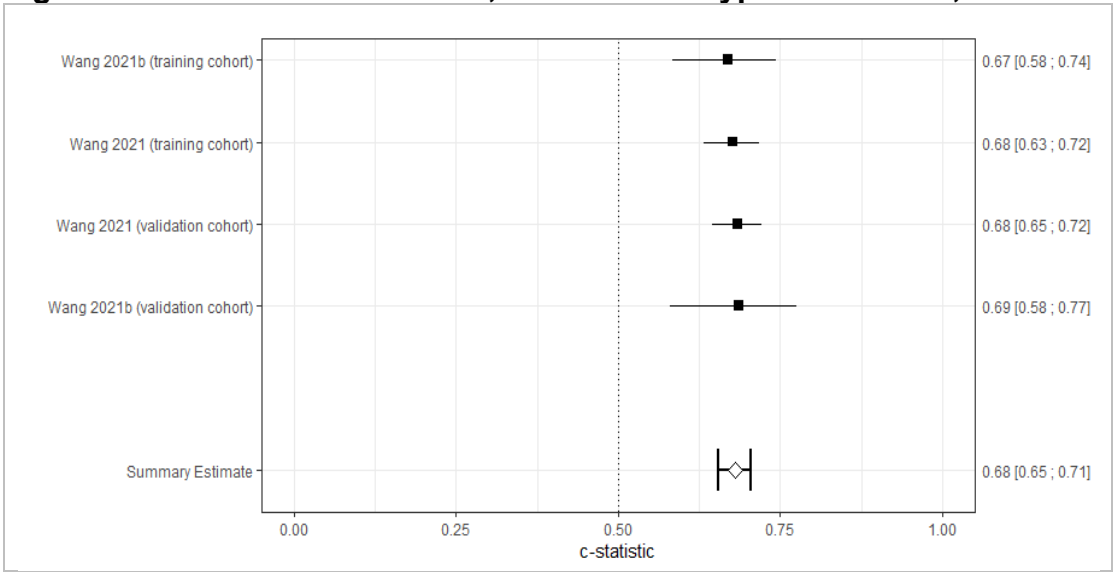
TNM 2016

Figure 28: TNM: progression-free survival, clear cell subtype - c-statistic, FE



I^2 = 0.00%

Figure 29: TNM: overall survival, clear cell subtype - c-statistic, FE



I^2 = 0.00%

Figure 30: TNM: Disease-free survival - Hazard ratio for stages 3 vs 1-2, clear cell subtype

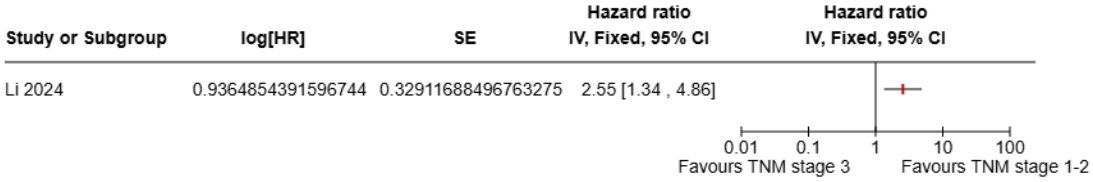
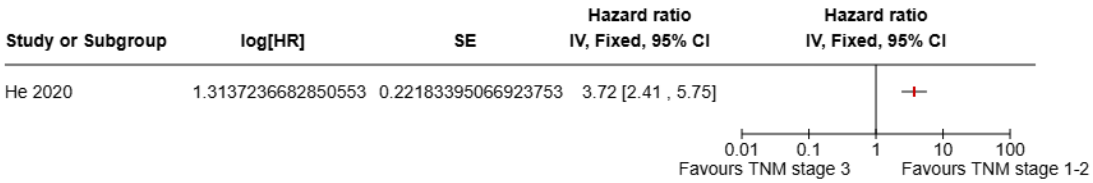
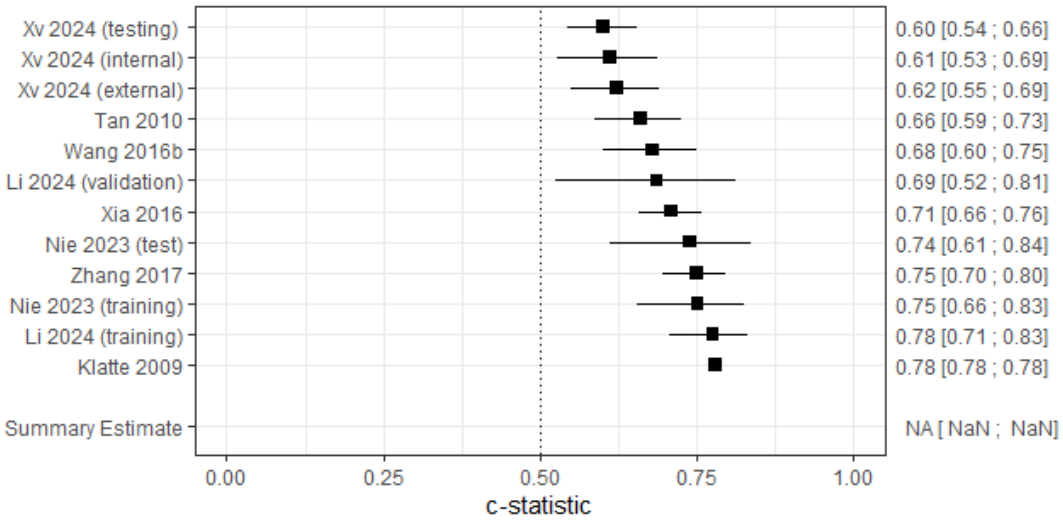


Figure 31: TNM: Overall survival - Hazard ratio for stages 3 vs 1-2, clear cell subtype



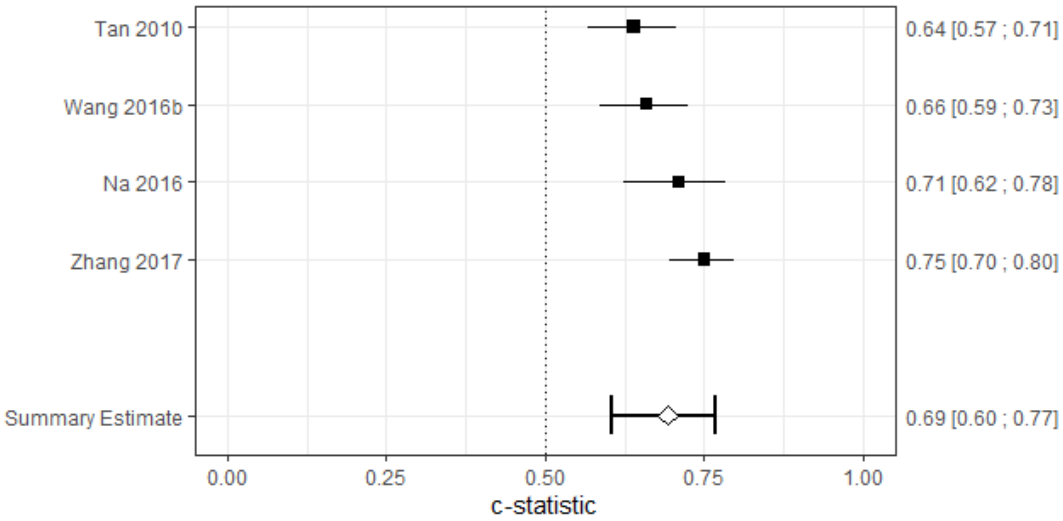
UISS

Figure 32: UISS: disease-free survival - c-statistic, clear cell subtype



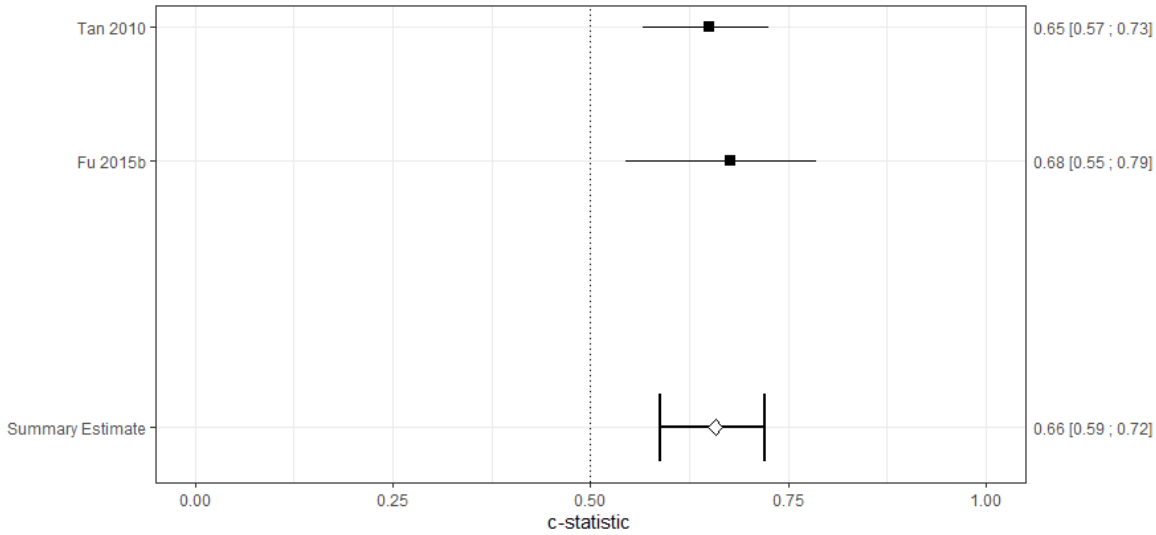
Evidence could not be pooled as I^2 was above 80%

Figure 33: UISS: overall survival - c-statistic, clear cell subtype, RE



I^2 = 62.37%

Figure 34: UISS: cancer-specific survival - c-statistic, clear cell subtype, FE



I^2 = 0.00%

Figure 35: UISS: Cancer-specific survival - Hazard ratio for high risk vs low risk, clear cell RCC

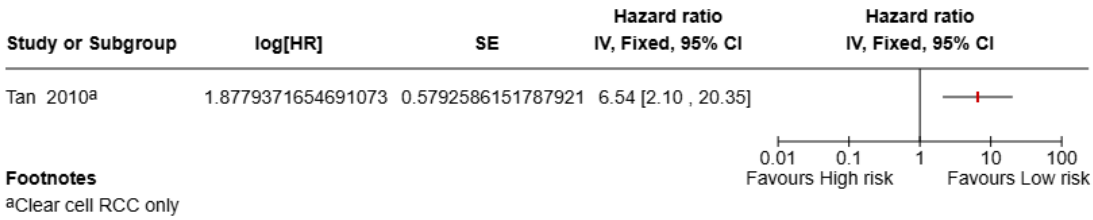


Figure 36: UISS: Disease-free survival - Hazard ratio for high risk vs low risk, clear cell RCC

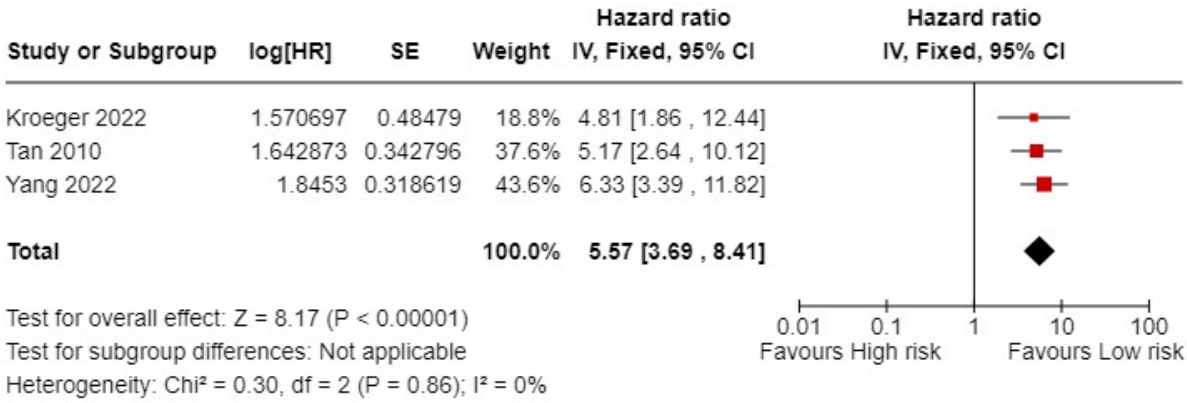


Figure 37: UISS: Overall survival - Hazard ratio for high risk vs low risk, clear cell RCC

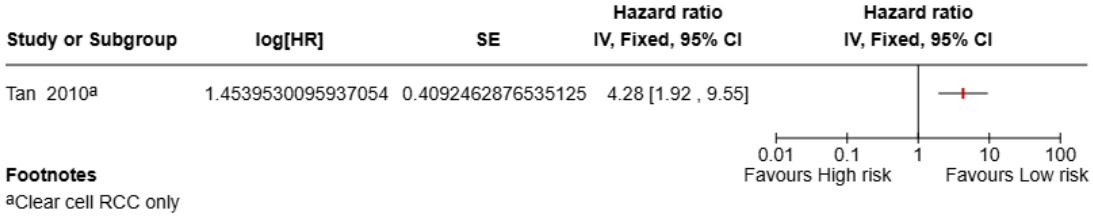


Figure 38: UISS: Cancer-specific survival - Hazard ratio for intermediate risk vs low risk, clear cell RCC

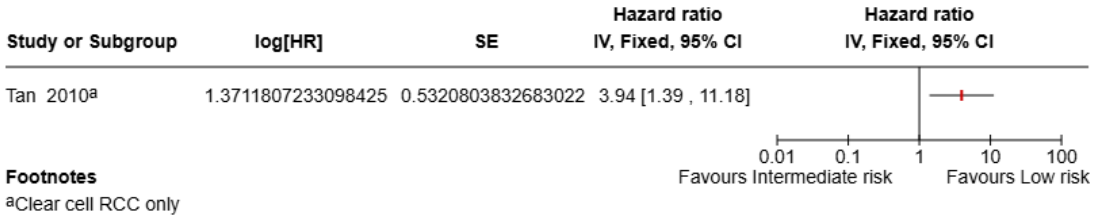


Figure 39: UISS: Disease-free survival - Hazard ratio for intermediate risk vs low risk, clear cell RCC

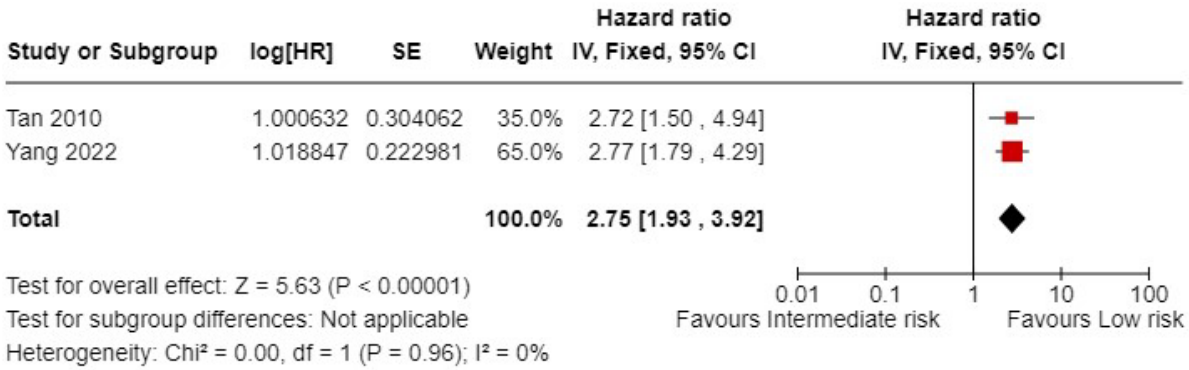


Figure 40: UISS: Overall survival - Hazard ratio for intermediate risk vs low risk, clear cell subtype

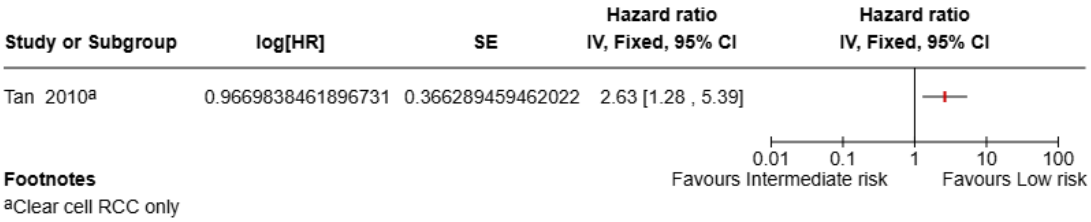
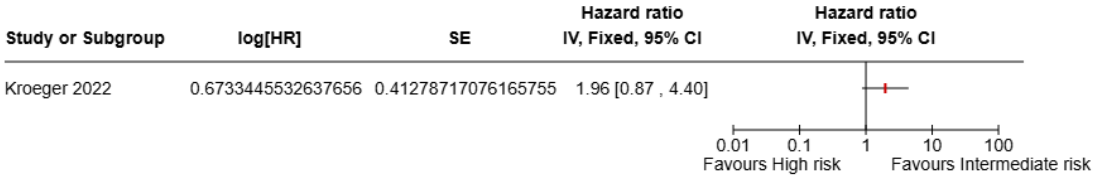


Figure 41: UISS: Disease-free survival - Hazard ratio for high risk vs intermediate risk, clear cell RCC



VENUSS

No evidence identified for this model.

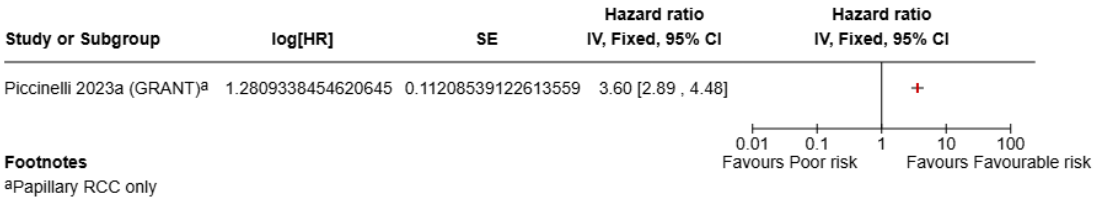
Zisman

No evidence identified for this model.

Papillary subtype

GRANT

Figure 42: GRANT: Cancer-specific survival - Hazard ratio for poor risk vs favourable risk, papillary RCC



Karakiewicz

No evidence identified for this model.

Kattan

No evidence identified for this model.

Leibovich 2003

Figure 43: Leibovich 2003: recurrence-free survival/disease-free survival - c-statistic, papillary subtype

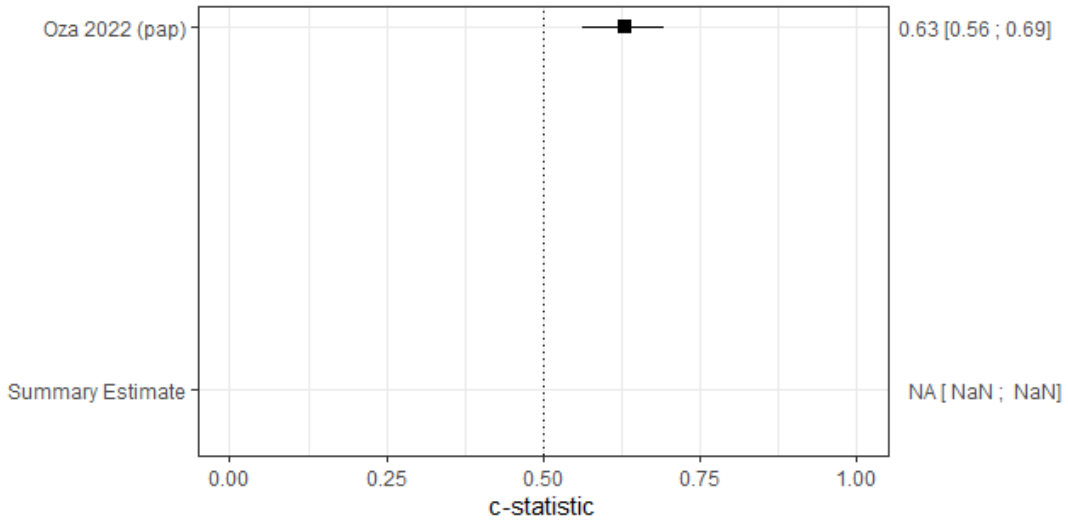
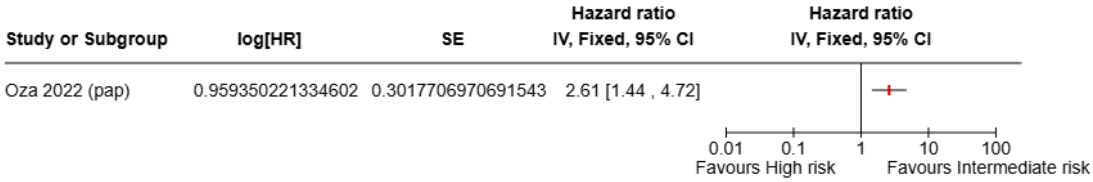


Figure 44: Leibovich 2003: disease-free survival, hazard ratio for high risk vs intermediate risk, papillary subtype



Leibovich 2018

Figure 45: Leibovich 2018: progression-free survival - c-statistic, papillary subtype

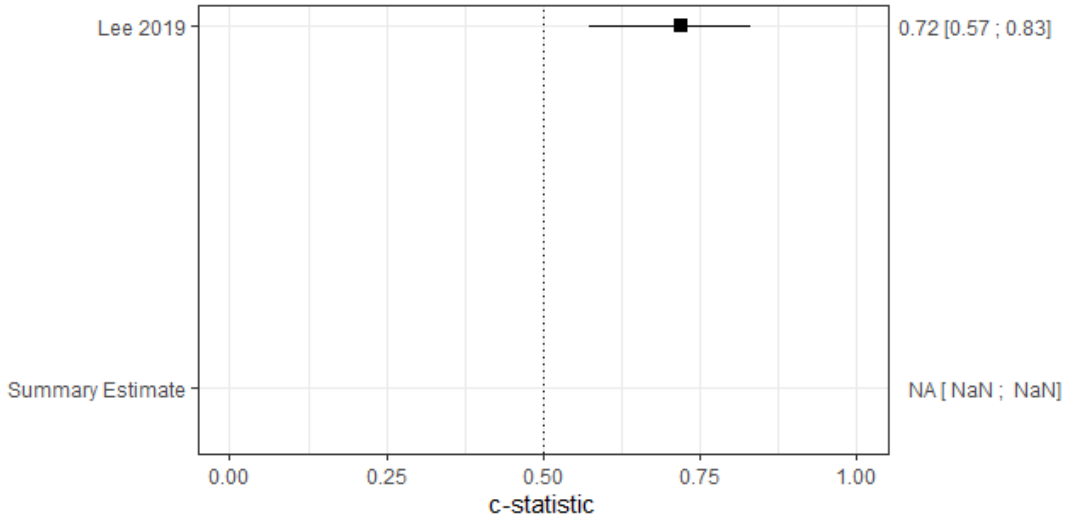


Figure 46: Leibovich 2018: cancer-specific survival - c-statistic, papillary subtype

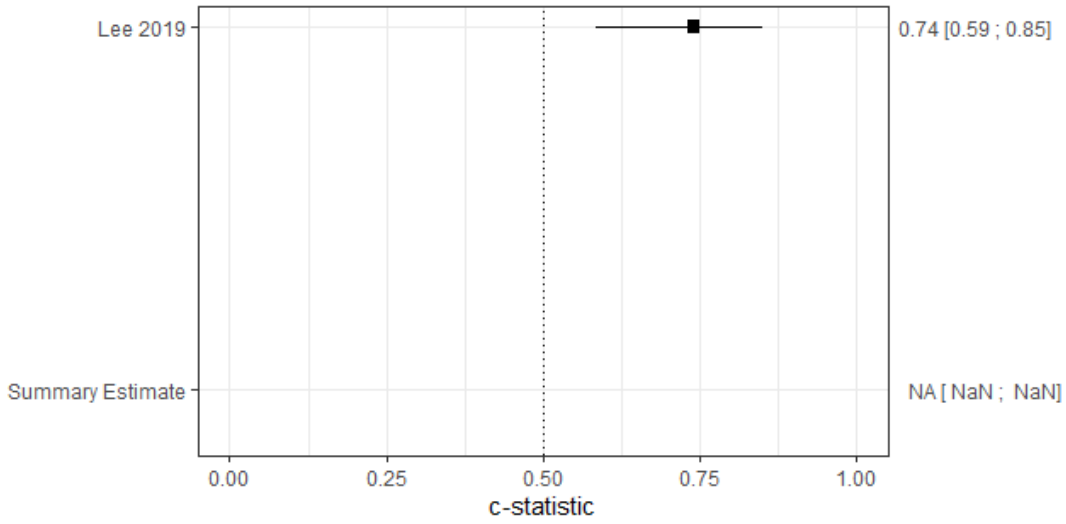


Figure 47: Leibovich 2018: recurrence-free survival/disease-free survival - c-statistic, papillary

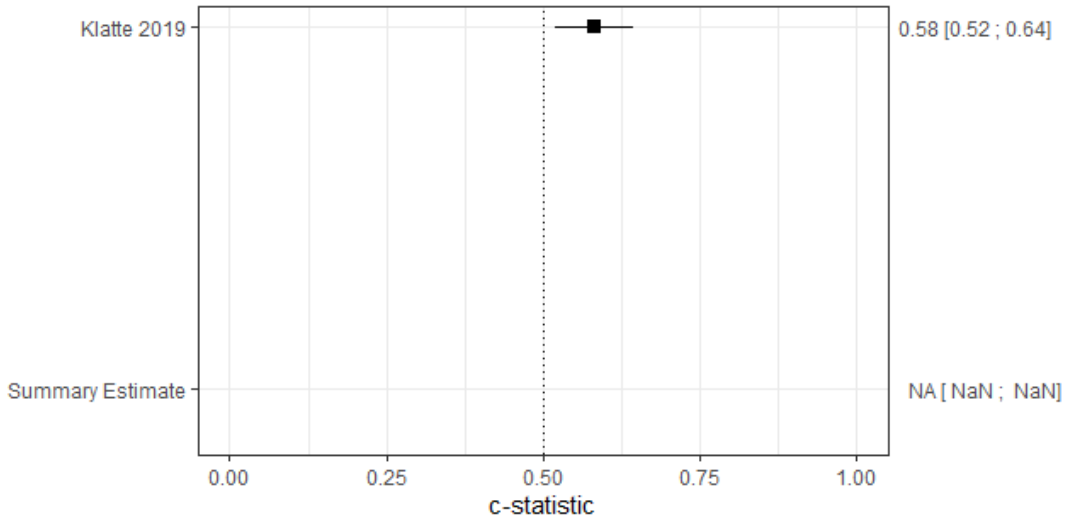
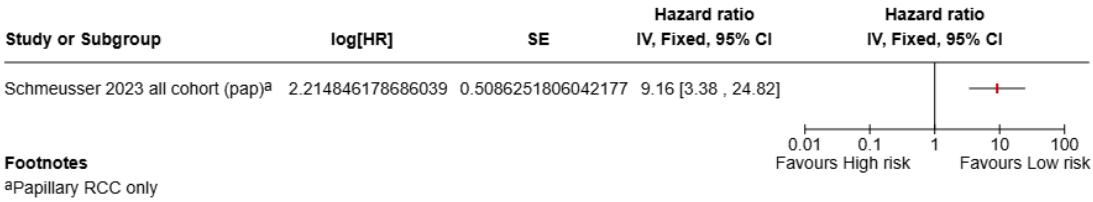


Figure 48: Leibovich 2018: Cancer-specific survival - Hazard ratio for high risk vs low risk, papillary RCC



Footnotes
[a]Papillary RCC only

Figure 49: Leibovich 2018: Cancer-specific survival - Hazard ratio for high risk vs low risk, papillary subtype [Black ethnicity only]

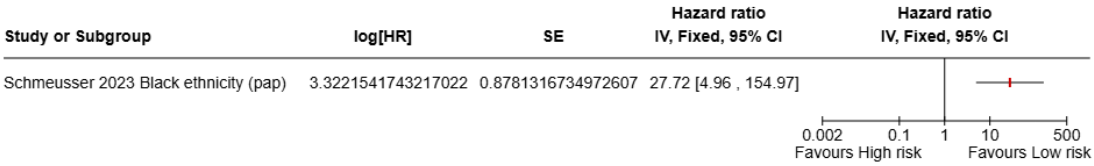
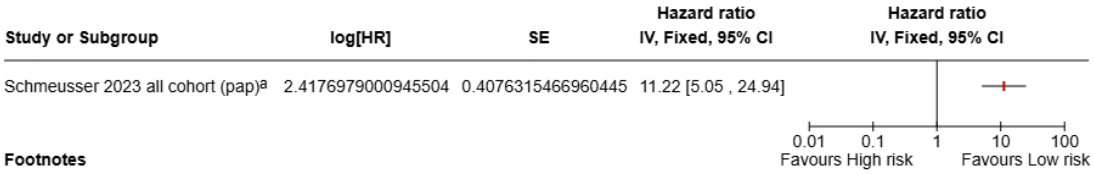


Figure 50: Leibovich 2018: Progression-free survival - Hazard ratio for high risk vs low risk, papillary RCC



Footnotes
[a]Papillary RCC only

Figure 51: Leibovich 2018: Progression-free survival - Hazard ratio for high risk vs low risk, papillary subtype [Black ethnicity only]

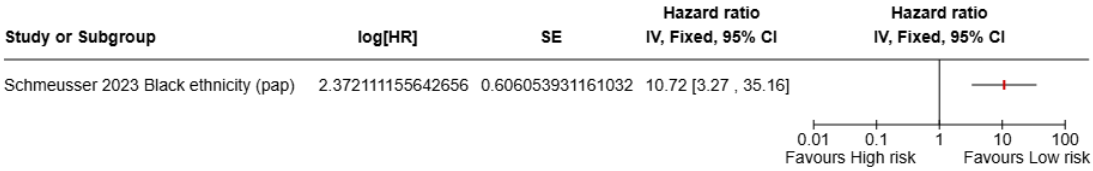
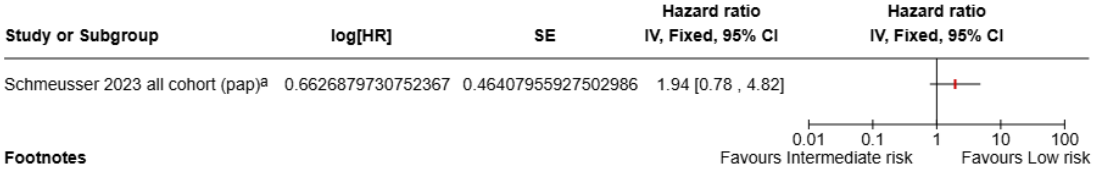


Figure 52: Leibovich 2018: Cancer-specific survival - Hazard ratio for intermediate risk vs low risk, papillary RCC



Footnotes
[a]Papillary RCC only

Figure 53: Leibovich 2018: Cancer-specific survival - Hazard ratio for intermediate risk vs low risk, papillary subtype [Black ethnicity only]

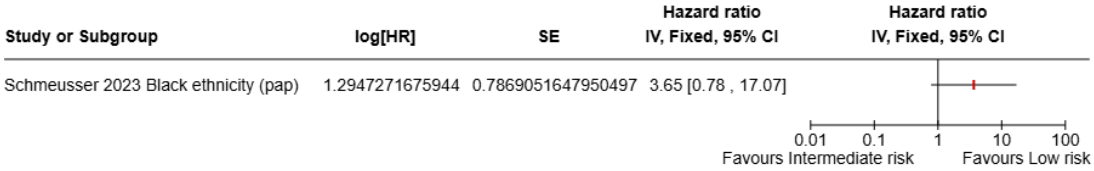


Figure 54: Leibovich 2018: Progression-free survival - Hazard ratio for intermediate risk vs low risk, papillary RCC

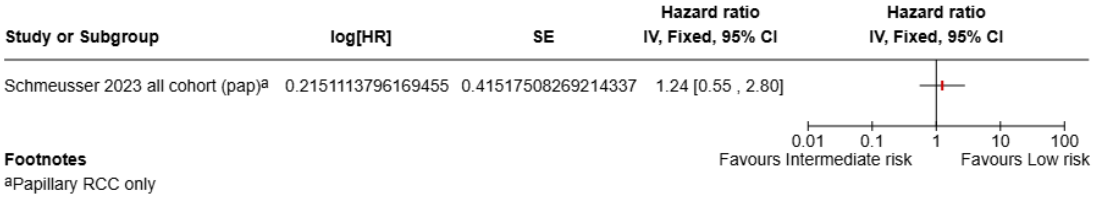
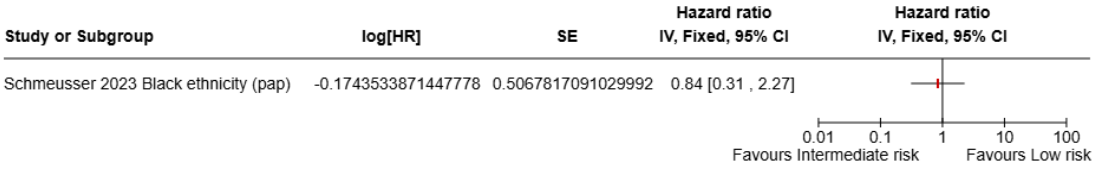


Figure 55: Leibovich 2018: Progression-free survival - Hazard ratio for intermediate risk vs low risk, papillary subtype [Black ethnicity only]



Sorbellini

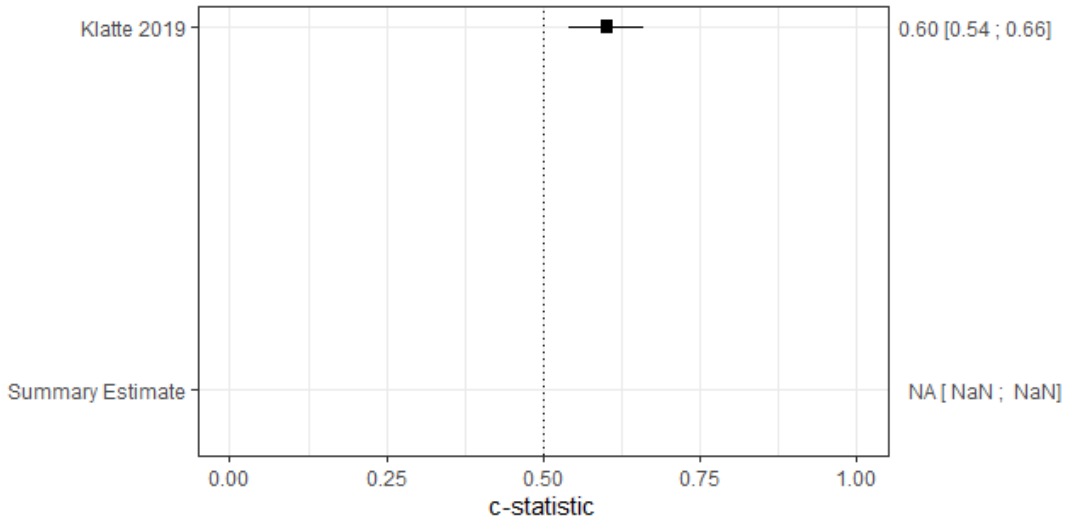
No evidence identified for this model.

SSIGN

No evidence identified for this model.

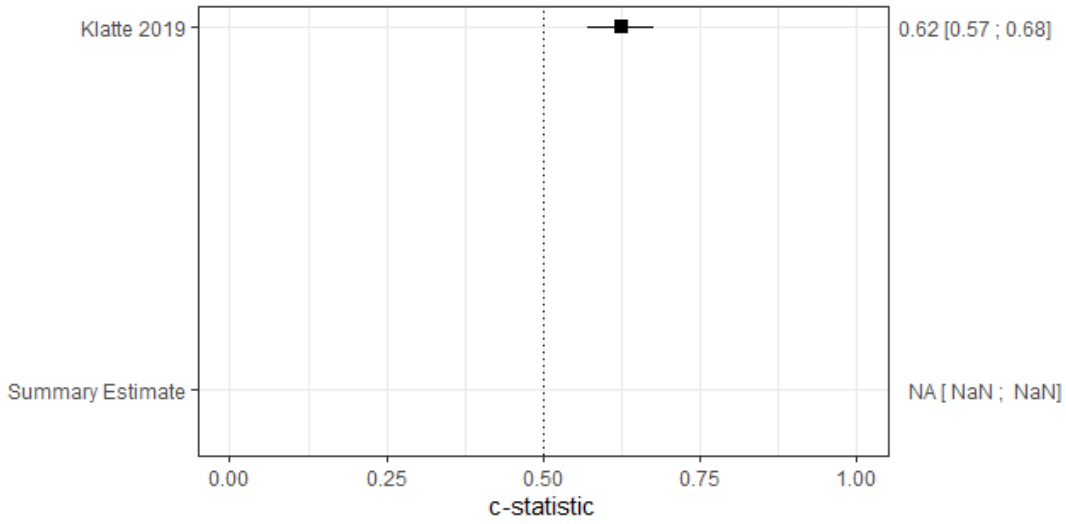
TNM 2016

Figure 56: TNM: recurrence-free survival/disease-free survival - c-statistic, papillary subtype



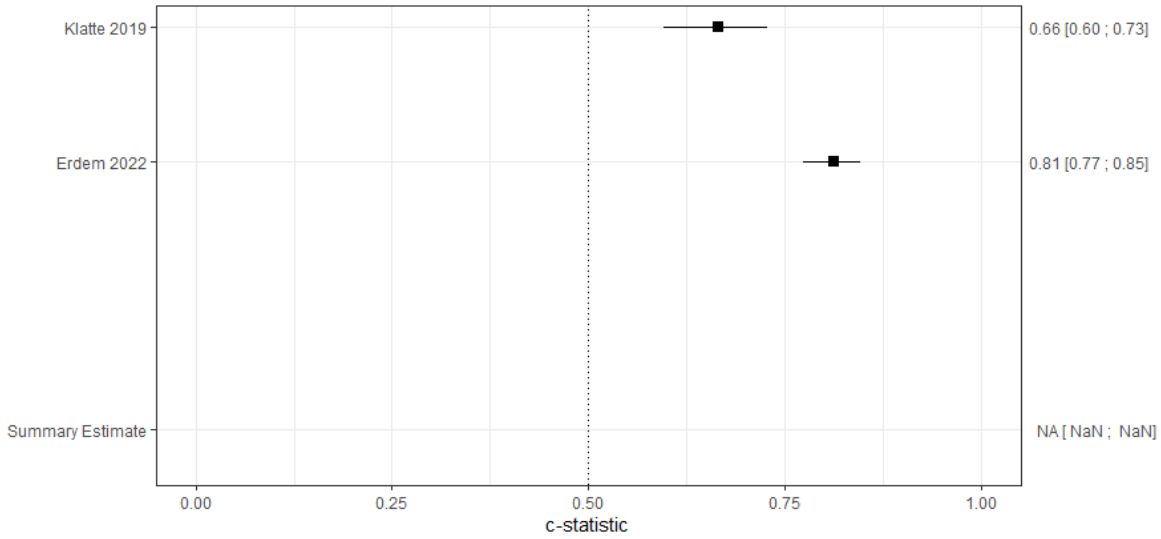
UISS

Figure 57: UISS: recurrence-free survival/disease-free survival - c-statistic, papillary subtype



VENUSS

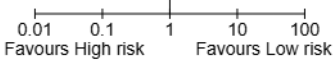
Figure 58: VENUSS: recurrence free survival/disease free survival - c-statistic, papillary subtype



Evidence could not be pooled as I^2 was above 80%

Figure 59: VENUSS: Cancer-specific survival - Hazard ratio for high risk vs low risk, papillary subtype

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI	Hazard ratio IV, Fixed, 95% CI
Piccinelli 2023a (VENUSS)[a]	2.5726122302071057	0.142393367692263	13.10 [9.91 , 17.32]	



Footnotes

[a]Papillary RCC only

Figure 60: VENUSS: Disease-free survival - Hazard ratio for high risk vs low risk, papillary subtype

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI	Hazard ratio IV, Fixed, 95% CI
Erdem 2022	2.884800712846709	0.1944270554001752	17.90 [12.23 , 26.20]	

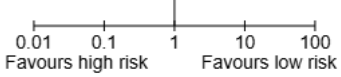
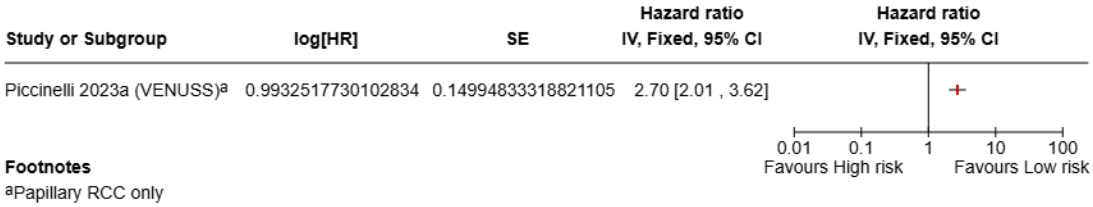


Figure 61: VENUSS: Cancer-specific survival - Hazard ratio for intermediate risk vs low risk, papillary subtype



Footnotes

[a]Papillary RCC only

Figure 62: VENUSS: Disease-free survival - Hazard ratio for intermediate risk vs low risk, papillary subtype

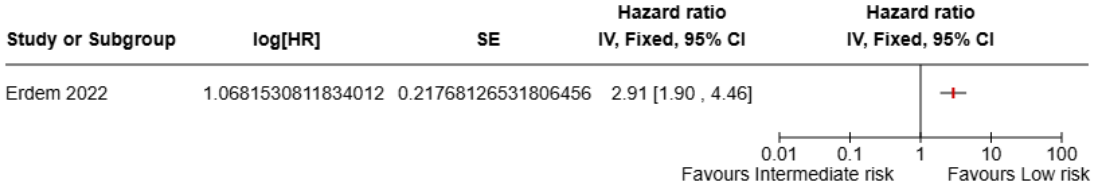
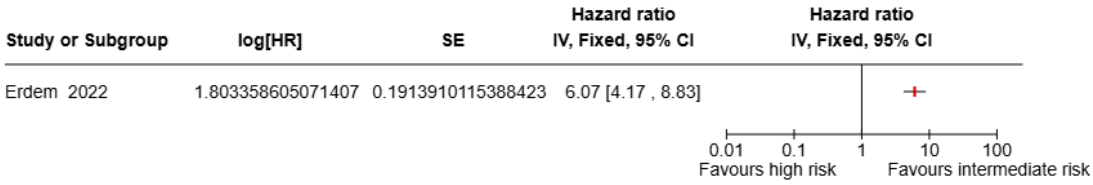


Figure 63: VENUSS: Disease-free survival - Hazard ratio for high risk vs intermediate risk, papillary subtype



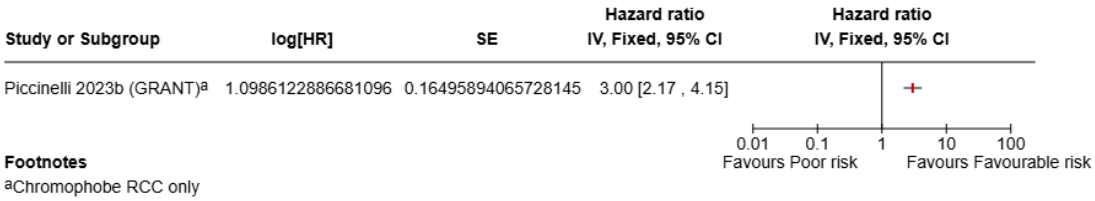
Zisman

No evidence identified for this model.

Chromophobe subtype

GRANT

Figure 64: GRANT: Cancer-specific survival - Hazard ratio for poor risk vs favourable risk, chromophobe RCC



Karakiewicz

No evidence identified for this model.

Kattan

No evidence identified for this model.

Leibovich 2003

Figure 65: Leibovich 2003: recurrence-free survival/disease-free survival - c-statistic, chromophobe

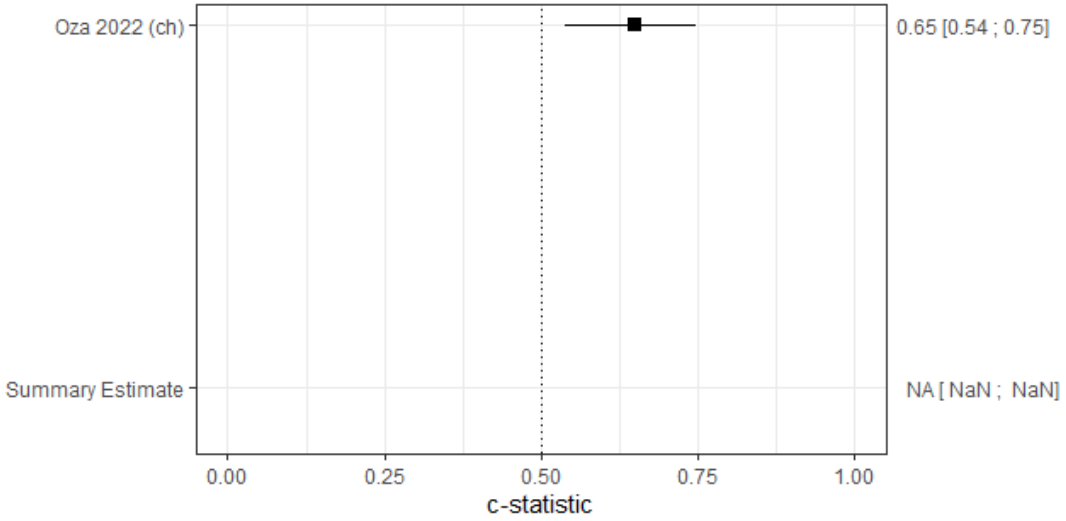
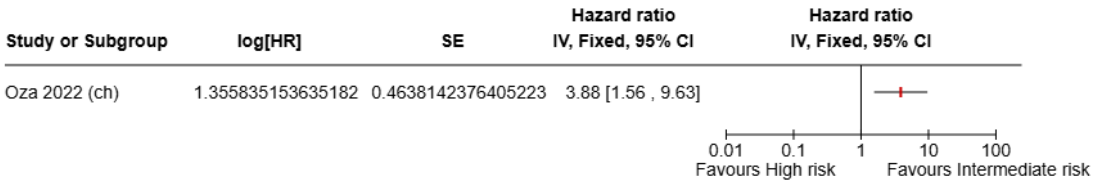


Figure 66: Leibovich 2003: Disease-free survival - Hazard ratio for high risk vs intermediate risk, chromophobe RCC



Leibovich 2018

Figure 67: Leibovich 2018: Cancer-specific survival - Hazard ratio for high risk vs low risk, chromophobe RCC

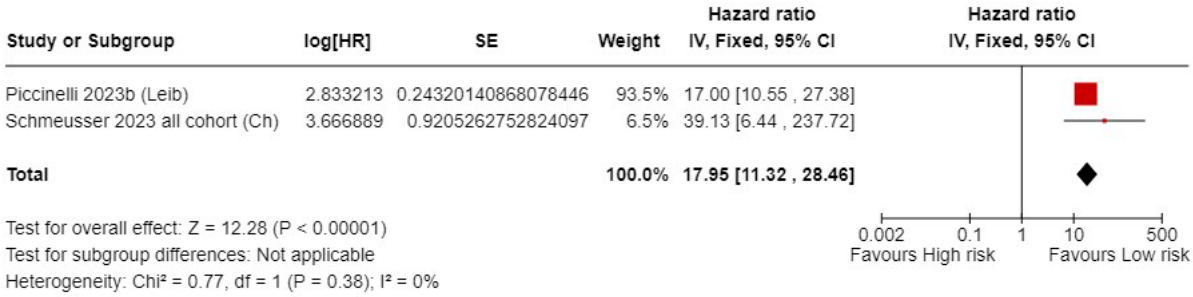


Figure 68: Leibovich 2018: Progression-free survival - Hazard ratio for high risk vs low risk, chromophobe RCC

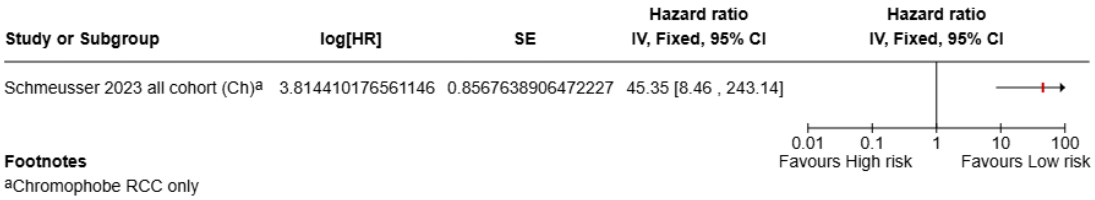


Figure 69: Leibovich 2018: Cancer-specific survival - Hazard ratio for intermediate risk vs low risk, chromophobe RCC

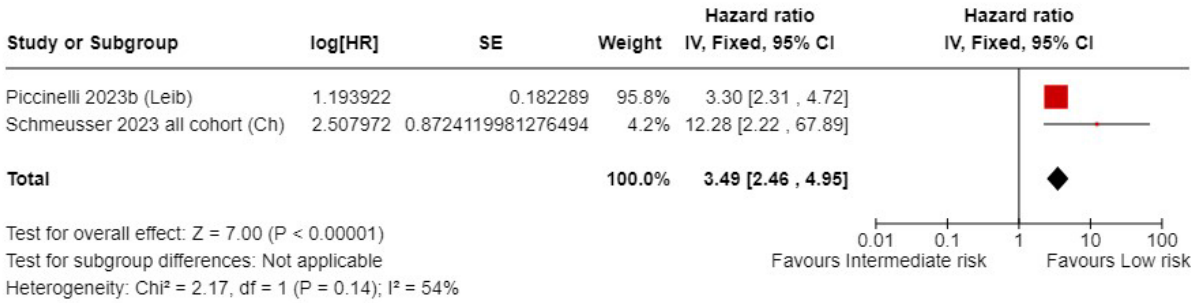
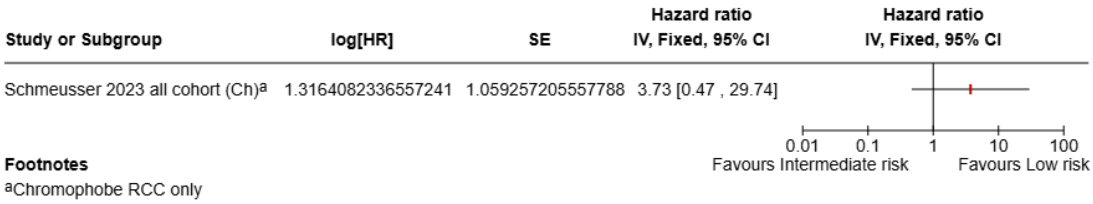


Figure 70: Leibovich 2018: Progression-free survival - Hazard ratio for intermediate risk vs low risk, chromophobe RCC



Sorbellini

No evidence identified for this model.

SSIGN

No evidence identified for this model.

TNM 2016

No evidence identified for this model.

UISS

No evidence identified for this model.

VENUSS

No evidence identified for this model.

Zisman

No evidence identified for this model.

All subtypes

GRANT

Figure 71: GRANT: overall-survival - c-statistic, all types

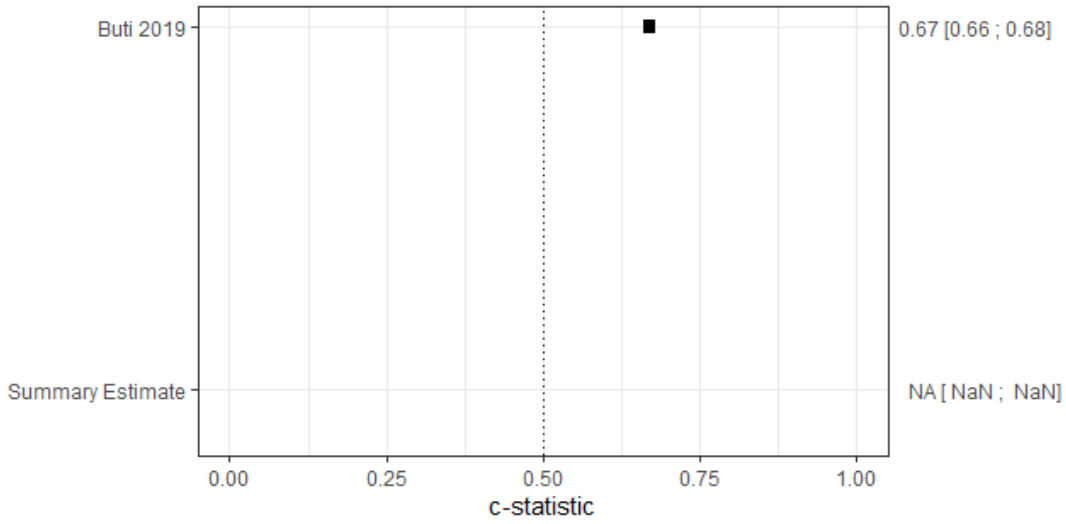
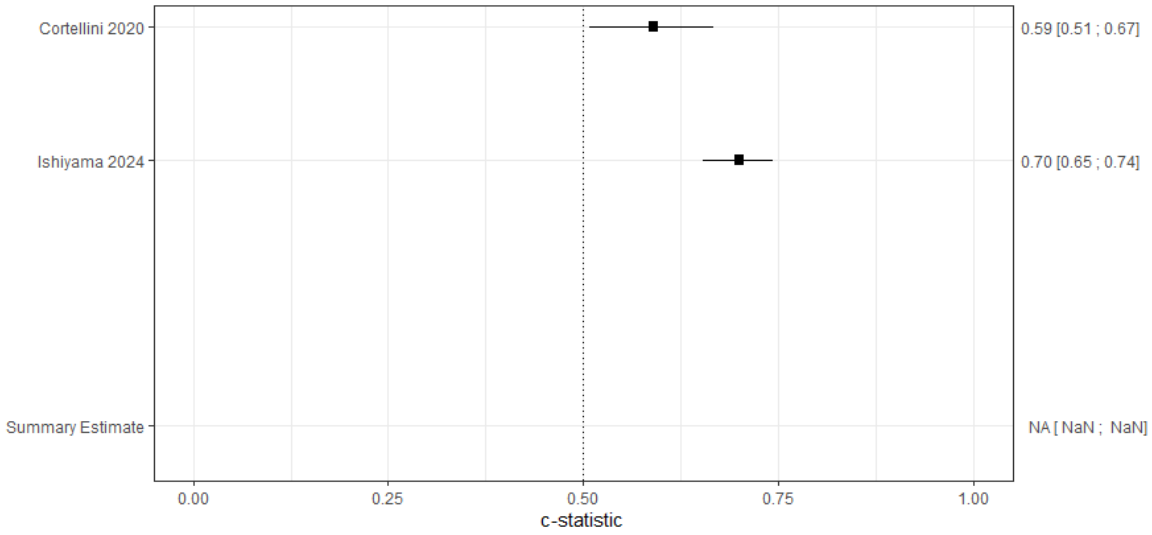


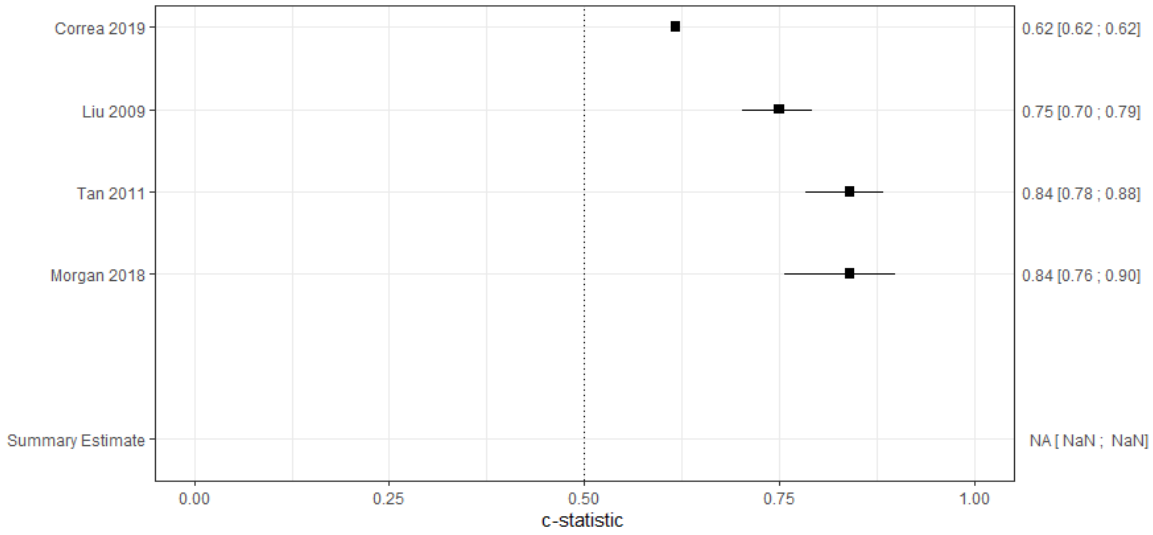
Figure 72: GRANT: recurrence-free survival/disease-free survival - c-statistic, all types



Evidence could not be pooled as I^2 was above 80%.

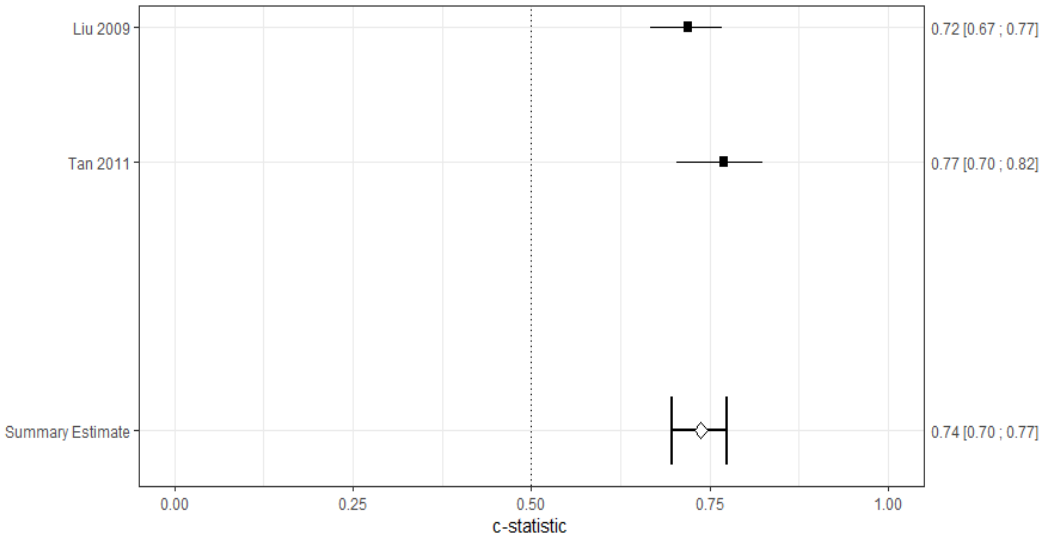
Karakiewicz

Figure 73: Karakiewicz: cancer-specific survival - c-statistic, all types



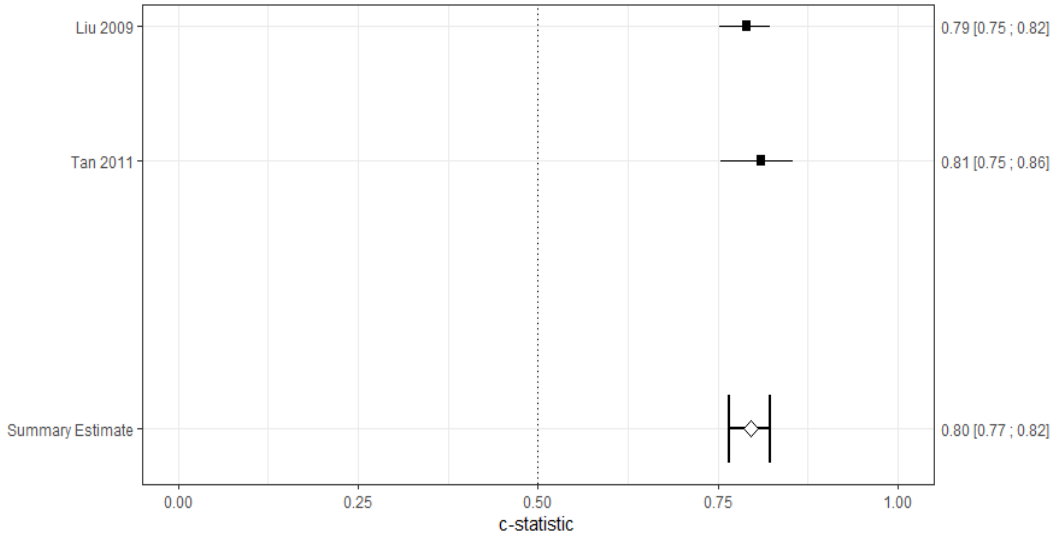
Evidence could not be pooled as I^2 was above 80%.

Figure 74: Karakiewicz: overall survival - c-statistic, all subtypes, FE



I^2 = 36.48%

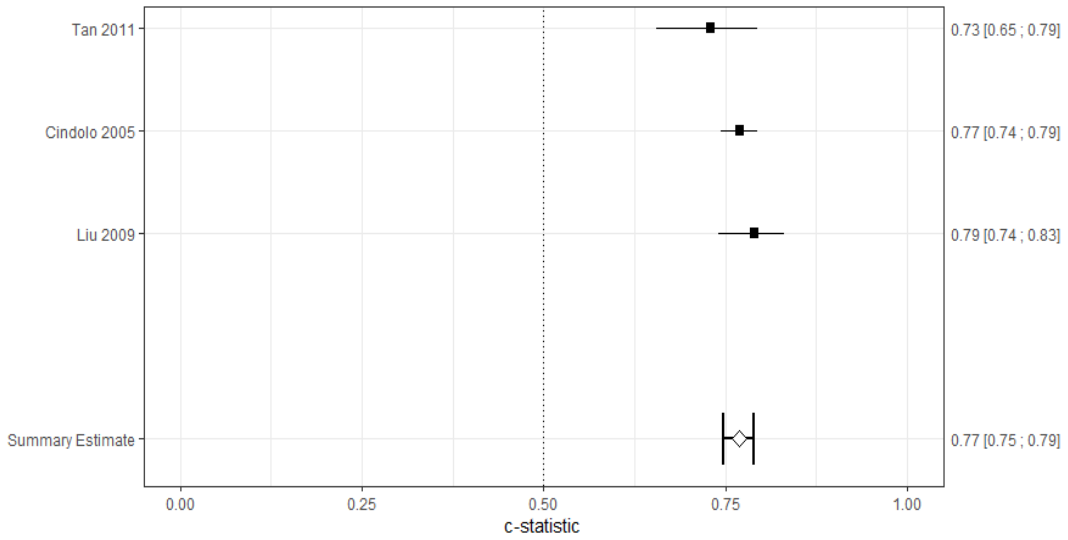
Figure 75: Karakiewicz: recurrence-free survival/disease-free survival - c-statistic, all subtypes, FE



I^2 = 0.00%

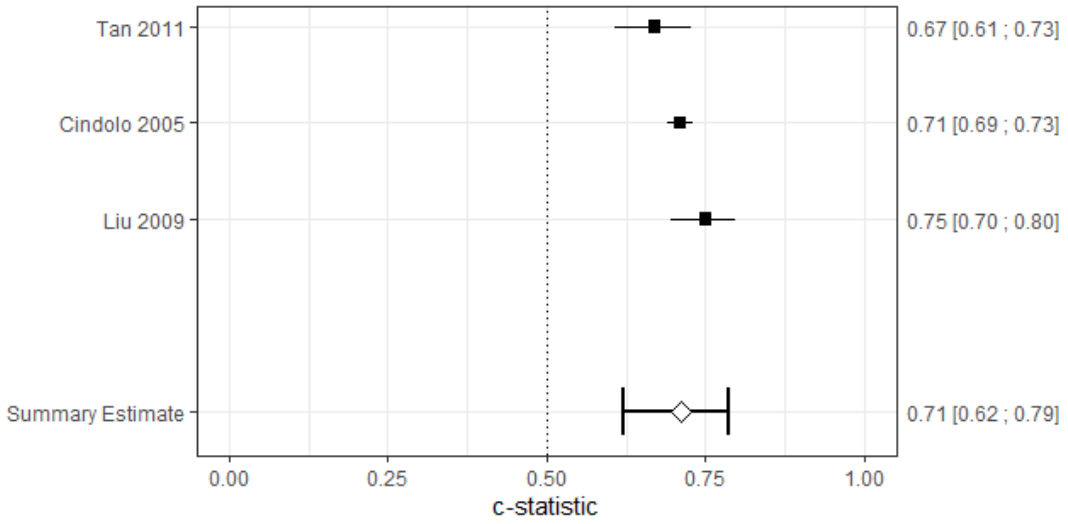
Kattan

Figure 76: Kattan: cancer-specific survival - c-statistic, all subtypes, FE



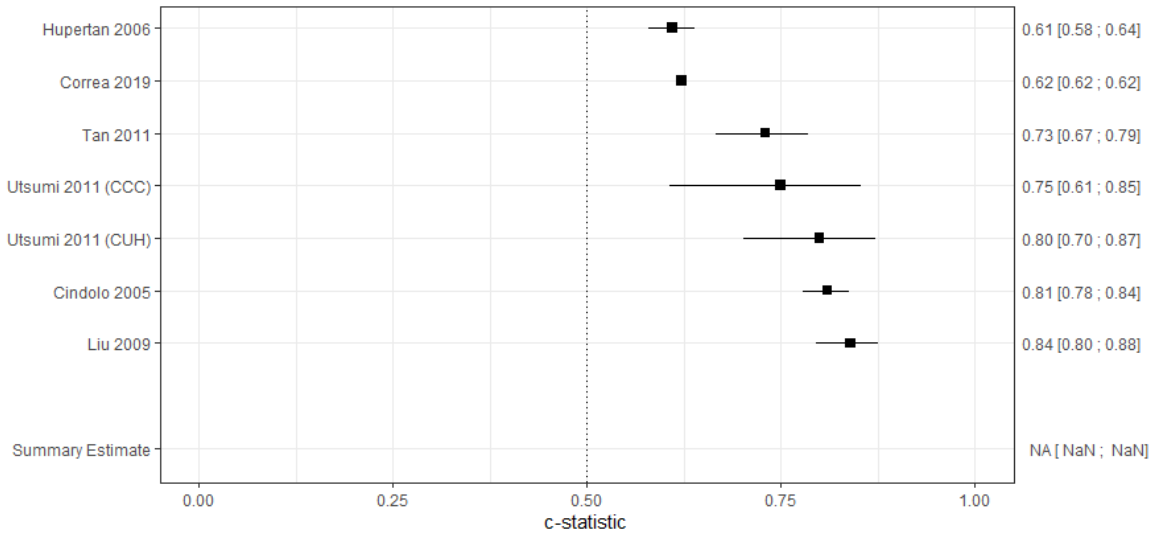
I^2 = 0.41%

Figure 77: Kattan: overall survival - c-statistic, all subtypes, RE



I^2 = 51.66%

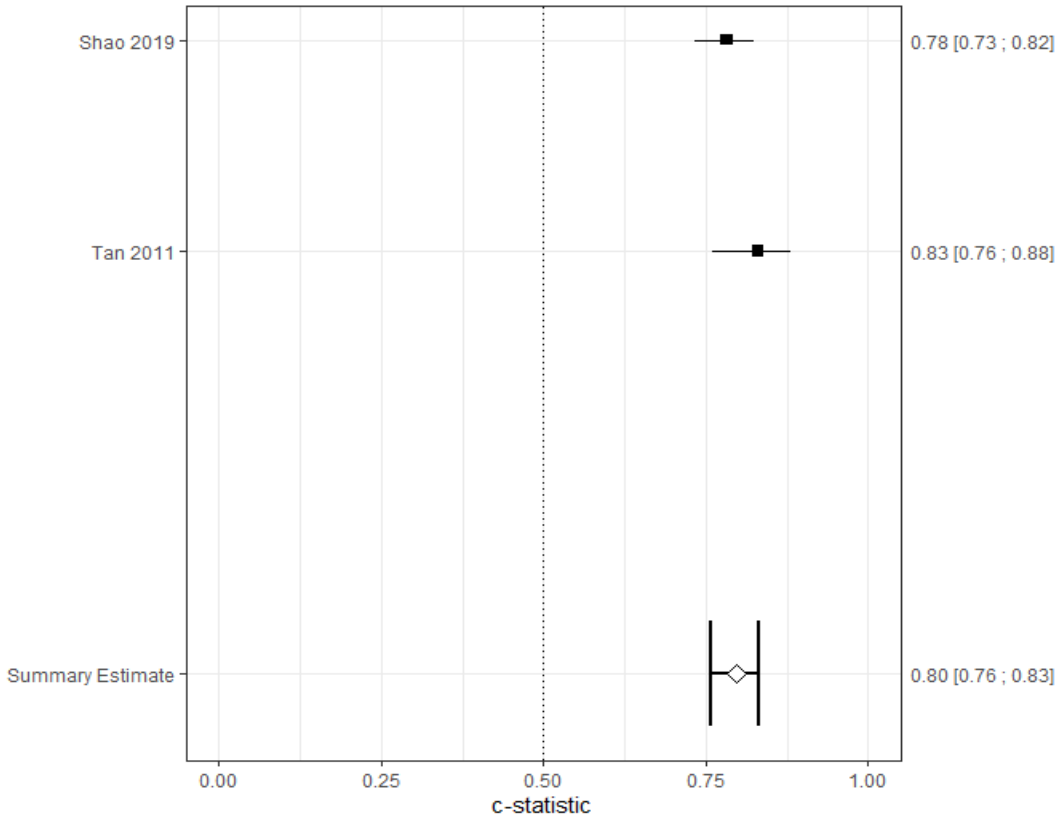
Figure 78: Kattan: recurrence-free survival/disease-free survival- c-statistic, all subtypes



Evidence could not be pooled as I^2 was above 80%.

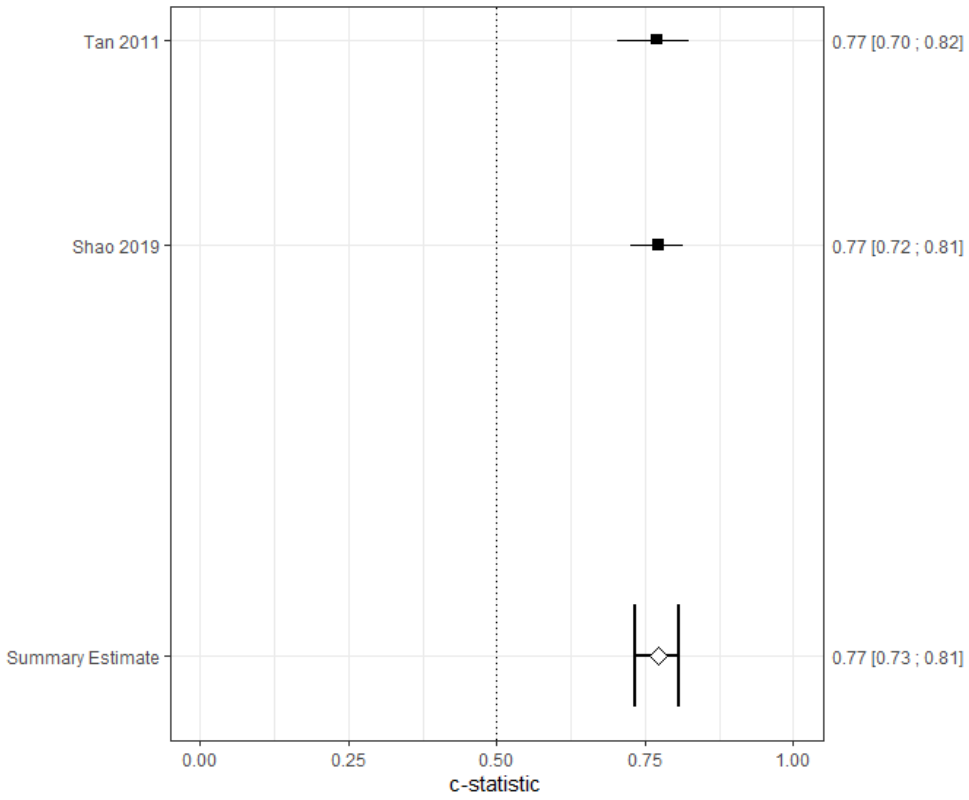
Leibovich 2003

Figure 79: Leibovich 2003: cancer-specific survival - c-statistic, all subtypes



I^2 = 35.42%

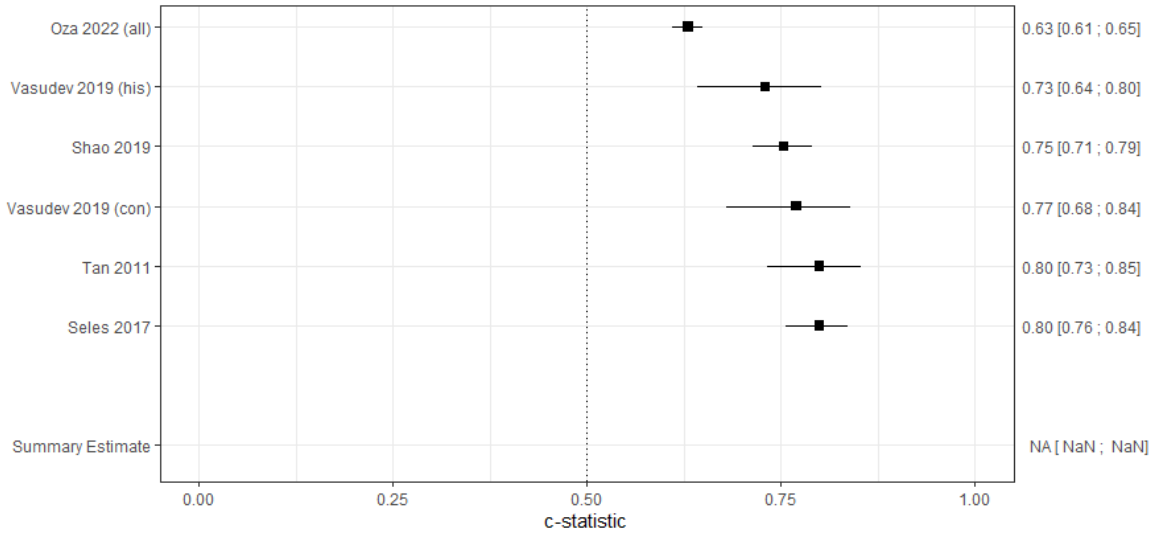
Figure 80: Leibovich 2003: overall survival - c-statistic, all subtypes



I^2 = 0.00%

Leibovich 2003: recurrence-free survival/disease-free survival - c-statistic, all subtypes

Figure 81: Leibovich 2003: recurrence-free survival/disease-free survival - c-statistic, all subtypes



Evidence could not be pooled as I^2 was above 80%.

Figure 82: Leibovich 2003: Disease-free survival - Hazard ratio for high risk vs low risk, all subtypes

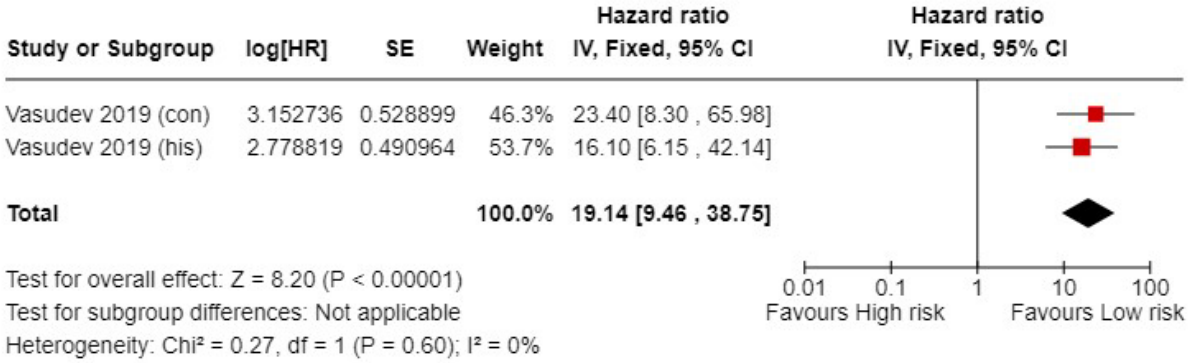


Figure 83: Leibovich 2003: Disease-free survival - Hazard ratio for intermediate risk vs low risk, all subtypes

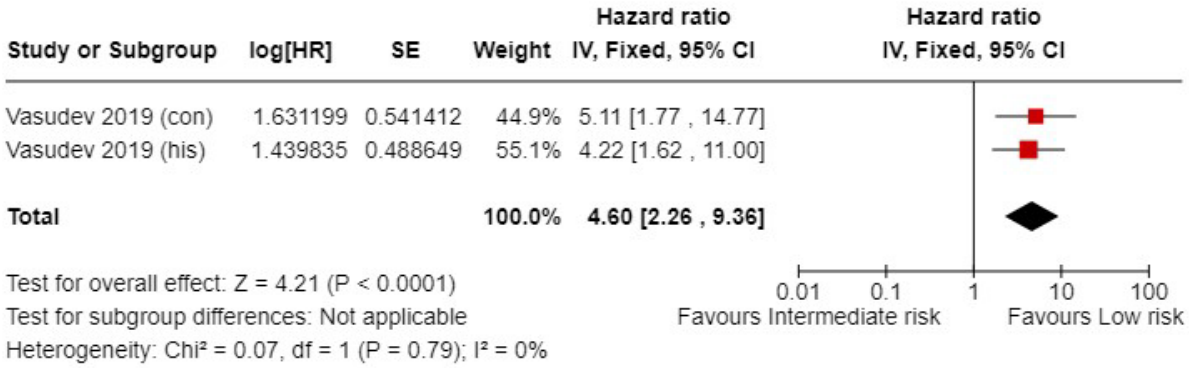
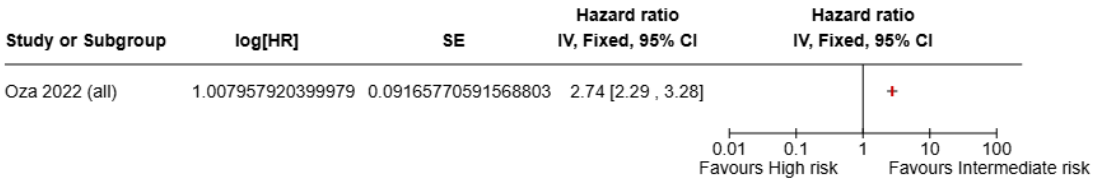


Figure 84: Leibovich 2003: Disease-free survival - Hazard ratio for high risk vs intermediate risk, all subtypes

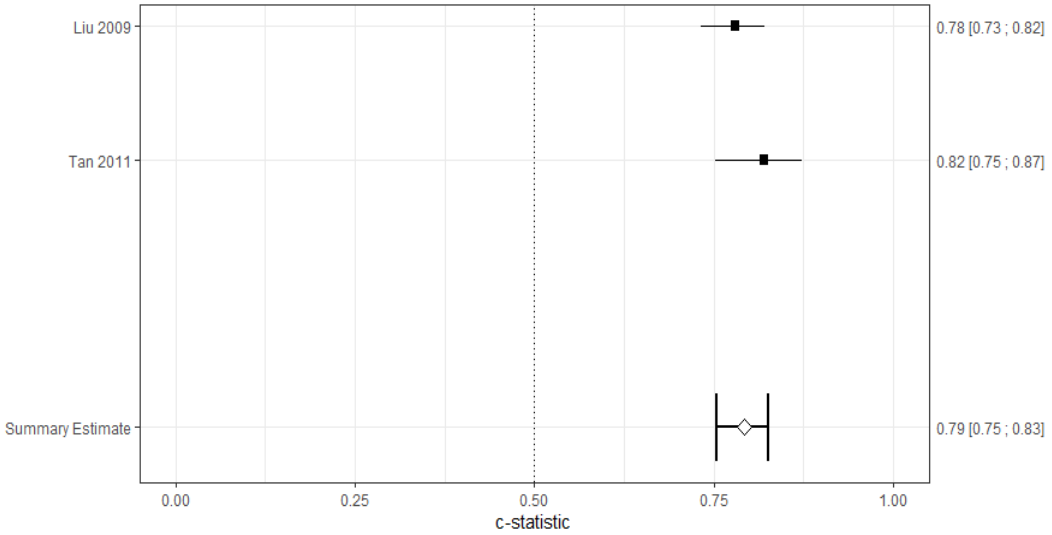


Leibovich 2018

No evidence identified for this model.

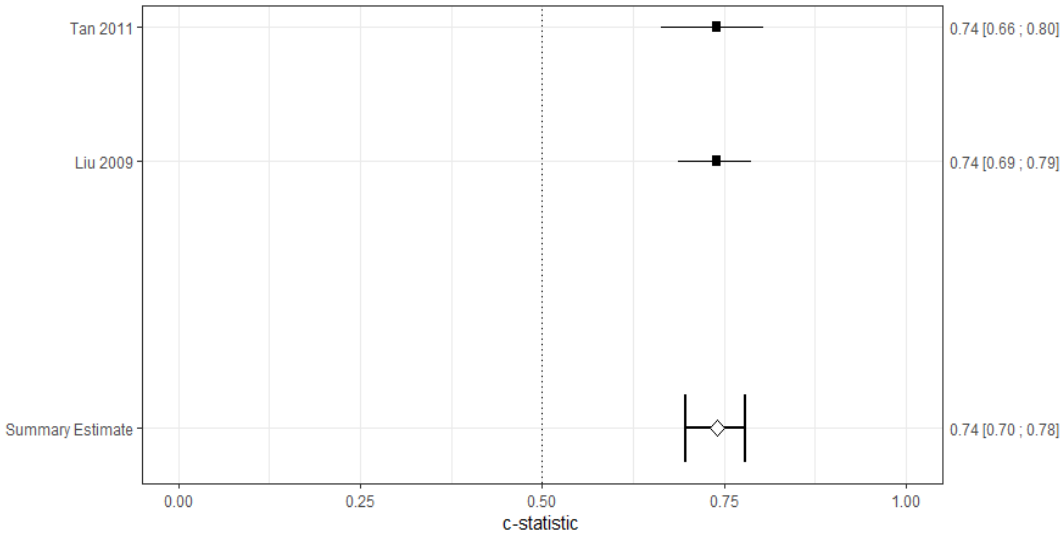
Sorbellini

Figure 85: Sorbellini: cancer-specific survival - c-statistic, all subtypes, FE



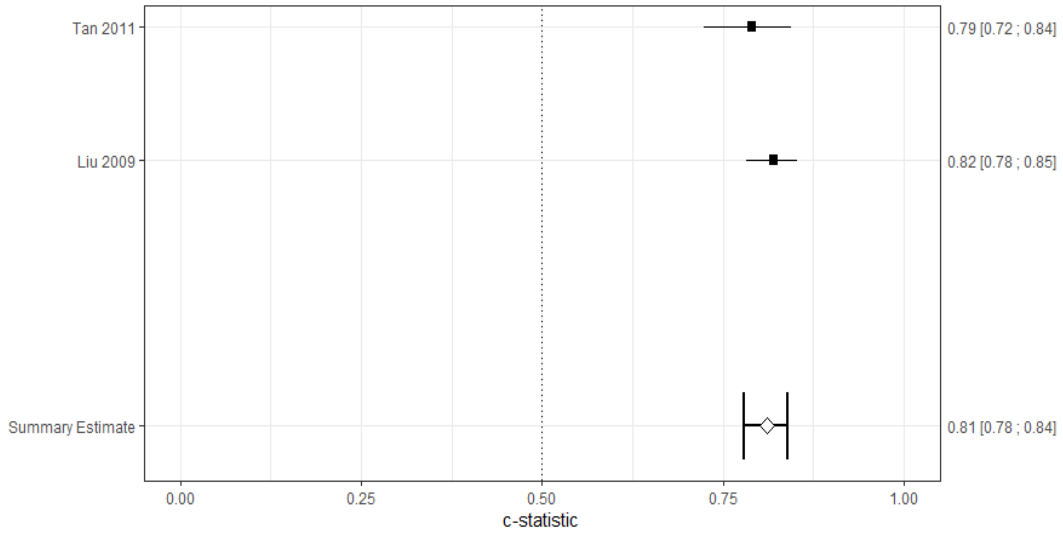
I^2 = 8.49%

Figure 86: Sorbellini: overall survival, all subtypes - c-statistic, FE



I^2 = 0.00%

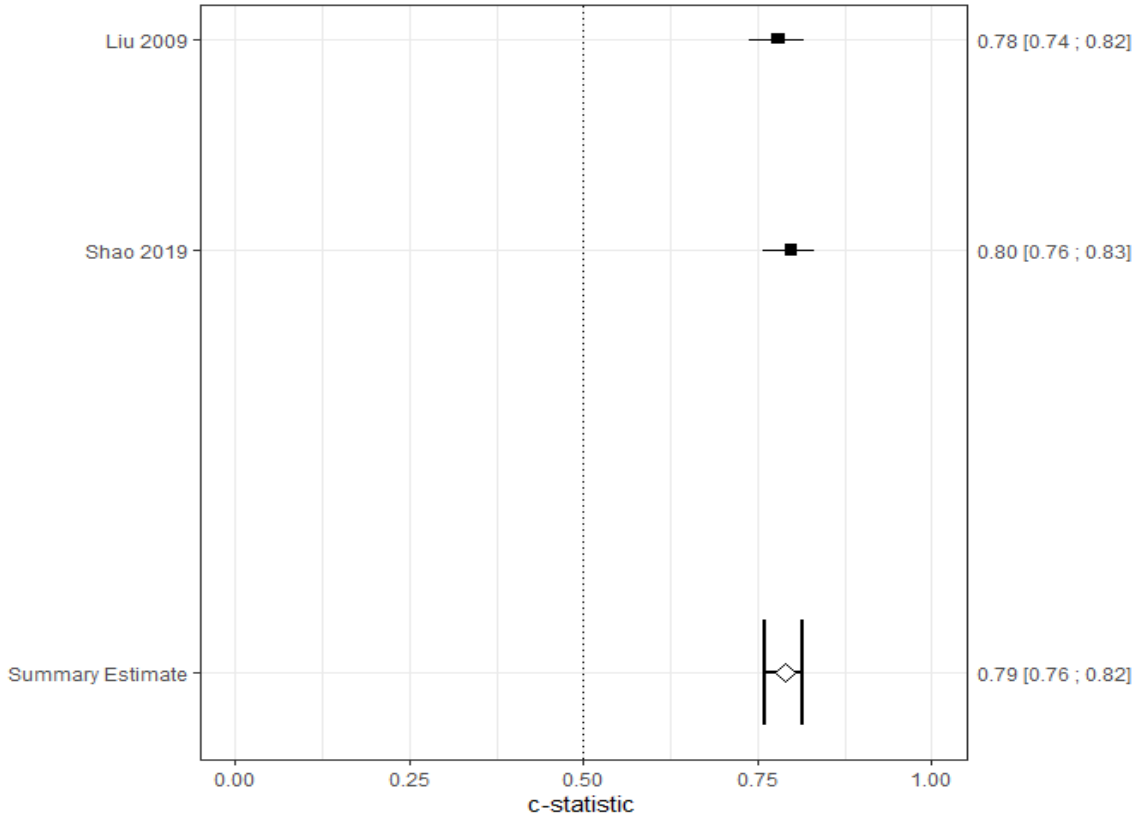
Figure 87: Sorbellini: recurrence-free survival/disease-free survival - c-statistic, all subtypes, FE



I^2 = 0.00%

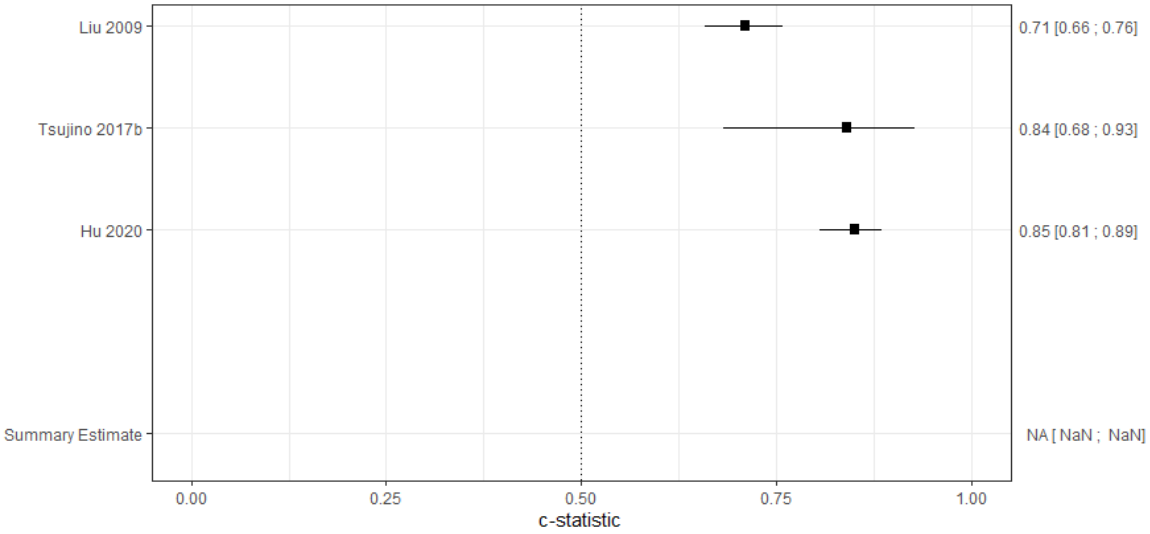
SSIGN

Figure 88: SSIGN: recurrence-free survival/disease-free survival - c-statistic, all subtypes



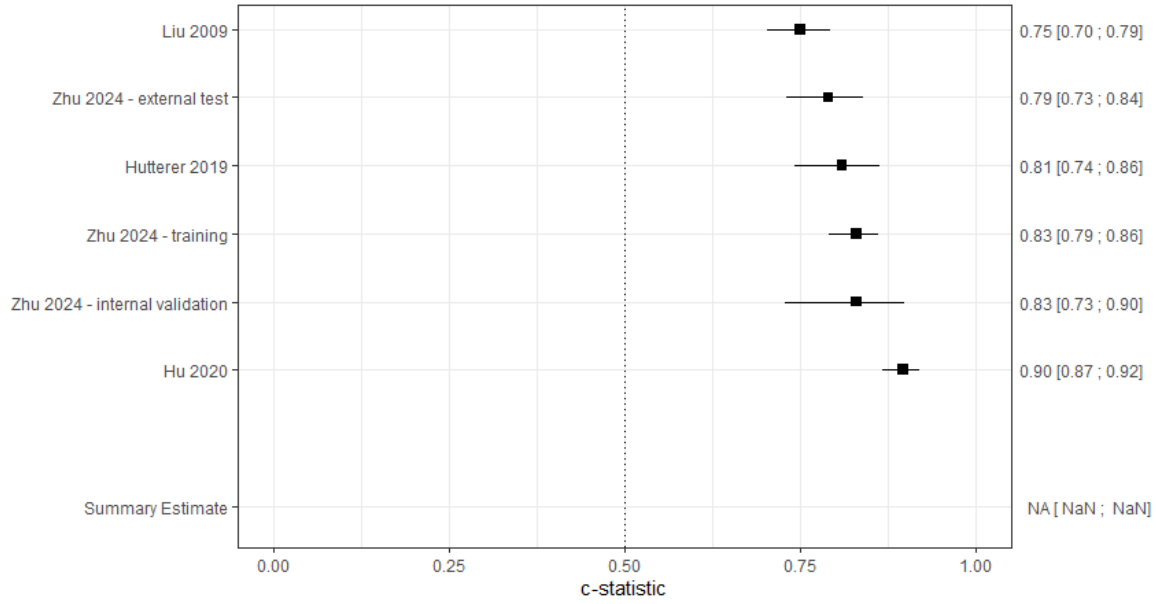
I^2 =0.00%

Figure 89: SSIGN: overall survival, all subtypes - c-statistic



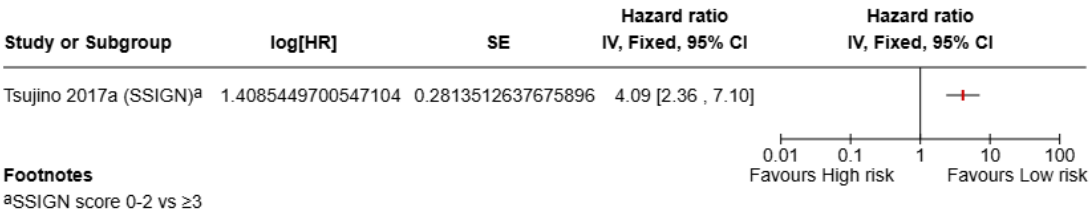
Evidence could not be pooled as I^2 was above 80%.

Figure 90: SSIGN: cancer-specific survival - c-statistic, all subtypes



Evidence could not be pooled as I^2 was above 80%.

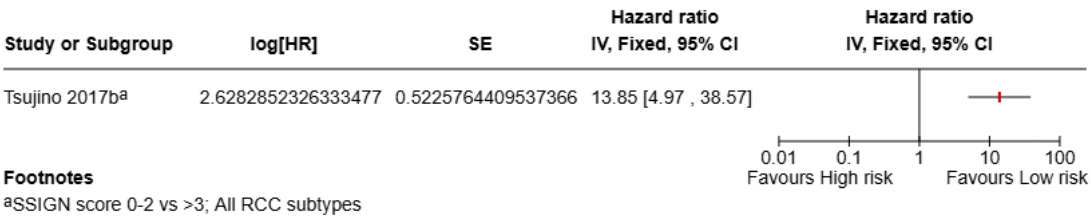
Figure 91: SSIGN: Disease-free survival - Hazard ratio for high risk vs low risk, all subtypes



Footnotes

[a]SSIGN score 0-2 vs ≥3

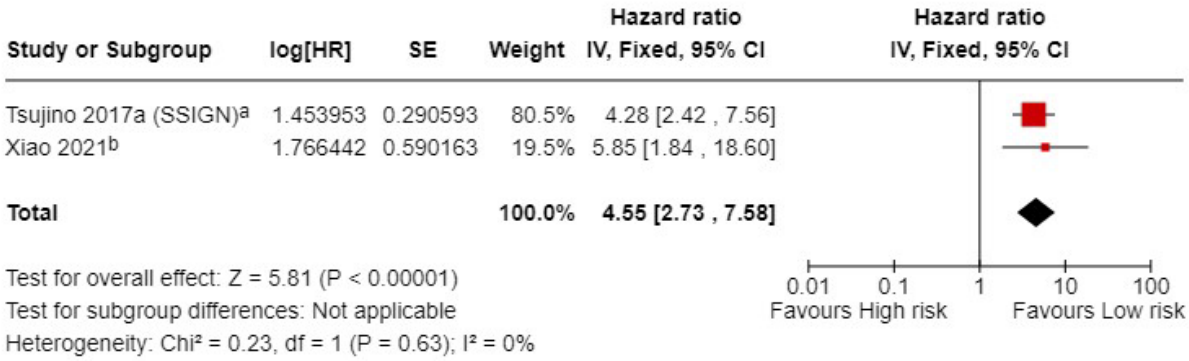
Figure 92: SSIGN: Cancer-specific survival - Hazard ratio for high risk vs low risk, all subtypes



Footnotes

[a]SSIGN score 0-2 vs >3; All RCC subtypes

Figure 93: SSIGN: Overall survival - Hazard ratio for high risk vs low risk, all subtypes

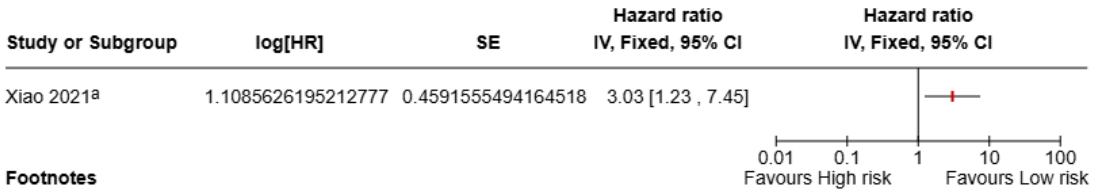


Test for overall effect: Z = 5.81 (P < 0.00001)
Test for subgroup differences: Not applicable
Heterogeneity: Chi² = 0.23, df = 1 (P = 0.63); I² = 0%

Footnotes

[a]SSIGN score 0-2 vs ≥3
[b]SSIGN low risk 2-4; intermediate risk 5-7; high risk 8-11

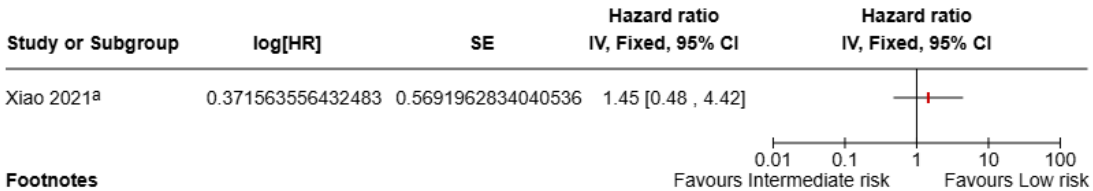
Figure 94: SSIGN: Progression-free survival - Hazard ratio for high risk vs low risk, all subtypes



Footnotes

[a]SSIGN low risk 2-4; intermediate risk 5-7; high risk 8-11

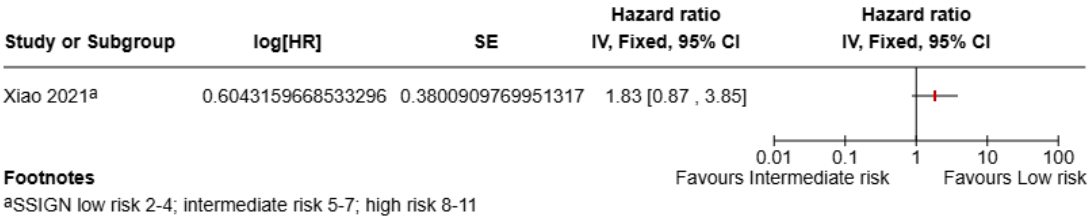
Figure 95: SSIGN: Overall survival - Hazard ratio for intermediate risk vs low risk, all subtypes



Footnotes

[a]SSIGN low risk 2-4; intermediate risk 5-7; high risk 8-11

Figure 96: SSIGN: Progression-free survival - Hazard ratio for intermediate risk vs low risk, all subtypes



Footnotes

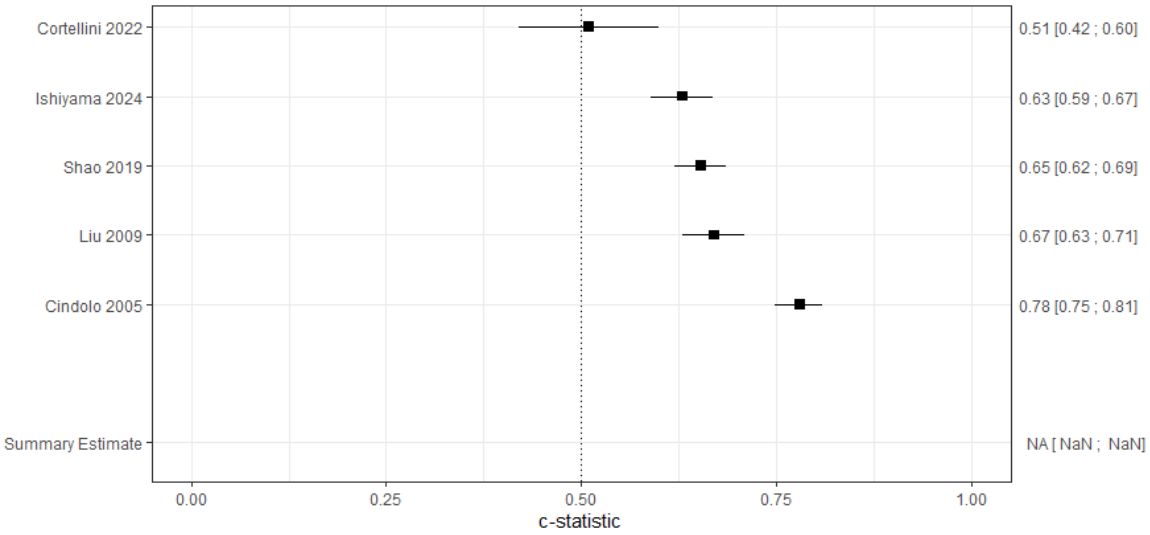
[a]SSIGN low risk 2-4; intermediate risk 5-7; high risk 8-11

TNM 2016

No evidence identified for this model.

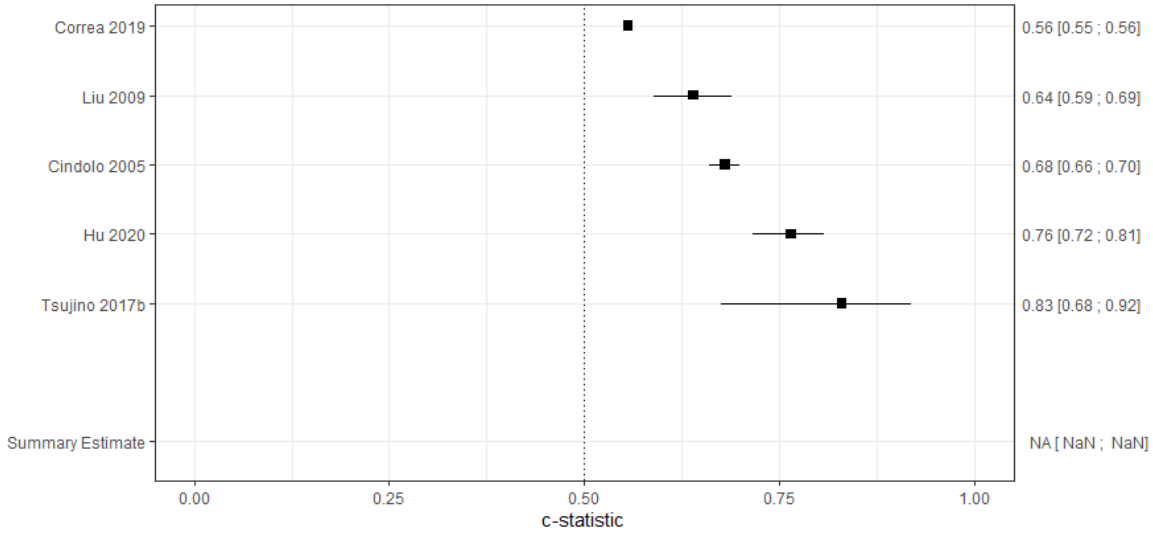
UISS

Figure 97: UISS: recurrence-free/disease-free survival - c-statistic, all subtypes



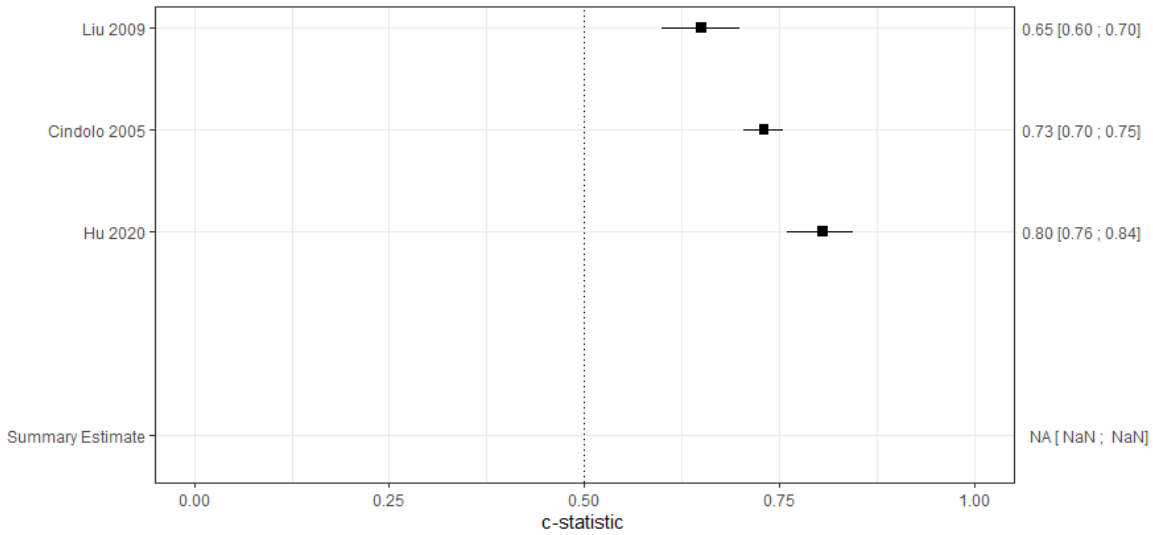
Evidence could not be pooled as I^2 was above 80%.

Figure 98: UISS: overall survival - c-statistic, all subtypes



Evidence could not be pooled as I^2 was above 80%.

Figure 99: UISS: cancer-specific survival - c-statistic, all subtypes



Evidence could not be pooled as I^2 was above 80%.

Figure 100: UISS: Cancer-specific survival - Hazard ratio for high risk vs low risk, all subtypes

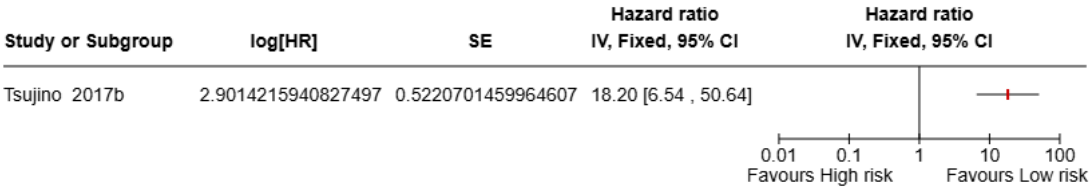


Figure 101: UISS: Disease-free survival - Hazard ratio for high risk vs low risk, all subtypes

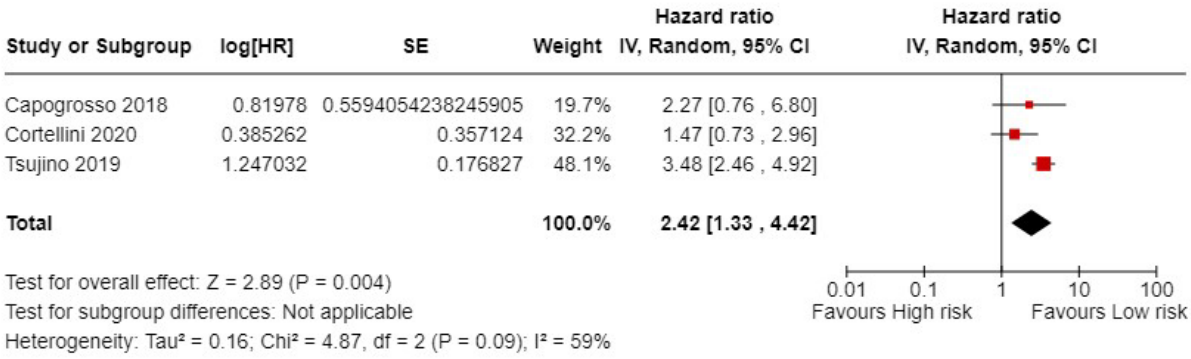


Figure 102: UISS: Overall survival - Hazard ratio for high risk vs low risk, all subtypes

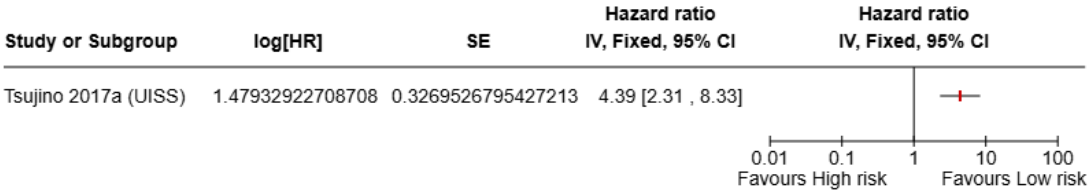


Figure 103: UISS: Disease-free survival - Hazard ratio for intermediate risk vs low risk, all subtypes

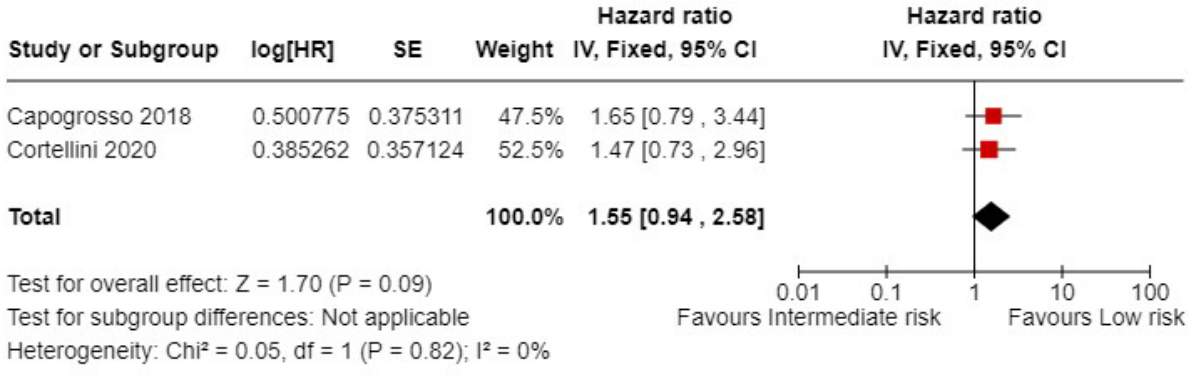


Figure 104: UISS: Overall survival - Hazard ratio for intermediate risk vs low risk, all subtypes

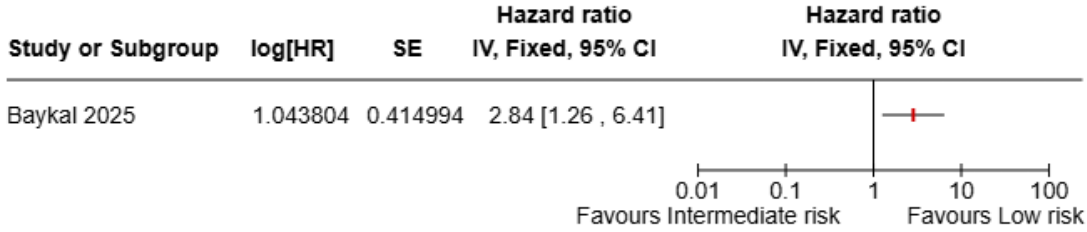


Figure 105: UISS: Disease-free survival - Hazard ratio for high risk vs intermediate risk, all subtypes

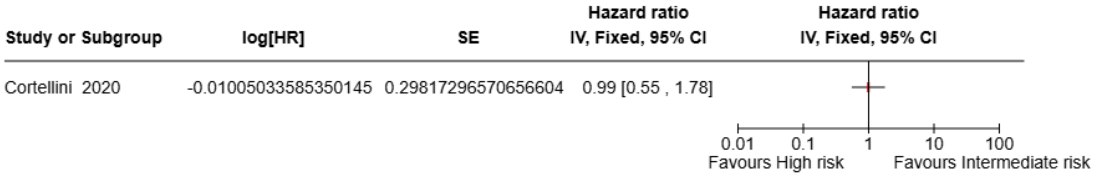
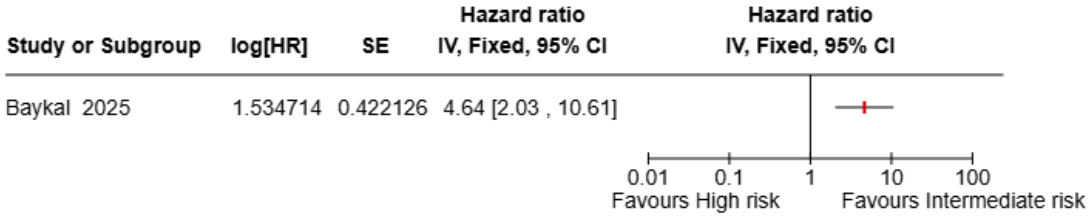
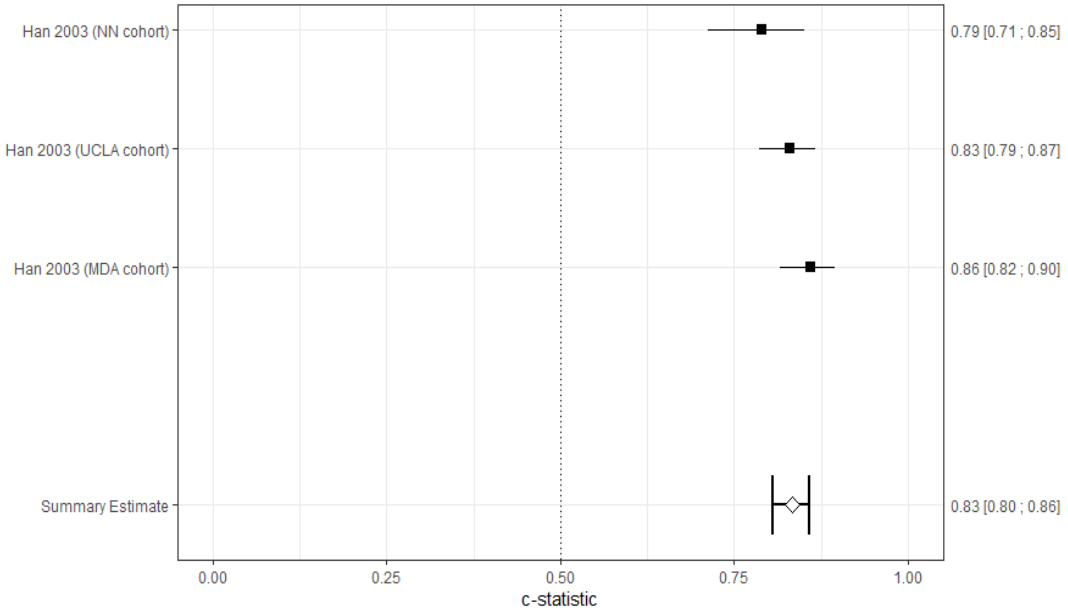


Figure 106: UISS: Overall survival - Hazard ratio for high risk vs intermediate risk, all subtypes



Zisman

Figure 107: Zisman: cancer-specific survival - c-statistic, all subtypes



I^2 = 35.88%

Appendix F – GRADE tables

Clear cell subtype

GRANT

No evidence identified for this model.

Karakiewicz

No evidence identified for this model.

Kattan

Table 41: Clinical evidence profile (C-statistics): Kattan model, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Kattan model for prediction of recurrence-free survival/disease-free survival for clear cell RCC, median 81 months follow-up								
1 (Suzuki 2011)	Retrospective cohort	211	0.73 (0.72, 0.73)	Very serious[a]	Not serious	Serious[b]	Not serious	Very low

a. Downgraded twice because study is at high risk of bias
b. Downgraded once as single study

Leibovich 2003

Table 42: Clinical evidence profile (C-statistics): Leibovich 2003 model, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model for prediction of progression-free survival for clear cell RCC, median 38 months follow-up								
1 (Huang 2017)	Retrospective cohort	268	0.76 (0.68, 0.83)	Very serious[a]	Not serious	Serious[b]	Very serious[c]	Very low
Leibovich 2003 model for prediction of cancer-specific survival for clear cell RCC, median 50 months follow-up								
2 (Hutterer 2014, Tan 2010)	Retrospective cohort	1033	0.79 (0.11, 0.99)	Very serious[a]	Not serious	Very serious[d]	Very serious[c]	Very low
Leibovich 2003 model for prediction of overall survival for clear cell RCC, median 67 months follow-up								
5 (An 2015, Chen 2017, Tan 2010, Wang 2016b, Zhang 2017)	Retrospective cohort	1575	0.74 (0.64, 0.81)	Very serious[a]	Not serious	Very serious[d]	Very serious[c]	Very low
Leibovich 2003 model for prediction of recurrence-free survival/disease-free survival for clear cell RCC, median 67 months follow-up								
1 (An 2015)	Retrospective cohort	191	0.67 (0.57, 0.76)	Serious[e]	Not serious	Serious[b]	Serious[f]	Very low
1 (Beisland 2015)	Retrospective cohort	386	0.86 (0.79, 0.94)					
1 (Correa 2019)	Retrospective cohort	1647	0.625 (0.623, 0.626)					
1 (Fu 2016)	Retrospective cohort	472	0.836 (0.79, 0.882)					

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
1 (Jensen 2009)	Retrospective cohort	121	0.74 (0.65, 0.83)					
1 (Oza 2022)	Retrospective cohort	1445	0.64 (0.59, 0.69)					
1 (Pichler 2011)	Retrospective cohort	1754	0.78 (0.75, 0.8)					
1 (Rini 2015)	Retrospective cohort	626	0.74 (0.69, 0.79)					
1 (Tan 2010)	Retrospective cohort	355	0.7 (0.63, 0.77)					
1 (Wang 2016b)	Retrospective cohort	268	0.74 (0.67, 0.81)					
1 (Xia 2016)	Retrospective cohort	290	0.72 (0.66, 0.77)					
1 (Xv 2024) (testing cohort)	Retrospective cohort	364	0.63 (0.573, 0.687)					
1 (Xv 2024) (internal cohort)	Retrospective cohort	156	0.609 (0.535, 0.683)					
1 (Xv 2024) (external cohort)	Retrospective cohort	187	0.663 (0.539, 0.786)					
1 (Zhang 2017)	Retrospective cohort	585	0.8 (0.76, 0.85)					

a. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias
b. Downgraded once as I^2 40-60%, or the point estimates span 2 categories of c-statistic classification accuracy, or data came from a single study
c. Downgraded twice as 95% confidence interval crossed 3 or more categories of c-statistic classification accuracy
d. Downgraded twice as I^2 >60%, or the point estimates span 3 categories of c-statistic classification accuracy
e. Downgraded once as >50% of the population weight across the studies came from studies at some concerns or high risk of bias
f. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Table 43: Clinical evidence profile (Hazard ratios): Leibovich 2003 model high risk vs low risk, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model – high risk vs low risk - for prediction of disease-free survival for clear cell RCC, median 53.8 months follow-up								
4 (Beisland 2015, Flippot 2017, Rini 2015, Tan 2010a)	Retrospective cohort	1270	8.92 (4.45, 17.90)	Serious[a]	Not serious	Serious[b]	Not serious	Low
Leibovich 2003 model – high risk vs low risk - for prediction of recurrence for clear cell, median 124 months follow-up								
1 (Jensen 2009)	Retrospective cohort	69	RR 3.12 (1.51, 6.46)	Very serious[c]	Not serious	Serious[b]	Serious[d]	Very low
Leibovich 2003 model – high risk vs low risk - for prediction of cancer-specific survival for clear cell RCC, median 56 months follow-up								
1 (Tan 2010a)	Retrospective cohort	189	10.84 (4.00, 29.39)	Very serious[c]	Not serious	Serious[b]	Serious[d]	Very low
Leibovich 2003 model – high risk vs low risk - for prediction of overall survival for clear cell RCC, median 56 months follow-up								
1 (Tan 2010a)	Retrospective cohort	189	5.17 (2.59, 10.32)	Very serious[c]	Not serious	Serious[b]	Serious[d]	Very low

a. Downgraded once as >50% of the weight in a meta-analysis came from studies at some concerns or high risk of bias
b. Downgraded once as I^2 40-60%, or data on the outcome was only available from one study
c. Downgraded twice because the study was at high risk of bias
d. Downgraded once as sample size <500

Table 44: Clinical evidence profile (Hazard ratios): Leibovich 2003 model intermediate risk vs low risk, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model – intermediate risk vs low risk - for prediction of disease-free survival for clear cell RCC, median 53.9 months follow-up								
4 (Beisland 2015, Flippot 2017, Rini 2015, Tan 2010a)	Retrospective cohort	1414	2.82 (1.96, 4.06)	Serious[a]	Not serious	Not serious	Not serious	Moderate
Leibovich 2003 model – intermediate risk vs low risk - for prediction of recurrence for clear cell RCC, median 124 months follow-up								
1 (Jensen 2009)	Retrospective cohort	78	RR 2.00 (0.93, 4.28)	Very serious[b]	Not serious	Serious[c]	Very serious[d]	Very low
Leibovich 2003 model – intermediate risk vs low risk - for prediction of cancer-specific survival for clear cell RCC, median 56 months follow-up								
1 (Tan 2010a)	Retrospective cohort	303	3.41 (1.30, 8.96)	Very serious[b]	Not serious	Serious[c]	Serious[e]	Very low
Leibovich 2003 model – intermediate risk vs low risk - for prediction of overall survival for clear cell RCC, median 56 months follow-up								
1 (Tan 2010a)	Retrospective cohort	303	2.05 (1.09, 3.86)	Very serious[b]	Not serious	Serious[c]	Serious[e]	Very low

a. Downgraded once as >50% of the weight in a meta-analysis came from studies at some concerns or high risk of bias
b. Downgraded twice because the study is at high risk of bias
c. Downgraded once as single study
d. Downgraded twice as sample size <500 and 95% confidence intervals crossed the line of no effect
e. Downgraded once as sample size <500

Table 45: Clinical evidence profile (Hazard ratios): Leibovich 2003 model high risk vs intermediate risk, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model – high risk vs intermediate risk - for prediction of disease-free survival for clear cell RCC, median 63.7 months follow-up								
2 (Flippot 2017, Oza 2022)	Retrospective cohort	1612	3.23 (2.13, 4.89)	Serious[a]	Not serious	Not serious	Not serious	Moderate
Leibovich 2003 model – high risk vs intermediate risk - for prediction of recurrence for clear cell RCC, median 124 months follow-up								
1 (Jensen 2009)	Retrospective cohort	95	RR 1.56 (1.10, 2.21)	Very serious[b]	Not serious	Serious[c]	Serious[d]	Very low

a. Downgraded once as >50% of the weight in a meta-analysis came from studies at some concerns or high risk of bias
b. Downgraded twice because the study is at high risk of bias
c. Downgraded once as single study
d. Downgraded once as sample size <500

Leibovich 2018

Table 46: Clinical evidence profile (C-statistics): Leibovich 2018, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2018 model for prediction of progression-free survival for clear cell RCC, median 76 months follow-up								
1 (Lee 2019)	Retrospective cohort	829	0.81 (0.77, 0.85)	Serious[a]	Not serious	Serious[b]	Serious[c]	Very low
Leibovich 2018 model for prediction of cancer-specific survival for clear cell RCC, median 76 months follow-up								
1 (Lee 2019)	Retrospective cohort	829	0.83 (0.79, 0.87)	Serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded once because the study has some concerns for risk of bias
b. Downgraded once as single study
c. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Sorbellini

Table 47: Clinical evidence profile (C-statistics): Sorbellini model, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Sorbellini model for prediction of recurrence-free survival/disease free survival for clear cell RCC, median 36 months follow-up								
2 (Lee 2018, Sorbellini 2005)	Retrospective	1842	0.81 (0.76, 0.86)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low

a. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias
b. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

SSIGN

Table 48: Clinical evidence profile (C-statistics): SSIGN model, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
SSIGN prognostic model for the prediction of progression-free survival in people with clear cell RCC, median 60 months follow-up								
8 (Wang 2021 (training), Wang 2021 (validation), Wang 2021b (training), Wang 2021b (validation), Zhu 2021 (cohort 1),	Retrospective cohort	1250	0.68 (0.64, 0.71)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Zhu 2021 (cohort 2), Zhu 2021 (training), Zhu 2021 (validation))								
SSIGN prognostic model for prediction of recurrence-free/disease-free survival in people with clear cell RCC, median 61.1 months follow-up								
14 (Haddad 2017 (training), Haddad 2017 (validation), Kang 2020 (training), Kang 2020 (validation), Liu 2016, Li 2024 (training), Li 2024 (validation), Lucca 2015, Nie 2023 (training), Nie 2023 (test), Wen 2023 (training), Wen 2023 (validation),	Retrospective cohort	4,148	0.73 (0.68, 0.76)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Xiong 2017, Zhang 2017)								
SSIGN prognostic model for prediction of overall survival in people with clear cell RCC, median 60 months follow-up								
12 (Chen 2017, Liu 2016, Na 2016, Wang 2021 (Training), Wang 2021 (Validation), Wang 2021b (Training), Wang 2021b (Validation), Zhang 2017, Zhu 2021 (cohort 1), Zhu 2021 (cohort 2), Zhu 2021 (training), Zhu 2021 (validation))	Retrospective cohort	2436	0.71 (0.68, 0.74)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low
SSIGN prognostic model for prediction of cancer-specific survival in people with clear cell RCC, median 111.6 months follow-up								
1 (Fu 2015)	Retrospective cohort	180	0.645 (0.513, 0.777)	Serious[d]	Not serious	Very serious[e]	Not serious	Very low
1 (Viers 2014)	Retrospective cohort	827	0.81 (0.78, 0.84)					
1 (Correa 2019)	Retrospective cohort	1647	0.69 (0.686, 0.689)					

a. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
b. Downgraded twice as I^2 > 60% c. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy d. Downgraded once as >50% of the studies by population weight came from studies at unclear or high risk of bias e. Downgraded twice as the point estimates span 3 or more categories of c-statistic classification accuracy								

Table 49: Clinical evidence profile (Hazard ratios): SSIGN model high risk vs low risk, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
SSIGN prognostic model – high risk vs low risk - for the prediction of disease-free survival in people with clear cell RCC, median 56.75 months follow-up								
1 (Haddad 2017)	Retrospective cohort	367	3.13 (1.69, 5.79)	Not serious	Not serious	Serious[a]	Not serious	Moderate
1 (Yang 2022)	Retrospective cohort	866	13.55 (8.41, 21.84)					
SSIGN prognostic model – high risk vs low risk - for the prediction of overall survival in people with clear cell RCC [Zhu 2021 removed], median follow-up not reported								
2 (Wang 2021b (training), Wang 2021b (validation))	Retrospective cohort	300	8.28 (4.33, 15.82)	Very serious[b]	Not serious	Not serious	Serious[c]	Very low
SSIGN prognostic model – high risk vs low risk - for the prediction of progression-free survival in people with clear cell RCC [Zhu 2021 removed], follow-up not reported								
2 (Wang 2021b (training),	Retrospective cohort	300	16.83 (8.94, 31.69)	Very serious[b]	Not serious	Not serious	Serious[c]	Very low

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Wang 2021b (validation))								

a. Downgraded once as pooled I^2 was above 80%, however, the point estimates did not span the line of no effect
b. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias
c. Downgraded once as sample size <500

Table 50: Clinical evidence profile (Hazard ratios): SSIGN model intermediate risk vs low risk, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
SSIGN prognostic model – intermediate risk vs low risk - for the prediction of recurrence-free survival in people with clear cell RCC, median 50 months follow-up								
1 (Yang 2022)	Retrospective cohort	231	4.71 (3.18, 6.97)	Not serious	Not serious	Serious[a]	Serious[b]	Low

a. Downgraded once as single study
b. Downgraded once as sample size <500

TNM 2016

Table 51: Clinical evidence profile (C-statistics): TNM 2016 model, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
TNM (not specified) prognostic model for prediction of progression-free survival in people with clear cell RCC, median 60 months follow-up								
4 (Wang 2021 (training),	Retrospective cohort	610	0.64 (0.63, 0.66)	Very serious[a]	Not serious	Not serious	Not serious	Low

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Wang 2021 (validation), Wang 2021b (training), Wang 2021b (validation))								
TNM (not specified) prognostic model for overall survival in people with clear cell RCC, median 60 months follow-up								
4 (Wang 2021 (training) Wang 2021 (validation) Wang 2021b (training) Wang 2021b (validation))	Retrospective cohort	610	0.68 (0.65, 0.71)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low

a. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias
b. Downgraded once as 95% confidence interval crossed one of the clinical decision thresholds

Table 52: Clinical evidence profile (Hazard ratios): TNM model stages 3 vs 1-2, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
TNM model – stages 3 vs 1-2 – for the prediction of disease-free survival in people with clear cell RCC, median 49.6 months follow-up								
1 (Li 2024)	Retrospective cohort	344	2.55 (1.34, 4.86)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
TNM model – stages 3 vs 1-2 – for the prediction of overall survival in people with clear cell RCC, follow-up not reported								
1 (He 2020)	Prospective cohort	Not reported	3.72 (2.41, 5.75)	Not serious	Not serious	Serious[b]	Serious[d]	Low

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty

a. Downgraded twice because the study is at high risk of bias
b. Downgraded once as single study
c. Downgraded once as sample size <500
d. Downgraded once as sample size not reported

UISS

Table 53: Clinical evidence profile (C-statistics): UISS model, clear cell RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
UISS prognostic model for prediction of disease-free survival in people with clear cell RCC, median 57.1 months follow-up								
1 (Tan 2010)	Retrospective cohort	355	0.66 (0.59, 0.73)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
1 (Klatte 2009)	Retrospective cohort	170	0.78 (0.776, 0.784)					
1 (Zhang 2017)	Retrospective cohort	585	0.75 (0.7, 0.8)					
1 (Xia 2016)	Retrospective cohort	290	0.71 (0.66, 0.76)					
1 (Wang 2016b)	Retrospective cohort	268	0.68 (0.6, 0.75)					
1 (Li 2024) (training)	Retrospective cohort	254	0.776 (0.714, 0.839)					
1 (Li 2024) (validation)	Retrospective cohort	110	0.686 (0.538, 0.834)					

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
1 (Nie 2023) (training)	Retrospective cohort	558	0.751 (0.665, 0.836)					
1 (Nie 2023) (test)	Retrospective cohort	241	0.739 (0.625, 0.852)					
1 (Xv 2024) (training)	Retrospective cohort	364	0.601 (0.544, 0.658)					
1 (Xv 2024) (internal)	Retrospective cohort	156	0.611 (0.531, 0.691)					
1 (Xv 2024) (external)	Retrospective cohort	187	0.62 (0.55, 0.69)					
UISS prognostic model for prediction of overall survival in people with clear cell RCC, median 67 months follow-up								
4 (Na 2016, Tan 2010, Wang 2016b, Zhang 2017)	Retrospective cohort	1,370	0.69 (0.60, 0.77)	Serious[d]	Not serious	Very serious[e]	Serious[f]	Very low
UISS prognostic model for prediction of cancer-specific survival in people with clear cell RCC, median 83 months follow-up								
2 (Fu 2015, Tan 2010)	Retrospective cohort	535	0.66 (0.59, 0.72)	Serious[d]	Not serious	Not serious	Serious[f]	Very low

a. Downgraded twice as >50% of the studies by population weight came from studies at high risk of bias
b. Downgraded once as the point estimates span 2 categories of c-statistic classification accuracy
c. Downgraded once as >50% of the studies by population weight have 95% CIs that cross one of the decision thresholds
d. Downgraded once as >50% of the weight in the meta-analysis came from studies at unclear or high risk of bias

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty

e. Downgraded twice as I^2>60%
f. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Table 54: Clinical evidence profile (Hazard ratios): UISS model high risk vs low risk, clear cell subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
UISS prognostic model – high risk vs low risk - for the prediction of cancer-specific survival in people with clear cell RCC, median 56 months follow-up								
1 (Tan 2010)	Retrospective cohort	154	6.54 (2.10, 20.35)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
UISS prognostic model – high risk vs low risk - for the prediction of disease-free survival in people with clear cell RCC, median 50 months follow-up								
3 (Kroeger 2022, Tan 2010b, Yang 2022)	Retrospective cohort	677	5.57 (3.69, 8.41)	Serious[d]	Not serious	Not serious	Not serious	Moderate
UISS prognostic model – high risk vs low risk - for the prediction of overall survival in people with clear cell RCC, median 56 months follow-up								
1 (Tan 2010)	Retrospective cohort	154	4.28 (1.92, 9.55)	Serious[e]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded twice because the study is at high risk of bias
b. Downgraded once as single study
c. Downgraded once as sample size<500
d. Downgraded once as >50% of the weight in the meta-analysis came from studies at some concerns or high risk of bias
e. Downgraded once because study has some concerns for risk of bias

Table 55: Clinical evidence profile (Hazard ratios): UISS model intermediate risk vs low risk, clear cell subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
UISS prognostic model – intermediate risk vs low risk - for the prediction of cancer-specific survival in people with clear cell RCC, median 56 months follow-up								
1 (Tan 2010)	Retrospective cohort	308	3.94 (1.39, 11.18)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
UISS prognostic model – intermediate risk vs low risk - for the prediction of disease-free survival in people with clear cell RCC, median 53 months follow-up								
2 (Tan 2010, Yang 2022)	Retrospective cohort	1,103	2.75 (1.93, 3.92)	Not serious	Not serious	Not serious	Not serious	High
UISS prognostic model – intermediate risk vs low risk - for the prediction of overall survival in people with clear cell RCC, median 56 months follow-up								
1 (Tan 2010)	Retrospective cohort	308	2.63 (1.28, 5.39)	Serious[d]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded twice because the study is at high risk of bias
b. Downgraded once as single study
c. Downgraded once as sample size<500
d. Downgraded once because study has some concerns for risk of bias

Table 56: Clinical evidence profile (Hazard ratios): UISS model high risk vs intermediate risk, clear cell subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
UISS prognostic model – high risk vs intermediate risk - for the prediction of disease-free survival in people with clear cell RCC, median 43.3 months follow-up								
1 (Kroeger 2022)	Retrospective cohort	135	1.96 (0.87, 4.40)	Very serious[a]	Not serious	Serious[b]	Very serious[c]	Very low

a. Downgraded twice because the study is at high risk of bias
b. Downgraded once as single study

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
c. Downgraded twice as sample size >500 and 95% confidence intervals cross the line of no effect								

VENUSS

No evidence identified for this model.

Zisman

No evidence identified for this model.

Papillary subtype

GRANT

Table 57: Clinical evidence profile (Hazard ratios): GRANT model poor risk vs favourable risk, papillary RCC subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
GRANT prognostic model – poor risk vs favourable risk – for the prediction of cancer-specific survival in people with papillary RCC, median 60 months follow-up								
1 (Piccinelli 2023a)	Retrospective cohort	4,184	3.60 (2.89, 4.48)	Not serious	Not serious	Serious[a]	Not serious	Moderate
a. Downgraded once as single study								

Karakiewicz

No evidence identified for this model.

Kattan

No evidence identified for this model.

Leibovich 2003

Table 58: Clinical evidence profile (C-statistics): Leibovich 2003 model, papillary RCC subtype

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model for prediction of recurrence-free survival/disease-free survival for papillary RCC, median 86.4 months follow-up								
1 (Oza 2022)	Retrospective	128	0.63 (0.56, 0.69)	Serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded once because the study has some concerns for risk of bias
b. Downgraded once as single study
c. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Table 59: Clinical evidence profile (Hazard ratios): Leibovich 2003 model high risk vs intermediate risk, papillary RCC subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model – high risk vs intermediate risk - for prediction of disease-free survival for papillary RCC, median 87.6 months follow-up								
1 (Oza 2022)	Retrospective cohort	128	2.61 (1.44, 4.72)	Serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded once because the study has some concerns for risk of bias
b. Downgraded once as single study
c. Downgraded once as sample size <500

Leibovich 2018

Table 60: Clinical evidence profile (C-statistics): Leibovich 2018 model, papillary RCC subtype

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2018 model for prediction of progression-free survival for papillary RCC, median 69.5 months follow-up								
1 (Lee 2019)	Retrospective cohort	113	0.72 (0.57, 0.83)	Serious[a]	Not serious	Serious[b]	Very serious[c]	Very low
Leibovich 2018 model for prediction of cancer-specific survival for papillary RCC, median 69.5 months follow-up								
1 (Lee 2019)	Retrospective cohort	113	0.74 (0.59, 0.85)	Serious[a]	Not serious	Serious[b]	Very serious[c]	Very low
Leibovich 2018 model for prediction of recurrence-free survival/disease free survival for papillary RCC, median 53 months follow-up								
1 (Klatte 2019)	Retrospective cohort	556	0.58 (0.52, 0.64)	Not serious	Not serious	Serious[b]	Serious[d]	Low

a. Downgraded once because study has some concerns for risk of bias
b. Downgraded once as single study
c. Downgraded twice as 95% confidence interval crossed 3 or more categories of c-statistic classification accuracy
d. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Table 61: Clinical evidence profile (Hazard ratios): Leibovich 2018 model high risk vs low risk, papillary RCC subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2018 model – high risk vs low risk - for prediction of cancer-specific survival for papillary RCC, median 52 months follow-up								
1 (Schmeusser 2023)	Retrospective cohort	190	9.16 (3.38, 24.82)	Not serious	Not serious	Serious[a]	Serious[b]	Low
Leibovich 2018 model – high risk vs low risk - for prediction of cancer-specific survival for papillary RCC (Black ethnicity), median 52 months follow-up								

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
1 (Schmeusser 2023)	Retrospective cohort	88	27.72 (4.96, 155.03)	Not serious	Not serious	Serious[a]	Serious[b]	Low
Leibovich 2018 model – high risk vs low risk - for prediction of progression-free survival for papillary RCC, median 52 months follow-up								
1 (Schmeusser 2023)	Retrospective cohort	190	11.22 (5.05, 24.96)	Not serious	Not serious	Serious[a]	Serious[b]	Low
Leibovich 2018 model – high risk vs low risk - for prediction of progression-free survival for papillary RCC (Black ethnicity), median 52 months follow-up								
1 (Schmeusser 2023)	Retrospective cohort	88	10.72 (3.27, 35.18)	Not serious	Not serious	Serious[a]	Serious[b]	Low

a. Downgraded once as data on the outcome was only available from one study
b. Downgraded once as sample size <500

Table 62: Clinical evidence profile (Hazard ratios): Leibovich 2018 model intermediate risk vs low risk, papillary RCC subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2018 model – intermediate risk vs low risk - for prediction of cancer-specific survival for papillary RCC, median 52 months follow-up								
1 (Schmeusser 2023)	Retrospective cohort	357	1.94 (0.78, 4.81)	Not serious	Not serious	Serious[a]	Very serious[b]	Very low
Leibovich 2018 model – intermediate risk vs low risk - for prediction of cancer-specific survival for papillary RCC (Black ethnicity), median 52 months follow-up								
1 (Schmeusser 2023)	Retrospective cohort	195	3.65 (0.78, 17.05)	Not serious	Not serious	Serious[a]	Very serious[b]	Very low
Leibovich 2018 model – intermediate risk vs low risk - for prediction of progression-free survival for papillary RCC, median 52 months follow-up								
1 (Schmeusser 2023)	Retrospective cohort	357	1.24 (0.55, 2.8)	Not serious	Not serious	Serious[a]	Very serious[b]	Very low

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2018 model – intermediate risk vs low risk - for prediction of progression-free survival for papillary RCC (Black ethnicity), median 52 months follow-up								
1 (Schmeusser 2023)	Retrospective cohort	195	0.84 (0.31, 2.26)	Not serious	Not serious	Serious[a]	Very serious[b]	Very low

a. Downgraded once as single study
b. Downgraded twice as sample size <500 and 95% confidence intervals cross the line of no effect

Sorbellini

No evidence identified for this model.

SSIGN

No evidence identified for this model.

TNM 2016

Table 63: Clinical evidence profile (C-statistics): TNM 2016 model, papillary RCC

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
TNM (not specified) prognostic model for prediction of recurrence-free/disease-free survival in people with papillary RCC, median 53 months follow-up								
1 (Klatte 2019)	Retrospective cohort	556	0.60 (0.54, 0.66)	Not serious	Not serious	Serious[a]	Serious[b]	Low

a. Downgraded once as single study
b. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

UISS

Table 64: Clinical evidence profile (C-statistics): UISS model, papillary RCC subtype

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
UISS prognostic model for prediction of disease-free survival in people with papillary RCC, median 53 months follow-up								
1 (Klatte 2019)	Retrospective cohort	556	0.62 (0.57, 0.68)	Not serious	Not serious	Serious[a]	Serious[b]	Low

a. Downgraded once as single study
b. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

VENUSS

Table 65: Clinical evidence profile (C-statistics): VENUSS model, papillary RCC subtype

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
VENUSS prognostic model for the prediction of disease-free survival in people with papillary RCC, median 33 months follow-up								
1 (Klatte 2019)	Retrospective cohort	980	0.812 (0.775, 0.848)	Not serious	Not serious	Very serious[a]	Serious[b]	Very low
1 (Erdem 2022)	Retrospective cohort	556	0.665 (0.605, 0.737)					

a. Downgraded twice as the point estimates span ≥3 categories of c-statistic classification accuracy
b. Downgraded once as >50% of the studies by population weight have 95% CIs that cross one of the decision thresholds

Table 66: Clinical evidence profile (Hazard ratios): VENUSS model high risk vs low risk, papillary subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
VENUSS prognostic model – high risk vs low risk - for the prediction of cancer-specific survival in people with papillary RCC, median 58.8 months follow-up								
1 (Piccinelli, 2023a)	Retrospective cohort	3,180	13.10 (9.91, 17.32)	Not serious	Not serious	Serious[a]	Not serious	Moderate
VENUSS prognostic model – high risk vs low risk - for the prediction of disease-free survival in people with papillary RCC, median 48 months follow-up								
1 (Erdem 2022)	Retrospective cohort	746	17.90 (12.23, 26.20)	Not serious	Not serious	Serious[a]	Not serious	Moderate

a. Downgraded once as single study

Table 67: Clinical evidence profile (Hazard ratios): VENUSS model intermediate risk vs low risk, papillary subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
VENUSS prognostic model – intermediate risk vs low risk - for the prediction of cancer-specific survival in people with papillary RCC, median 58.8 months follow-up								
1 (Piccinelli, 2023a)	Retrospective cohort	3,886	2.70 (2.01, 3.62)	Not serious	Not serious	Serious[a]	Not serious	Moderate
VENUSS prognostic model – intermediate risk vs low risk - for the prediction of disease-free survival in people with papillary RCC, median 48 months follow-up								
1 (Erdem 2022)	Retrospective cohort	851	2.91 (1.90, 4.46)	Not serious	Not serious	Serious[a]	Not serious	Moderate

a. Downgraded once as single study

Table 68: Clinical evidence profile (Hazard ratios): VENUSS model high risk vs intermediate risk, papillary subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
VENUSS prognostic model – intermediate risk vs low risk - for the prediction of disease-free survival in people with papillary RCC, median 48 months follow-up								
1 (Erdem 2022)	Retrospective cohort	363	6.07 (4.17, 8.83)	Not serious	Not serious	Serious[a]	Serious[b]	Moderate

a. Downgraded once as single study
b. Downgraded once as sample size<500

Zisman

No evidence identified for this model.

Chromophobe subtype

GRANT

Table 69: Clinical evidence profile (Hazard ratio): GRANT model poor risk vs favourable risk, chromophobe RCC subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
GRANT prognostic model – poor risk vs favourable risk – for the prediction of cancer-specific survival in people with chromophobe RCC, median 58.8 months follow-up								
1 (Piccinelli 2023b)	Retrospective cohort	2761	3.00 (2.17, 4.15)	Serious[a]	Not serious	Serious[b]	Not serious	Low

a. Downgraded once because the study has some concerns for risk of bias
b. Downgraded once as single study

Karakiewicz

No evidence identified for this model.

Kattan

No evidence identified for this model.

Leibovich 2003

Table 70: Clinical evidence profile (C-statistic): Leibovich 2003 model, chromophobe RCC subtype

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model for prediction of recurrence-free survival/disease-free survival for chromophobe subtype RCC, median 86.4 months follow-up								
1 (Oza 2022)	Retrospective cohort	96	0.65 (0.54, 0.75)	Serious[a]	Not serious	Serious[b]	Very serious[c]	Very low

a. Downgraded once because the study has some concerns for risk of bias
b. Downgraded once as single study
c. Downgraded twice as 95% confidence interval crossed 3 or more categories of c-statistic classification accuracy

Table 71: Clinical evidence profile (Hazard ratio): Leibovich 2003 model high risk vs intermediate risk, chromophobe RCC subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model – high risk vs intermediate risk - for prediction of disease-free survival for chromophobe RCC, median 87.6 months follow-up								
1 (Oza 2022)	Retrospective cohort	96	3.88 (1.56, 9.63)	Serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded once because the study has some concerns for risk of bias

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
b. Downgraded once as single study c. Downgraded once as sample size <500								

Leibovich 2018

Table 72: Clinical evidence profile (Hazard ratio): Leibovich 2018 model high risk vs low risk, chromophobe RCC subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2018 model – high risk vs low risk - for prediction of cancer-specific survival for chromophobe RCC, median 56 months follow-up								
2 (Piccinelli 2023b, Schmeusser 2023)	Retrospective cohort	2560	17.95 (11.32, 28.46)	Not serious	Not serious	Not serious	Not serious	High
Leibovich 2018 model – high risk vs low risk - for prediction of progression-free survival for chromophobe RCC, median 52 months								
1 (Schmeusser 2023)	Retrospective cohort	167	45.35 (8.46, 243.18)	Not serious	Not serious	Serious[a]	Serious[b]	Low
a. Downgraded once as data on the outcome was only available from one study b. Downgraded once as sample size <500								

Table 73: Clinical evidence profile (Hazard ratio): Leibovich 2018 model intermediate risk vs low risk, chromophobe RCC subtype

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2018 model – intermediate risk vs low risk - for prediction of cancer-specific survival for chromophobe RCC, median 56 months follow-up								

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
2 (Piccinelli 2023b, Schmeusser 2023)	Retrospective cohort	2882	3.49 (2.46, 4.95)	Not serious	Not serious	Serious[a]	Not serious	Moderate
Leibovich 2018 model – intermediate risk vs low risk - for prediction of progression-free survival for chromophobe RCC, median 52 months								
1 (Schmeusser 2023)	Retrospective cohort	174	3.73 (0.47, 29.88)	Not serious	Not serious	Serious[a]	Very serious[b]	Very low

a. Downgraded once as I^2 40-60%, or data on the outcome was only available from one study
b. Downgraded twice as sample size <500 and 95% confidence intervals cross the line of no effect

Sorbellini

No evidence identified for this model.

SSIGN

No evidence identified for this model.

TNM 2016.

No evidence identified for this model.

UISS

No evidence identified for this model.

VENUSS

No evidence identified for this model.

Zisman

No evidence identified for this model.

All subtypes

GRANT

Table 74: Clinical evidence profile (C-statistics): GRANT model, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
GRANT model for prediction of overall survival for all types of RCC, median 60 months follow-up								
1 (Buti 2019)	Retrospective cohort	73217	0.67 (0.66, 0.68)	Very serious[a]	Not serious	Serious[b]	Not serious	Very low
GRANT model for prediction of recurrence-free survival/disease free survival for all types of RCC, median 57.9 months follow-up								
1 (Ishiyama 2024)	Retrospective cohort	235	0.7 (0.66, 0.75)	Very serious[c]	Not serious	Very serious[d]	Serious[e]	Very low
1 (Cortellini 2020)	Retrospective cohort	134	0.59 (0.51, 0.67)					

a. Downgraded twice because the study is at high risk of bias
b. Downgraded once as data from the outcome was only available from one study
c. Downgraded twice as >50% of the studies by population weight came from studies at high risk of bias
d. Downgraded twice as the point estimates span 3 or more categories of c-statistic classification accuracy
e. Downgraded once as >50% of the studies by population weight have 95% CIs that cross 2 categories of c-statistic classification accuracy

Karakiewicz

Table 75: Clinical evidence profile (C-statistics): Karakiewicz model, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Karakiewicz model for prediction of cancer-specific survival for all subtypes of RCC, median 77.9 months follow-up								
1 (Correa 2019)	Retrospective cohort	1647	0.617 (0.616, 0.619)	Serious[a]	Not serious	Serious[b]	Not serious	Low
1 (Liu 2009)	Retrospective cohort	653	0.75 (0.71, 0.8)					
1 (Morgan 2018)	Retrospective cohort	656	0.84 (0.77, 0.91)					
1 (Tan 2011)	Retrospective cohort	390	0.84 (0.79, 0.89)					
Karakiewicz model for prediction of overall survival for all subtypes of RCC, median 62.5 months follow-up								
2 (Liu 2009, Tan 2011)	Retrospective cohort	1043	0.74 (0.70, 0.77)	Very serious[c]	Not serious	Not serious	Not serious	Moderate
Karakiewicz model for prediction of recurrence-free survival/disease-free survival for all subtypes of RCC, median 62.5 months follow-up								
2 (Liu 2009, Tan 2011)	Retrospective cohort	1043	0.8 (0.77, 0.82)	Very serious[c]	Not serious	Not serious	Serious[d]	Moderate

a. Downgraded once as >50% of the studies by population weight came from studies at some concerns or high risk of bias
b. Downgraded once as the point estimates span ≥2 categories of c-statistic classification accuracy
c. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias
d. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Kattan

Table 76: Clinical evidence profile (C-statistics): Kattan model, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Kattan model for prediction of cancer-specific survival for all subtypes of RCC, median 60 months follow-up								
3 (Cindolo 2005, Liu 2009, Tan 2011)	Retrospective cohort	3447	0.77 (0.75, 0.79)	Very serious[a]	Not serious	Serious[b]	Not serious	Very low
Kattan model for prediction of overall survival for all subtypes of RCC, median 60 months follow-up								
3 (Cindolo 2005, Liu 2009, Tan 2011)	Retrospective cohort	3447	0.71 (0.62, 0.79)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
Kattan model for prediction of recurrence-free survival/disease-free survival for all subtypes of RCC, median 60 months follow-up								
1 (Cindolo 2005)	Retrospective cohort	2404	0.81 (0.78, 0.84)	Very serious[d]	Not serious	Serious[b]	Serious[c]	Very low
1 (Correa 2019)	Retrospective cohort	1647	0.622 (0.621, 0.623)					
1 (Hupertan 2006)	Retrospective cohort	565	0.61 (0.58, 0.64)					
1 (Liu 2009)	Retrospective cohort	653	0.84 (0.80, 0.88)					
1 (Tan 2011)	Retrospective cohort	390	0.73 (0.67, 0.79)					
1 (Utsumi 2011) (CUH cohort)	Retrospective cohort	152	0.75 (0.62, 0.87)					
1 (Utsumi 2011) (CCC cohort)	Retrospective cohort	65	0.8 (0.71, 0.88)					

a. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias
b. Downgraded once as I^2 40 - 60%, or the point estimates span 2 categories of c-statistic classification accuracy

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty

c. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy
d. Downgraded twice as >50% of the studies by population weight came from studies at high risk of bias

Leibovich 2003

Table 77: Clinical evidence profile (C-statistics): Leibovich 2003 model, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model for prediction of cancer-specific survival for all subtypes of RCC, median 62 months follow-up								
2 (Shao 2020, Tan 2011)	Retrospective cohort	1524	0.80 (0.76, 0.83)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low
Leibovich 2003 model for prediction of overall survival for all subtypes of RCC, median 62 months follow-up								
2 (Shao 2020, Tan 2011)	Retrospective cohort	1524	0.77 (0.73, 0.81)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low
Leibovich 2003 model for prediction of recurrence-free survival/disease-free survival for all subtypes of RCC, median 68 months follow-up								
1 (Oza 2022)	Retrospective cohort	1445	0.63 (0.61, 0.65)	Very serious[d]	Not serious	Very serious[c]	Not serious	Very low
1 (Shao 2020)	Retrospective cohort	1202	0.75 (0.72, 0.79)					
1 (Seles 2017)	Retrospective cohort	676	0.8 (0.76, 0.84)					
1 (Tan 2011)	Retrospective cohort	322	0.8 (0.74, 0.86)					

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
1 (Vasudev 2019) (his)	Retrospective cohort	191	0.73 (0.65, 0.81)					
1 (Vasudev 2019) (con)	Retrospective cohort	384	0.77 (0.69, 0.85)					

a. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias
b. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy
c. Downgraded twice as the point estimates span ≥3 categories of c-statistic classification accuracy
d. Downgraded twice as >50% of the studies by population weight came from studies at high risk of bias

Table 78: Clinical evidence profile (Hazard ratios): Leibovich 2003 high risk vs low risk, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model – high risk vs low risk - for prediction of disease-free survival for all subtypes RCC, median 90.6 months								
2 (Vasudev 2019 (con), Vasudev 2019 (his))	Retrospective cohort	326	19.14 (9.46, 38.75)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low

a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias
b. Downgraded once as sample size <500

Table 79: Clinical evidence profile (Hazard ratios): Leibovich 2003 intermediate risk vs low risk, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model – intermediate risk vs low risk - for prediction of disease-free survival for all types RCC, median 90.6 months								

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
2 (Vasudev 2019 (con), Vasudev 2019 (his))	Retrospective cohort	459	4.60 (2.26, 9.36)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low

a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias
b. Downgraded once as sample size <500

Table 80: Clinical evidence profile (Hazard ratios): Leibovich 2003 high risk vs intermediate risk, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Leibovich 2003 model – high risk vs intermediate risk - for prediction of disease-free survival for all types RCC, median								
1 (Oza 2022)	Retrospective cohort	1669	2.74 (2.29, 3.28)	Serious[a]	Not serious	Serious[b]	Not serious	Low

a. Downgraded once because the study has some concerns for risk of bias
b. Downgraded once as single study

Leibovich 2018

No evidence identified for this model.

Sorbellini

Table 81: Clinical evidence profile (C-statistics): Sorbellini model, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Sorbellini model for prediction of cancer-specific survival for all types of RCC, median 62.5 months								
2 (Liu 2009, Tan 2011)	Retrospective	975	0.79 (0.75, 0.83)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low
Sorbellini model for prediction of overall survival for all types of RCC, median 62.5 months								
2 (Liu 2009, Tan 2011)	Retrospective	975	0.74 (0.70, 0.78)	Very serious[a]	Not serious	Not serious	Not serious	Low
Sorbellini model for prediction of recurrence-free survival/disease free survival for all types of RCC, median 62.5 months								
2 (Liu 2009, Tan 2011)	Retrospective	975	0.81 (0.78, 0.84)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low

a. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias
b. Downgraded twice as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

SSIGN

Table 82: Clinical evidence profile (C-statistics): SSIGN model, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
SSIGN prognostic model for prediction of recurrence-free/disease-free survival in people with RCC all types, median 64 months follow-up								
2 (Liu 2009, Shao 2020)	Retrospective cohort	1855	0.79 (0.76, 0.82)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
SSIGN prognostic model for prediction of overall survival in people with RCC all types, median 65 months follow-up								
1 (Tsujino 2017b)	Retrospective cohort	219	0.84 (0.72, 0.96)	Very serious[c]	Not serious	Serious[d]	Serious[b]	Very low
1 (Liu 2009)	Retrospective cohort	653	0.71 (0.66, 0.76)					
1 (Hu 2020)	Retrospective cohort	648	0.85 (0.811, 0.89)					
SSIGN prognostic model for prediction of cancer-specific survival in people with RCC all types, median 64 months follow-up								
1 (Liu 2009)	Retrospective cohort	653	0.75 (0.71, 0.8)	Very serious[c]	Not serious	Serious[d]	Serious[b]	Very low
1 (Hu 2020)	Retrospective cohort	648	0.896 (0.87, 0.922)					
1 (Hutterer 2019)	Retrospective cohort	382	0.81 (0.75, 0.87)					
1 (Zhu 2024) (external test)	Retrospective cohort	736	0.79 (0.66, 0.76)					
1 (Zhu 2024) (training)	Retrospective cohort	1185	0.83 (0.79, 0.86)					
1 (Zhu 2024) (internal validation)	Retrospective cohort	297	0.83 (0.73, 0.90)					

a. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias
b. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy
c. Downgraded twice as >50% of the studies by population weight came from studies at high risk of bias
d. Downgraded once as the point estimates span 2 categories of c-statistic classification accuracy

Table 83: Clinical evidence profile (Hazard ratios): SSIGN model high risk vs low risk, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
SSIGN prognostic model – high risk vs low risk - for the prediction of disease-free survival in people with RCC all types, median 60 months follow-up								
1 (Tsujino 2017a)	Retrospective cohort	268	4.09 (2.36, 7.10)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
SSIGN prognostic model – high risk vs low risk - for the prediction of cancer-specific survival in people with RCC all types, median 57 months follow-up								
1 (Tsujino 2017b)	Retrospective cohort	219	13.85 (4.97, 38.57)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
SSIGN prognostic model – high risk vs low risk - for the prediction of overall survival in people with RCC all types, median 39.5 months follow-up								
2 (Tsujino 2017a, Xiao 2021b)	Retrospective cohort	338	4.55 (2.73, 7.58)	Very serious[d]	Not serious	Not serious	Serious[c]	Very low
SSIGN prognostic model – high risk vs low risk - for the prediction of progression-free survival in people with RCC all types, median 19 months follow-up								
1 (Xiao 2021b)	Retrospective cohort	70	3.03 (1.23, 7.46)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded twice because the study is at high risk of bias
b. Downgraded once as single study
c. Downgraded once as sample size <500
d. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias

Table 84: Clinical evidence profile (Hazard ratios): SSIGN model intermediate risk vs low risk, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
SSIGN prognostic model – intermediate risk vs low risk - for the prediction of overall survival in people with RCC all types, median 19 months follow-up								

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
1 (Xiao 2021)	Retrospective cohort	125	1.45 (0.48, 4.42)	Very serious[a]	Not serious	Serious[b]	Very serious[c]	Very low
SSIGN prognostic model – intermediate risk vs low risk - for the prediction of progression-free survival in people with RCC all types, median 19 months follow-up								
1 (Xiao 2021)	Retrospective cohort	125	1.83 (0.87, 3.85)	Very serious[a]	Not serious	Serious[b]	Very serious[c]	Very low

a. Downgraded once because the study is at high risk of bias
b. Downgraded once as single study
c. Downgraded twice as sample size <500 and 95% confidence intervals cross the line of no effect

TNM 2016

No evidence identified for this model.

UISS

Table 85: Clinical evidence profile (C-statistics): UISS model, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
UISS prognostic model for prediction of recurrence-free/disease-free survival in people with RCC all types, median 63 months follow-up								
1 (Cindolo 2005)	Retrospective cohort	2404	0.78 (0.75, 0.81)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low
1 (Liu 2009)	Retrospective cohort	653	0.67 (0.63, 0.71)					

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
1 (Ishiyama 2024)	Retrospective cohort	235	0.63 (0.59, 0.67)					
1 (Cortellini 2020)	Retrospective cohort	134	0.51 (0.42, 0.6)					
1 (Shao 2020)	Retrospective cohort	1202	0.653 (0.62, 0.686)					
UISS prognostic model for prediction of overall survival in people with RCC all types, median 60 months follow-up								
1 (Tsujino 2017b)	Retrospective cohort	219	0.83 (0.71, 0.95)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low
1 (Cindolo 2005)	Retrospective cohort	2404	0.68 (0.66, 0.7)					
1 (Liu 2009)	Retrospective cohort	653	0.64 (0.59, 0.69)					
1 (Hu 2020)	Retrospective cohort	648	0.765 (0.719, 0.81)					
1 (Correa 2019)	Retrospective cohort	1647	0.556 (0.555, 0.557)					
UISS prognostic model for prediction of cancer-specific survival in people with RCC all types, median 65 follow-up								
1 (Cindolo 2005)	Retrospective cohort	2404	0.73 (0.71, 0.76)	Very serious[a]	Not serious	Very serious[b]	Not serious	Very low
1 (Liu 2009)	Retrospective cohort	653	0.65 (0.6, 0.7)					
1 (Hu 2020)	Retrospective cohort	647	0.805 (0.763, 0.847)					

a. Downgraded twice as >50% of the studies by population weight came from studies at high risk of bias
b. Downgraded twice as the point estimates span ≥3 categories of c-statistic classification accuracy

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
c. Downgraded once as >50% of the studies by population weight have 95% CIs that cross 2 categories of c-statistic classification accuracy								

Table 86: Clinical evidence profile (Hazard ratios): UISS model high risk vs low risk, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
UISS prognostic model – high risk vs low risk - for the prediction of cancer-specific survival in people with RCC all types, median 57 months follow-up								
1 (Tsujino 2017b)	Retrospective cohort	219	18.20 (6.54, 50.64)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
UISS prognostic model – high risk vs low risk - for the prediction of disease-free survival in people with RCC all types, median 73 months follow-up								
3 (Capogrosso 2018, Cortellini 2020, Tsujino 2019)	Retrospective cohort	1,262	2.42 (1.33, 4.42)	Serious[d]	Not serious	Serious[e]	Not serious	Low
UISS prognostic model – high risk vs low risk - for the prediction of overall survival in people with RCC all types, median 60 months follow-up								
1 (Tsujino 2017a)	Retrospective cohort	268	4.39 (2.31, 8.33)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded twice because the study is at high risk of bias
b. Downgraded once as single study
c. Downgraded once as sample size<500
d. Downgraded once as >50% of the weight in a meta-analysis came from studies at some concerns or high risk of bias
e. Downgraded once as I^2 40-60%

Table 87: Clinical evidence profile (Hazard ratios): UISS model intermediate risk vs low risk, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
UISS prognostic model – intermediate risk vs low risk - for the prediction of disease-free survival in people with RCC all types, median 78 months follow-up								
2 (Capogrosso 2018, Cortellini 2020)	Retrospective cohort	1,443	1.55 (0.94, 2.58)	Serious[a]	Not serious	Not serious	Serious[b]	Low
UISS prognostic model – intermediate risk vs low risk - for the prediction of overall survival in people with RCC all types, median 49 months follow-up								
1 (Baykal 2025)	Retrospective cohort	197	2.84 (1.26, 6.41)	Very serious[c]	Not serious	Serious[d]	Serious[e]	Very low

a. Downgraded once as >50% of the weight in a meta-analysis came from studies at some concerns or high risk of bias
b. Downgraded once as 95% confidence intervals crossed the line of no effect
c. Downgraded twice because the study is at high risk of bias
d. Downgraded once as single study
e. Downgraded once as sample size <500

Table 88: Clinical evidence profile (Hazard ratios): UISS model high risk vs intermediate risk, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
UISS prognostic model – high risk vs intermediate risk - for the prediction of disease-free survival in people with RCC all types, median 96 months follow-up								
1 (Cortellini 2020)	Retrospective cohort	113	0.99 (0.55, 1.78)	Serious[a]	Not serious	Serious[b]	Very serious[c]	Very low
UISS prognostic model – high risk vs intermediate risk - for the prediction of overall survival in people with RCC all types, median 49 months follow-up								
1 (Baykal 2025)	Retrospective cohort	197	4.64 (2.03, 10.61)	Very serious[d]	Not serious	Serious[b]	Serious[e]	Very low

a. Downgraded once because the study has some concerns for risk of bias
b. Downgraded once as single study

No. of studies/cohorts	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
c. Downgraded twice as sample size <500 and 95% confidence intervals cross the line of no effect d. Downgraded twice because the study is at high risk of bias e. Downgraded once as sample size <500								

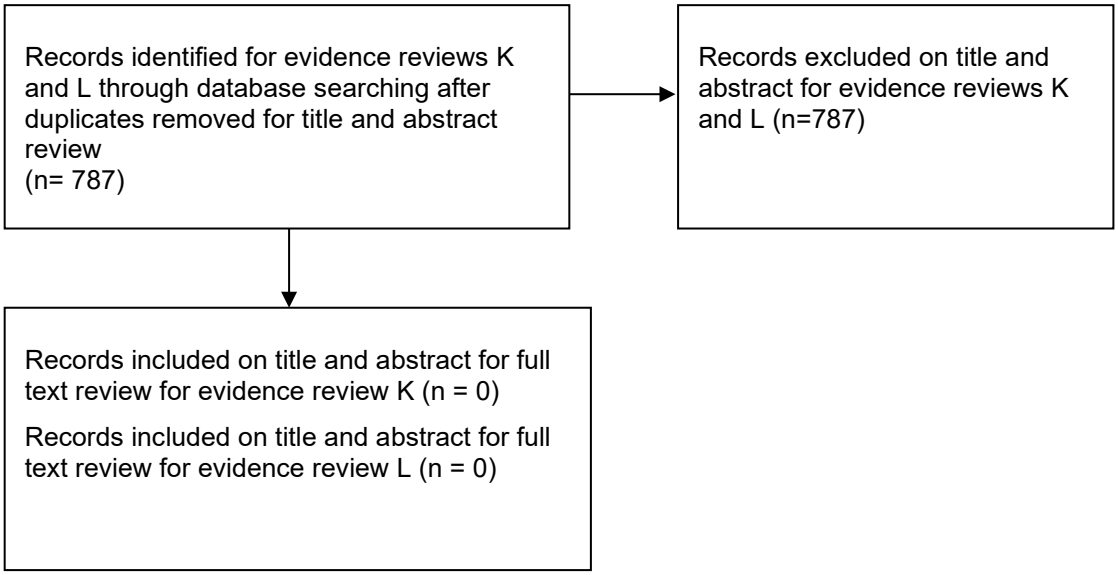
Zisman

Table 89: Clinical evidence profile (C-statistics): Zisman model, all RCC subtypes

No. of studies/cohorts	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Certainty
Zisman prognostic model for the prediction of cancer-specific survival in people with RCC all types, median 33 months follow-up								
3 (Han 2003 (NN cohort), Han 2003 (MDA cohort), Han 2003 (UCLA cohort))	Retrospective cohort	1,060	0.83 (0.80, 0.86)	Very serious[a]	Not serious	Not serious	Not serious	Low
a. Downgraded twice as >50% of the weight in the meta-analysis came from studies at high risk of bias								

Appendix G – Economic evidence study selection

Figure 108: Economic evidence study selection



Appendix H – Economic evidence tables

No economic evidence was identified for this review question.

Appendix I – Health economic model

No economic modelling was conducted for this review question.

Appendix J – Excluded studies

Table 90: Excluded clinical studies

Study	Reason for exclusion
Abd Ghafar, Nahjatul Kursyiah, Alip, Adlinda, Ong, Teng Aik et al. (2018) Efficacy, safety, and prognostic indicators of first-line sunitinib in patients with metastatic renal cell carcinoma: A single center experience. Journal of cancer research and therapeutics 14(6): 1303-1311	- Data not reported in an extractable format
Abel, E Jason, Master, Viraj A, Spiess, Philippe E et al. (2024) The Selection for Cytoreductive Nephrectomy (SCREEN) Score: Improving Surgical Risk Stratification by Integrating Common Radiographic Features. European urology oncology 7(2): 266-274	- Does not report data by specific treatment line
Abel, E Jason, Masterson, Timothy A, Karam, Jose A et al. (2017) Predictive Nomogram for Recurrence following Surgery for Nonmetastatic Renal Cell Cancer with Tumor Thrombus. The Journal of urology 198(4): 810-816	- C statistic without SE / 95% CI ("parked" studies code) *AUC for SSIGN, Sorbellini and UISS models with no CI / SE*
Aktepe, Oktay Halit, Guner, Gurkan, Guven, Deniz Can et al. (2021) The platelet to lymphocyte ratio predicts overall survival better than the neutrophil to lymphocyte ratio in metastatic renal cell carcinoma. Turkish journal of medical sciences 51(2): 757-765	- Does not report data by specific treatment line
Albiges, Laurence, Flechon, Aude, Chevreau, Christine et al. (2021) Real-world evidence of cabozantinib in patients with metastatic renal cell carcinoma: Results from the CABOREAL Early Access Program. European journal of cancer (Oxford, England : 1990) 142: 102-111	- Does not report data by specific treatment line
An, Huimin, Zhu, Yu, Xu, Le et al. (2015) Notch1 predicts recurrence and survival of patients with clear-cell renal cell carcinoma after surgical resection. Urology 85(2): 483e9-483e14	- C statistic without SE / 95% CI ("parked" studies code) *OS and RFS, c index for TNM, UISS and SSIGN, no CI/SE*
Arikan, Rukiye, Demircioglu, Ozlem, Ozguven, Salih et al. (2024) Prognostic value of psoas muscle index in metastatic renal cell carcinoma patients treated with anti-VEGF therapy. Indian journal of cancer 61(4): 789-796	- Judged likely that there was overlap between databases in other included study

Study	Reason for exclusion
Arikan, Rukiye, Ozguven, Salih, Telli, Tugba Akin et al. (2023) Prognostic significance of 18F-FDG PET/CT indices in metastatic renal cell cancer and evaluation of revised IMDC risk model by including 18F-FDG PET-CT parameters. Acta radiologica (Stockholm, Sweden : 1987) 64(5): 2040-2049	- Judged likely that there was overlap between databases in other included study *Bayoglu 2023 included due to larger sample size*
Badiola, Laura Basterretxea, Milagro, Nuria Lainez, Lavin, Diego Cacho et al. (2024) RENO Study: Clinical characteristics, treatment patterns and survival results in patients with metastatic renal cell carcinoma in Northern Spain. Seminars in oncology 51(34): 77-86	- Exclude - Results reported in non-extractable format
Bai, Junjie, Lu, Qing, Wen, Yahui et al. (2024) Development and validation of a nomogram for predicting the impact of tumor size on cancer-specific survival of locally advanced renal cell carcinoma: a SEER-based study. Aging 16(4): 3823-3836	- Exclude - Study didn't assess a prognostic model of interest
Bamias, A, Tzannis, K, Beuselinck, B et al. (2013) Development and validation of a prognostic model in patients with metastatic renal cell carcinoma treated with sunitinib: a European collaboration. British journal of cancer 109(2): 332-41	- Does not report data by specific treatment line
Beulque, Yana, Kinget, Lisa, Roussel, Eduard et al. (2024) Baseline neutrophil-to-eosinophil-ratio and outcome in metastatic clear-cell renal cell carcinoma treated with nivolumab or ipilimumab/nivolumab. Acta oncologica (Stockholm, Sweden) 63: 658-668	- Does not report data by specific treatment line
Beyplnar, I.; Sozel, Y.; Onder, A.H. (2023) Assessing the prognostic value of IMDC risk score for nivolumab-treated patients with renal cancer and malignant melanoma. Cancer Biomarkers 38(3): 367-377	- Exclude - Study reported the outcome as median - Exclude - Study reported the HR without comparing it with a reference group/breaking it down into categories
Bezan, Angelika, Mrsic, Edvin, Krieger, Daniel et al. (2015) The Preoperative AST/ALT (De Ritis) Ratio Represents a Poor Prognostic Factor in a Cohort of Patients with Nonmetastatic Renal Cell Carcinoma. The Journal of urology 194(1): 30-5	- C statistic without SE / 95% CI ("parked" studies code)

Study	Reason for exclusion
Bhindi, Bimal, Abel, E Jason, Albiges, Laurence et al. (2019) Systematic Review of the Role of Cytoreductive Nephrectomy in the Targeted Therapy Era and Beyond: An Individualized Approach to Metastatic Renal Cell Carcinoma. European urology 75(1): 111-128	- Systematic review used as a source of primary studies
Bimbatti, Davide, Pierantoni, Francesco, Lai, Eleonora et al. (2023) Advanced Non-Clear Cell Renal Cell Carcinoma Treatments and Survival: A Real-World Single-Centre Experience. Cancers 15(17)	- Exclude - Results reported as % or median
Blackmur, James P, Gaba, Fortis, Fernando, Dilini et al. (2021) Leibovich score is the optimal clinico-pathological system associated with recurrence of non-metastatic clear cell renal cell carcinoma. Urologic oncology 39(7): 438e11-438e21	- Exclude - Outcome reported as AUC
Blute, M.L. (2008) 1. Redefining pT3 renal cell carcinoma in the modern era: A proposal for a revision of the current TNM primary tumor classification system. Margulis V, Tamboli P, Matin SF, Meisner M, Swanson DA, Wood CG, Department of Urology, The University of Texas, M. D. Anderson Cancer Center, Houston, TX. Urologic Oncology: Seminars and Original Investigations 26(1): 99-100	- Exclude - conference abstract
Boegemann, Martin, Goebell, Peter Jurgen, Woike, Michael et al. (2021) Assessment of prognosis by established prognosis scores and physicians' judgement in mRCC patients: an analysis of the STAR-TOR registry. Translational andrology and urology 10(10): 4062-4074	- Exclude - Results reported as % or median
Brookman-May, Sabine D, May, Matthias, Shariat, Shahrokh F et al. (2013) Time to recurrence is a significant predictor of cancer-specific survival after recurrence in patients with recurrent renal cell carcinoma--results from a comprehensive multi-centre database (CORONA/SATURN-Project). BJU international 112(7): 909-16	- Exclude - Study didn't assess a prognostic model of interest
Bugdayci Basal, Fatma, Karacin, Cengiz, Bilgetekin, Irem et al. (2021) Can Systemic Immune-Inflammation Index Create a New Perspective for the IMDC Scoring System in Patients with Metastatic Renal Cell	- Data only reported for multivariate analysis

Study	Reason for exclusion
Carcinoma?. Urologia internationalis 105(78): 666-673	
Buti, S, Puligandla, M, Bersanelli, M et al. (2017) Validation of a new prognostic model to easily predict outcome in renal cell carcinoma: the GRANT score applied to the ASSURE trial population. Annals of oncology : official journal of the European Society for Medical Oncology 28(11): 2747-2753	- Not a peer-reviewed publication
Cai, Wen, Kong, Wen, Dong, Baijun et al. (2017) Pretreatment Serum Prealbumin as an Independent Prognostic Indicator in Patients With Metastatic Renal Cell Carcinoma Using Tyrosine Kinase Inhibitors as First-Line Target Therapy. Clinical genitourinary cancer 15(3): e437-e446	- Judged likely that there was overlap between databases in other included study *Cai 2017a included due to larger sample size*
Cheng, Yuling; Kou, Wei; Zhu, Yu (2023) Preoperative Inflammation-Associated Blood Cell Markers in Patients with Non-Metastatic Clear Cell Renal Cell Carcinoma: A Retrospective Study. International journal of general medicine 16: 3067-3080	- C statistic without SE / 95% CI ("parked" studies code) *OS and CSS, SSIGN and CSS*
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. Clinical genitourinary cancer 16(6): e1189-e1199	- Exclude - Study doesn't report an outcome of interest
Chong, Yue, Zhou, Haibin, Zhang, Peng et al. (2025) Establishing cM0 (i+) stage criteria in localized renal cell carcinoma based on postoperative circulating tumor cells monitoring. BMC cancer 25(1): 436	- Exclude - Outcome reported as AUC
Choueiri TK, 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): 60-66	- Exclude - Study doesn't report an outcome of interest
Chow, G K; Myles, J; Novick, A C (2001) The Cleveland Clinic experience with papillary (chromophil) renal cell carcinoma: clinical outcome with histopathological correlation. The Canadian journal of urology 8(2): 1223-8	- Exclude - Study didn't assess a prognostic model of interest

Study	Reason for exclusion
Chrom, Pawel, Stec, Rafal, Bodnar, Lubomir et al. (2018) Incorporating Neutrophil-to-lymphocyte Ratio and Platelet-to-lymphocyte Ratio in Place of Neutrophil Count and Platelet Count Improves Prognostic Accuracy of the International Metastatic Renal Cell Carcinoma Database Consortium Model. Cancer research and treatment 50(1): 103-110	- Judged likely that there was overlap between databases in other included study *Chrom 2019 included due to larger sample size*
Cindolo, Luca, Chiodini, Paolo, Brookman-May, Sabine et al. (2013) Assessing the accuracy and generalizability of the preoperative and postoperative Karakiewicz nomograms for renal cell carcinoma: results from a multicentre European and US study. BJU international 112(5): 578-84	- Does not separate out metastatic and non-metastatic participants
Cindolo, Luca, Chiodini, Paolo, Gallo, Ciro et al. (2008) Validation by calibration of the UCLA integrated staging system prognostic model for nonmetastatic renal cell carcinoma after nephrectomy. Cancer 113(1): 65-71	- Secondary publication with no new data *Secondary publication of Cindolo 2005*
Coffin, Gregoire, Hupertan, Vincent, Taksin, Lionel et al. (2011) Impact of elective versus imperative indications on oncologic outcomes after open nephron-sparing surgery for the treatment of sporadic renal cell carcinomas. Annals of surgical oncology 18(4): 1151-7	- Exclude - Study didn't assess a prognostic model of interest
Cortes, Julian A, Saitta, Cesare, Yuen, Kit L et al. (2024) Combined Charlson comorbidity/C-Reactive Protein Index Is a Novel Predictor in Renal Cell Carcinoma: Analysis of the International Marker Consortium for Renal Cancer (INMARC) Registry. Clinical genitourinary cancer 22(5): 102126	- Exclude - Outcome reported as AUC
Cortes, Julian A, Saitta, Cesare, Yuen, Kit L et al. (2024) Combined Charlson comorbidity/C-Reactive Protein Index Is a Novel Predictor in Renal Cell Carcinoma: Analysis of the International Marker Consortium for Renal Cancer (INMARC) Registry. Clinical genitourinary cancer 22(5): 102126	- Exclude - C-index without SE/95%CI
Dai, Chenchen, Huang, Jiaqi, Li, Yaohui et al. (2021) Tumor contour irregularity on	- Does not separate out metastatic and non-metastatic participants

Study	Reason for exclusion
preoperative imaging: a practical and useful prognostic parameter for papillary renal cell carcinoma. European radiology 31(6): 3745-3753	
Dal Bianco, M, Artibani, W, Bassi, P F et al. (1988) Prognostic factors in renal cell carcinoma. European urology 15(12): 73-6	- TNM prior to 2016
Damassi, Alessandra, Cremante, Malvina, Signori, Alessio et al. (2024) Prognostic Stratification by the Meet-URO Score in Real-World Older Patients With Metastatic Renal Cell Carcinoma (mRCC) Receiving Cabozantinib: A Subanalysis of the Prospective ZEBRA Study (Meet-URO 9). Clinical genitourinary cancer 22(2): 126-133e2	- Does not report data by specific treatment line
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	- Does not report data by specific treatment line
De Giorgi, Ugo, Rihawi, Karim, Aieta, Michele et al. (2014) Lymphopenia and clinical outcome of elderly patients treated with sunitinib for metastatic renal cell cancer. Journal of geriatric oncology 5(2): 156-63	- Judged likely that there was overlap between databases in other included study *Lolli 2016 included due to larger sample size*
De Giorgi, Ugo, Scarpi, Emanuela, Sacco, Cosimo et al. (2014) Standard vs adapted sunitinib regimen in elderly patients with metastatic renal cell cancer: results from a large retrospective analysis. Clinical genitourinary cancer 12(3): 182-9	- Judged likely that there was overlap between databases in other included study *Lolli 2016 included due to larger sample size*
de Martino, M., Leitner, C.V., Hofbauer, S.L. et al. (2016) Serum Adiponectin Predicts Cancer-specific Survival of Patients with Renal Cell Carcinoma. European Urology Focus 2(2): 197-203	- Study does not contain a relevant outcome
de Martino, Michela, Klatte, Tobias, Haitel, Andrea et al. (2012) Serum cell-free DNA in renal cell carcinoma: a diagnostic and prognostic marker. Cancer 118(1): 82-90	- Study does not contain a relevant outcome
Dong, Yi, Wang, Zheng, Lu, Xin et al. (2020) Clinical outcomes of 168 Chinese patients after local surgery for bone	- Data not reported in an extractable format

Study	Reason for exclusion
metastases arising from advanced renal cell carcinoma. Cancer 126suppl9: 2079-2085	
Donskov, Frede, Michaelson, M Dror, Puzanov, Igor et al. (2015) Sunitinib-associated hypertension and neutropenia as efficacy biomarkers in metastatic renal cell carcinoma patients. British journal of cancer 113(11): 1571-80	- Exclude - Study integrate biomarkers into the MSKCC and IMDC prognostic models
Drljevic-Nielsen, Aska, Donskov, Frede, Mains, Jill Rachel et al. (2022) Prognostic Utility of Parameters Derived From Pretreatment Dual-Layer Spectral-Detector CT in Patients With Metastatic Renal Cell Carcinoma. AJR. American journal of roentgenology 218(5): 867-876	- C statistic without SE / 95% CI ("parked" studies code)
Du, Meijun, Giridhar, Karthik V, Tian, Yijun et al. (2017) Plasma exosomal miRNAs-based prognosis in metastatic kidney cancer. Oncotarget 8(38): 63703-63714	- Does not report data by specific treatment line
Elcicek, O.F. and Kucukoner, M. (2024) Prognostic Factors and Treatment Outcomes in Renal Cell Carcinoma: A Comprehensive Analysis. Namik Kemal Medical Journal 12(3): 217	- Exclude - study does not contain a relevant outcome
El-Mokadem, Ismail, Kidd, Thomas, Pratt, Norman et al. (2016) Tumour suppressor gene (CDKNA2) status on chromosome 9p in resected renal tissue improves prognosis of localised kidney cancer. Oncotarget 7(45): 73045-73054	- C statistic without SE / 95% CI ("parked" studies code) *Disease specific survival: SSIGN c indexRFS: Leibovich c index*
Ernst, Matthew S, Navani, Vishal, Wells, J Connor et al. (2023) Outcomes for International Metastatic Renal Cell Carcinoma Database Consortium Prognostic Groups in Contemporary First-line Combination Therapies for Metastatic Renal Cell Carcinoma. European urology 84(1): 109-116	- Exclude - Results reported as % or median
Erol, Cihan, Yekeduz, Emre, Tural, Deniz et al. (2023) Clinical Features and Prognostic Factors of Metastatic Non-Clear Cell Renal Cell Carcinoma: A Multicenter Study from the Turkish Oncology Group Kidney Cancer Consortium. Urologia internationalis 107(6): 595-601	- Data only reported for multivariate analysis
Fan, Bo, Wang, Wei, Zhang, Xianping et al. (2019) Prevalence and prognostic value of	- C statistic without SE / 95% CI ("parked" studies code)

Study	Reason for exclusion
FBXO11 expression in patients with clear cell renal cell carcinoma. BMC cancer 19(1): 534	*OS: UISS and SSIGN c statistic*
Faraj Tabrizi, P., Zeuschner, P., Katzendorn, O. et al. (2024) Robot-assisted partial nephrectomy of multiple tumors: a multicenter analysis. Minerva Urology and Nephrology 76(6): 698	- Exclude - Hazard ratios presented for biomarker stratified by model of interest
Fei, LI, Xiaodong, WEN, Hongqiang, CHAI et al. (2024) Development and validation of a prognostic nomogram for locally advanced renal cell carcinoma patients after surgery. Journal of Modern Urology: 334-341	- Exclude - non-English language
Ficarra, Vincenzo, Martignoni, Guido, Lohse, Christine et al. (2006) External validation of the Mayo Clinic Stage, Size, Grade and Necrosis (SSIGN) score to predict cancer specific survival using a European series of conventional renal cell carcinoma. The Journal of urology 175(4): 1235-9	- C statistic without SE / 95% CI ("parked" studies code)
Ficarra, Vincenzo, Novara, Giacomo, Galfano, Antonio et al. (2004) Application of TNM, 2002 version, in localized renal cell carcinoma: is it able to predict different cancer-specific survival probability?. Urology 63(6): 1050-4	- Exclude - Population non mRCC
Ficarra, Vincenzo, Novara, Giacomo, Galfano, Antonio et al. (2009) The 'Stage, Size, Grade and Necrosis' score is more accurate than the University of California Los Angeles Integrated Staging System for predicting cancer-specific survival in patients with clear cell renal cell carcinoma. BJU international 103(2): 165-70	- Study does not contain a relevant outcome *Included in Usher-Smith but AUC only*
Ficarra, Vincenzo, Righetti, Rita, Pilloni, Stefania et al. (2002) Prognostic factors in patients with renal cell carcinoma: retrospective analysis of 675 cases. European urology 41(2): 190-8	- Exclude - Study didn't assess a prognostic model of interest
Fina, Widia, Agus Rizal, AH Hamid, Chaidir A, Mochtar et al. (2016) Clinical Factors Predictive of Metastases from Renal Cell Carcinomas. Asian Pacific journal of cancer prevention : APJCP 17(9): 4503-4506	- Exclude - Study uses AJCC TNM 2010 classification - Exclude - TNM model broken down

Study	Reason for exclusion
Fu, Hangcheng, Liu, Yidong, Xu, Le et al. (2015) Galectin-9 predicts postoperative recurrence and survival of patients with clear-cell renal cell carcinoma. Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine 36(8): 5791-9	- C statistic without SE / 95% CI ("parked" studies code)
Fu, Hangcheng, Liu, Yidong, Xu, Le et al. (2016) Low Expression of Mucin-4 Predicts Poor Prognosis in Patients With Clear-Cell Renal Cell Carcinoma. Medicine 95(17): e3225	- TNM 2010
Fu, Qiang, Liu, Zheng, Pan, Deng et al. (2014) Tumor miR-125b predicts recurrence and survival of patients with clear-cell renal cell carcinoma after surgical resection. Cancer science 105(11): 1427-34	- Study reports on the same dataset as an included study, without providing additional information
Fujii, Yasuhisa, Saito, Kazutaka, Iimura, Yasumasa et al. (2008) External validation of the Mayo Clinic cancer specific survival score in a Japanese series of clear cell renal cell carcinoma. The Journal of urology 180(4): 1290-6	- C statistic without SE / 95% CI ("parked" studies code) *SSIGN CSS*
Fujikawa, K, Sasaki, M, Aoyama, T et al. (1997) Role of volume weighted mean nuclear volume for predicting disease outcome in patients with renal cell carcinoma. The Journal of urology 157(4): 1237-41	- Exclude - Study didn't assess a prognostic model of interest
Fujiwara, Ryo, Yuasa, Takeshi, Yamamoto, Shinya et al. (2023) Geriatric Nutritional Risk Index as a Predictor of Prognosis in Metastatic Renal Cell Carcinoma Treated with Nivolumab. Nutrition and cancer 75(2): 670-677	- Does not report data by specific treatment line
Fukuda, Hironori, Takagi, Toshio, Kondo, Tsunenori et al. (2018) Prognostic value of the Glasgow Prognostic Score for patients with metastatic renal cell carcinoma treated by cytoreductive nephrectomy. International journal of clinical oncology 23(3): 539-546	- Does not report data by specific treatment line
Fukushima, Hiroshi, Nakanishi, Yasukazu, Kataoka, Madoka et al. (2016) Prognostic Significance of Sarcopenia in Patients with Metastatic Renal Cell Carcinoma. The Journal of urology 195(1): 26-32	- Does not report data by specific treatment line

Study	Reason for exclusion
Fukushima, Tatsuo, Tsujino, Takuya, Sakamoto, Moritoshi et al. (2025) Deciphering RCC immunotherapy outcomes: insights from a Japanese multi-institutional study on the CANLPH score's impact. World journal of urology 43(1): 135	- Study does not contain a relevant outcome *Reports CSS*
Galfano, Antonio, Novara, Giacomo, Iafrate, Massimo et al. (2008) Mathematical models for prognostic prediction in patients with renal cell carcinoma. Urologia internationalis 80(2): 113-23	- Systematic review used as a source of primary studies
Gettman, M T, Blute, M L, Spotts, B et al. (2001) Pathologic staging of renal cell carcinoma: significance of tumor classification with the 1997 TNM staging system. Cancer 91(2): 354-61	- Exclude - Study didn't assess a prognostic model of interest
Gofrit, O N, Shapiro, A, Kovalski, N et al. (2001) Renal cell carcinoma: evaluation of the 1997 TNM system and recommendations for follow-up after surgery. European urology 39(6): 669-675	- Exclude - Population non mRCC
Gontero, Paolo, Sun, Maxine, Antonelli, Alessandro et al. (2013) External validation of the preoperative Karakiewicz nomogram in a large multicentre series of patients with renal cell carcinoma. World journal of urology 31(5): 1285-90	- Exclude - Outcome reported as AUC
Gu, Liangyou, Ma, Xin, Xie, Yongpeng et al. (2017) Pretreatment Lymphocyte to Monocyte Ratio is an Independent Prognostic Factor in Metastatic Clear Cell Renal Cell Carcinoma. Clinical genitourinary cancer 15(3): e369-e377	- C statistic without SE / 95% CI ("parked" studies code)
Gu, Weijie, Zhang, Guiming, Sun, Lijiang et al. (2015) Nutritional screening is strongly associated with overall survival in patients treated with targeted agents for metastatic renal cell carcinoma. Journal of cachexia, sarcopenia and muscle 6(3): 222-30	- Model / factor assessed is not included in the protocol
Gui, Cheng-Peng, Chen, Yu-Hang, Zhao, Hong-Wei et al. (2023) Multimodal recurrence scoring system for prediction of clear cell renal cell carcinoma outcome: a discovery and validation study. The Lancet. Digital health 5(8): e515-e524	- Exclude - Outcome reported as AUC
Gupta, Alind, Arora, Paul, Brenner, Darren et al. (2021) Risk Prediction Using Bayesian	- Exclude - Outcome reported as AUC

Study	Reason for exclusion
Networks: An Immunotherapy Case Study in Patients With Metastatic Renal Cell Carcinoma. JCO clinical cancer informatics 5: 326-337	
Hahn, A.W., Surasi, D.S., Viscuse, P.V. et al. (2024) Treatment Outcomes in Patients with Metastatic Renal Cell Carcinoma with Sarcomatoid and/or Rhabdoid Dedifferentiation after Progression on Immune Checkpoint Therapy. Oncologist 29(5): 392-399	- Data only reported for multivariate analysis
Hahn, Andrew W, Alhalabi, Omar, Msaouel, Pavlos et al. (2020) Validation of prognostic scoring systems for patients with metastatic renal cell carcinoma enrolled in phase I clinical trials. ESMO open 5(6): e001073	- Does not report data by specific treatment line
Haider, M.A., Vosough, A., Khalvati, F. et al. (2017) CT texture analysis: A potential tool for prediction of survival in patients with metastatic clear cell carcinoma treated with sunitinib. Cancer Imaging 17(1): 4	- Exclude - Results reported in non-extractable format
Han, Jang Hee, Jeong, Seung-Hwan, Han, Sanghun et al. (2022) Association between decreased ipsilateral renal function and aggressive behavior in renal cell carcinoma. BMC cancer 22(1): 1143	- Data not reported in an extractable format
Harada, Ken-Ichi, Sato, Ryo, Bando, Yukari et al. (2023) Efficacy and safety of pembrolizumab and axitinib as first-line treatment for patients with advanced renal cell carcinoma: Real-world experience in Japan. International journal of urology : official journal of the Japanese Urological Association 30(9): 772-777	- Data not reported for model of interest
Heng, Daniel Y C, Xie, Wanling, Regan, Meredith M et al. (2009) Prognostic factors for overall survival in patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor-targeted agents: results from a large, multicenter study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 27(34): 5794-9	- Exclude - Outcome reported as AUC
Heng, Daniel Y C, Xie, Wanling, Regan, Meredith M et al. (2013) External validation and comparison with other models of the International Metastatic Renal-Cell Carcinoma Database Consortium	- Does not report data by specific treatment line

Study	Reason for exclusion
prognostic model: a population-based study. The Lancet. Oncology 14(2): 141-8	
Herrmann, Edwin, Trojan, Lutz, Becker, Frank et al. (2010) Prognostic factors of papillary renal cell carcinoma: results from a multi-institutional series after pathological review. The Journal of urology 183(2): 460-6	- Exclude - Study didn't assess a prognostic model of interest
Higgins, Michelle I, Martini, Dylan J, Patil, Dattatraya H et al. (2021) Sarcopenia and modified Glasgow Prognostic Score predict postsurgical outcomes in localized renal cell carcinoma. Cancer 127(12): 1974-1983	- Exclude - Outcome reported as AUC
Horie, Shigemitsu, Naito, Sei, Hatakeyama, Shingo et al. (2023) Preoperative prognostic model for localized and locally advanced renal cell carcinoma: Michinoku Japan Urological Cancer Study Group. International journal of clinical oncology 28(11): 1538-1544	- Model / factor assessed is not included in the protocol
Hou, Min, Xing, Haiyan, He, Shuangshuang et al. (2022) The Predictive Value of Three Variables in Patients with Metastatic Renal Cell Carcinoma Treated with Immune-Based Combination Therapies in Randomized Clinical Trials: A Systematic Review and Meta-Analysis. Journal of oncology 2022: 7733251	- Systematic review used as a source of primary studies
Iimura, Yasumasa, Saito, Kazutaka, Fujii, Yasuhisa et al. (2009) Development and external validation of a new outcome prediction model for patients with clear cell renal cell carcinoma treated with nephrectomy based on preoperative serum C-reactive protein and TNM classification: the TNM-C score. The Journal of urology 181(3): 1004-1012	- Exclude - Study didn't assess a prognostic model of interest
Ishikawa, Gaku, Tamura, Keita, Tsuchiya, Yoshihiro et al. (2025) Comparing Immuno-oncology Combination Therapy With Tyrosine Kinase Inhibitor Monotherapy for Advanced Renal Cell Carcinoma. Anticancer research 45(1): 379-386	- Exclude - Study doesn't report an outcome of interest
Isik, Deniz, Kinikoglu, Oguzcan, Akdag, Goncagul et al. (2024) Clinical Effectiveness of Targeted Therapies Following Nivolumab Therapy in Patients with Metastatic Renal Cell Carcinoma: A	- Exclude - Study doesn't report an outcome of interest

Study	Reason for exclusion
Real-World Study. Medicina (Kaunas, Lithuania) 60(7)	
Jiang, Liming, Wang, Chengcheng, Tong, Yuexin et al. (2023) Web-based nomogram and risk stratification system constructed for predicting the overall survival of older adults with primary kidney cancer after surgical resection. Journal of cancer research and clinical oncology 149(13): 11873-11889	- Exclude - Study didn't assess a prognostic model of interest
Johnson, T V, Abbasi, A, Owen-Smith, A et al. (2010) Absolute preoperative C-reactive protein predicts metastasis and mortality in the first year following potentially curative nephrectomy for clear cell renal cell carcinoma. The Journal of urology 183(2): 480-5	- Study does not contain a relevant outcome *Multivariable analysis only*
Joshi, A, Ramaswamy, A, Noronha, V et al. (2016) Efficacy and safety of sorafenib in advanced renal cell cancer and validation of Heng criteria. Indian journal of cancer 53(3): 423-428	- Exclude - Results reported as % or median
Juul, Simon, Donskov, Frede, Clark, Peter E et al. (2022) GRade, Age, Nodes, and Tumor (GRANT) compared with Leibovich score to predict survival in localized renal cell carcinoma: A nationwide study. International journal of urology : official journal of the Japanese Urological Association 29(7): 641-645	- C statistic without SE / 95% CI ("parked" studies code) *GRANT and Leibovich, c index for OS and RFS*
Kammerer-Jacquet, Solene-Florence, Brunot, Angelique, Bensalah, Karim et al. (2017) Hilar fat infiltration: A new prognostic factor in metastatic clear cell renal cell carcinoma with first-line sunitinib treatment. Urologic oncology 35(10): 603e7-603e14	- Exclude - doesn't state what risk groups the HRs relate to
Kang, Minyong, Yu, Jiwoong, Sung, Hyun Hwan et al. (2018) Prognostic impact of the pretreatment aspartate transaminase/alanine transaminase ratio in patients treated with first-line systemic tyrosine kinase inhibitor therapy for metastatic renal cell carcinoma. International journal of urology : official journal of the Japanese Urological Association 25(6): 596-603	- Judged likely that there was overlap between databases in other included study *Kim 2018 included due to larger sample size*
Karakiewicz, Pierre I, Briganti, Alberto, Chun, Felix K-H et al. (2007) Multi-institutional validation of a new renal	- Study does not contain a relevant outcome

Study	Reason for exclusion
cancer-specific survival nomogram. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 25(11): 1316-22	
Karakiewicz, Pierre I, Hutterer, Georg C, Trinh, Quoc-Dien et al. (2007) C-reactive protein is an informative predictor of renal cell carcinoma-specific mortality: a European study of 313 patients. Cancer 110(6): 1241-7	- TNM 2002
Karakiewicz, Pierre I, Suardi, Nazareno, Capitanio, Umberto et al. (2009) Conditional survival predictions after nephrectomy for renal cell carcinoma. The Journal of urology 182(6): 2607-12	- Study does not contain a relevant outcome
Kawai, Y, Osawa, T, Kobayashi, K et al. (2015) Factors Prognostic for Survival in Japanese Patients Treated with Sunitinib as First-line Therapy for Metastatic Clear Cell Renal Cell Cancer. Asian Pacific journal of cancer prevention : APJCP 16(14): 5687-90	- Exclude - doesn't state what risk groups the HRs relate to
Khene, Zine-Eddine, Larcher, Alessandro, Bernhard, Jean-Christophe et al. (2021) External Validation of the ASSURE Model for Predicting Oncological Outcomes After Resection of High-risk Renal Cell Carcinoma (RESCUE Study: UroCCR 88). European urology open science 33: 89-93	- Data not reported in an extractable format *Data presented as graphs only*
Kikuchi, Hiroshi, Osawa, Takahiro, Matsushita, Yuto et al. (2025) Validation of five prognostic models treated with axitinib beyond first-line nivolumab plus ipilimumab therapy for metastatic renal cell carcinoma: a Japanese multicenter retrospective study. Japanese journal of clinical oncology	- Judged likely that there was overlap between databases in other included study
Kim, Hyung L, Seligson, David, Liu, Xueli et al. (2004) Using protein expressions to predict survival in clear cell renal carcinoma. Clinical cancer research : an official journal of the American Association for Cancer Research 10(16): 5464-71	- Exclude - Study didn't assess a prognostic model of interest
Kim, S.H., Kim, J.K., Park, E.Y. et al. (2019) Liver metastasis and Heng risk are prognostic factors in patients with non-nephrectomized synchronous metastatic renal cell carcinoma treated with systemic therapy. PLoS ONE 14(2): e0211105	- Exclude - duplicate paper

Study	Reason for exclusion
Kim, Simon P, Alt, Angela L, Weight, Christopher J et al. (2011) Independent validation of the 2010 American Joint Committee on Cancer TNM classification for renal cell carcinoma: results from a large, single institution cohort. The Journal of urology 185(6): 2035-9	- Exclude - Study didn't assess a prognostic model of interest
Kim, Sung Han, Kim, Sohee, Joo, Jungnam et al. (2016) A retrospective study of predictive factors for unexpectedly prolonged or shortened progression-free survival and overall survival among patients with metastatic renal cell carcinoma who received first-line targeted therapy. BMC cancer 16: 577	- Exclude - Results reported in non-extractable format
Kim, Sung Han, Kwon, Whi-An, Kim, Sohee et al. (2018) The neutrophil-to-lymphocyte ratio makes the Heng risk model improve better the prediction of overall survival in metastatic renal cell cancer patients. Japanese journal of clinical oncology 48(9): 835-840	- Does not report data by specific treatment line
Klumper, Niklas, Ralser, Damian J, Zarbl, Romina et al. (2021) <ovid:i>CTLA4</ovid:i> promoter hypomethylation is a negative prognostic biomarker at initial diagnosis but predicts response and favorable outcome to anti-PD-1 based immunotherapy in clear cell renal cell carcinoma. Journal for immunotherapy of cancer 9(8)	- Model / factor assessed is not included in the protocol
Kohli, M., Tan, W., Vire, B. et al. (2021) Prognostic value of plasma HPG80 (Circulating progastrin) in metastatic renal cell carcinoma. Cancers 13(3): 1-13	- Exclude - Study doesn't report an outcome of interest
Konishi, Sakae, Hatakeyama, Shingo, Numakura, Kazuyuki et al. (2019) Validation of the IMDC Prognostic Model in Patients With Metastatic Renal-Cell Carcinoma Treated With First-Line Axitinib: A Multicenter Retrospective Study. Clinical genitourinary cancer 17(5): e1080-e1089	- Data not reported in an extractable format
Kotecha, Ritesh R, Flippot, Ronan, Nortman, Taylor et al. (2021) Prognosis of Incidental Brain Metastases in Patients With Advanced Renal Cell Carcinoma. Journal of the National Comprehensive Cancer Network : JNCCN 19(4): 432-438	- Exclude - Study doesn't report an outcome of interest

Study	Reason for exclusion
Kubackova, Katerina, Melichar, Bohuslav, Bortlicek, Zbynek et al. (2015) Comparison of Two Prognostic Models in Patients with Metastatic Renal Cancer Treated with Sunitinib: a Retrospective, Registry-Based Study. Targeted oncology 10(4): 557-63	- Exclude - Results reported as % or median
Kwon, Whi-An, Cho, In-Chang, Yu, Ami et al. (2013) Validation of the MSKCC and Heng risk criteria models for predicting survival in patients with metastatic renal cell carcinoma treated with sunitinib. Annals of surgical oncology 20(13): 4397-404	- Does not report data by specific treatment line
Lamb, G W A, Aitchison, M, Ramsey, S et al. (2012) Clinical utility of the Glasgow Prognostic Score in patients undergoing curative nephrectomy for renal clear cell cancer: basis of new prognostic scoring systems. British journal of cancer 106(2): 279-83	- Study does not contain a relevant outcome *Included in Usher-Smith but AUC only*
Lamb, G W A, McMillan, D C, Ramsey, S et al. (2006) The relationship between the preoperative systemic inflammatory response and cancer-specific survival in patients undergoing potentially curative resection for renal clear cell cancer. British journal of cancer 94(6): 781-4	- Study does not contain a relevant outcome
Lauridsen, K.M., Moller, H.J., Kristensen, M.W. et al. (2025) Soluble CD206 in metastatic renal cell carcinoma: Relation to clinical-biochemical parameters and patient outcome. International Journal of Cancer 156(4): 875	- Exclude - Study didn't analyse a prognostic model listed in the protocol
Lee, Alvin, Lee, Han Jie, Huang, Hong Hong et al. (2020) Prognostic Significance of Inflammation-associated Blood Cell Markers in Nonmetastatic Clear Cell Renal Cell Carcinoma. Clinical genitourinary cancer 18(4): 304-313	- C statistic without SE / 95% CI ("parked" studies code) *CSS Leibovich and UISS c index*
Lee, Chung-Han, Hotker, Andreas M, Voss, Martin H et al. (2016) Bevacizumab Monotherapy as Salvage Therapy for Advanced Clear Cell Renal Cell Carcinoma Pretreated With Targeted Drugs. Clinical genitourinary cancer 14(1): 56-62	- Does not report data by specific treatment line
Lee, Chunwoo, You, Dalsan, Park, Junsoo et al. (2011) Validation of the 2009 TNM Classification for Renal Cell Carcinoma: Comparison with the 2002 TNM	- Exclude - Study didn't assess a prognostic model of interest

Study	Reason for exclusion
Classification by Concordance Index. Korean journal of urology 52(8): 524-30	
Lee, In Hee, Kang, Byung Woog, Kim, Jong Gwang et al. (2020) Comparison of three risk stratification models for non-clear cell renal cell carcinoma patients treated with temsirolimus as first-line therapy. The Korean journal of internal medicine 35(1): 185-193	- Exclude - Study doesn't report an outcome of interest
Leibovich, BC Cheville, JC Lohse, CM Zincke, H Kwon, ED Frank, I Thompson, RH Blute, ML (2005) Cancer specific survival for patients with pT3 renal cell carcinoma - Can the 2002 primary tumor classification be improved?. JOURNAL OF UROLOGY 173(3): 716 - 719	- Exclude - Prognostic factor - Exclude - non-metastatic
Leibovich, BC, Blute, ML, Cheville, JC et al. (2003) Prediction of progression after radical nephrectomy for patients with clear cell renal cell carcinoma: a stratification tool for prospective clinical trials. Cancer 97(7): 1663-71	- Exclude - Study uses TNM 2002 classification - Exclude - TNM model broken down
Lemelin, Audreylie, Takemura, Kosuke, Heng, Daniel Y C et al. (2023) Prognostic Models in Metastatic Renal Cell Carcinoma. Hematology/oncology clinics of North America 37(5): 925-935	- Review article but not a systematic review
Li, Shuaishuai, Zhu, Jiawei, He, Zhenwei et al. (2022) Development and validation of nomograms predicting postoperative survival in patients with chromophobe renal cell carcinoma. Frontiers in oncology 12: 982833	- Exclude - Study didn't assess a prognostic model of interest
Li, Xiaoxia, Lin, Dengqiang, Xiong, Ying et al. (2025) Node-RADS category on preoperative CT predicts prognosis in patients with papillary renal cell carcinoma. European radiology	- Exclude - C-index without SE/95%CI - Exclude - AUC reported without other relevant outcomes
Lin, Haiyue, Sun, Qi, Li, Zeyang et al. (2023) Comparison and validation of different risk models for papillary renal cell carcinoma. Urologic oncology 41(8): 358e1-358e7	- C statistic without SE / 95% CI ("parked" studies code) *TNM, UISS, SSIGN, Leibovich, VENUSS , RFS, CSS and OS.*
Lin, Haiyue, Wang, Caiying, Zhao, Yun et al. (2024) Validation of novel grading schemes and refinement of the Leibovich risk groups for chromophobe renal cell	- C statistic without SE / 95% CI ("parked" studies code)

Study	Reason for exclusion
carcinoma. World journal of urology 43(1): 45	
Lin, Mingxin; Wang, Cong; Zhou, Jianan (2023) Development and validation of prognostic nomogram for elderly patients with clear cell renal cell carcinoma based on the SEER database. Medicine 102(42): e35694	- Exclude - Results reported in non-extractable format
Liu, Bing, Cui, Zhiming, Xu, Shenhao et al. (2024) Computed Tomography Measures of Perinephric Adipose Tissue and C-Reactive Protein-to-Albumin Ratio are Associated with Common Prognostic Models for Nonmetastatic Clear Cell Renal Cell Carcinoma Patients. Archivos espanoles de urologia 77(9): 1054-1061	- Exclude - Study doesn't report an outcome of interest
Liu, Weisi, Liu, Haiou, Liu, Yidong et al. (2014) Prognostic significance of p21-activated kinase 6 expression in patients with clear cell renal cell carcinoma. Annals of surgical oncology 21suppl4: 575-83	- C statistic without SE / 95% CI ("parked" studies code)
Liu, Weisi, Liu, Yidong, Liu, Haiou et al. (2015) Snail predicts recurrence and survival of patients with localized clear cell renal cell carcinoma after surgical resection. Urologic oncology 33(2): 69e1-10	- C statistic without SE / 95% CI ("parked" studies code)
Liu, Yao, Liu, J, Liu, C et al. (2024) Expression and Significance of BCCIP and Glutathione Peroxidase 4 in Clear Cell Renal Cell Carcinoma. Bulletin of experimental biology and medicine 176(3): 363-368	- Exclude - Study didn't assess a prognostic model of interest
Liu, Yidong, Liu, Haiou, Liu, Weisi et al. (2015) beta1,6-N-acetylglucosaminyltransferase V predicts recurrence and survival of patients with clear-cell renal cell carcinoma after surgical resection. World journal of urology 33(11): 1791-9	- C statistic without SE / 95% CI ("parked" studies code)
Liu, Yidong, Liu, Weisi, Xu, Le et al. (2014) GALNT4 predicts clinical outcome in patients with clear cell renal cell carcinoma. The Journal of urology 192(5): 1534-41	- TNM 2010 *(Usher-Smith 2022 paper)*
Liu, Zheng, Liu, Yidong, Xu, Le et al. (2015) P2X7 receptor predicts postoperative cancer-specific survival of patients with	- C statistic without SE / 95% CI ("parked" studies code) *TNM, UISS, SSIGN c index, 6.2% metastatic*

Study	Reason for exclusion
clear-cell renal cell carcinoma. Cancer science 106(9): 1224-31	
Longoni, Mattia, Rosiello, Giuseppe, Scilipoti, Pietro et al. (2025) Recurrence after surgery for clear cell and papillary renal cell carcinoma: Head-to head comparison of validated risk scores. Urologic oncology	- Exclude - Outcome reported as AUC
Lv, Zheng, Feng, Hua-Yi, Wang, Tao et al. (2022) Preoperative systemic inflammation response index indicates poor prognosis in patients treated with resection of renal cell carcinoma with inferior vena cava tumor thrombus. Urologic oncology 40(4): 167e9-167e19	- Does not separate out people with metastatic and non-metastatic RCC
M W Kattan 1, V Reuter, R J Motzer, J Katz PR (2001) A postoperative prognostic nomogram for renal cell carcinoma. 1(166): 63-67	- Not a relevant study design *Derivation only (validation conducted by boot-strapping)*
Maffezzoli, Michele, Signori, Alessio, Campobasso, Davide et al. (2025) External Validation of the GRade, Age, Nodes and Tumor (GRANT) Score for Patients with Surgically Treated Papillary Renal Cell Carcinoma. Technology in cancer research & treatment 24: 15330338251329848	- C statistic without SE / 95% CI ("parked" studies code)
Majidova, Nargiz, Seyyar, Mustafa, Bayraktar, Demet Isik et al. (2024) Which factors help to determine the long-term response to first-line tyrosine kinase inhibitors in patients with metastatic renal cell carcinoma: A Turkish multi-centre study. Biomolecules & biomedicine 24(6): 1776-1784	- Exclude - Study doesn't report an outcome of interest
Marconi, L, de Bruijn, R, van Werkhoven, E et al. (2018) External validation of a predictive model of survival after cytoreductive nephrectomy for metastatic renal cell carcinoma. World journal of urology 36(12): 1973-1980	- Exclude - New model, not included in the protocol
Martella, Oreste, Galatioto, Giuseppe Paradiso, Necozione, Stefano et al. (2011) Integrated staging systems for conventional renal cell carcinoma: a comparison of two prognostic models. Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica 83(3): 121-7	- Exclude - Outcome reported as AUC

Study	Reason for exclusion
Martini, Dylan J, Liu, Yuan, Shabto, Julie M et al. (2020) Novel Risk Scoring System for Patients with Metastatic Renal Cell Carcinoma Treated with Immune Checkpoint Inhibitors. The oncologist 25(3): e484-e491	- C statistic without SE / 95% CI ("parked" studies code)
Martini, Dylan J, Olsen, T Anders, Goyal, Subir et al. (2021) Body Composition Variables as Radiographic Biomarkers of Clinical Outcomes in Metastatic Renal Cell Carcinoma Patients Receiving Immune Checkpoint Inhibitors. Frontiers in oncology 11: 707050	- C statistic without SE / 95% CI ("parked" studies code)
Massaad, Elie, Saylor, Philip J, Hadzipasic, Muhamed et al. (2021) The effectiveness of systemic therapies after surgery for metastatic renal cell carcinoma to the spine: a propensity analysis controlling for sarcopenia, frailty, and nutrition. Journal of neurosurgery. Spine 35(3): 356-365	- Does not report data by specific treatment line
Massari, Francesco, Di Nunno, Vincenzo, Guida, Annalisa et al. (2021) Addition of Primary Metastatic Site on Bone, Brain, and Liver to IMDC Criteria in Patients With Metastatic Renal Cell Carcinoma: A Validation Study. Clinical genitourinary cancer 19(1): 32-40	- Data not reported for model of interest
Mattila, Kalle E, Laajala, Teemu D, Tornberg, Sara V et al. (2021) A three-feature prediction model for metastasis-free survival after surgery of localized clear cell renal cell carcinoma. Scientific reports 11(1): 8650	- Data not reported in an extractable format *Unclear data*
May, Matthias, Surcel, Cristian, Capitanio, Umberto et al. (2017) Prognostic and discriminative power of the 7th TNM classification for patients with surgically treated papillary renal cell carcinoma: results of a multi-institutional validation study (CORONA subtype project). Scandinavian journal of urology 51(4): 269-276	- Exclude - Study didn't assess a prognostic model of interest
McKay, Rana R, Kroeger, Nils, Xie, Wanling et al. (2014) Impact of bone and liver metastases on patients with renal cell carcinoma treated with targeted therapy. European urology 65(3): 577-84	- Data not reported for model of interest

Study	Reason for exclusion
Minervini, Andrea, Di Cristofano, Claudio, Collecchi, Paola et al. (2005) Intracapsular clear cell renal carcinoma: ploidy status improves the prognostic value of the 2002 TNM classification. The Journal of urology 174(4pt1): 1203-1207	- Exclude - Population non mRCC - Exclude - Study didn't assess a prognostic model of interest
Minervini, R, Minervini, A, Fontana, N et al. (2000) Evaluation of the 1997 tumour, nodes and metastases classification of renal cell carcinoma: experience in 172 patients. BJU international 86(3): 199-202	- Exclude - Study didn't assess a prognostic model of interest
Mischinger, Johannes, Frohlich, Eleonore, Mannweiler, Sebastian et al. (2019) Prognostic value of B7-H1, B7-H3 and the stage, size, grade and necrosis (SSIGN) score in metastatic clear cell renal cell carcinoma. Central European journal of urology 72(1): 23-31	- Study does not contain a relevant outcome
Mizuno, Ryuichi, Miyajima, Akira, Hibi, Taizo et al. (2017) Impact of baseline visceral fat accumulation on prognosis in patients with metastatic renal cell carcinoma treated with systemic therapy. Medical oncology (Northwood, London, England) 34(4): 47	- Data only reported for multivariate analysis
Mollica, V., Rizzo, A., Tassinari, E. et al. (2021) Prognostic and predictive factors to nivolumab in patients with metastatic renal cell carcinoma: A single center study. Anti-Cancer Drugs 32(1): 74-81	- Exclude - Prognostic model doesn't compare the different risk groups
Mollica, Veronica, Rizzo, Alessandro, Tassinari, Elisa et al. (2021) Prognostic and predictive factors to nivolumab in patients with metastatic renal cell carcinoma: a single center study. Anti-cancer drugs 32(1): 74-81	- Exclude - Results reported in non-extractable format - Exclude - Results reported as % or median
Motzer, RJ, Bacik, J, Murphy, BA et al. (2002) Interferon-alfa as a comparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 20(1): 289-96	- Exclude - Study didn't analyse a prognostic model listed in the protocol
Murianni, Veronica, Signori, Alessio, Buti, Sebastiano et al. (2024) Time to strategy failure and treatment beyond progression in pretreated metastatic renal cell carcinoma patients receiving nivolumab: post-hoc	- Exclude - prognostic model report the result from multivariate analysis

Study	Reason for exclusion
analysis of the Meet-URO 15 study. Frontiers in oncology 14: 1307635	
Nagpal, Ria, Campione, Marina, Rebuzzi, Sara Elena et al. (2025) Prognostic Value of G8 Geriatric Screening and Meet-URO Scores in Metastatic Renal Cell Carcinoma Patients Receiving First-Line Ipilimumab-Nivolumab Combination Immunotherapy. Technology in cancer research & treatment 24: 15330338251316626	- Judged likely that there was overlap between databases in other included study
Naito, Sei, Kato, Tomoyuki, Numakura, Kazuyuki et al. (2021) Prognosis of Japanese metastatic renal cell carcinoma patients in the targeted therapy era. International journal of clinical oncology 26(10): 1947-1954	- C statistic without SE / 95% CI ("parked" studies code) - Exclude - Outcome reported as AUC
Ng, Chi-Fai, Wan, Siu-Ho, Wong, Annie et al. (2007) Use of the University of California Los Angeles Integrated Staging System (UISS) to predict survival in localized renal cell carcinoma in an Asian population. International urology and nephrology 39(3): 699-703	- Exclude - Results were reported in %
Niu, Tian, Liu, Yidong, Zhang, Yuan et al. (2016) Increased expression of MUC3A is associated with poor prognosis in localized clear-cell renal cell carcinoma. Oncotarget 7(31): 50017-50026	- C statistic without SE / 95% CI ("parked" studies code)
Noe, Allard, de Bruijn, Roderick E, Blank, Christian et al. (2016) Comparison of pre-treatment MSKCC and IMDC prognostic risk models in patients with synchronous metastatic renal cell carcinoma treated in the era of targeted therapy. World journal of urology 34(8): 1067-72	- Exclude - Results reported in non-extractable format - Exclude - Results reported as % or median
Novara, Giacomo, Ficarra, Vincenzo, Antonelli, Alessandro et al. (2010) Validation of the 2009 TNM version in a large multi-institutional cohort of patients treated for renal cell carcinoma: are further improvements needed?. European urology 58(4): 588-95	- Exclude - Study didn't assess a prognostic model of interest
Ohashi, Riuko, Martignoni, Guido, Hartmann, Arndt et al. (2020) Multi-institutional re-evaluation of prognostic factors in chromophobe renal cell carcinoma: proposal of a novel two-tiered grading scheme. Virchows Archiv : an	- Exclude - Study didn't assess a prognostic model of interest

Study	Reason for exclusion
international journal of pathology 476(3): 409-418	
Ohsugi, Haruyuki, Yoshida, Takashi, Ohe, Chisato et al. (2021) The SSPN Score, a Novel Scoring System Incorporating PBRM1 Expression, Predicts Postoperative Recurrence for Patients with Non-metastatic Clear Cell Renal Cell Carcinoma. Annals of surgical oncology 28(4): 2359-2366	- Data not reported in an extractable format
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. Urologic oncology 39(12): 836e11-836e17	- C statistic without SE / 95% CI ("parked" studies code)
Omae, Kenji; Kondo, Tsunenori; Tanabe, Kazunari (2015) High preoperative C-reactive protein values predict poor survival in patients on chronic hemodialysis undergoing nephrectomy for renal cancer. Urologic oncology 33(2): 67e9-13	- Exclude - Study didn't assess a prognostic model of interest
Osorio, Lucia, Grazioso, Tatiana P, de Velasco, Guillermo et al. (2024) Retrospective study assessing the role of the androgen receptor in clear cell renal cell cancer patients treated with VEGFR inhibitors in monotherapy. Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico	- Exclude - Study didn't analyse a prognostic model listed in the protocol
Palumbo, Carlotta, Mistretta, Francesco A, Knipper, Sophie et al. (2020) Conditional Survival of Patients With Nonmetastatic Renal Cell Carcinoma: How Cancer-Specific Mortality Changes After Nephrectomy. Journal of the National Comprehensive Cancer Network : JNCCN 18(1): 44-51	- Exclude - Population non mRCC
Palumbo, Carlotta, Perri, Davide, Zacchero, Monica et al. (2022) Risk of recurrence after nephrectomy: Comparison of predictive ability of validated risk models. Urologic oncology 40(4): 167e1-167e7	- C statistic without SE / 95% CI ("parked" studies code)
Pan, Deng, Xu, Le, Liu, Haiou et al. (2015) High expression of interleukin-11 is an independent indicator of poor prognosis in	- C statistic without SE / 95% CI ("parked" studies code)

Study	Reason for exclusion
clear-cell renal cell carcinoma. Cancer science 106(5): 592-7	
Pan, Deng, Xu, Le, Liu, Haiou et al. (2015) Interleukin-11 receptor predicts post-operative clinical outcome in patients with early-stage clear-cell renal cell carcinoma. Japanese journal of clinical oncology 45(2): 202-9	- C statistic without SE / 95% CI ("parked" studies code) *RFS and OS Leibovich c index*
Papworth, K., Bergh, A., Grankvist, K. et al. (2013) Osteopontin but not parathyroid hormone-related protein predicts prognosis in human renal cell carcinoma. Acta Oncologica 52(1): 159-165	- Exclude - Study didn't assess a prognostic model of interest
Parker, William P, Cheville, John C, Frank, Igor et al. (2017) Application of the Stage, Size, Grade, and Necrosis (SSIGN) Score for Clear Cell Renal Cell Carcinoma in Contemporary Patients. European urology 71(4): 665-673	- Does not separate out metastatic and non-metastatic participants
Patard, Jean-Jacques, Dorey, Frederick J, Cindolo, Luca et al. (2004) Symptoms as well as tumor size provide prognostic information on patients with localized renal tumors. The Journal of urology 172(6pt1): 2167-71	- Exclude - Study uses TNM 2002 classification
Patard, Jean-Jacques, Kim, Hyung L, Lam, John S et al. (2004) Use of the University of California Los Angeles integrated staging system to predict survival in renal cell carcinoma: an international multicenter study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 22(16): 3316-22	- Exclude - C-index without SE/95%CI
Patel, N., Hakansson, A., Ohtake, S. et al. (2023) Transcriptomic recurrence score improves recurrence prediction for surgically treated patients with intermediate-risk clear cell kidney cancer. Cancer Medicine 12(5): 6437-6444	- Study does not contain a relevant outcome
Perez-Valderrama, B, Arranz Arija, J A, Rodriguez Sanchez, A et al. (2016) Validation of the International Metastatic Renal-Cell Carcinoma Database Consortium (IMDC) prognostic model for first-line pazopanib in metastatic renal carcinoma: the Spanish Oncologic Genitourinary Group (SOGUG) SPAZO study. Annals of oncology : official journal of	- Exclude - Results reported in non-extractable format

Study	Reason for exclusion
the European Society for Medical Oncology 27(4): 706-11	
Petraki, Constantina D, Gregorakis, Alkiviadis K, Vaslamatzis, Michael M et al. (2006) Prognostic implications of the immunohistochemical expression of human kallikreins 5, 6, 10 and 11 in renal cell carcinoma. Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine 27(1): 1-7	- Exclude - Study uses TNM 2002 classification - Exclude - TNM model broken down
Peyton, Charles C, Abel, E Jason, Chipollini, Juan et al. (2020) The Value of Neutrophil to Lymphocyte Ratio in Patients Undergoing Cytoreductive Nephrectomy with Thrombectomy. European urology focus 6(1): 104-111	- C statistic without SE / 95% CI ("parked" studies code)
Piccinelli, M.L., Barletta, F., Tappero, S. et al. (2023) Development and External Validation of a Novel Nomogram Predicting Cancer-specific Mortality-free Survival in Surgically Treated Papillary Renal Cell Carcinoma Patients. European Urology Focus 9(5): 799-806	- Study does not contain a relevant outcome
Pichler, M, Hutterer, G C, Stoeckigt, C et al. (2013) Validation of the pre-treatment neutrophil-lymphocyte ratio as a prognostic factor in a large European cohort of renal cell carcinoma patients. British journal of cancer 108(4): 901-7	- C statistic without SE / 95% CI ("parked" studies code)
Pichler, Martin, Hutterer, Georg C, Chromecki, Thomas F et al. (2012) Prognostic value of the Leibovich prognosis score supplemented by vascular invasion for clear cell renal cell carcinoma. The Journal of urology 187(3): 834-9	- C statistic without SE / 95% CI ("parked" studies code)
Pichler, Martin, Hutterer, Georg C, Chromecki, Thomas F et al. (2013) Comparison of the 2002 and 2010 TNM classification systems regarding outcome prediction in clear cell and papillary renal cell carcinoma. Histopathology 62(2): 237-46	- TNM 2002 - TNM 2010
Pichler, Martin, Hutterer, Georg C, Chromecki, Thomas F et al. (2013) Predictive ability of the 2002 and 2010 versions of the Tumour-Node-Metastasis classification system regarding metastasis-	- Exclude - Study didn't assess a prognostic model of interest

Study	Reason for exclusion
free, cancer-specific and overall survival in a European renal cell carcinoma single-centre series. BJU international 111(4ptb): e191-5	
Pichler, Martin, Hutterer, Georg C, Chromecki, Thomas F et al. (2011) External validation of the Leibovich prognosis score for nonmetastatic clear cell renal cell carcinoma at a single European center applying routine pathology. The Journal of urology 186(5): 1773-7	- Exclude - Population non mRCC
Polanco Pujol, L, Herranz Amo, F, Cano Velasco, J et al. (2020) Recurrence risk groups after nephrectomy for renal cell carcinoma. Actas urologicas espanolas 44(2): 111-118	- Exclude - Study didn't assess a prognostic model of interest
Poprach, Alexandr, Pavlik, Tomas, Melichar, Bohuslav et al. (2014) Clinical and laboratory prognostic factors in patients with metastatic renal cell carcinoma treated with sunitinib and sorafenib after progression on cytokines. Urologic oncology 32(4): 488-95	- Exclude - Prognostic factors - Exclude - model not in protocol or new model
Poprach, Alexandr, Rumanova, Kristina, Lakomy, Radek et al. (2019) Tyrosine kinase inhibitors in the first-line treatment for metastatic nonclear cell renal carcinoma: A retrospective analysis of a national database. Urologic oncology 37(4): 294e1-294e8	- Data only reported for multivariate analysis
Powles T, Kayani I, Blank C et al. (2011) The safety and efficacy of sunitinib before planned nephrectomy in metastatic clear cell renal cancer. Annals of oncology : official journal of the European Society for Medical Oncology 22(5): 1041-1047	- Exclude - Study didn't assess a prognostic model of interest
Procopio, G, Verzoni, E, Iacovelli, R et al. (2012) Prognostic factors for survival in patients with metastatic renal cell carcinoma treated with targeted therapies. British journal of cancer 107(8): 1227-32	- Does not report data by specific treatment line, or treatment line unclear
Qu, Le, Wang, Ze-Lin, Chen, Qi et al. (2018) Prognostic Value of a Long Non-coding RNA Signature in Localized Clear Cell Renal Cell Carcinoma. European urology 74(6): 756-763	- Study reports on the same dataset as an included study, without providing additional information *Changhai Hospital for SSIGN and TNM reported in Wang 2021 for a more recent time period*

Study	Reason for exclusion
Qu, Yang, Liu, Li, Wang, Jiajun et al. (2016) Dot1l expression predicts adverse postoperative prognosis of patients with clear-cell renal cell carcinoma. Oncotarget 7(51): 84775-84784	- C statistic without SE / 95% CI ("parked" studies code)
Ramsey, Sara, Lamb, Gavin W A, Aitchison, Michael et al. (2008) Prospective study of the relationship between the systemic inflammatory response, prognostic scoring systems and relapse-free and cancer-specific survival in patients undergoing potentially curative resection for renal cancer. BJU international 101(8): 959-63	- Exclude - study does not contain a relevant outcome
Rebuzzi, Sara Elena, Cerbone, Luigi, Signori, Alessio et al. (2022) Application of the Meet-URO score to metastatic renal cell carcinoma patients treated with second- and third-line cabozantinib. Therapeutic advances in medical oncology 14: 17588359221079580	- Does not report data by specific treatment line
Rebuzzi, Sara Elena, Signori, Alessio, Banna, Giuseppe Luigi et al. (2022) The prognostic value of the previous nephrectomy in pretreated metastatic renal cell carcinoma receiving immunotherapy: a sub-analysis of the Meet-URO 15 study. Journal of translational medicine 20(1): 435	- Does not report data by specific treatment line - Data not reported in an extractable format
Rebuzzi, Sara Elena, Signori, Alessio, Banna, Giuseppe Luigi et al. (2021) Inflammatory indices and clinical factors in metastatic renal cell carcinoma patients treated with nivolumab: the development of a novel prognostic score (Meet-URO 15 study). Therapeutic advances in medical oncology 13: 17588359211019642	- Does not report data by specific treatment line
Rosiello, Giuseppe, Larcher, Alessandro, Fallara, Giuseppe et al. (2022) Head-to-head comparison of all the prognostic models recommended by the European Association of Urology Guidelines to predict oncologic outcomes in patients with renal cell carcinoma. Urologic oncology 40(6): 271e19-271e27	- Exclude - AUC reported without other relevant outcomes
Roussel, Eduard, Kinget, Lisa, Verbiest, Annelies et al. (2021) C-reactive protein and neutrophil-lymphocyte ratio are prognostic in metastatic clear-cell renal cell carcinoma	- Data only reported for multivariate analysis - C statistic without SE / 95% CI ("parked" studies code)

Study	Reason for exclusion
patients treated with nivolumab. Urologic oncology 39(4): 239e17-239e25	
Rouvinov, Keren, Mermershtain, Wilmosh, Dresler, Hadas et al. (2017) Circulating Cell-Free DNA Levels in Patients with Metastatic Renal Cell Carcinoma. Oncology research and treatment 40(11): 707-710	- Data not reported in an extractable format *HR was reported, but did not compare one or more risk groups to one or more other risk groups, or did not provide enough information to extract this.*
Ruatta, F, Derosa, L, Escudier, B et al. (2019) Prognosis of renal cell carcinoma with bone metastases: Experience from a large cancer centre. European journal of cancer (Oxford, England : 1990) 107: 79-85	- Data only reported for multivariate analysis
Russo, Giorgio Ivan, Di Rosa, Alessandro, Favilla, Vincenzo et al. (2015) Accuracy capabilities comparisons between Karakiewicz, Kattan and Cindolo nomograms in predicting outcomes for renal cancer carcinoma: A systematic review and meta-analysis. Canadian Urological Association journal = Journal de l'Association des urologues du Canada 9(56): e359-66	- Systematic review used as a source of primary studies
Saal, J, Bald, T, Holzel, M et al. (2022) In the phase III IMmotion151 trial of metastatic renal cell carcinoma the easy-to-implement modified Glasgow prognostic score predicts outcome more accurately than the IMDC score. Annals of oncology : official journal of the european society for medical oncology 33(9): 982-984	- Letter to the editor
Sacre, Anne, Barthelemy, Philippe, Korenbaum, Clement et al. (2016) Prognostic factors in second-line targeted therapy for metastatic clear-cell renal cell carcinoma after progression on an anti-vascular endothelial growth factor receptor tyrosine kinase inhibitor. Acta oncologica (Stockholm, Sweden) 55(3): 329-40	- Exclude - Prognostic model doesn't compare the different risk groups
Sagie, Shira, Sarfaty, Michal, Levartovsky, Meital et al. (2022) RCC Real-World Data: Prognostic Factors and Risk Stratification in the Immunotherapy Era. Cancers 14(13)	- Does not report data by specific treatment line
Salama, M E, Guru, K, Stricker, H et al. (2005) pT1 substaging in renal cell carcinoma: validation of the 2002 TNM staging modification of malignant renal epithelial tumors. The Journal of urology 173(5): 1492-5	- Exclude - Population non mRCC

Study	Reason for exclusion
Sandlund, Johanna, Ljungberg, Borje, Wikstrom, Pernilla et al. (2009) Hypoxia-inducible factor-2alpha mRNA expression in human renal cell carcinoma. Acta oncologica (Stockholm, Sweden) 48(6): 909-14	- Exclude - Study didn't assess a prognostic model of interest
Santoni, Matteo, Buti, Sebastiano, Conti, Alessandro et al. (2015) Prognostic significance of host immune status in patients with late relapsing renal cell carcinoma treated with targeted therapy. Targeted oncology 10(4): 517-22	- Data not reported in an extractable format *HR reported, however, this was reported for the whole model and did not specify comparison between risk groups*
Santoni, Matteo, Conti, Alessandro, Procopio, Giuseppe et al. (2015) Bone metastases in patients with metastatic renal cell carcinoma: are they always associated with poor prognosis?. Journal of experimental & clinical cancer research : CR 34: 10	- Data not reported in an extractable format *HR reported for MSKCC, however this is given for the model as a whole and does not specify comparisons between risk groups*
Sanz Del Pozo, Monica, Orlandi Oliveira, Walter, Linacero Gracia, Alvaro et al. (2024) Validation and Comparison of Prognostic Models in Renal Carcinoma in a Tertiary Hospital. Archivos espanoles de urologia 77(6): 622-631	- C statistic without SE / 95% CI ("parked" studies code)
Sastre-Heres, Alejandro Jose, Iglesias, Irene, Alaguero-Calero, Miguel et al. (2019) Comparative Study of Different Classification Models in Renal-Cell Carcinoma. Pathology oncology research : POR 25(4): 1357-1362	- Exclude - Results reported as % or median
Sekiya, Ken, Ito, Masaya, Takemura, Kosuke et al. (2021) Prognostic significance of the controlling nutritional status score in patients with metastatic renal cell carcinoma diagnosed before an era of first-line immune-oncology combination therapies. Japanese journal of clinical oncology 51(10): 1570-1576	- Does not report data by specific treatment line
Shao, Ning, Wang, Hong-Kai, Zhu, Yao et al. (2018) Modification of American Joint Committee on cancer prognostic groups for renal cell carcinoma. Cancer medicine 7(11): 5431-5438	- Exclude - Study didn't assess a prognostic model of interest
Shin Lee, Ji, Seok Kim, Hyung, Bok Kim, Young et al. (2003) Expression of PTEN in renal cell carcinoma and its relation to	- Exclude - Study used the TNM 1997 system to classify the stages

Study	Reason for exclusion
tumor behavior and growth. Journal of surgical oncology 84(3): 166-72	
Shin, Seung Jea, Kim, Taejin, Sung, Hyun Hwan et al. (2019) Novel Predictive Models of Early Death Less Than 1 Year in Patients With Metastatic Renal Cell Carcinoma After Treatment With First-line Tyrosine Kinase Inhibitors. Clinical genitourinary cancer 17(6): e1137-e1146	- C statistic without SE / 95% CI ("parked" studies code)
Shinohara, Nobuo, Abe, Takashige, Mochizuki, Tango et al. (2013) Is Memorial Sloan-Kettering Cancer Center risk classification appropriate for Japanese patients with metastatic renal cell carcinoma in the cytokine era?. Urologic oncology 31(7): 1276-82	- Does not report data by specific treatment line, or treatment line unclear
Siemer, S, Lehmann, J, Loch, A et al. (2005) Current TNM classification of renal cell carcinoma evaluated: revising stage T3a. The Journal of urology 173(1): 33-7	- Exclude - Study didn't assess a prognostic model of interest
Sim, S H, Messenger, M P, Gregory, W M et al. (2012) Prognostic utility of pre-operative circulating osteopontin, carbonic anhydrase IX and CRP in renal cell carcinoma. British journal of cancer 107(7): 1131-7	- C statistic without SE / 95% CI ("parked" studies code)
Stukalin, I., Connor Wells, J., Fraccon, A. et al. (2018) Fourth-line therapy in metastatic renal cell carcinoma (mRCC): Results from the international mRCC database consortium (IMDC). Kidney Cancer 2(1): 31-36	- Study does not contain a relevant outcome
Stukalin, I., Wells, C., Fraccon, A.P. et al. (2017) Fourth-line targeted therapy in metastatic renal cell carcinoma (mRCC): Results from the International mRCC Database Consortium (IMDC). Journal of Clinical Oncology 35(6supplement1)	- Exclude - Prognostic model doesn’t compare the different risk groups
Takemura, K, Yuasa, T, Lemelin, A et al. (2024) Prognostic significance of absolute lymphocyte count in patients with metastatic renal cell carcinoma receiving first-line combination immunotherapies: results from the International Metastatic Renal Cell Carcinoma Database Consortium. ESMO open 9(7): 103606	- C statistic without SE / 95% CI ("parked" studies code)

Study	Reason for exclusion
Takemura, Kosuke, Lemelin, Audreylie, Ernst, Matthew S et al. (2024) Outcomes of Patients with Brain Metastases from Renal Cell Carcinoma Receiving First-line Therapies: Results from the International Metastatic Renal Cell Carcinoma Database Consortium. European urology 86(6): 488-492	- Data only reported for multivariate analysis
Tanaka, Nobuyuki, Mizuno, Ryuichi, Yasumizu, Yota et al. (2017) Prognostic value of neutrophil-to-lymphocyte ratio in patients with metastatic renal cell carcinoma treated with first-line and subsequent second-line targeted therapy: A proposal of the modified-IMDC risk model. Urologic oncology 35(2): 39e19-39e28	- C statistic without SE / 95% CI ("parked" studies code)
Teishima, J., Inoue, S., Hayashi, T. et al. (2020) Impact of the systemic immune-inflammation index for the prediction of prognosis and modification of the risk model in patients with metastatic renal cell carcinoma treated with first-line tyrosine kinase inhibitors. Canadian Urological Association Journal 14(11)	- Exclude - model not in protocol or new model
Terakawa, Tomoaki, Miyake, Hideaki, Kusuda, Yuji et al. (2013) Expression level of vascular endothelial growth factor receptor-2 in radical nephrectomy specimens as a prognostic predictor in patients with metastatic renal cell carcinoma treated with sunitinib. Urologic oncology 31(4): 493-8	- Judged likely that there was overlap between databases in other included study *Miyake 2015 and Miyake 2014 extracted due to larger sample size*
Tian, Jihua, Zeng, Xing, Guan, Wei et al. (2022) Prognostic indicators for survival in renal cell carcinoma with venous thrombus and development of predictive nomograms. Translational andrology and urology 11(10): 1374-1388	- Exclude - Study didn't assess a prognostic model of interest
Tian, S, Sun, S, Mao, W et al. (2021) Development and Validation of Prognostic Nomogram for Young Patients with Kidney Cancer. International journal of general medicine 14: 5091-5103	- Exclude - Study used the TNM 1997 system to classify the stages
Tjokrowidjaja, A, Goldstein, D, Hudson, HM et al. (2020) The impact of neutrophil-lymphocyte ratio on risk reclassification of patients with advanced renal cell cancer to guide risk-directed therapy. Acta oncologica (Stockholm, Sweden) 59(1): 20-27	- C statistic without SE / 95% CI ("parked" studies code)

Study	Reason for exclusion
Tran, Hai T, Liu, Yuan, Zurita, Amado J et al. (2012) Prognostic or predictive plasma cytokines and angiogenic factors for patients treated with pazopanib for metastatic renal-cell cancer: a retrospective analysis of phase 2 and phase 3 trials. The Lancet. Oncology 13(8): 827-37	- Exclude - Study doesn't report an outcome of interest
Uzun, Mehmet, Yildirim, Eda Caliskan, Ekinci, Ferhat et al. (2022) Is CRP/Albumin Ratio (CAR) a New Parameter to be Added to Risk Stratification Systems in Metastatic Renal Cell Carcinoma Patients?. Journal of the College of Physicians and Surgeons--Pakistan : JCPSP 32(11): 1425-1429	- Data only reported for multivariate analysis
Veeratterapillay, R, Simren, R, El-Sherif, A et al. (2012) Accuracy of the revised 2010 TNM classification in predicting the prognosis of patients treated for renal cell cancer in the north east of England. Journal of clinical pathology 65(4): 367-71	- Exclude - Study didn't assess a prognostic model of interest
Veeratterapillay, Rajan, Rakhra, Simren, El-Sherif, Amira et al. (2012) Can the Kattan nomogram still accurately predict prognosis in renal cell carcinoma using the revised 2010 tumor-nodes-metastasis reclassification?. International journal of urology : official journal of the Japanese Urological Association 19(8): 773-6	- Data not reported in an extractable format
Verine, J, Colin, D, Nheb, M et al. (2018) Architectural Patterns are a Relevant Morphologic Grading System for Clear Cell Renal Cell Carcinoma Prognosis Assessment: Comparisons With WHO/ISUP Grade and Integrated Staging Systems. The American journal of surgical pathology 42(4): 423-441	- Exclude - AUC reported without other relevant outcomes
Vermaat, J S, van der Tweel, I, Mehra, N et al. (2010) Two-protein signature of novel serological markers apolipoprotein-A2 and serum amyloid alpha predicts prognosis in patients with metastatic renal cell cancer and improves the currently used prognostic survival models. Annals of oncology : official journal of the European Society for Medical Oncology 21(7): 1472-1481	- Does not report data by specific treatment line
Vermaat, Joost S, Gerritse, Frank L, van der Veldt, Astrid A et al. (2012) Validation of serum amyloid alpha as an independent biomarker for progression-free and overall	- Exclude - Outcome reported as AUC

Study	Reason for exclusion
survival in metastatic renal cell cancer patients. European urology 62(4): 685-95	
Voskuil-Galos, Diana, Calinici, Tudor, Piciu, Andra et al. (2024) Evaluation of prognostic factors for late recurrence in clear cell renal carcinoma: an institutional study. Frontiers in oncology 14: 1446953	- Exclude - Population non mRCC *Non-metastatic population and IMDC*
Wang, Chao, Li, Yan, Chu, Chuan-Min et al. (2019) Gankyrin is a novel biomarker for disease progression and prognosis of patients with renal cell carcinoma. EBioMedicine 39: 255-264	- Study reports on the same dataset as an included study, without providing additional information
Wang, Hanfeng, Li, Xintao, Huang, Qingbo et al. (2021) Prognostic role of bland thrombus in patients treated with resection of renal cell carcinoma with inferior vena cava tumor thrombus. Urologic oncology 39(5): 302e1-302e7	- Does not separate out metastatic and non-metastatic participants
Wang, J., Liu, Y., Yang, Y. et al. (2016) High expression of galectin-7 associates with poor overall survival in patients with non-metastatic clear-cell renal cell carcinoma. Oncotarget 7(27): 41986-41995	- Exclude - C-index without SE/95%CI
Wang, Jinkui, Zhanghuang, Chenghao, Tan, Xiaojun et al. (2022) Development and Validation of a Competitive Risk Model in Elderly Patients With Chromophobe Cell Renal Carcinoma: A Population-Based Study. Frontiers in public health 10: 840525	- TNM model broken down
Wang, L., Cai, W., Kong, W. et al. (2018) Plasma fibrinogen as prognostic predictor in patients with metastatic renal cell carcinoma receiving target therapy. Translational Cancer Research 7(6): 1384-1392	- Judged likely that datasets overlapped with another included study
Wang, Xuhui (2024) Clinical and molecular prognostic nomograms for patients with papillary renal cell carcinoma. Discover oncology 15(1): 780	- Does not separate out people with metastatic and non-metastatic RCC
Warren, Hannah, Fernando, Archana, Thomas, Kay et al. (2019) Surgery for high-risk locally advanced (pT3c) renal tumours: oncological outcomes and prognostic significance of a modified International Metastatic Renal Cell Cancer Database Consortium (IMDC) score. BJU international 124(3): 462-468	- Data not reported for model of interest

Study	Reason for exclusion
Wei, Jin Huan, Feng, Zi Hao, Cao, Yun et al. (2019) Predictive value of single-nucleotide polymorphism signature for recurrence in localised renal cell carcinoma: a retrospective analysis and multicentre validation study. The Lancet. Oncology 20(4): 591-600	- Exclude - AUC reported without other relevant outcomes
Westerman, Mary E, Shapiro, Daniel D, Tannir, Nizar M et al. (2020) Survival following cytoreductive nephrectomy: a comparison of existing prognostic models. BJU international 126(6): 745-753	- Does not report data by specific treatment line
Wong, Emily C L and Kapoor, Anil (2020) Does Bone-targeted Therapy Benefit Patients with Metastatic Renal Cell Carcinoma?. Translational oncology 13(2): 241-244	- Exclude - Results reported in non-extractable format
Wu, Qian, Yang, Liu, Liu, Haiou et al. (2015) Elevated Expression of N-Acetylgalactosaminyltransferase 10 Predicts Poor Survival and Early Recurrence of Patients with Clear-Cell Renal Cell Carcinoma. Annals of surgical oncology 22(7): 2446-53	- C statistic without SE / 95% CI ("parked" studies code)
Xia, Yu, Liu, Li, Long, Qilai et al. (2016) Decreased expression of CTR2 predicts poor prognosis of patients with clear cell renal cell carcinoma. Urologic oncology 34(1): 5e1-9	- Exclude - Study didn't assess a prognostic model of interest
Xiao, Ruotao, Liu, Cheng, He, Wei et al. (2021) Prognostic Factors and a Nomogram Predicting Overall Survival and Cancer-Specific Survival for Patients with Collecting Duct Renal Cell Carcinoma. BioMed research international 2021: 6736008	- Exclude - TNM model broken down
Xiao, Ruotao, Qin, Yanchun, Liu, Lei et al. (2021) Development and validation of nomogram based on a novel platelet index score to predict prognosis in patients with renal cell carcinoma. Journal of Cancer 12(21): 6301-6309	- Does not separate out people with metastatic and non-metastatic RCC
Xie, Ruiyang, Shang, Bingqing, Shi, Hongzhe et al. (2023) Neutrophil extracellular traps in relationship to efficacy of systemic therapy for metastatic renal cell carcinoma. Cancer medicine 12(24): 21807-21819	- Exclude - Prognostic model compares all 3 at once

Study	Reason for exclusion
Xie, Yongpeng, Ma, Xin, Li, Hongzhao et al. (2017) Prognostic Value of Clinical and Pathological Features in Chinese Patients with Chromophobe Renal Cell Carcinoma: A 10-Year Single-Center Study. Journal of Cancer 8(17): 3474-3479	- Exclude - Study uses AJCC TNM 2010 classification
Xing, Jiajun, Liu, Yiyang, Wang, Zhongyuan et al. (2023) Incremental value of radiomics with machine learning to the existing prognostic models for predicting outcome in renal cell carcinoma. Frontiers in oncology 13: 1036734	- Study does not contain a relevant outcome
Xiong, Ying, Liu, Li, Bai, Qi et al. (2020) Individualized immune-related gene signature predicts immune status and oncologic outcomes in clear cell renal cell carcinoma patients. Urologic oncology 38(1): 7e1-7e8	- Model / factor assessed is not included in the protocol *Assesses stage, but does not specify TNM or other*
Xu, Le, Chang, Yuan, An, Huimin et al. (2015) High APOBEC3B expression is a predictor of recurrence in patients with low-risk clear cell renal cell carcinoma. Urologic oncology 33(8): 340e1-8	- C statistic without SE / 95% CI ("parked" studies code)
Yamaguchi, Yoshitomo, Tanaka, Hajime, Kimura, Koichiro et al. (2023) Prognostic impact of the radiological infiltrative feature of primary renal tumor in metastatic renal cell carcinoma. International journal of urology : official journal of the Japanese Urological Association 30(10): 913-921	- Exclude - Outcome out of scope - Exclude - Study doesn't report an outcome of interest
Yamamoto, Yoshiaki, Matsuyama, Hideyasu, Matsumoto, Hiroaki et al. (2020) Prognostic value of risk stratification using blood parameters for nivolumab in Japanese patients with metastatic renal-cell carcinoma. Japanese journal of clinical oncology 50(2): 214-220	- Exclude - Results reported in non-extractable format - Exclude - Outcome out of scope - Exclude - Study doesn't report an outcome of interest
Yang, Liu, Wu, Qian, Xu, Le et al. (2015) Increased expression of colony stimulating factor-1 is a predictor of poor prognosis in patients with clear-cell renal cell carcinoma. BMC cancer 15: 67	- C statistic without SE / 95% CI ("parked" studies code)
Yang, Xiaoxiao, Han, Bo, Xie, Qian et al. (2025) Low Expression of Mitochondrial Ribosomal Protein S5 is Associated With Poor Prognosis in Patients With Clear Cell Renal Cell Carcinoma. Applied	- Exclude - Study reported the HR without comparing it with a reference group/breaking it down into categories

Study	Reason for exclusion
immunohistochemistry & molecular morphology : AIMM 33(1): 22-28	
Yao, C., Feng, B., Li, S. et al. (2024) Predicting postoperative prognosis in clear cell renal cell carcinoma using a multiphase CT-based deep learning model. Abdominal Radiology	- Exclude - Prognostic model compares all 3 at once
Yildiz, I, Sen, F, Kilic, L et al. (2013) Prognostic factors associated with the response to sunitinib in patients with metastatic renal cell carcinoma. Current oncology (Toronto, Ont.) 20(6): e546-53	- Exclude - Results reported in non-extractable format
Yilmaz, Hatice; Yilmaz, Ali; Demirag, Guzin (2021) Prognostic significance of hemoglobin-to-red cell distribution width ratio in patients with metastatic renal cancer. Future oncology (London, England) 17(29): 3853-3864	- Exclude - Prognostic model doesn't compare the different risk groups
Yip, Steven M, Wells, Connor, Moreira, Raphael et al. (2018) Checkpoint inhibitors in patients with metastatic renal cell carcinoma: Results from the International Metastatic Renal Cell Carcinoma Database Consortium. Cancer 124(18): 3677-3683	- Exclude - Results reported as % or median
Yuasa, Takeshi, Tsuchiya, Norihiko, Urakami, Shinji et al. (2012) Clinical efficacy and prognostic factors for overall survival in Japanese patients with metastatic renal cell cancer treated with sunitinib. BJU international 109(9): 1349-54	- Exclude - Prognostic model doesn't compare the different risk groups
Yuasa, Takeshi, Urakami, Shinji, Yamamoto, Shinya et al. (2011) Treatment outcome and prognostic factors in renal cell cancer patients with bone metastasis. Clinical & experimental metastasis 28(4): 405-11	- Exclude - Results reported in non-extractable format
Yukihiro, Kazuma, Teishima, Jun, Goto, Keisuke et al. (2022) Impact of modified Glasgow prognostic score on predicting prognosis and modification of risk model for patients with metastatic renal cell carcinoma treated with first line tyrosine kinase inhibitor. Urologic oncology 40(10): 455e11-455e18	- C statistic without SE / 95% CI ("parked" studies code)
Zastrow, Stefan, Brookman-May, Sabine, Cong, Thi Anh Phuong et al. (2015) Decision curve analysis and external	- TNM 2002

Study	Reason for exclusion
validation of the postoperative Karakiewicz nomogram for renal cell carcinoma based on a large single-center study cohort. World journal of urology 33(3): 381-8	- C statistic without SE / 95% CI ("parked" studies code)
Zelenkevich, I., Sukonko, O., Mirylenka, L. et al. (2014) Is current staging system accurately predicts survival of stage I and II renal cell carcinoma?. European Urology, Supplements 13(1): e315	- Exclude - Population non mRCC
Zhang, Hai-Liang, Sheng, Xi-Nan, Li, Xue-Song et al. (2017) Sorafenib versus sunitinib as first-line treatment agents in Chinese patients with metastatic renal cell carcinoma: the largest multicenter retrospective analysis of survival and prognostic factors. BMC cancer 17(1): 16	- Exclude - Results reported in non-extractable format
Zhang, Yushi, Li, Yongqiang, Cai, Yi et al. (2016) Efficacy of sorafenib correlates with Memorial Sloan-Kettering Cancer Center (MSKCC) risk classification and bone metastasis in Chinese patients with metastatic renal cell carcinoma. Cellular oncology (Dordrecht) 39(1): 15-21	- Data only reported for multivariate analysis
Zhang, Zhilei, Yu, Yongbo, Zheng, Jilu et al. (2021) Prognostic significance of preoperative neutrophil-to-lymphocyte ratio in papillary renal cell carcinoma patients after receiving curative surgery based on a retrospective cohort. BMC urology 21(1): 43	- Exclude - Study didn't assess a prognostic model of interest
Zhanghuang, Chenghao, Wang, Jinkui, Zhang, Zhaoxia et al. (2022) A nomogram for predicting cancer-specific survival and overall survival in elderly patients with nonmetastatic renal cell carcinoma. Frontiers in surgery 9: 1018579	- TNM model broken down - Model / factor assessed is not included in the protocol
Zheng, Jianyi, Li, Shijie, Zhao, Yiqiao et al. (2022) Nomograms for predicting overall and cancer-specific survival of patients with chromophobe renal cell carcinoma after nephrectomy: a retrospective SEER-based study. BMJ open 12(9): e062129	- TNM model broken down - Model / factor assessed is not included in the protocol
Zhou, Lin, Chang, Yuan, Xu, Le et al. (2016) The Presence of Vascular Mimicry Predicts High Risk of Clear Cell Renal Cell Carcinoma after Radical Nephrectomy. The Journal of urology 196(2): 335-42	- C statistic without SE / 95% CI ("parked" studies code) *RFS: Leibovich c index* - TNM 2010

Study	Reason for exclusion
Zhu, D., Shi, X., Gao, S. et al. (2021) RNF43 is a novel tumor-suppressor and prognostic indicator in clear cell renal cell carcinoma. Oncology Research 29(3): 159	- Does not separate out people with metastatic and non-metastatic RCC
Zhu, Jun, Liu, Zhifu, Zhang, Zhongyuan et al. (2020) Development and internal validation of nomograms for the prediction of postoperative survival of patients with grade 4 renal cell carcinoma (RCC). Translational andrology and urology 9(6): 2629-2639	- Exclude - model not in protocol or new model
Zhu, Yu, Xu, Le, An, Huimin et al. (2015) p21-activated kinase 1 predicts recurrence and survival in patients with non-metastatic clear cell renal cell carcinoma. International journal of urology : official journal of the Japanese Urological Association 22(5): 447-53	- C statistic without SE / 95% CI ("parked" studies code)
Zigeuner, Richard, Hutterer, Georg, Chromecki, Thomas et al. (2010) External validation of the Mayo Clinic stage, size, grade, and necrosis (SSIGN) score for clear-cell renal cell carcinoma in a single European centre applying routine pathology. European urology 57(1): 102-9	- TNM model broken down - Data not reported in an extractable format
Zubac, Dragomir P, Bostad, Leif, Gestblom, Charlotta et al. (2007) Renal cell carcinoma: a clinicopathological follow-up study after radical nephrectomy. Scandinavian journal of urology and nephrology 41(3): 191-7	- Exclude - Study didn't assess a prognostic model of interest
Zubac, Dragomir P, Bostad, Leif, Kihl, Bjorn et al. (2009) The expression of thrombospondin-1 and p53 in clear cell renal cell carcinoma: its relationship to angiogenesis, cell proliferation and cancer specific survival. The Journal of urology 182(5): 2144-9	- Exclude - Study uses TNM 2002 classification - Exclude - TNM model broken down

Economic references excluded at full text (n=0)

Appendix K– Research recommendations – full details

K1.1 Research recommendation

Which risk prediction tools, biomarkers or factors can most accurately predict the risk of progression, metastasis, or both of localised renal cell carcinoma (RCC) in people who are undergoing active surveillance across a broad population with different characteristics (for example ethnicity and sex), including all subtypes of RCC?

K1.1.1 Why this is important

Currently prognostic tools for predicting outcomes in renal cell carcinoma rely on information from a tissue specimen following surgery of the tumour. Some patients choose to decline or delay surgery in favour of active surveillance. Predicting the risk progression and metastasis for these people is limited to clinical judgement alone as no surgical specimen of the tumour is available.

K1.1.2 Rationale for research recommendation

Table 91: Rationale for research recommendation

Importance to 'patients' or the population	There are no validated prognostic tools for predicting recurrence or survival in those suspected renal cell carcinoma who choose to undergo active surveillance. It would be useful to be able to predict the risk of progression and metastasis for these people as people, as people at higher risk may choose not to have active surveillance and instead have surgery if they are aware of this.
Relevance to NICE guidance	Predicting renal cell carcinoma has been considered in this guideline and there is a lack of data on prognostic tools for those who have not had primary surgery of the tumour.
Relevance to the NHS	A prognostic tool would assist healthcare professionals in making a clinical judgement around treatment options and follow-up schedules.
National priorities	Low
Current evidence base	No studies were identified to assess the risk of progression and metastasis for people undergoing active surveillance.
Equality considerations	None known

K1.1.3 Modified PICO table

Table 92: Modified PICO table

Population	Adults (18 or years or over) with suspected or biopsy-confirmed renal cell carcinoma (RCC), who have not had surgery or ablation of the primary renal tumour and are undergoing active surveillance. Excluded: Adults with metastatic RCC
Predictor (Predictive prognostic model or score)	The development and validation of prognostic models to predict survival outcomes (or biomarkers or clinical factors, which may include pathological features, to help develop such a tool)

Outcomes	• Progression free survival • Overall survival • Cancer specific survival
Study design	• Prospective and retrospective cohort studies (specifically validation studies of models or derivation studies that also include independent validation data)
Timeframe	5 years
Additional information	Subgroup data should be available by: • Ethnicity • Sex • RCC subtype

K1.2 Research recommendation

Which risk prediction tools, biomarkers or clinical factors can most accurately predict the risk of recurrence in people with localised or locally advanced chromophobe renal cell carcinoma across a broad population with different characteristics (for example ethnicity and sex)?

K1.2.1 Why this is important

The chromophobe renal cell carcinoma is a rare tumour type. Currently validated risk prediction models include prognostic factors that are not appropriate for chromophobe subtypes therefore scores cannot be calculated.

K1.2.2 Rationale for research recommendation

Table 93: Rationale for research recommendation

Importance to 'patients' or the population	There are no validated risk prediction tools for predicting recurrence or survival in people with chromophobe renal cell carcinoma. Patient management and care is based on clinical assessment only. A risk prediction tool would guide treatment and follow up.
Relevance to NICE guidance	Chromophobe renal cell carcinoma has been considered in this guideline and there is a lack of data on risk prediction tools for this subtype.
Relevance to the NHS	A risk prediction tool would assist healthcare professionals in making a clinical judgement around treatment options and follow-up schedules.
National priorities	Low
Current evidence base	No models that had been specifically developed for use in people who had been treated for chromophobe RCC were identified and other models contained factors that were not appropriate for chromophobe RCC.
Equality considerations	None known

K1.2.3 Modified PICO table

Table 94: Modified PICO table

Population	Adults (18 or years or over) with suspected or confirmed chromophobe renal cell carcinoma (RCC) that is localised or locally advanced Excluded: Adults with metastatic RCC
Predictor (Predictive prognostic model or score)	The development and validation of prognostic tools to predict survival or recurrence outcomes (or biomarkers or clinical factors, which may include pathological features, to help develop such a tool)
Outcomes	• Progression free survival • Recurrence free survival • Disease-free survival, including cancer-free survival
Study design	• Prospective and retrospective cohort studies (specifically validation and derivation cohorts)
Timeframe	5 years after developing tool
Additional information	Subgroup data should be available by: • Ethnicity • Sex

K1.3 Research recommendation

Which risk prediction tools, biomarkers or clinical factors can most accurately predict the risk of recurrence in people with localised renal cell carcinoma who are having thermal ablation or stereotactic ablative radiotherapy, and have not had surgery?

K1.3.1 Why this is important

Currently prognostic tools for predicting outcomes in renal cell carcinoma rely on histology information from a tissue specimen following surgery of the tumour. For some people, surgery is contraindicated so they may have ablative therapy or SABR, meaning that they may either not have a tissue specimen, or will only have histology from a biopsy. No evidence was identified for people who had not undergone surgery, and so the accuracy of the risk prediction tools in these people is unclear.

K1.3.2 Rationale for research recommendation

Table 95: Rationale for research recommendation

Importance to 'patients' or the population	There are no validated prognostic tools for predicting recurrence or survival in those suspected renal cell carcinoma who have not had surgery of the primary tumour. Some patients are frail or have comorbidities that mean surgery is contraindicated, therefore patient management and care is based on clinical assessment only.
Relevance to NICE guidance	Predicting renal cell carcinoma has been considered in this guideline and there is a lack of data on risk prediction tools for those who have not had primary surgery of the tumour.

Relevance to the NHS	A risk prediction tool would assist healthcare professionals in making a clinical judgement around treatment options and follow-up schedules.
National priorities	Low
Current evidence base	No studies of risk prediction tools were identified that specifically allowed risk to be calculated for people who had not had surgery.
Equality considerations	None known

K1.3.3 Modified PICO table

Table 96: Modified PICO table

Population	Adults (18 or years or over) with suspected or biopsy-confirmed renal cell carcinoma (RCC) that is localised, who have not had surgery of the primary renal tumour Excluded: Adults with metastatic RCC
Predictor (Predictive prognostic model or score)	The development and validation of a prognostic tools to predict survival or recurrence outcomes (or biomarkers or clinical factors, which may include pathological features, to help develop such a tool)
Outcomes	• Recurrence free survival • Disease-free survival, including cancer-free survival • Overall survival • Cancer specific survival
Study design	• Prospective and retrospective cohort studies (specifically derivation and validation cohorts)
Timeframe	5 years after developing tool
Additional information	Subgroup data should be available by: • Ethnicity • Sex • RCC subtype