National Institute for Health and Care Excellence

Kidney cancer: diagnosis and management

[L] Evidence review for risk prediction tools for metastatic renal cell carcinoma

NICE guideline NG256

Evidence underpinning recommendations 1.13.1 to 1.13.5 and a research recommendation in the NICE guideline

March 2026

FINAL

NICE National Institute for Health and Care Excellence®

Disclaimer

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

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

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 All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

ISBN: 978-1-4731-9352-9

Contents

1 Risk prediction model to predict survival and progression in adults with metastatic renal cell carcinoma

1.1 Review question

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

1.1.1 Introduction

Various tools have been developed to assess the prognosis of people with metastatic renal cell carcinoma (RCC). These tools have evolved over time, mainly due to the introduction of targeted therapy for metastatic RCC. These tools can be used to predict prognosis and are important for guiding treatment decisions. Currently there is no national guideline in the UK that informs clinicians of the most appropriate tools to use, leading to variation in practice and patient care. This review aims to identify which tools best predict survival and disease progression in people with metastatic renal cell carcinoma of carious subtypes.

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria

Population	Adults (18 years or over) with suspected or confirmed metastatic renal cell carcinoma
Risk prediction tools	• IMDC • MSKCC • Meet-URO
Outcomes	• Progression-free survival • Overall 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

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, in the methods document and in the section below.

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

Methods and technical decisions specific to this review looking at tools to predict outcomes in metastatic RCC are summarised below:

1. Studies that included people with non-metastatic RCC were excluded, regardless of the proportion compared with metastatic population.
2. Studies that reported populations of both metastatic and unresectable RCC were included. Where outcomes were not separated for these populations, the study was considered to be partially indirect.
3. 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 them.
4. 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.
5. Studies that only report an AUC for the risk prediction tools for survival outcomes have been excluded.
6. 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 tool of interest.
7. For consistency with the review on non-metastatic RCC prediction tools, for risk of bias using the PROBAST tool, we did not complete domain 4.6. In addition, we did not complete domains 4.5, 4.8 and 4.9 which are for derivation studies only.
8. For the imprecision domain in GRADE for HR data, as agreed with the committee, we used the line of no effect and a sample size of <500 as the two thresholds for downgrading.
9. 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.
10. Studies that did not report outcomes separately for specific treatment lines were excluded.
11. A decision was made to introduce a protocol deviation and stratify by treatment line. This was because the committee agreed that a person's risk can change depending on the line of SACT they receive, and therefore the results would differ according to treatment line. Additionally, the risk prediction tools were not developed to be used in people prior to cytoreductive nephrectomy, and therefore it was important to assess this population separately.
12. The protocol stated that we would include specifically validation studies of models or derivation studies that also include validation data, however, only 6 validation studies were identified in the searches. Therefore, a protocol deviation was introduced to include other cohort studies that evaluated the performance of relevant risk prediction models.

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. Further details and 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).

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 studies were ordered for closer inspection. 52 of these studies met the criteria specified in the review protocol for metastatic RCC risk prediction tools (appendix A). For a summary of the 52 included studies see Table 3.

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

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

1.1.4.2 Excluded studies

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

1.1.5 Summary of studies included in prognostic evidence

Table 2 Summary of risk prediction tools for metastatic RCC

Risk prediction tool	Development population	Original outcome	Prediction timepoint	Risk factors included	Interpretation of scoring
MSKCC	Metastatic RCC	Overall survival	2 years	• Time from diagnosis to systemic treatment • Haemoglobin • Calcium • Lactate dehydrogenase (LDH) • Karnofsky performance status	Score 0: Good risk; median survival 20 months Score 1-2: Intermediate risk; median survival 10 months Score ≥3: High risk; median survival 4 months
IMDC	Metastatic RCC	Overall survival	2 years	• Time from diagnosis to systemic treatment • Karnofsky performance status • Haemoglobin • Corrected calcium • Neutrophils • Platelets	Score 0: Favourable risk; median survival 43.2 months Score 1-2: Intermediate risk; median survival 22.5 months Score ≥3: Poor risk; median survival 7.8 months
Meet-URO	Metastatic RCC after second or further treatment line	Overall survival	2 years	• Lymphocyte count • Neutrophil count • Time from diagnosis to systemic treatment • Karnofsky performance status • Haemoglobin	Score 0-1: Group 1 Score 2-3: Group 2 Score 4-5: Group 3 Score 6-8: Group 4 Score 9: Group 5

Risk prediction tool	Development population	Original outcome	Prediction timepoint	Risk factors included	Interpretation of scoring
				• Calcium • Platelets • Bone metastases	Where lower scores mean lower risk

Table 3: Summary of studies included in the prognostic evidence

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Abuhelwa (2022) N = 527 Retrospective cohort study Follow-up: Median 19 months	US, Czechia. France, Germany, Italy, Poland, Romania, Spain, UK, Australia, Bosnia and Herzegovina, Brazil, Canada, Denmark, Japan, Republic of Korea, Mexico, Russia, Singapore, Taiwan, Thailand, Turkey	People with mRCC with clear cell and/or sarcomatoid components who had not previously received systemic therapy.	First line therapy with atezolizumab plus bevacizumab	IMDC/Heng	Overall survival Progression-free survival	Model discrimination (C-stats) Hazard ratio	High
Aktepe (2021) N=40 Retrospective cohort study Follow-up: Median 21 months	Turkey	People aged 18 years and older who had no previous history of treatment with any targeted therapy (sunitinib, sorafenib) and immune-checkpoint inhibitors. All participants had previously been treated with immune therapy (interferon).	First-line therapy with pazopanib	IMDC/Heng	Overall survival Progression-free survival	Hazard ratio	High
Aktepe (2022) N=86	Turkey	People with metastatic RCC aged 18 years or older who were treated with targeted	First-line targeted therapy	IMDC/Heng	Overall survival	Hazard ratio	High

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Retrospective cohort study Follow-up: Median: 21.6 months		therapy with history of nephrectomy for localised or metastatic disease at initial presentation.					
Bamias (2010) N=109 Retrospective cohort study Follow-up: Median 15.8 months	Greece	People with advanced RCC treated with targeted agents.	First-line sunitinib	MSKCC	Overall survival	Event data	High
Bayoglu (2023) N=185 Retrospective cohort study Follow-up: Not reported	Turkey	People with metastatic RCC who received first-line tyrosine-kinase inhibitors.	First-line treatment with tyrosine-kinase inhibitors (pazopanib/sunitinib)	IMDC/Heng	Progression-free survival Overall survival	Hazard ratio	High
Beuselinck (2014) N=200 Retrospective cohort study Follow-up: Median 67 months	Belgium and France	People with clear cell metastatic RCC who started sunitinib therapy. Participants could have received previous immunotherapy or chemotherapy.	First-line sunitinib	IMDC/Heng	Progression-free survival Overall survival	Model discrimination (C-stats) Hazard ratio	High
Bolzacchini (2022) N = 100	Italy	Patients with mRCC.	First-line sunitinib	IMDC/Heng MSKCC	Overall survival	Hazard ratio	Moderate

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Retrospective cohort study Follow-up: Up to 24 months or until death					Progression-free survival		
Cai (2017a) N = 178 Retrospective cohort study Follow-up: Median 22 months	China	People with mRCC with Karnofsky performance status (KPS) of 70 to 100.	First-line treatments with sorafenib or sunitinib	IMDC/Heng	Overall survival Progression-free survival	Model discrimination (C-stats) Hazard ratio	High
Cai (2017c) N=184 Retrospective cohort study Follow-up: Not reported	China	People with mRCC who had a KPS score of 70 to 100.	First-line treatment with sorafenib or sunitinib	MSKCC	Overall survival Progression-free survival	Model discrimination (C-stats) Hazard ratio	High
Cetin (2013) N=118 Retrospective cohort study Follow-up: Median 15 months	Turkey	People with mRCC aged 18 to 80 years with a WHO performance status of 0-1.	First-line treatment with IFN-alpha	MSKCC	Progression-free survival Overall survival	Hazard ratio	Moderate
Chen (2019) N = 213	China	Adults with mRCC. All participants had received radical, nephron-sparing, or	First-line treatment with sunitinib or sorafenib	IMDC/Heng	Overall survival	Model discrimination (C-stats)	Moderate

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Retrospective cohort study Follow-up: Not reported		cytoreductive surgery before systemic therapy			Progression-free survival	Hazard ratio	
Chrom (2019) N = 502 Retrospective cohort study Follow-up: Median 52.5 months	Poland	People with mRCC of any histopathological subtype who had an absence of other malignancies.	First-line treatment with TKI (sunitinib and pazopanib)	IMDC/Heng	Overall survival	Model discrimination (C-stats)	Low
de Velasco (2017) N = 54 Retrospective cohort study Follow-up: Not reported	US	People with mRCC	VEGF-targeted first-line therapy (sunitinib, pazopanib, axitinib, Sorafenib, and Bevacizumab)	IMDC/Heng MSKCC	Overall survival	Model discrimination (C-stats)	Moderate
Derosa (2019) Discovery set: N = 222 Validation set: N = 947 Retrospective cohort study	Discovery set: France Validation set: US, Argentina, Australia, Austria, Canada, Chile, China, Denmark, Finland, France, Germany, Hungary, Italy,	Discovery set: People with mRCC who had progressive disease after first-line targeted treatment Validation set: People with mRCC who had previously received first line treatment with sunitinib or bevacizumab, alone or in combination	Discovery set: People who received a second line targeted treatment with VEGF inhibitor or mTOR inhibitor, after progressive disease on first-line targeted treatment Validation set: People receiving axitinib,	IMDC/Heng MSKCC	Overall survival	Model discrimination (C-stats) Hazard ratio Event data	High

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Follow-up: Discovery set: median 49.4 months Validation set: median 16.3 months	Republic of Korea, Netherlands, Singapore, Spain, Sweden, Switzerland, UK		sorafenib or temsirolimus following first-line treatment with sunitinib or bevacizumab alone or in combination				
Fiala (2020) N=2390 Retrospective cohort study Follow-up: PFS: 10.6 months OS: 28.5 months	Czech Republic	Adults with mRCC.	First-line treatment with sunitinib.	MSKCC	Progression-free survival Overall survival	Hazard ratio	High
Fujita (2024) N=52 Retrospective cohort study Follow-up: median 20 months	Japan	People with advanced non-clear cell RCC	Second-line TKI therapy following IO combination therapy	IMDC/Heng	Progression-free survival Overall survival	Hazard ratio	High
Giridhar (2017) N = 47 Retrospective cohort study Follow-up: Median 3.6 years	USA	People with mRCC.	First-line treatment	MSKCC	Overall survival	Event data	High

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Guida (2024) N=172 Retrospective cohort study Follow-up: median 19.3 months	Italy	People with mRCC	First-line pembrolizumab/axitinib	IMDC/Heng	Progression-free survival Overall survival	Hazard ratio	High
Gu (2017) N = 101 Retrospective cohort study Follow-up: Median 30.8 months	China	People with clear cell carcinoma and Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1. Participants were in a clinically stable condition without severe comorbidities and with no limitations on food access or intake	First-line treatment with TKIs/mTOR inhibitors (sunitinib, sorafenib, pazopanib, fabitinib, axtinib, and everolimus)	IMDC/Heng	Overall survival Progression-free survival	Hazard ratio	Moderate
Hara (2024) N=99 Retrospective cohort study Follow-up: median 29.5 months	Japan	People with mRCC	First-line combination therapy with dual immune checkpoint inhibitors	IMDC/Heng	Progression-free survival Overall survival	Hazard ratio	High
Kikuta 2025 - IOIO N=105 Retrospective cohort study	Japan	People with mRCC	First-line treatment with immune-oncologic drug doublet combinations	IMDC/Heng	Progression-free survival Overall survival	Hazard ratio	High

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Follow-up: median 15.8 months							
Kikuta (2025) - IOTKI N=43 Retrospective cohort study Follow-up: median 15.8 months	Japan	People with mRCC	First-line treatment with immune oncologic drug tyrosine kinase inhibitor combinations	IMDC/Heng	Progression-free survival Overall survival	Hazard ratio	High
Kim (2018b) N=554 Retrospective cohort study Follow-up: Median 16.4 months	Korea	People with mRCC.	First-line treatment with TKI (sunitinib or pazopanib PZ)	IMDC/Heng MSKCC	Overall survival	Hazard ratio	Moderate
Kim (2019a) N=156 Retrospective cohort study Follow-up: Median 5 months	Korea	People with metastatic non-clear cell RCC	First-line therapy with VEGF-TKIs, mTORi, or cytokines	MSKCC IMDC/Heng	Progression-free survival	Model discrimination (C-stats)	High
Kim (2019b) N = 70 Retrospective cohort study	Korea	People with mRCC with naive, unresectable primary renal lesions who did not undergo nephrectomy.	First-line treatment with VEGF-targeted therapy (either sunitinib, sorafenib or pazopanib)	IMDC/Heng	Overall survival Progression-free survival	Hazard ratio	Moderate

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Follow-up: Median 30.9 months							
Ko (2015) N=1021 Retrospective cohort study Follow-up: Median 12.6 months	Canada, USA, Greece, Japan, Singapore, South Korea, and Denmark	People with mRCC.	Second-line targeted therapy with either an anti-VEGT drug or an mTOR inhibitor	IMDC/Heng MSKCC	Overall survival	Model discrimination (C-stats) Hazard ratio	Low
Kroeger (2013) N = 2215 Retrospective cohort study Follow-up: Median 22.3 months	20 academic centres from Canada, USA, Japan, South Korea, Singapore, and Denmark	People with mRCC.	First-line targeted therapy which included anti-VEGF therapy, sutent, sorafenib, axitinib, bevacizumab, pazopanib, and tivozanib.	IMDC/Heng MSKCC	Overall survival	Model discrimination (C-stats) Hazard ratio	High
Laukhtina (2020) N = 613 Retrospective cohort study Follow-up: Median 31 months	Tertiary centres in the United States and Europe	People with mRCC.	Treatment with cytoreductive nephrectomy	IMDC/Heng	Overall survival	Hazard ratio	Low
Lee (2017) N = 244 Retrospective cohort study	South Korea	People diagnosed with mRCC and initially treated with nephrectomy	Cytoreductive nephrectomy following nephrectomy	IMDC/Heng	Overall survival	Hazard ratio	High

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Follow-up: median 13 months							
Li (2020) N=355 Retrospective cohort study Follow-up: Median PFS: 14.2 months Median OS: 32.7 months	China	People with mRCC.	First-line treatment with TKIs	IMDC/Heng	Overall survival Progression-free survival	Hazard ratio	Moderate
Lin (2018) N=108 Retrospective cohort study Follow-up: Median 23.35 months	China	People with mRCC and no history of other malignancy.	First-line treatment with sunitinib or sorafenib	IMDC/Heng	Progression-free survival Overall survival	Hazard ratio	Moderate
Lolli (2016) N=335 Retrospective cohort study Follow-up: Median 49 months	Italy	People with unresectable or metastatic RCC.	First-line treatment with sunitinib	IMDC/Heng MSKCC	Progression-free survival Overall survival	Hazard ratio	High
Lu (2016) N = 67	China	People with RCC and bone metastasis.	First-line treatment with sunitinib	MSKCC	Overall survival	Model discrimination (C-stats)	Moderate

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Retrospective cohort study Follow-up: Not reported						Hazard ratio	
Marchioni (2021) N=519 Retrospective cohort study Follow-up: Median: 18.1 months	North America and Europe	People with mRCC.	Treatment with cytoreductive nephrectomy	MSKCC IMDC/Heng	Overall survival	Model discrimination (C-stats)	Moderate
Matsushita (2024) N = 243 Retrospective cohort study Follow-up:	Japan	People who were diagnosed with mRCC and were previously treated with first-line immune-oncology combination therapy.	Second-line treatment TKI therapy (cabozantinib, axitinib, pazopanib, sunitinib, and sorafenib)	IMDC/Heng MSKCC	Overall survival Progression-free survival	Hazard ratio	Low
Miyake (2014) N=110 Retrospective cohort study Follow-up: Median 19 months	Japan	People with mRCC.	First-line therapy with sunitinib	MSKCC	Progression-free survival	Hazard ratio	High
Miyake (2016a) N=185 Retrospective cohort study	Japan	People with mRCC.	First-line molecular-targeted therapy with sunitinib and sorafenib.	IMDC/Heng	Progression-free survival Overall survival	Hazard ratio	High

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Follow-up: Median 33.6 months							
Miyake (2016b) N = 271 Retrospective cohort study Follow-up: 70 months	Japan	People with mRCC who had disease progression on first-line targeted therapy. People who received immunotherapy using interferon-alpha and/or interleukin-2 before first-line therapy were also eligible.	Second-line therapy with either sunitinib, sorafenib or temsirolimus.	IMDC/Heng MSKCC	Overall survival	Hazard ratio	High
Miyake (2017) N = 124 Retrospective cohort study Follow-up: 41 months	Japan	People with mRCC who had disease progression on first-line systemic therapy.	Second-line treatment with axitanib (participants had received sunitinib, sorafenib, temsirolimus, and cytokine therapy, in the first-line setting)	IMDC/Heng MSKCC	Progression-free survival	Hazard ratio	High
Miyazaki (2015) N=271 Retrospective cohort study Follow-up: Median 19 months	Japan	People with mRCC who were TKI naïve.	First-line treatment with sorafenib or sunitinib	MSKCC	Overall survival	Hazard ratio	High
Ning (2022) N=358	China	People with mRCC.	First-line treatment with anti-VEGF therapy (sunitanib, axitinib, pazopanib,	IMDC/Heng	Overall survival Progression-free survival	Model discrimination (C-stats)	Moderate

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Retrospective cohort study Follow-up: Median OS: 22 Median PFS: 9.1			sorafenib, and bevacizumab).				
Rebuzzi (2022) N = 306 Retrospective cohort study Follow-up: Median 12.2 months	Italy	Adults with metastatic clear cell or non-clear cell RCC and IMDC intermediate/poor risk.	First-line treatment with nivolumab plus ipilimumab	IMDC/Heng Meet-URO	Overall survival Progression-free survival	Hazard ratio	Moderate
Rini (2019) N = 861 Randomised controlled trial Follow-up: median 12.8 months	Brazil, Canada, Czech Republic, France, Germany, Hungary, Ireland, Japan, Poland, Russia, South Korea, Spain, Taiwan, Ukraine, UK, US	Adults with newly diagnosed or recurrent stage IV clear cell RCC who have not previously received systemic therapy for advanced disease	1st line treatment with pembrolizumab + axitinib or sunitinib	IMDC/Heng	Overall survival Progression-free survival	Number of events	High
Schuttke (2024) N = 61 Retrospective cohort study Follow-up: Median 12.4 months	Germany	People with mRCC.	1st line checkpoint inhibitors therapy (ipilimumab/nivolumab)	IMDC/Heng	Overall survival Progression-free survival	Hazard ratio	Moderate

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Shin (2021) KRoCS model developing cohort: N=619 External validation cohort: N=171 Retrospective cohort study Follow-up: Median 36 months	Korea	People with mRCC.	First-line treatment with single targeted therapy agent, including tyrosine kinase inhibitor or mammalian target of rapamycin inhibitor.	IMDC/Heng MSKCC	Overall survival	Model discrimination (C-stats)	High
Smith (2013) N=82 Retrospective cohort study Follow-up: Median PFS: 17 months	USA	People with mRCC.	First-line treatment with VEGF-targeted therapy with either sorafenib or sunitinib	MSKCC	Progression-free survival	Sensitivity/ specificity	High
Soerensen (2016) N= 735 Retrospective cohort study Follow-up: Median 50.2 months	Denmark	People with mRCC.	First line treatment with TKI (sorafenib and sunitinib) or interleukin-2 (IL2)-based immunotherapy.	IMDC/Heng	Overall survival	Model discrimination (C-stats) Hazard ratio	High
Tamura (2021) N = 325	Japan	People with mRCC.	1st line treatments including axitinib, everolimus, pazopanib,	MSKCC IMDC/Heng	Overall survival Mortality	Model discrimination (C-stats)	High

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Retrospective cohort study Follow-up: Median 19 months			sorafenib, sunitinib, and temsirolimus.			Hazard ratio Event data	
Tanaka (2016) First line: N = 312 Second line: N=168 Retrospective cohort study Follow-up: First line: Median 18.1 months Second line: Median 12.7 months	Japan	People with mRCC.	First-line targeted therapy with either anti-VEGF targeted drugs or mTOR inhibitors, or second-line targeted therapy if participants had received immunotherapy as part of their treatment.	MSKCC IMDC/Heng	Overall survival	Event data	Low
Toyoda (2024) N=75 Retrospective cohort Follow-up: not reported	Japan	People with metastatic RCC treated with ICI-based combination therapy with non-clear cell RCC	First-line treatment with IO-based combination therapy	IMDC/Heng	Overall Survival Progression-free survival	Hazard ratio	High
Ueda (2018) N = 35 Retrospective cohort Follow-up: not reported	Japan	People with locally advanced and metastatic RCC who had failure of first-line TKI [Baseline characteristics showed that all participants had at least one organ with metastasis]	Second-line treatment with axitinib as second-line therapy	MSKCC IMDC/Heng	Overall Survival Progression-free survival	Hazard ratio	High

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Voss (2018) COMPARZ trial N = 927 RECORD-3 trial N = 471 Retrospective cohort study Follow-up: Not reported	US	COMPARZ trial: People aged 18 years and older, who had advanced or metastatic RCC with a clear cell histologic component, who had not received systemic treatment previously. Participants had measurable disease according to the Response Evaluation Criteria in Solid Tumours (RECIST) guidelines, a Karnofsky performance-status score of at least 70, and adequate organ function. RECORD-3 trial: People aged 18 years and older who had measurable clear cell or non-clear cell mRCC, with or without nephrectomy, and no prior systemic therapy. Participants had a Karnofsky performance status of 70% or greater; adequate hematologic, liver, and kidney function; and normal left ventricular ejection fraction.	COMPARZ trial: first-line treatment with pazopanib or sunitinib RECORD-3 trial: first-line everolimus followed by sunitinib at progression or first-line sunitinib followed by everolimus	MSKCC	Overall survival Progression-free survival	Model discrimination (C-stats)	Moderate

Study details	Setting/Location	Population	Treatment line	Risk prediction tool(s)	Outcomes predicted	Outcome measure	Risk of bias
Yao (2018) N = 218 Retrospective cohort study Follow-up: 60 months	China	Patients with mRCC.	VEGF-TKI as first-line treatment (Sunitinib or Sorafenib)	IMDC/Heng	Overall survival Progression-free survival	Hazard ratio	High

Abbreviations: ICI: immune checkpoint inhibitor, IFN-alpha: Interferon alpha, IMDC: International Metastatic Database Consortium, IO: immune-oncology, mRCC: metastatic renal cell carcinoma, MSKCC: Memorial Sloan Kettering Cancer Centre, mTOR: mammalian target of rapamycin, N: number of patients, RCC: renal cell carcinoma, VEFG: vascular endothelial growth factor, TKI: tyrosine kinase inhibitors

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 4.

Table 4 Interpretation of risk prediction tool 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 the risk groups if the 95% CI crosses the line of no effect.

Prior to cytoreductive nephrectomy

Table 5: Summary of findings for IMDC: cytoreductive nephrectomy (c-statistics)

Number of studies	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
Mixed RCC subtypes					
1 [Marchioni 2021]	Overall survival	519	0.60 (0.56, 0.64)	Very low	Poor

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

Table 6: Summary of findings for IMDC: cytoreductive nephrectomy (hazard ratio)

Number of studies	Outcome	Sample size	Effect estimate (hazard ratio)	Certainty	Interpretation
Poor risk vs favourable risk – mixed RCC subtypes					
2 [Laukhtina 2020, Lee 2017]	Overall survival	514	HR 1.58 (1.19, 2.09)	High	Risk of mortality significantly higher in poor risk group
Intermediate risk vs favourable risk – mixed RCC subtypes					
2 [Laukhtina 2020, Lee 2017]	Overall survival	773	HR 1.19 (0.99, 1.43)	Moderate	Could not differentiate

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

Table 7: Summary of findings for MSKCC: cytoreductive nephrectomy treatment (c-statistics)

Number of studies	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
Mixed RCC subtypes					
1 [Marchioni 2021]	Overall survival	519	0.60 (0.57, 0.64)	Very low	Poor

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

No evidence was identified for Meet-URO prior to treatment with cytoreductive nephrectomy.

Prior to first-line SACT

Table 8: Summary of findings for IMDC: first-line SACT (c-statistics)

Number of studies	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
Clear cell RCC subtype					
3 [Beuselinck 2014, de Velasco 2017, Shin 2021 (model cohort), Shin 2021 (external validation cohort)]	Overall survival	1,044	0.65 (0.62, 0.67)	Low	Poor
1 [Beuselinck 2024]	Progression-free survival	200	0.63 (0.58, 0.67)	Very low	Poor
Mixed RCC subtypes					

8 [Abduhelwa 2022, Cai 2017a, Chrom 2019, Chen 2019, Kroeger 2013, Ning 2022, Soerensen 2016, Tamura 2021]	Overall survival	5,053	0.65 (0.62, 0.68)	Very low	Poor
4 [Abduhelwa 2022, Cai 2017a, Kim 2019a, Ning 2022]	Progression-free survival	1,219	0.62 (0.56, 0.69)	Very low	Poor

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

Table 9: Summary of findings for IMDC: first-line SACT (hazard ratios and risk ratios)

Number of studies	Outcome	Sample size	Effect estimate (hazard ratio/risk ratio)	Certainty	Interpretation
Poor risk vs favourable risk – non-clear cell RCC subtype					
1 [Aktepe 2021b]	Overall survival	25	HR 10.20 (2.42, 42.97)	Very low	Risk of mortality significantly higher in poor risk group
1 [Aktepe 2021b]	Progression-free survival	25	HR 15.64 (4.52, 54.08)	Very low	Risk of disease progression significantly higher in poor risk group
Poor risk vs favourable risk – mixed RCC subtypes					
15 [Abuhelwa 2022, Aktepe 2022, Bayoglu 2023, Bolzacchini 2022, Cai 2017a, Chen 2019, Guida 2024, Kim 2018b (IMDC), Kroeger 2013, Li 2020, Lin 2018, Lolli 2016 (IMDC), Soerense 2016, Tamura 2021, Yao 2018]	Overall survival	2,645	HR 5.52 (4.15, 7.34)	Very low	Risk of mortality significantly higher in poor risk group
10 [Abduhelwa 2022, Bayoglu 2023, Bolzacchini 2022, Cai 2017a, Chen 2019, Guida 2024, Li 2020, Lin 2018, Lolli 2016 (IMDC), Yao 2018]	Progression-free survival	1,115	HRs not pooled due to high heterogeneity Median (IQR) 3.55 (2.05, 4.97)	Very low	Risk of disease progression significantly higher in poor risk group
Poor risk vs favourable risk – mixed RCC subtypes					

Number of studies	Outcome	Sample size	Effect estimate (hazard ratio/risk ratio)	Certainty	Interpretation
2 [Tamura 2021 (IMDC), Tanaka 2016 (first line, IMDC)]	Overall survival	252	RR 3.42 (2.42, 4.83)	Very low	Risk of mortality significantly higher in poor risk group
Poor risk vs favourable risk – clear cell RCC subtype					
2 [Beuselinck 2014; Gu 2017]	Overall survival	123	HR 6.07 (2.66, 13.88)	Very low	Risk of mortality significantly higher in poor risk group
2 [Beuselinck 2014; Gu 2017]	Progression-free survival	123	HR 4.67 (2.64, 8.25)	Very low	Risk of disease progression significantly higher in poor risk group
Poor risk vs favourable risk – clear cell RCC subtype					
1 (Rini 2019)	Overall survival	377	RR 6.74 (4.05, 11.22)	Very low	Risk of mortality significantly higher in poor risk group
1 (Rini 2019)	Progression-free survival	377	RR 2.02 (1.63, 2.50)	Very low	Risk of mortality significantly higher in poor risk group
Intermediate risk vs favourable risk – non-clear cell RCC subtype					
1 [Aktepe 2021b]	Overall survival	26	HR 0.90 (0.26, 3.97)	Very low	Could not differentiate
1 [Aktepe 2021b]	Progression-free survival	26	HR 1.32 (0.47, 3.73)	Very low	Could not differentiate
Intermediate risk vs favourable risk – mixed RCC subtypes					

Number of studies	Outcome	Sample size	Effect estimate (hazard ratio/risk ratio)	Certainty	Interpretation
15 [Abduhelwa 2022, Aktepe 2022, Bayoglu 2023, Bolzacchini 2022, Cai 2017a, Chen 2019, Guida 2024, Kim 2018b (IMDC), Kroeger 2013, Li 2020, Lin 2018, Lolli 2016 (IMDC), Soerense 2016, Tamura 2021, Yao 2018]	Overall survival	4,653	HR 1.83 (1.61, 2.08)	Low	Risk of mortality significantly higher in intermediate risk group
10 [Abduhelwa 2022, Bayoglu 2023, Bolzacchini 2022, Cai 2017a, Chen 2019, Guida 2024, Li 2020, Lin 2018, Lolli 2016 (IMDC), Yao 2018]	Progression-free survival	2,031	HR 1.41 (1.15, 1.73)	Very low	Risk of disease progression significantly higher in intermediate risk group
Intermediate risk vs favourable risk – mixed RCC subtypes					
2 [Tamura 2021 (IMDC), Tanaka 2016 (first line, IMDC)]	Overall survival	461	RR 2.16 (1.52, 3.07)	Very low	Risk of mortality significantly higher in intermediate risk group
Intermediate risk vs favourable risk – clear cell RCC subtype					
2 [Beuselinck 2014; Gu 2017]	Overall survival	229	HR 2.98 (1.33, 6.67)	Very low	Risk of mortality significantly higher in intermediate risk group
2 [Beuselinck 2014; Gu 2017]	Progression-free survival	229	HR 2.75 (1.70, 4.44)	Very low	Risk of disease progression significantly higher in intermediate risk group
Intermediate risk vs favourable risk – clear cell RCC subtype					
1 (Rini 2019)	Overall survival	753	RR 3.04 (1.85, 4.98)	Very low	Risk of mortality significantly higher in intermediate risk group

Number of studies	Outcome	Sample size	Effect estimate (hazard ratio/risk ratio)	Certainty	Interpretation
1 (Rini 2019)	Progression-free survival	753	RR 1.43 (1.18, 1.74)	Very low	Risk of mortality significantly higher in intermediate risk group
Poor risk vs intermediate risk – mixed RCC subtypes					
3 [Hara 2024; Kikuta 2025 – IOIO; Kikuta 2025 – IOTKI; Rebuzzi 2022]	Overall survival	553	HR 3.08 (2.34, 4.07)	Moderate	Risk of mortality significantly higher in poor risk group
3 [Hara 2024; Kikuta 2025 – IOIO; Kikuta 2025 – IOTKI; Rebuzzi 2022]	Progression-free survival	553	HR 1.96 (1.58, 2.43)	Moderate	Risk of disease progression significantly higher in poor risk group
Poor risk vs intermediate risk – mixed RCC subtypes					
2 (Tamura 2021 (IMDC); Tanaka 2016 (first line, IMDC))	Overall survival	491	RR 1.58 (1.38, 1.81)	Very low	Risk of mortality significantly higher in poor risk group
Poor risk vs intermediate risk – clear cell RCC					
1 (Rini 2019)	Overall survival	592	RR 2.22 (1.67, 2.95)	Very low	Risk of mortality significantly higher in poor risk group
1 (Rini 2019)	Progression-free survival	592	RR 1.41 (1.20, 1.66)	Very low	Risk of mortality significantly higher in poor risk group
Poor risk vs favourable + intermediate risk – non-clear cell RCC					
1 [Toyoda 2024]	Overall survival	75	HR 3.17 (1.48, 6.78)	Very low	Risk of mortality is significantly higher in the poor risk group

Number of studies	Outcome	Sample size	Effect estimate (hazard ratio/risk ratio)	Certainty	Interpretation
1 [Toyoda 2024]	Progression-free survival	75	HR 1.14 (0.61, 2.14)	Very low	Risk of disease progression significantly higher in the poor risk group
Poor risk vs favourable + intermediate risk – mixed RCC subtypes					
3 [Kim 2019b, Miyake 2016a (IMDC), Schuttke 2024]	Overall survival	402	HR 2.36 (1.64, 3.39)	Very low	Risk of mortality significantly higher in poor risk group
2 [Kim 2019b, Schuttke 2024]	Progression-free survival	131	HR 1.77 (1.15, 2.79)	Low	Risk of disease progression significantly higher in poor risk group

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

Table 10: Summary of findings for MSKCC: first-line SACT (c-statistics)

Number of studies	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
Clear cell RCC					
2 [de Velasco 2017, Voss 2018]	Overall survival	981	0.59 (0.56, 0.63)	Low	Very poor
1 [Voss 2018]	Progression-free survival	927	0.57 (0.53, 0.60)	Very low	Very poor
Mixed RCC subtypes					

Number of studies	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
7 [Cai 2017c, Kroeger 2013, Lu 2016, Shin 2021 (external validation cohort), Shin 2021 (model cohort), Tamura 2021, Voss 2018]	Overall survival	4,052	0.66 (0.64, 0.68)	Low	Poor
2 [Cai 2017c, Kim 2019a]	Progression-free survival	340	0.67 (0.62, 0.71)	Very low	Poor

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

Table 11: Summary of findings for MSKCC: first-line SACT (hazard ratios and risk ratios)

Number of studies	Outcome	Sample size	Effect estimate (hazard ratios/risk ratios)	Certainty	Interpretation
Poor risk vs favourable risk – mixed RCC subtype					
5 [Cetin 2013, Fiala 2020, Kim 2018b, Lolli 2016, Tamura 2021]	Overall survival	1,361	HR 4.49 (3.75, 5.38)	Low	Risk of mortality significantly higher in poor risk group
3 [Cetin 2013, Fiala 2020, Lolli 2016]	Progression-free survival	886	HR 2.86 (2.39, 3.43)	Very low	Risk of disease progression significantly higher in poor risk group
Poor risk vs favourable risk – mixed RCC subtype					
3 [Bamias 2010, Tamura 2021, Tanaka 2016]	Overall survival	269	RR 3.44 (2.46, 4.81)	Moderate	Risk of mortality significantly higher in poor risk group
Poor risk vs favourable risk – clear cell RCC					
1 [Giridhar 2017]	Overall survival	35	RR 1.86 (1.17, 2.95)	Very low	Risk of mortality significantly higher in poor risk group
Intermediate risk vs favourable risk – mixed RCC subtype					

Number of studies	Outcome	Sample size	Effect estimate (hazard ratios/risk ratios)	Certainty	Interpretation
5 [Cetin 2013, Fiala 2020, Kim 2018b, Lolli 2016, Tamura 2021]	Overall survival	3,232	HR 1.73 (1.56, 1.93)	Low	Risk of mortality significantly higher in intermediate risk group
3 [Cetin 2013, Fiala 2020, Lolli 2016]	Progression-free survival	1,904	HR 1.51, (1.37, 1.65)	Low	Risk of disease progression significantly higher in intermediate risk group
Intermediate risk vs favourable risk – mixed RCC subtype					
3 [Bamias 2010, Tamura 2021, Tanaka 2016]	Overall survival	577	RR 2.24 (1.60, 3.14)	High	Risk of mortality significantly higher in intermediate risk group
Intermediate risk vs favourable risk – clear cell RCC					
1 [Giridhar 2017]	Overall survival	431	RR 1.03 (0.53, 2.02)	Very low	Could not differentiate
Poor risk vs intermediate risk – mixed RCC subtypes					
3 [Bamias 2010, Tamura 2021, Tanaka 2016]	Overall survival	577	RR 1.54 (1.36, 1.75)	Low	Risk of mortality significantly higher in poor risk group
Poor risk vs intermediate risk – clear cell RCC					
1 [Giridhar 2017]	Overall survival	167	RR 1.80 (0.97, 3.34)	Very low	Could not differentiate
Poor risk vs favourable + intermediate risk – mixed RCC subtypes					
2 [Miyake 2016a, Miyazake 2015]	Overall survival	456	HR 3.89 (2.06, 7.36)	Very low	Risk of mortality significantly higher in poor risk group
1 [Miyake 2014]	Progression free survival	110	HR 3.89 (1.74, 8.70)	Very low	Risk of disease progression significantly higher in poor risk group

Number of studies	Outcome	Sample size	Effect estimate (hazard ratios/risk ratios)	Certainty	Interpretation
Intermediate + poor risk vs favourable risk – mixed RCC subtypes					
1 [Lu 2016]	Overall survival	67	HR 2.25 (1.26, 4.02)	Very low	Risk of mortality significantly higher in intermediate + poor risk group

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

Table 12: Summary of findings for Meet-URO: first-line SACT (hazard ratios)

Number of studies	Outcome	Sample size	Effect estimate (hazard ratios)	Certainty	Interpretation
Score 5 vs score 2 – mixed RCC subtype					
1 [Rebuzzi 2022a]	Overall survival	117	HR 16.03 (7.74, 33.20)	Very low	Risk of mortality significantly higher with score 5
1 [Rebuzzi 2022a]	Progression-free survival	117	HR 6.56 (3.97, 10.83)	Very low	Risk of disease progression significantly higher with score 5
Score 4 vs score 2 – clear cell RCC					
1 [Rebuzzi 2022a]	Overall survival	190	HR 6.07 (3.16, 11.66)	Very low	Risk of mortality significantly higher with score 4
1 [Rebuzzi 2022a]	Progression-free survival	190	HR 2.77 (1.88, 4.08)	Very low	Risk of disease progression significantly higher with score 4

Score 3 vs score 2 – mixed RCC subtype					
1 [Rebuzzi 2022a]	Overall survival	177	HR 3.09 (1.54, 6.20)	Very low	Risk of mortality significantly higher with score 3
1 [Rebuzzi 2022a]	Progression-free survival	177	HR 2.05 (1.38, 3.05)	Very low	Risk of disease progression significantly higher with score 3

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

Prior to second-line SACT

Table 13: Summary of findings for IMDC: second-line SACT (c-statistics)

Number of studies	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
Mixed RCC subtypes					
2 [Derosa 2019 (discovery), Derosa 2019 (validation), Ko 2015]	Overall survival	2,190	0.64 (0.58, 0.69)	Very low	Poor

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

Table 14: Summary of findings for IMDC: second-line SACT (hazard ratios and risk ratios)

Number of studies	Outcome	Sample size	Effect estimate (hazard ratio)	Certainty	Interpretation
Poor risk vs favourable risk – mixed RCC subtypes					
2 [Derosa 2019 (discovery, IMDC), Derosa 2019 (validation, IMDC), Ko 2015]	Overall survival	654	HR 5.87 (4.48, 7.69)	Low	Risk of mortality significantly higher in poor risk group
Poor risk vs favourable risk – mixed RCC subtypes					

Number of studies	Outcome	Sample size	Effect estimate (hazard ratio)	Certainty	Interpretation
2 [Derosa 2019 (discovery), Derosa 2019 (validation), Tanaka 2016 (second-line)]	Overall survival	366	RR 2.53 (1.56, 4.11)	Very low	Risk of mortality significantly higher in poor risk group
Intermediate risk vs favourable risk – mixed RCC subtypes					
2 [Derosa 2019 (discovery, IMDC), Derosa 2019 (validation, IMDC), Ko 2015]	Overall survival	1,436	HR 1.85 (1.42, 2.40)	Low	Risk of mortality significantly higher in intermediate risk group
Intermediate risk vs favourable risk – mixed RCC subtypes					
2 [Derosa 2019 (discovery). Derosa 2019 (validation), Tanaka 2016 (second-line)]	Overall survival	956	RR 1.52 (1.14, 2.04)	Moderate	Risk of mortality significantly higher in intermediate risk group
Poor risk vs Favourable + intermediate risk – mixed RCC subtypes					
3 [Matsushita 2024 (IMDC), Miyake 2016b (IMDC), Ueda 2018 (IMDC)]	Overall survival	549	HR 2.79 (1.62, 4.83)	Very low	Risk of mortality significantly higher in poor risk group

Number of studies	Outcome	Sample size	Effect estimate (hazard ratio)	Certainty	Interpretation
3 [Matsushita 2024 (IMDC), Miyake 2017, Ueda 2018 (IMDC)]	Progression-free survival	402	HR 1.23 (0.53, 2.88)	Very low	Could not differentiate
Poor risk vs intermediate risk – non-clear cell RCC					
1 [Fujita 2024]	Overall survival	52	HR 2.74 (1.15, 6.52)	Very low	Risk of mortality significantly higher in poor risk group
1 [Fujita 2024]	Progression-free survival	52	HR 1.98 (1.02, 3.83)	Very low	Risk of progression significantly higher in the poor risk group

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

Table 15: Summary of findings for MSKCC: second-line SACT (c-statistics)

Number of studies	Outcome	Sample size	Effect estimate (c-statistic)	Certainty	Interpretation of discriminative ability
Mixed RCC subtypes					
3 [Derosa 2019 (discovery) Derosa 2019 (validation) Ko 2015]	Overall survival	2,190	0.62 (0.55, 0.69)	Very low	Poor

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

Table 16: Summary of findings for MSKCC: second-line SACT (hazard ratios and risk ratios)

Number of studies	Outcome	Sample size	Effect estimate (hazard ratios/risk ratios)	Certainty	Interpretation
Poor risk vs favourable risk – mixed RCC subtype					
2 [Derosa 2019 (discovery), Derosa 2019 (validation)]	Overall survival	525	HR 8.20 (3.80, 17.71)	Low	Risk of mortality significantly higher in poor risk group
3 [Derosa 2019 (discovery), Derosa 2019 (validation), Tanaka 2016]	Overall survival	545	RR 2.29 (1.37, 3.82)	Very low	Risk of mortality significantly higher in poor risk group

Number of studies	Outcome	Sample size	Effect estimate (hazard ratios/risk ratios)	Certainty	Interpretation
Intermediate risk vs favourable risk – mixed RCC subtype					
2 [Derosa 2019 (discovery), Derosa 2019 (validation)]	Overall survival	1,070	HR 2.29 (1.93, 2.72)	Low	Risk of mortality significantly higher in intermediate risk group
3 [Derosa 2019 (discovery), Derosa 2019 (validation), Tanaka 2016]	Overall survival	1,195	HRs not pooled due to high heterogeneity Median (IQR) 1.47 (1.35, 1.61)	Very low	Risk of mortality significantly higher in intermediate risk group
Poor risk vs intermediate risk – mixed RCC subtype					
3 [Derosa 2019 (discovery), Derosa 2019 (validation), Tanaka 2016]	Overall survival	728	RR 1.57 (0.99, 2.48)	Very low	Could not differentiate
Poor risk vs favourable + intermediate risk – mixed RCC subtype					
3 [Matsushita 2024, Miyake 2016b, Udea 2018]	Overall survival	549	3.16 (2.13, 4.67)	High	Risk of mortality significantly higher in poor risk group
3 [Matsushita 2024, Miyake 2017, Udea 2018]	Progression-free survival	402	2.24 (1.60, 3.13)	Moderate	Risk of disease progression significantly higher in poor risk group

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

Prior to subsequent-line SACT

No evidence was identified for use of risk prediction models prior to subsequent-line SACT.

See appendix F for full GRADE tables.

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 – Literature search strategies. This search retrieved 787 studies, and none of these studies were considered relevant or applicable for either review question at title and abstract screening.

1.1.7.1 Included studies

No studies were included for this evidence review (see Appendix G – Economic evidence study selection).

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 discussed the outcomes specified in the protocol. They agreed that the most useful outcome that the risk prediction tools predict for metastatic renal cell carcinoma would be overall survival (OS), in terms of management, as well as being important to the individual. Lay members highlighted that predicting both OS and progression-free survival (PFS) information would be important to them as PFS could affect quality of life. However, it was noted that people can have PFS benefits but without quality-of-life benefits.

In order for prediction tools to be useful for guiding management of metastatic RCC, the committee agreed that they need to be able to discriminate well between different risk groups, and they 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. They can be linked directly to decision making by identifying all those at risk of progression or death and therefore guiding management. 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 (high risk and low risk) and the risk of an event associated with the classification.

1.1.12.2 The certainty of the evidence

Evidence was identified for each of the tools in the protocol: IMDC, MSKCC and Meet-Uro. Most of the evidence was assessed to be low or very low certainty with the majority downgraded for risk of bias. Concerns around the risk of bias included limited information provided by studies on the analysis, inappropriate handling of missing data and insufficient numbers of outcome events. Evidence was downgraded for inconsistency due to variation in the results from individual studies. Evidence was also downgraded for imprecision due to the HR or RR results coming from analyses where the sample size was smaller than 500 or the 95% CI crossed the line of no effect, and for c-statistics where the effect estimate crossed more than one category of classification accuracy.

The evidence for discrimination in this review was limited to results reported using c-statistics as the data needed to calculate sensitivity and specificity was not reported in the studies. The committee were aware of the limitations of the c-statistic, which looks at classification accuracy but places equal weight on false positives and false negatives. They noted that in practice the tools would be used to classify people into different risk groups to help identify those at high-risk of disease progression or death, who may benefit from systemic anti-cancer therapy or other treatments. In the absence of sensitivity and specificity data, the committee agreed that c-statistic data could provide information to guide clinicians to select a suitable tool to help clinicians with treatment decisions coupled with a larger risk of the outcome of interest, shown by the hazard ratio (HR) or risk ratio (RR), in more severe groups compared to less severe risk groups.

There was no data available for different subgroups of interest within individual studies, however, analyses were stratified by RCC subtype and line of SACT where possible at the study level. The committee highlighted that IMDC was developed for clear cell RCC and has been validated in the non-clear cell population. Most of the available evidence identified was related to clear cell RCC or not reported by subtype and there was therefore more uncertainty around the use of these tools in non-clear cell RCC subtypes.

1.1.12.3 Benefits and harms

The evidence was presented to the committee based on where in the treatment pathway the risk prediction tools were applied in the studies. This was prior to cytoreductive nephrectomy, prior to first-line systemic anti-cancer therapy (SACT) and prior to second-line SACT. No evidence was identified for the tools being applied prior to subsequent-line SACT.

Risk prediction tools applied prior to cytoreductive nephrectomy (no SACT)

There was some evidence identified for the use of IMDC and MSKCC prior to cytoreductive nephrectomy. C-statistics showed that both tools had poor ability to discriminate between different risk groups for overall survival. However, the evidence came from just one study. Clinical data from 1 study with participants who had either clear cell or non-clear cell RCC (data not provided separately for subtypes) using IMDC, suggested there was a statistically significant higher risk of mortality (reported as a hazard ratio, HR) in the poor risk group compared to the favourable risk group, but it was not possible from the evidence to differentiate between intermediate risk and favourable risk groups. However, the magnitude of the increased risk was relatively small compared to the results from studies using the tool prior to first-line SACT.

The committee noted that IMDC and MSKCC are used in practice in some places as part of decision making prior to cytoreductive nephrectomy, and that cytoreductive nephrectomy would not generally be performed in people with a poor IMDC risk score. The committee also highlighted the importance of evaluating the extent of disease, the fitness of the person, and the person's symptoms when assessing suitability for cytoreductive nephrectomy.

Risk prediction tools applied prior to first-line SACT

The evidence reported c-statistics as a measure for the ability of IMDC and MSKCC to discriminate between the different risk groups for OS and PFS outcomes, when the tools are applied prior to first-line SACT. These ranged between very poor and poor discriminative ability for MSKCC and poor discriminative ability for IMDC. No c-statistic data related to Meet-URO was identified.

The majority of the evidence came from studies where people had either clear cell or non-clear cell RCC and outcomes were not reported separately for subtypes, or the studies did not specify the subtype. However, the committee noted that most of the participants of these studies were likely to have had clear cell RCC subtype as this is the most common subtype.

Clinical evidence reporting HRs was identified for all 3 risk prediction tools, while some studies reported results as RRs. In summary, the evidence shows that IMDC, MSKCC, and Meet-URO were able to differentiate well between the different risk categories in most studies where data was available for participants with non-clear cell RCC, clear cell RCC, or a mixed population of both subtypes. The magnitude of the HRs (or RRs) varied but for IMDC, for example, there was a large or very large increased risk of progression or mortality in the poor risk category compared to the favourable one. Similarly, when comparing the poor and intermediate risk groups for IMDC the risk was higher in the poor risk group, however, results were mixed when comparing intermediate and favourable risk groups. The evidence showed that MSKCC was able to differentiate between poor and favourable risk groups for overall survival and progression-free survival, however, results were mixed when comparing both poor with intermediate risk groups and intermediate with favourable risk groups. Where a difference between risk groups could not be detected, this could be due to an insufficient sample size or due to the relatively poor discriminative ability of these tools (as assessed by the c-statistic above).

Although the results reported as HR showed statistically significant differences in risk of mortality and progression across the risk groups, the committee highlighted that there is some subjectivity in how people are classified into the groups by the tools because they all use the Karnofsky performance score (KPS) to rate performance status. This score consists of an 11-point rating system and is subjective in nature. This means that the resulting risk classification can change depending on how the KPS is applied and ultimately impact eligibility for SACT. Therefore, the committee stressed the need for clinical judgment to be used together with any risk tools to inform decisions around treatment options.

Risk prediction tools applied prior to second-line SACT

In summary, risk prediction tools applied before second-line SACT showed that c-statistics values of the IMDC and MSKCC tools had poor discriminative ability to predict OS in a mixed RCC study population. There was no c-statistic data for PFS. There was limited HR and RR data for IMDC and MSKCC. However, where evidence was available the higher of the two risk groups being compared generally showed an increased risk of mortality or progression, except for the poor versus intermediate MSKCC risk group comparison, where risk of

mortality could not be differentiated. There was no data for Meet-URO for this stage in the pathway.

The committee highlighted potential complexities in applying these risk prediction tools to predict overall survival risk in people undergoing second-line or subsequent treatments, as prior interventions may potentially bias predictive results due to selection bias. People requiring second-line treatment due to recurrence or progression may have a renal lesion that is more aggressive. The committee agreed that factors such as how long individuals have been on treatment and their response, frailty, and other risk factors would be important at this stage in the pathway.

Drafting the recommendations

The committee noted that the MSKCC, IMDC and Meet-Uro risk prediction tools were developed at different treatment eras for kidney cancer. MSKCC was developed before the anti-angiogenic era, while IMDC and Meet-Uro were developed when anti-angiogenic drugs were available. From their experience, the most used risk prediction tool in current clinical practice is the IMDC tool. The committee agreed that in practice they usually group IMDC poor and intermediate-risk groups together and discussed the possibility of combining data by different risk groups in this manner. However, the available data was not presented in a manner to allow this re-analysis, and although some studies did group risk categories together for analysis, this involved mostly the favourable and intermediate risk groups being combined, rather than poor and intermediate risk groups being combined, which would have been the committee's desired option. The committee were aware that NICE technology appraisals (TAs) of metastatic RCC treatments include IMDC risk stratification as part of their eligibility criteria and also consider poor and intermediate-risk groups together.

The committee discussed the importance of having the information needed to calculate the risk score available for the risk prediction tool to be useful. They noted that the MSKCC risk prediction tool requires measurement of lactate dehydrogenase (LDH) which is not always readily available. IMDC does not require LDH to calculate a score which makes it easier to implement. Using MSKCC represents an additional cost to the NHS because it requires measurement of LDH. Meet-URO classifies people differently compared to IMDC and MSKCC and does not map easily to favourable, intermediate, and poor risk groups. In addition, Meet-URO requires data on the presence of bone metastases which would need a dedicated bone scan. The committee advised that indications for a bone scan are more symptom-based, and a bone scan is usually performed only when there is a report of pain. The committee agreed that individuals with bone metastases generally perform worse, and it is common to observe variability in how these individuals are classified into risk groups.

Whilst the discriminative ability for each of the risk prediction tools was not rated as good or above based on c-statistics, IMDC and MSKCC were able to classify people into poor risk and favourable risk groups sufficiently well, so that there was a statistically significant difference in risk between the 2 groups for OFS and PFS. Therefore, the committee agreed that the tools could still provide useful information to support the decision-making process about future treatment options. As the IMDC tool is already used commonly in practice, is used when determining eligibility for some SACT according to associated TAs and does not require the additional tests of LDH and bone scans needed for MSKCC and Meet-Uro respectively, the committee made a recommendation to consider the use of IMDC when making decisions about treatment options for metastatic RCC. The committee agreed that IMDC can be useful for predicting OS, however, there was less evidence around the use of

IMDC for predicting PFS, and available c-statistic evidence was very low certainty, so they limited their recommendation to using this tool to predict OS.

The committee agreed that risk prediction tools can be used to predict OS as part of the decision-making process about future treatment options. However, they agreed that because the discriminative ability of existing risk prediction tools was poor at best, these tools should only be used alongside clinical judgment when determining future treatment approaches. The committee highlighted that the decision-making process around treatment options should involve a comprehensive assessment of the individual clinical characteristics such as their fitness, frailty and any comorbidities.

The majority of the evidence came from studies where the risk prediction tools were applied before first-line systemic therapy. Whilst the use of IMDC has been validated beyond first-line systemic therapy, the committee agreed that users need to be aware that there is more uncertainty around the usefulness and accuracy of the tools in predicting OS prior to people receiving second- and subsequent-line systemic therapy, due to the potential bias that could be introduced by previous interventions received. Other factors that might be relevant when decisions are made about second- or subsequent-line therapy and would be expected to fall under the use of clinical judgement included how long individuals have been on a treatment, response to that treatment, previous experiences of side effects.

There was no evidence on the use of risk prediction tools in people with rare renal carcinoma subtypes such as medullary carcinoma, collecting duct carcinoma and there was also no evidence on the use of these tools in people with heritable RCC predisposition syndromes. Therefore, the recommendation highlighted the uncertainty around the usefulness and accuracy of the IMDC in these populations and when making decisions about second- or subsequent-line therapy.

The committee were aware that some technology appraisals (TAs) or NHS clinical commissioning criteria used specific risk prediction tools (such as the IMDC) to help determine which treatments are suitable for people. To future proof the guideline the committee recommended that where this happens and SACT is indicated, the relevant tool should be used in addition to the IMDC.

To reduce variation in clinical practice, improve record keeping and promote use of risk prediction tools, the committee recommended that the results of the risk score are recorded clearly in the person's clinical records before any decisions about future treatment options are made.

The committee highlighted that there is variation in practice around the information that is provided to people with metastatic RCC about risk prediction tools, with some people not receiving enough information about their risk of progression or survival, and often not understanding what the scores mean in terms of management and care options going forward. The committee agreed that it was important to share information about the name of the tool, the purpose of using it, what the results mean for the person and how they can be used to inform treatment decisions, as well as highlighting where there are more uncertainties associated with using the tool (such as in people with rarer RCC subtypes because most of the data supporting the tool comes from people with clear cell RCC).

The committee also drafted a research recommendation to promote the development and validation of a new risk prediction tool (or the identification of biomarkers or clinical factors that could be used to develop such a tool) for people with metastatic RCC because the

existing tools had poor discriminative ability. Most of the evidence came from people with clear cell RCC, because the populations in studies that did not stratify by RCC subtype were made up mostly of people with clear cell RCC. Therefore, the committee noted that there was little data on the usefulness of these tools for rarer RCC subtypes, and that it would be useful to be able to predict outcomes including survival, risk of disease progression, or response to treatment. They therefore specified that the tool or tools should accurately predict these outcomes in all subtypes of metastatic renal cell carcinoma.

1.1.12.4 Cost effectiveness and resource use

No published economic evidence was identified and original economic modelling was not conducted 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. These tools are expected to lead to better management options and potentially improve outcomes (at no additional cost), and therefore their use is likely cost-effective. The recommendations made on risk prediction tools for metastatic RCC are broadly aligned with current clinical practice, and are not expected to have a substantial resource impact but encourage standardisation of practice.

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.13.1 to 1.13.5 and the research recommendation on Risk prediction tools for metastatic renal cell carcinoma.

1.1.14 References – included studies

1.1.14.1 Prognostic

Abuhelwa, A.Y., Bellmunt, J., Kichenadasse, G. et al. (2022) C-reactive protein provides superior prognostic accuracy than the IMDC risk model in renal cell carcinoma treated with Atezolizumab/Bevacizumab. Frontiers in Oncology 12: 918993

Aktepe, O.H. and Erman, M. (2021) Survival outcomes of patients in advanced non-clear renal cell carcinoma treated with pazopanib: A retrospective single institution experience. UHOD - Uluslararasi Hematoloji-Onkoloji Dergisi 31(3): 170-177

Aktepe, Oktay Halit, Gundogdu, Fatma, Kosemehmetoglu, Kemal et al. (2022) THSD7A expression: a novel immunohistochemical determinant in predicting overall survival of metastatic renal cell carcinoma treated with targeted therapy. Irish journal of medical science 191(4): 1561-1567

Bamias, Aristotelis, Karadimou, Alexandra, Lampaki, Sofia et al. (2010) Prognostic stratification of patients with advanced renal cell carcinoma treated with sunitinib: comparison with the Memorial Sloan-Kettering prognostic factors model. BMC cancer 10: 45

Bayoglu, Ibrahim Vedat, Huseynov, Javid, Topal, Alper et al. (2023) PNI as a Potential Add-On Biomarker to Improve the IMDC Intermediate Prognostic Score. Journal of clinical medicine 12(19)

Beuselinck, Benoit, Vano, Yann-Alexandre, Oudard, Stephane et al. (2014) Prognostic impact of baseline serum C-reactive protein in patients with metastatic renal cell carcinoma (RCC) treated with sunitinib. BJU international 114(1): 81-9

Bolzacchini, Elena, Giordano, Monica, Bertu, Lorenza et al. (2022) Prognostic role of hematologic parameters of metastatic renal cell carcinoma treated with sunitinib. Tumori 108(5): 502-509

Cai, Wen, Zhang, Jin, Chen, Yonghui et al. (2017) Association of post-treatment hypoalbuminemia and survival in Chinese patients with metastatic renal cell carcinoma. Chinese journal of cancer 36(1): 47

Cai, Wen, Zhong, Hai, Kong, Wen et al. (2017) Significance of preoperative prognostic nutrition index as prognostic predictors in patients with metastatic renal cell carcinoma with tyrosine kinase inhibitors as first-line target therapy. International urology and nephrology 49(11): 1955-1963

Cetin, Bulent, Berk, Veli, Kaplan, Mehmet Ali et al. (2013) Is the pretreatment neutrophil to lymphocyte ratio an important prognostic parameter in patients with metastatic renal cell carcinoma?. Clinical genitourinary cancer 11(2): 141-8

Chen, Xiang, Yao, JiaXi, Liu, Li et al. (2019) Serum Alpha1-Globulin as a Novel Prognostic Factor in Metastatic Renal Cell Carcinoma Treated with Tyrosine Kinase Inhibitors. Targeted oncology 14(2): 187-195Choueiri TK, Powles T, Burotto M et al. (2021) Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. The New England journal of medicine 384(9): 829-841

Chrom, Pawel, Zolnierek, Jakub, Bodnar, Lubomir et al. (2019) External validation of the systemic immune-inflammation index as a prognostic factor in metastatic renal cell carcinoma and its implementation within the international metastatic renal cell carcinoma database consortium model. International journal of clinical oncology 24(5): 526-532

de Velasco, Guillermo, Culhane, Aedin C, Fay, Andre P et al. (2017) Molecular Subtypes Improve Prognostic Value of International Metastatic Renal Cell Carcinoma Database Consortium Prognostic Model. The oncologist 22(3): 286-292

Derosa, Lisa, Bayar, Mohamed Amine, Albiges, Laurence et al. (2019) A new prognostic model for survival in second line for metastatic renal cell carcinoma: development and external validation. Angiogenesis 22(3): 383-395

Fiala, Ondrej, Finek, Jindrich, Poprach, Alexandr et al. (2020) Outcomes According to MSKCC Risk Score with Focus on the Intermediate-Risk Group in Metastatic Renal Cell Carcinoma Patients Treated with First-Line Sunitinib: A Retrospective Analysis of 2390 Patients. Cancers 12(4)

Fujita, Kazutoshi, Matsushita, Yuto, Toyoda, Shingo et al. (2024) The efficacy of second-line tyrosine kinase inhibitor for patients with metastatic non-clear cell renal cell carcinoma following first-line immune-oncology combination therapy. World journal of urology 42(1): 536

Giridhar, Karthik V, Sosa, Carlos P, Hillman, David W et al. (2017) Whole Blood mRNA Expression-Based Prognosis of Metastatic Renal Cell Carcinoma. International journal of molecular sciences 18(11)

Guida, Annalisa, Gili, Alessio, Mosillo, Claudia et al. (2024) Efficacy and Safety of Pembrolizumab plus Axitinib combination for Metastatic Renal Cell Carcinoma in a Real-World Scenario: Data From the Prospective ProPAXI Study. Clinical genitourinary cancer 22(6): 102225

Gu, Weijie, Wu, Junlong, Liu, Xiaohang et al. (2017) Early skeletal muscle loss during target therapy is a prognostic biomarker in metastatic renal cell carcinoma patients. Scientific reports 7(1): 7587Hara, Takuto, Ueki, Hideto, Okamura, Yasuyoshi et al. (2025) Comparative prognostic value of tumor volume in IOIO and IOTKI treatment for metastatic renal cancer. Urologic oncology 43(1): 63e19-63e27

Kikuta, Masato, Naito, Sei, Osawa, Takahiro et al. (2025) Real-world short-term outcomes and treatment regimen comparisons in patients with metastatic renal cell carcinoma treated with first-line immune combinations. BMC cancer 25(1): 117

Kim, Jung Kwon, Kim, Sung Han, Song, Mi Kyung et al. (2019) Application of the International Metastatic Renal Cell Carcinoma Database Consortium and Memorial Sloan Kettering Cancer Center Risk Models in Patients with Metastatic Non-Clear Cell Renal Cell Carcinoma: A Multi-Institutional Retrospective Study Using the Korean Metastatic Renal Cell Carcinoma Registry. Cancer research and treatment 51(2): 758-768

Kim, Myung Soo, Chung, Ho Seok, Hwang, Eu Chang et al. (2018) Efficacy of First-Line Targeted Therapy in Real-World Korean Patients with Metastatic Renal Cell Carcinoma: Focus on Sunitinib and Pazopanib. Journal of Korean medical science 33(51): e325

Kim, Sung Han, Kim, Jung Kwon, Park, Eun Young 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

Ko, Jenny J, Xie, Wanling, Kroeger, Nils et al. (2015) The International Metastatic Renal Cell Carcinoma Database Consortium model as a prognostic tool in patients with metastatic renal cell carcinoma previously treated with first-line targeted therapy: a population-based study. The Lancet. Oncology 16(3): 293-300

Kroeger, Nils, Xie, Wanling, Lee, Jae-Lyn et al. (2013) Metastatic non-clear cell renal cell carcinoma treated with targeted therapy agents: characterization of survival outcome and application of the International mRCC Database Consortium criteria. Cancer 119(16): 2999-3006

Laukhtina, Ekaterina, Pradere, Benjamin, D Andrea, David et al. (2020) Association of preoperative serum De Ritis ratio with oncological outcomes in patients treated with cytoreductive nephrectomy for metastatic renal cell carcinoma. Urologic oncology 38(12): 936e7-936e14

Lee H, Kim YJ, Hwang EC et al. (2017) Preoperative cholesterol level as a new independent predictive factor of survival in patients with metastatic renal cell carcinoma treated with cytoreductive nephrectomy. BMC cancer 17(1): 364

Li, Tao, Li, Heng, Xie, Sheng et al. (2020) Lactate Dehydrogenase-to-Lymphocyte Ratio Represents a Powerful Prognostic Tool of Metastatic Renal Cell Carcinoma Patients Treated with Tyrosine Kinase Inhibitors. Pathology oncology research : POR 26(2): 1319-1324

Lin, Zhiyuan, Liu, Li, Xia, Yu et al. (2018) Tumor infiltrating CD19+ B lymphocytes predict prognostic and therapeutic benefits in metastatic renal cell carcinoma patients treated with tyrosine kinase inhibitors. Oncoimmunology 7(10): e1477461

Lee H, Kim YJ, Hwang EC et al. (2017) Preoperative cholesterol level as a new independent predictive factor of survival in patients with metastatic renal cell carcinoma treated with cytoreductive nephrectomy. BMC cancer 17(1): 364

Lolli, Cristian, Basso, Umberto, Derosa, Lisa et al. (2016) Systemic immune-inflammation index predicts the clinical outcome in patients with metastatic renal cell cancer treated with sunitinib. Oncotarget 7(34): 54564-54571

Lu, Xiaolin, Gu, Weijie, Zhang, Hailiang et al. (2016) Oligometastatic state predicts a favorable outcome for renal cell carcinoma patients with bone metastasis under the treatment of sunitinib. Oncotarget 7(18): 26879-87

Marchioni, Michele, Kriegmair, Maximilian, Heck, Mathias et al. (2021) Development of a Novel Risk Score to Select the Optimal Candidate for Cytoreductive Nephrectomy Among Patients with Metastatic Renal Cell Carcinoma. Results from a Multi-institutional Registry (REMARCC). European urology oncology 4(2): 256-263

Matsushita, Yuto, Kojima, Takahiro, Osawa, Takahiro et al. (2024) Prognostic outcomes in patients with metastatic renal cell carcinoma receiving second-line treatment with tyrosine kinase inhibitor following first-line immune-oncology combination therapy. International journal of urology : official journal of the Japanese Urological Association 31(5): 526-533

Miyake, Hideaki, Harada, Ken-Ichi, Ozono, Seiichiro et al. (2017) Assessment of Efficacy, Safety, and Quality of Life of 124 Patients Treated With Axitinib as Second-Line Therapy for Metastatic Renal-Cell Carcinoma: Experience in Real-World Clinical Practice in Japan. Clinical genitourinary cancer 15(1): 122-128

Miyake, Hideaki, Harada, Ken-Ichi, Ozono, Seiichiro et al. (2016) Prognostic Significance of Early Tumor Shrinkage Under Second-Line Targeted Therapy for Metastatic Renal Cell Carcinoma: A Retrospective Multi-Institutional Study in Japan. Molecular diagnosis & therapy 20(4): 385-92

Miyake, Hideaki, Miyazaki, Akira, Harada, Ken-Ichi et al. (2014) Assessment of efficacy, safety and quality of life of 110 patients treated with sunitinib as first-line therapy for metastatic renal cell carcinoma: experience in real-world clinical practice in Japan. Medical oncology (Northwood, London, England) 31(6): 978

Miyake, Hideaki, Miyazaki, Akira, Imai, Satoshi et al. (2016) Early Tumor Shrinkage Under Treatment with First-line Tyrosine Kinase Inhibitors as a Predictor of Overall Survival in Patients with Metastatic Renal Cell Carcinoma: a Retrospective Multi-Institutional Study in Japan. Targeted oncology 11(2): 175-82

Miyazaki, Akira, Miyake, Hideaki, Harada, Ken-Ichi et al. (2015) Prognostic outcome in patients treated with tyrosine kinase inhibitors as first-line molecular-targeted therapy for metastatic renal cell carcinoma: Experience in real-world clinical practice in Japan. Molecular and clinical oncology 3(3): 601-606

Ning, Kang, Li, Zhen, Liu, Huiming et al. (2022) Perirenal Fat Thickness Significantly Associated with Prognosis of Metastatic Renal Cell Cancer Patients Receiving Anti-VEGF Therapy. Nutrients 14(16)

Rebuzzi, S E, Signori, A, Buti, S et al. (2022) Validation of the Meet-URO score in patients with metastatic renal cell carcinoma receiving first-line nivolumab and ipilimumab in the Italian Expanded Access Program. ESMO open 7(6): 100634

Rini BI, Plimack ER, Stus V et al. (2019) Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. The New England journal of medicine 380(12): 1116-1127

Schuttke, Vayda, Kusiek, Cathrin, Fuessel, Susanne et al. (2024) Early kinetics of C-reactive protein as prognosticator for survival in a real-world cohort of patients with metastatic renal cell cancer under first-line therapy with immune checkpoint inhibitors. Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico 26(5): 1117-1128

Shin, Dongrul, Jeong, Chang Wook, Song, Cheryn et al. (2021) Prognostic factors for overall survival in patients with clear cell metastatic renal cell carcinoma: Model development and external validation with Memorial Sloan Kettering Cancer Center model and the international metastatic renal cell carcinoma database consortium model. Medicine 100(31): e26826

Smith, Andrew D, Shah, Shetal N, Rini, Brian I et al. (2013) Utilizing pre-therapy clinical schema and initial CT changes to predict progression-free survival in patients with metastatic renal cell carcinoma on VEGF-targeted therapy: a preliminary analysis. Urologic oncology 31(7): 1283-91

Soerensen, Anne V, Geertsen, Poul F, Christensen, Ib J et al. (2016) A five-factor biomarker profile obtained week 4-12 of treatment for improved prognostication in metastatic renal cell carcinoma: Results from DARENCA study 2. Acta oncologica (Stockholm, Sweden) 55(3): 341-8

Tamura, Keita, Ando, Ryosuke, Takahara, Kiyoshi et al. (2021) Development of novel ACN (albumin, C-reactive protein and neutrophil-to-lymphocyte ratio) prognostication model for

patients with metastatic renal cell carcinoma receiving first-line molecular-targeted therapy. Urologic oncology 39(1): 78e1-78e8

Tanaka, Nobuyuki, Mizuno, Ryuichi, Ito, Keiichi et al. (2016) External Validation of the MSKCC and IMDC Risk Models in Patients Treated with Targeted Therapy as a First-line and Subsequent Second-line Treatment: A Japanese Multi-institutional Study. European urology focus 2(3): 303-309

Toyoda, Shingo, Fukuokaya, Wataru, Mori, Keiichiro et al. (2024) Clinical outcomes and prognostic factors in metastatic nonclear cell renal cell carcinoma treated with immuno-oncology combination therapy. Japanese journal of clinical oncology 54(12): 1336-1342

Ueda, Kosuke, Suekane, Shigetaka, Hirano, Taishi et al. (2018) Efficacy of Axitinib as Second-line Treatment in Locally Advanced and Metastatic Renal Cell Carcinoma. Anticancer research 38(9): 5387-5392

Voss, Martin H, Reising, Albert, Cheng, Yuan et al. (2018) Genomically annotated risk model for advanced renal-cell carcinoma: a retrospective cohort study. The Lancet. Oncology 19(12): 1688-1698

Yao, Jia-Xi, Chen, Xiang, Xi, Wei et al. (2018) Immunoscore System for Predicting Clinical Outcome of Metastatic Renal Cell Carcinoma Patients Treated with Tyrosine Kinase Inhibitors. Journal of Cancer 9(22): 4099-4107

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

<table>
<tr><td>16.</td><td>Analysis of sub-groups</td><td colspan="3">RCC subtypes, for example, clear cell RCC, papillary RCC.</td></tr>
<tr><td>17.</td><td>Type and method of review</td><td colspan="3">X Intervention
Diagnostic
Prognostic
Qualitative
Epidemiologic
Service Delivery
Other (please specify)</td></tr>
<tr><td>18.</td><td>Language</td><td colspan="3">English</td></tr>
<tr><td>19.</td><td>Country</td><td colspan="3">England</td></tr>
<tr><td>20.</td><td>Anticipated or actual start date</td><td colspan="3">August 2024</td></tr>
<tr><td>21.</td><td>Anticipated completion date</td><td colspan="3">March 2026</td></tr>
<tr><td>22.</td><td>Stage of review at time of this submission</td><td>Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td></td><td></td><td>Preliminary searches</td><td></td><td>X</td></tr>
<tr><td></td><td></td><td>Piloting of the study selection process</td><td></td><td>X</td></tr>
<tr><td></td><td></td><td>Formal screening of search results against eligibility criteria</td><td></td><td>X</td></tr>
<tr><td></td><td></td><td>Data extraction</td><td></td><td>X</td></tr>
<tr><td></td><td></td><td>Risk of bias (quality) assessment</td><td></td><td>X</td></tr>
<tr><td></td><td></td><td>Data analysis</td><td></td><td>X</td></tr>
<tr><td>23.</td><td>Named contact</td><td colspan="3">Named contact
Centre for Guidelines, NICE

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

Organisational affiliation of the review
National Institute for Health and Care Excellence (NICE) and Guideline Development Team.</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>
</table>

25.	Funding sources/sponsor	This systematic review is being completed by the Guideline Development Team which receives funding from NICE.
26.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: Kidney Cancer (GID-NG10398).
28.	Other registration details	None
29.	Reference/URL for published protocol	None
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
31.	Keywords	Renal cell carcinoma, prognosis, prognostic scores
32.	Details of existing review of same topic by same authors	Not applicable
33.	Current review status	Ongoing Completed but not published X Completed and published Completed, published and being updated Discontinued
34.	Additional information	None

35.	Details of final publication	www.nice.org.uk

Economic review protocol

ID	Field	Content
1.	Review titles	K and L: Cost effectiveness of prognostic models to predict survival and/ or recurrence in adults with suspected or confirmed renal cell carcinoma (RCC)
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 L (current review) and review K as the question wanted to also include prognostic models that assessed surgical outcomes.

An exploratory search was performed prior to the search for review L (current review) and review K. 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 16/07/2024. 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 24/09/2024 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.

The analysts identified 5 additional papers that were added to the results. The RCT papers were identified via the reference lists of relevant systematic reviews.

Clinical searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled	16/07/2024	Wiley	Issue 7 of 12, July 2024	93

Trials (CENTRAL)				
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
Web of Science	24/09/2024	724

Rerun search database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	31/03/2025	Wiley	Issue 3 of 12, March 2025	94
Cochrane Database of Systematic Reviews (CDSR)	31/03/2025	Wiley	Issue 3 of 12, March 2025	0
Embase	31/03/2025	Ovid	1974 to 2025 March 28	1399
Epistemonikos	31/03/2025	Epistemonikos	n/a	219
INAHTA	31/03/2025	INAHTA	n/a	13
MEDLINE ALL	31/03/2025	Ovid	1946 to March 28, 2025	2222

Rerun additional search methods

Databases	Date searched	No. of results downloaded
Medline	01/04/2025	1026
Embase	01/04/2025	2153
Epistemonikos	01/04/2025	4628

No date limits were applied to the rerun strategies due to technical issues in the OVID databases. The duplicates were resolved in EPPI reviewer.

Web of Science was not required for reruns as the original additional search was looking for backward citations.

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
#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

Searches
#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)
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)

Searches
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)
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)

Searches
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 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

Searches
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)

Searches
19 follow-up studies.sh. (700226)
20 prognos:.tw. (853921)
21 predict:.tw. (2203246)
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)

Additional search methods

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

Searches
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)
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)

Searches
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)
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*

Searches
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 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: 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)

Searches
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)
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)

Searches
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)

Database name: Web of Science

Searches
doi.org/10.1016/j.ejca.2015.06.125, doi.org/10.3109/21681805.2014.980844, doi.org/10.1038/s41598-019-49250-6, doi.org/10.1016/j.juro.2018.01.072, doi.org/10.1002/cncr.23517, doi.org/10.1002/cncr.21331, doi.org/10.1111/j.1464-410X.2008.07901.x, doi.org/10.1007/s13277-015-3248-y, doi.org/10.1111/cas.12507, doi.org/10.1111/bju.13776, doi.org/10.1016/j.urolonc.2014.04.001, doi.org/10.1038/bjc.2011.556, doi.org/10.1111/j.1442-2042.2008.02229.x, doi.org/10.1016/j.juro.2014.04.084, doi.org/10.1245/s10434-014-3680-z, doi.org/10.1007/s00345-015-1559-7, doi.org/10.2147/OTT.S116953, doi.org/10.1016/j.juro.2011.10.155, doi.org/10.1111/his.12001, doi.org/10.1016/S1470-2045(15)70167-1, doi.org/10.1097/01.ju.0000148261.19532.2c, doi.org/10.1016/j.urology.2009.07.1289, doi.org/10.1002/cncr.26193, doi.org/10.1016/j.urology.2019.09.044, doi.org/10.1177/1010428317691417, doi.org/10.1111/iju.13936 doi.org/10.18632/oncotarget.15162, doi.org/10.1016/j.euf.2016.07.006, doi.org/10.1016/j.urolonc.2019.04.002, doi.org/10.18632/oncotarget.22688, doi.org/10.1245/s10434-017-5948-6, doi.org/10.1111/j.1442-2042.2011.02812.x, doi.org/10.1016/j.urolonc.2014.05.014, doi.org/10.18632/oncotarget.10492, doi.org/10.1016/S1470-2045(18)30932-X

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

Rerun search database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	07/05/2025	OVID	1886 to May 01, 2025	0
Embase	07/05/2025	Ovid	1974 to 2025 May 06	745
INAHTA	07/05/2025	INAHTA	N/A	13
MEDLINE ALL	07/05/2025	Ovid	1946 to May 06, 2025	295

EED and HTA were not included in the rerun searches as both databases only hold legacy information and are not updated.

No date limits were applied to the rerun strategies due to technical issues in the OVID databases. The duplicates were resolved in EPPI reviewer.

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)

Searches
2 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* 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)
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)

Searches
27 limit 26 to english language (6732)
28 27 not (letter or editorial).pt. (6710)
29 exp Health Economics/ (1083212)
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)

Searches	
66	health$ year$ equivalent$.tw. (41)
67	utilit$.tw. (402088)
68	(hui or hui1 or hui2 or hui3).tw. (3363)
69	disutili$.tw. (1375)
70	rosser.tw. (144)
71	quality of wellbeing.tw. (79)
72	quality of well-being.tw. (591)
73	qwb.tw. (276)
74	willingness to pay.tw. (14111)
75	standard gamble$.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

Searches
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

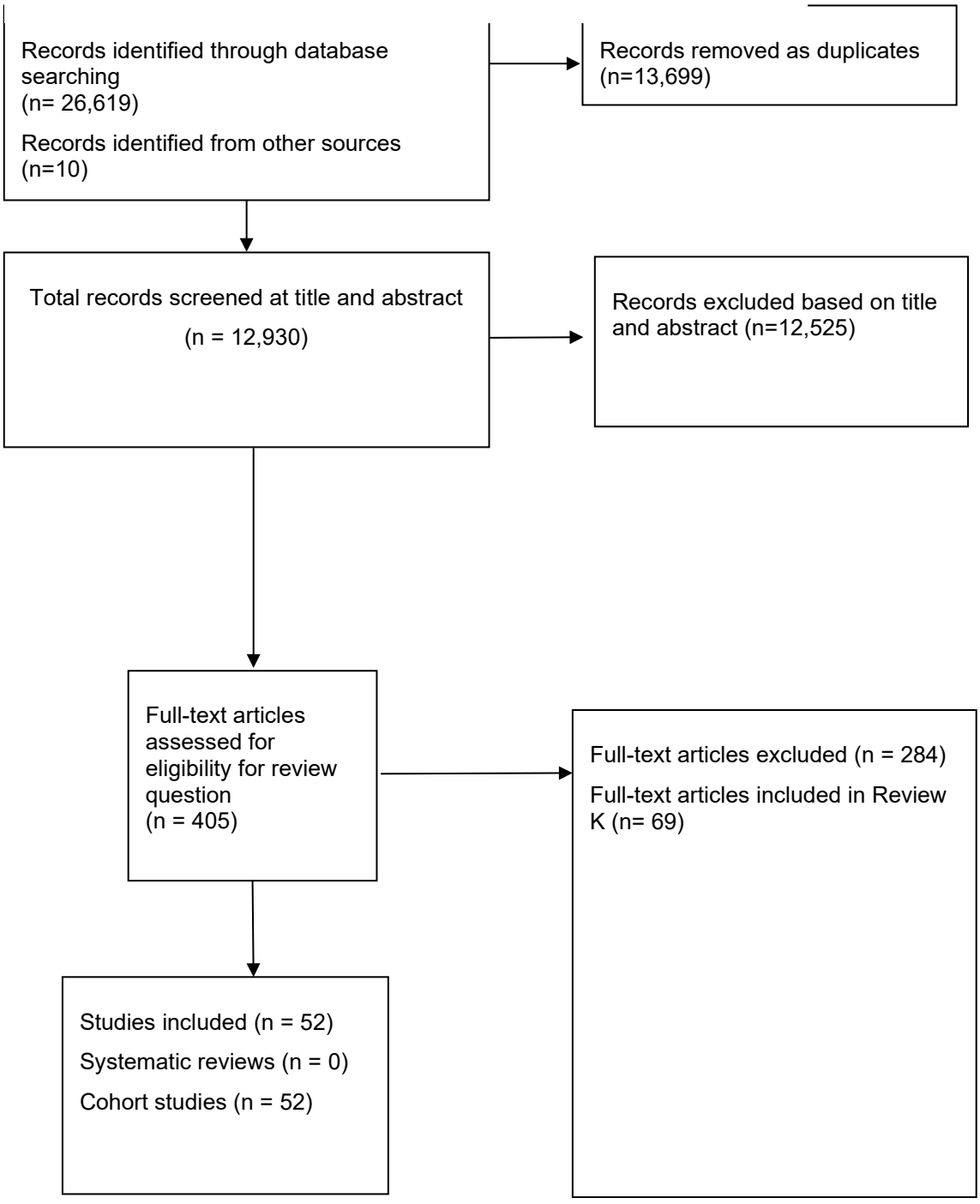
Searches
1 exp Kidney Neoplasms/ or exp nephrectomy/ (109936)
2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or 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)

Searches
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)
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)

Searches
62 disability adjusted life.tw. (6190)
63 daly$.tw. (5560)
64 Health Status Indicators/ (24132)
65 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (31978)
66 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2782)
67 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (8114)
68 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (42)
69 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (467)
70 (euroqol or euro qol or eq5d or eq 5d).tw. (18396)
71 (qol or hql or hqol or hrqol).tw. (79365)
72 (hye or hyes).tw. (77)
73 health$ 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

Abuhelwa, 2022

Bibliographic Reference	Abuhelwa, A.Y.; Bellmunt, J.; Kichenadasse, G.; McKinnon, R.A.; Rowland, A.; Sorich, M.J.; Hopkins, A.M.; C-reactive protein provides superior prognostic accuracy than the IMDC risk model in renal cell carcinoma treated with Atezolizumab/Bevacizumab; Frontiers in Oncology; 2022; vol. 12; 918993

Study Characteristics

Study design	Retrospective cohort study
Study location	US, Czechia. France, Germany, Italy, Poland, Romania, Spain, UK, Australia, Bosnia and Herzegovina, Brazil, Canada, Denmark, Japan, Republic of Korea, Mexico, Russia, Singapore, Taiwan, Thailand, Turkey
Study dates	IMotion150: recruitment between January 2014 and March 2015 IMmotion151: recruitment between May 2015 and October 2016
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	IMotion150: People with mRCC with clear cell and/or sarcomatoid components and adequate haematology and laboratory parameters. IMotion151: People with a component of clear cell or sarcomatoid histology who were previously untreated for mRCC
Exclusion criteria	IMotion150: Prior systemic therapy and active central nervous system disease.
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First line therapy with atezolizumab plus bevacizumab
Number of participants	N = 527

Description of cohorts	
Length of follow-up	Median 19 months (95% CI 18 to 19)
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Overall survival Progression-free survival
Source of funding	Cancer Council South Australia and National Breast Cancer Foundation, Australia
Additional comments	None

Study arms

IMDC Favourable risk (N = 134)

IMDC Intermediate risk (N = 342)

IMDC Poor risk (N = 76)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 552)
% Female Sample size	n = 163 ; % = 30
Age (years) Median (IQR)	62 (56 to 69)

Outcomes

Time-to-event

Outcome	IMDC Intermediate risk vs IMDC Favourable risk, N2 = 342, N1 = 134	IMDC Poor risk vs IMDC Favourable risk, N2 = 76, N1 = 134
Overall survival Hazard ratio/95% CI	2.9 (1.73 to 4.86)	8.35 (4.75 to 14.7)
Progression-free survival Hazard ratio/95% CI	1.44 (1.11 to 1.88)	2.68 (1.91 to 3.77)

Overall survival - Polarity - Lower values are better

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(Lack of information around whether all participants were included in the analysis and a measure of calibration was not reported.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Aktepe, 2021

Bibliographic Reference	Aktepe, O.H.; Erman, M.; Survival outcomes of patients in advanced non-clear renal cell carcinoma treated with pazopanib: A retrospective single institution experience; UHOD - Uluslararasi Hematoloji-Onkoloji Dergisi; 2021; vol. 31 (no. 3); 170-177

Study Characteristics

Study design	Retrospective cohort study
Study location	Turkey
Study dates	October 2009 to October 2020
Risk prediction model(s)	IMDC/Heng

Inclusion criteria	• Age ≥ 18 years • treatment with pazopanib for advanced non-clear cell RCC, • no previous history of treatment with any targeted therapy (sunitinib, sorafenib), and immune-checkpoint inhibitors • normal liver, and kidney function tests • all the patients had a previous history of immune therapy (interferon).
Exclusion criteria	Not specified
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	Treatment with pazopanib, 800 mg/day. Model used at initiation of treatment.
Number of participants	N=40
Length of follow-up	Median 21 months
Follow-up schedule	Not specified
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	Not specified
Additional comments	Kaplan-Meier analyses were performed for the estimation of PFS and OS. The Cox proportional hazards regression models were performed for the identification of predictive indicators of PFS and OS.

Study arms

IMDC favourable (N = 11)

IMDC intermediate (N = 15)

IMDC poor (N = 14)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 40)
% Female Sample size	n = 9 ; % = 22.5
Age Custom value	Median (range): 62 (45-78)
Nephrectomy status - Had surgery, unspecified Sample size	n = 32 ; % = 80
RCC subtypes - Papillary Sample size	n = 21 ; % = 52.5
RCC subtypes - Chromophobe Sample size	n = 6 ; % = 15
RCC subtypes - Sarcomatoid differentiation Sample size	n = 5 ; % = 12.5
RCC subtypes - Unclassified Sample size	n = 8 ; % = 20

Outcomes

IMDC

Outcome	IMDC intermediate vs IMDC favourable, N2 = 15, N1 = 11	IMDC poor vs IMDC favourable, N2 = 14, N1 = 11
Progression-free survival Hazard ratio/95% CI	1.32 (0.47 to 3.75)	15.64 (4.52 to 54.04)
Overall survival Hazard ratio/95% CI	0.9 (0.3 to 3.5)	10.2 (2.4 to 42.6)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(<50 events, no information on whether there was missing data or how it was handled. No model performance measure.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Aktepe, 2022

Bibliographic Reference	Aktepe, Oktay Halit; Gundogdu, Fatma; Kosemehmetoglu, Kemal; Yeter, Haci Hasan; Aksoy, Sercan; Guven, Deniz Can; Sahin, Taha Koray; Yuce, Deniz; Kertmen, Neyran; Dizdar, Omer; Yalcin, Suayib; Erman, Mustafa; THSD7A expression: a novel immunohistochemical determinant in predicting overall survival of metastatic renal cell carcinoma treated with targeted therapy.; Irish journal of medical science; 2022; vol. 191 (no. 4); 1561-1567

Study Characteristics

Study design	Retrospective cohort study
Study location	Turkey
Study dates	2008 to 2019
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	• Metastatic renal cell carcinoma • 18 or older • treated with targeted therapy between 2008 and 2019 at Hacettepe University Cancer Institute in Ankara Turkey • history of nephrectomy for localised or metastatic disease at initial presentation.
Exclusion criteria	• Treated with neoadjuvant or adjuvant therapies.
Selection of cohort	Single centre
Description of interventions/	Targeted therapy. Model used at baseline.

point in the pathway model is used	
Number of participants	N=86
Length of follow-up	Median: 21.6 months
Follow-up schedule	Not reported
Outcome(s) of interest	Overall survival
Source of funding	Department of Scientific Research Projects Coordination Unit of Hacettepe University
Additional comments	Kaplan–Meier method was used for estimation of OS, and the long-rank test was performed for evaluation of differences between prognostic subgroups.

Study arms

IMDC intermediate (N = 49)

IMDC poor (N = 28)

IMDC favourable (N = 8)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 86)
% Female Sample size	% = 29.1
Age Median (IQR)	61 (29 to 81)
RCC subtypes - Clear cell Sample size	% = 82.5
RCC subtypes - Non–clear cell	% = 17.5

Characteristic	Study (N = 86)
Sample size	
Metastases location - Lung Sample size	% = 67.1
Metastases location - Liver Sample size	% = 25.6
Metastases location - Bone Sample size	% = 26.8
Metastases location - Adrenal Sample size	% = 6.1
Metastases location - Brain Sample size	% = 2.4

Outcomes

IMDC

Outcome	IMDC intermediate vs IMDC favourable, N2 = 49, N1 = 8	IMDC poor vs IMDC favourable, N2 = 29, N1 = 8
Overall survival Hazard ratio/95% CI	1.08 (0.37 to 3.14)	4.82 (1.55 to 14.97)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(No information on whether there was missing outcome data or how it was handled. No information on model performance evaluations.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Bamias, 2010

Bibliographic Reference	Bamias, Aristotelis; Karadimou, Alexandra; Lampaki, Sofia; Lainakis, George; Malettou, Lia; Timotheadou, Eleni; Papazisis, Kostas; Andreadis, Charalambos; Kontovinis, Loukas; Anastasiou, Ioannis; Stravodimos, Kostas; Xanthakis, Ioannis; Skolarikos, Andreas; Christodoulou, Christos; Syrigos, Kostas; Papandreou, Christos; Razi, Evangelia; Dafni, Urania; Fountzilas, George; Dimopoulos, Meletios A; Prognostic stratification of patients with advanced renal cell carcinoma treated with sunitinib: comparison with the Memorial Sloan-Kettering prognostic factors model.; BMC cancer; 2010; vol. 10; 45

Study Characteristics

Study design	Retrospective cohort study
Study location	Greece
Study dates	2006-2008
Risk prediction model(s)	MSKCC
Inclusion criteria	• Advanced RCC treated with targeted agents
Exclusion criteria	Not specified
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Sunitinib was administered at the approved dose of 50 mg daily on a 4 weeks on-2 weeks off schedule.
Number of participants	N=109
Length of follow-up	15.8 months (range for surviving patients 0.1 to 31.5 months)
Follow-up schedule	Tumour evaluation was performed every 2-3 cycles of treatment
Outcome(s) of interest	Overall survival
Source of funding	Author received honoraria by industry
Additional comments	Cox proportional hazards model was used to assess the relationship of OS with various clinical and laboratory variables.

Study arms

MSKCC favourable (N = 15)

MSKCC intermediate (N = 56)

MSKCC poor (N = 25)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 109)
% Female Sample size	n = 29 ; % = 27
Age Custom value	Median (range): 59 (30-79)
Nephrectomy status - Yes Sample size	n = 86 ; % = 79
Nephrectomy status - No Sample size	n = 23 ; % = 21
RCC subtypes - Clear cell Sample size	n = 100 ; % = 91
RCC subtypes - Papillary Sample size	n = 2 ; % = 2
RCC subtypes - Chromophobe Sample size	n = 2 ; % = 2
RCC subtypes - Mixed Sample size	n = 3 ; % = 3
RCC subtypes - Unclassified Sample size	n = 2 ; % = 2
Metastases location - Lung	n = 75 ; % = 69

Characteristic	Study (N = 109)
Sample size	
Metastases location - Nodes Sample size	n = 38 ; % = 35
Metastases location - Liver Sample size	n = 10 ; % = 9
Metastases location - Renal bed Sample size	n = 27 ; % = 25
Metastases location - Bones Sample size	n = 39 ; % = 36
Metastases location - Brain Sample size	n = 8 ; % = 7

Outcomes

MSKCC

Outcome	MSKCC favourable, N = 15	MSKCC intermediate, N = 56	MSKCC poor, N = 25
Overall survival No of events	n = 1	n = 24	n = 18

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(Less than 50 events. No information on model performance measures.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Bayoglu, 2023

Bibliographic Reference	Bayoglu, Ibrahim Vedat; Huseynov, Javid; Topal, Alper; Sever, Nadiye; Majidova, Nargiz; Celebi, Abdussamet; Yasar, Alper; Arikan, Rukiye; Isik, Selver; Hacioglu, Muhammet Bekir; Ercelep, Ozlem; Sari, Murat; Erdogan, Bulent; Hacibekiroglu, Ilhan; Topaloglu, Sernaz; Kostek, Osman; Cicin, Irfan; PNI as a Potential Add-On Biomarker to Improve the IMDC Intermediate Prognostic Score.; Journal of clinical medicine; 2023; vol. 12 (no. 19)

Study Characteristics

Study design	Retrospective cohort study
Study location	Turkey
Study dates	Not reported
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	• Metastatic renal cell carcinoma • received tyrosine-kinase inhibitors in the first-line.
Exclusion criteria	Not specified
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First-line treatment with tyrosine-kinase inhibitors. Treatment agents were pazopanib (800 mg once daily) and sunitinib (50 mg once daily for 2 consecutive weeks followed by 1 week or 50 mg once daily for 4 consecutive weeks followed by 2 weeks). Model used before treatment.
Number of participants	N=185
Length of follow-up	Not specified
Follow-up schedule	Not specified
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	No funding received
Additional comments	Survival curves were obtained using the Kaplan–Meier method for each subgroup. Differences in survival between the groups were compared by log-rank test.

Study arms

IMDC favourable (N = 87)

IMDC intermediate (N = 62)

IMDC poor (N = 7)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 185)
% Female Sample size	n = 51 ; % = 27.5
Age Median (IQR)	61 (51 to 69)
Nephrectomy status - Prior nephrectomy Sample size	% = 79
RCC subtypes - Non–clear cell Sample size	% = 18.2
Metastases location - Lung Sample size	% = 79
Metastases location - Liver Sample size	% = 17.7
Metastases location - Brain Sample size	% = 9.4

Outcomes

IMDC

Outcome	IMDC intermediate vs IMDC favourable, N2 = 62, N1 = 87	IMDC poor vs IMDC favourable, N2 = 7, N1 = 87
Progression-free survival Hazard ratio/95% CI	3.7 (1.89 to 7.23)	6.2 (2.82 to 13.62)
Overall survival Hazard ratio/95% CI	1.72 (0.96 to 3.07)	3.41 (1.64 to 7.09)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(No information on the number of events. No information on whether all participants enrolled were analysed and no information on how (if any) missing data was dealt with. The percentages of number of participants in each risk group do not add to the total number of participants so might be missing data. No information on model performance measures.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Beuselinck, 2014

Bibliographic Reference	Beuselinck, Benoit; Vano, Yann-Alexandre; Oudard, Stephane; Wolter, Pascal; De Smet, Robert; Depoorter, Lore; Teghom, Corine; Karadimou, Alexandra; Zucman-Rossi, Jessica; Debruyne, Philip R; Van Poppel, Hendrik; Joniau, Steven; Lerut, Evelyne; Strijbos, Michiel; Dumez, Herlinde; Paridaens, Robert; Van Calster, Ben; Schoffski, Patrick; Prognostic impact of baseline serum C-reactive protein in patients with metastatic renal cell carcinoma (RCC) treated with sunitinib.; BJU international; 2014; vol. 114 (no. 1); 81-9

Study Characteristics

Study design	Retrospective cohort study

Study location	Belgium and France
Study dates	January 2005 to October 2012
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	• Clear cell metastatic renal cell carcinoma • started sunitinib therapy • previous immunotherapy or chemotherapy were allowed.
Exclusion criteria	• Previous targeted therapy
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Sunitinib therapy (50 mg/d, 4 weeks on, 2 weeks off). Model used at start of sunitinib therapy.
Number of participants	N=200
Length of follow-up	Median 67 months
Follow-up schedule	Thoracic and abdominal CT scan every 2-3 months.
Outcome(s) of interest	Model discrimination (C-stats) Overall survival Progression-free survival
Source of funding	Authors received grants from: Fondation Martine Midy (Paris, France); Research Foundation – Flanders (FWO) (Belgium); the Hellenic Society of Medical Oncology (HESMO, Athens, Greece). Also funding from Fonds voorWetenschappelijk Onderzoek Vlaanderen (Belgium) and Stichting tegen Kanker (Belgium).
Additional comments	Survival curves were generated using Kaplan–Meier analysis.

Study arms

IMDC favourable (N = 25)

IMDC intermediate (N = 110)

IMDC poor (N = 65)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 200)
% Female Sample size	n = 58 ; % = 29
Age Mean (SD)	59 (*NR*)
Nephrectomy status - No nephrectomy Sample size	n = 12 ; % = 6
Metastases location - Lung No of events	n = 150 ; % = 75
Metastases location - Lymph nodes No of events	n = 117 ; % = 59
Metastases location - Liver No of events	n = 45
Metastases location - Brain No of events	n = 22 ; % = 11
Metastases location - Bone No of events	n = 87 ; % = 44

Outcomes

IMDC

Outcome	IMDC poor vs IMDC favourable, N2 = 65, N1 = 25	IMDC intermediate vs IMDC favourable, N2 = 110, N1 = 25
Progression-free survival Hazard ratio/95% CI	4.59 (2.48 to 9.23)	2.54 (1.43 to 4.96)
Overall survival Hazard ratio/95% CI	4.57 (2.51 to 8.98)	2.12 (1.21 to 4.02)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High (*Lack of information around analysis*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Bolzacchini, 2022

Bibliographic Reference	Bolzacchini, Elena; Giordano, Monica; Bertu, Lorenza; Bregni, Marco; Nigro, Olga; Galli, Luca; Antonuzzo, Andrea; Artale, Salvatore; Barzaghi, Sabrina; Danova, Marco; Torchio, Martina; Pinotti, Graziella; Dentali, Francesco; Prognostic role of hematologic parameters of metastatic renal cell carcinoma treated with sunitinib.; Tumori; 2022; vol. 108 (no. 5); 502-509

Study Characteristics

Study design	Retrospective cohort study
Study location	Italy
Study dates	2006-2020
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	Patients with mRCC treated with sunitinib as first-line therapy

Exclusion criteria	NR
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Sunitinib was administered according to a 4/2 schedule (sunitinib 50 mg once a day, 4 weeks of treatment followed by 2 weeks without treatment), and modified (2:1 schedule) if necessary
Number of participants	N = 100 IMDC Score IMDC Favourable = 12 IMDC Intermediate = 67 IMDC Poor = 13
Length of follow-up	Up to 24 months or until death
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	The authors received no financial support for the research, authorship, and/or publication of this article
Additional comments	Univariate analysis using the Cox regression model was applied to study factors influencing progression and survival; hazard ratios (HRs) together with 95% confidence intervals were calculated

Study arms

IMDC Favourable (N = 12)

IMDC Intermediate (N = 67)

IMDC Poor (N = 13)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 100)
% Female No of events	n = 30 ; % = 30
Age Mean (SD)	63.2 (10.3)
Prior nephrectomy - Yes No of events	n = 79 ; % = 79
Prior nephrectomy - No No of events	n = 21 ; % = 21
Metastatic sites - >2 Metastatic sites No of events	n = 53 ; % = 53
MSKCC score - Favourable No of events	n = 16 ; % = 16
MSKCC score - Intermediate No of events	n = 62 ; % = 62
MSKCC score - Poor No of events	n = 11 ; % = 11
IMDC Score - Favourable No of events	n = 12 ; % = 12
IMDC Score - Intermediate	n = 67 ; % = 67

Characteristic	Study (N = 100)
No of events	
IMDC Score - Poor No of events	n = 13 ; % = 13

Outcomes

Survival

Outcome	IMDC Intermediate vs IMDC Favourable, N2 = 67, N1 = 12	IMDC Poor vs IMDC Favourable, N2 = 13, N1 = 12
Progression-free survival Hazard ratio/95% CI	1.91 (0.88 to 4.41)	4.41 (1.69 to 11.54)
Overall survival Hazard ratio/95% CI	2.31 (0.82 to 6.52)	7.02 (2.17 to 22.72)

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

Critical appraisal - GDT Crit App

Overall Risk of bias and Applicability	Risk of bias	Moderate *Lack of information around analysis*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Cai, 2017a

Bibliographic Reference	Cai, Wen; Zhong, Hai; Kong, Wen; Dong, Baijun; Chen, Yonghui; Zhou, Lixin; Xue, Wei; Huang, Yiran; Zhang, Jin; Huang, Jiwei; Significance of preoperative prognostic nutrition index as prognostic predictors in patients with metastatic renal cell carcinoma with tyrosine kinase inhibitors as first-line target therapy.; International urology and nephrology; 2017; vol. 49 (no. 11); 1955-1963

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	March 2006 to July 2015
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	People with mRCC receiving sorafenib or sunitinib as first-line therapy with Karnofsky performance status (KPS) of 70–100, and serum albumin levels and lymphocyte counts recorded within 1 week before treatment.
Exclusion criteria	People who had unstable or severe cardiac disease, uncontrolled brain metastases, concurrent malignancies and with incomplete data files.
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	Sorafenib or sunitinib as first-line therapy
Number of participants	N = 178
Length of follow-up	Median 22 months
Follow-up schedule	All patients were suggested to monthly have disease assessment after treatment. After completion of therapy, patients were followed up every month until they experienced discomfort or death. Progression-free survival (PFS) was evaluated according to RECIST criteria.
Outcome(s) of interest	Model discrimination (C-stats) Overall survival Progression-free survival
Source of funding	National Natural Science Foundation of China, the Shanghai Municipal Commission of Health and Family Planning and the Incubating Program for Clinical Research and Innovation of Renji Hospital.

Study arms

IMDC favourable risk (N = 83)

IMDC Intermediate risk (N = 69)

IMDC poor risk (N = 26)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 178)
% Female Sample size	n = 43 ; % = 24.2
Age - Younger than 65 years Sample size	n = 136 ; % = 76.4
Age - 65 years and older Sample size	n = 42 ; % = 23.6
Nephrectomy status Prior nephrectomy Sample size	n = 144 ; % = 80.9
RCC subtypes - Clear cell Sample size	n = 170 ; % = 95.5
RCC subtypes - Others Sample size	n = 8 ; % = 4.5
Metastases location - Lymph node Sample size	n = 132 ; % = 77.5
Metastases location - Bone Sample size	n = 44 ; % = 24.7
Metastases location - Liver Sample size	n = 20 ; % = 11.2

Characteristic	Study (N = 178)
Metastases location - Others Sample size	n = 14 ; % = 7.9

Outcomes

Time-to-event outcomes

Outcome	IMDC Intermediate risk vs IMDC favourable risk, N2 = 69, N1 = 83	IMDC poor risk vs IMDC favourable risk, N2 = 26, N1 = 83
Progression-free survival Hazard ratio/95% CI	1.83 (1.28 to 2.64)	4.59 (2.81 to 7.51)
Overall survival Hazard ratio/95% CI	1.97 (1.3 to 2.99)	6.37 (3.77 to 10.79)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(It was unclear for many participants had the outcome event. 30 participants were lost to follow-up and it appears that these were excluded from the analysis. The study did not report a measure of calibration.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Cai, 2017c

Bibliographic Reference	Cai, Wen; Zhang, Jin; Chen, Yonghui; Kong, Wen; Huang, Yiran; Huang, Jiwei; Zhou, Lixin; Association of post-treatment hypoalbuminemia and survival in Chinese patients with metastatic renal cell carcinoma.; Chinese journal of cancer; 2017; vol. 36 (no. 1); 47

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	March 2006 to September 2015
Risk prediction model(s)	MSKCC
Inclusion criteria	People with mRCC who received sorafenib or sunitinib as first-line therapy and had a KPS score of 70–100 with records of serum albumin levels before and after treatment.
Exclusion criteria	People who had unstable or severe cardiac disease, uncontrolled brain metastases, concurrent malignancies, or incomplete data files.
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	First-line treatment with sorafenib or sunitinib
Number of participants and recruitment methods	N=184
Length of follow-up	Not reported
Follow-up schedule	Participants were followed up within 1–2 weeks of the onset of targeted therapy, and their disease statuses were assessed every month or any time they felt discomfort after the treatment.
Outcome(s) of interest	Model discrimination (C-stats) Overall survival Progression-free survival
Source of funding	National Natural Science Foundation of China; incubating program for clinical research and innovation of Renji hospital; the Shanghai Municipal Commission of Health and Family Planning

Study arms

MSKCC favourable and intermediate risk (N = 155)

MSKCC poor risk (N = 29)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 184)
% Female Sample size	n = 47 ; % = 25.5
Age - Younger than 65 years Sample size	n = 141 ; % = 76.6
Age - 65 years and older Sample size	n = 43 ; % = 23.4
Nephrectomy status Prior nephrectomy Sample size	n = 146 ; % = 79.3
RCC subtypes - Clear cell Sample size	n = 179
RCC subtypes - Non–clear cell Sample size	n = 5 ; % = 2.7
Metastases location - Lung Sample size	n = 137 ; % = 74.5
Metastases location - Lymph node Sample size	n = 44 ; % = 23.9
Metastases location - Bone Sample size	n = 20 ; % = 10.9
Metastases location - Liver Sample size	n = 16 ; % = 8.7

Characteristic	Study (N = 184)
Metastases location - Others Sample size	n = 15 ; % = 8.2

Outcomes

Time-to-event

Outcome	MSKCC favourable and intermediate risk vs MSKCC poor risk, N2 = 155, N1 = 29
Progression-free survival Hazard ratio/95% CI	1.93 (1.55 to 2.4)
Overall survival Hazard ratio/95% CI	1.93 (1.55 to 2.4)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(Participants with incomplete datafiles were excluded. There was no measure of calibration reported.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Cetin, 2013

Bibliographic Reference	Cetin, Bulent; Berk, Veli; Kaplan, Mehmet Ali; Afsar, Baris; Tufan, Gulnihal; Ozkan, Metin; Isikdogan, Abdurahman; Benekli, Mustafa; Coskun, Ugur; Buyukberber, Suleyman; Is the pretreatment neutrophil to lymphocyte ratio an important prognostic parameter in patients with metastatic renal cell carcinoma?.; Clinical genitourinary cancer; 2013; vol. 11 (no. 2); 141-8

Study Characteristics

Study design	Retrospective cohort study

Study location	Turkey
Study dates	February 2008 to December 2011
Risk prediction model(s)	MSKCC
Inclusion criteria	• mRCC WHO performance status 0-1 • age 18-80 • IFN-a as first-line therapy
Exclusion criteria	Not specified
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First-line IFN-a. Model applied pretreatment.
Number of participants	N=118
Length of follow-up	Median 15 months (range 1 to 53)
Follow-up schedule	Regular physical examination and laboratory assessment (hematologic and serum chemical measurements), every 4 – 6 weeks, and computed tomography scans were performed according to the local standard every 12–18 weeks.
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	Not specified

Study arms

MSKCC low (favourable) (N = 16)

MSKCC intermediate (N = 70)

MSKCC poor (N = 13)

Unknown (N = 1)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 100)
% Female Sample size	n = 24 ; % = 24
Age Custom value	Median (range): 58 (24-80)
RCC subtypes - Clear cell Sample size	n = 73 ; % = 73
RCC subtypes - Non–clear cell Sample size	n = 24 ; % = 24
RCC subtypes - Unknown Sample size	n = 3 ; % = 3
Metastases location - Liver Sample size	n = 17 ; % = 17
Metastases location - Bone Sample size	n = 24 ; % = 24
Metastases location - Lung Sample size	n = 65 ; % = 65

Outcomes

MSKCC

Outcome	MSKCC intermediate vs MSKCC low (favourable), N2 = 70, N1 = 16	MSKCC poor vs MSKCC low (favourable), N2 = 13, N1 = 16
Progression-free survival Hazard ratio/95% CI	1.12 (0.58 to 2.15)	4.58 (2.01 to 10.4)
Overall survival	1.87 (0.78 to 4.47)	8.52 (3.11 to 23.36)

Outcome	MSKCC intermediate vs MSKCC low (favourable), N2 = 70, N1 = 16	MSKCC poor vs MSKCC low (favourable), N2 = 13, N1 = 16
Hazard ratio/95% CI		

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate *(Not all participants enrolled were included in the analysis but mention of censored data. No information on model performance measures.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Chen, 2019

Bibliographic Reference	Chen, Xiang; Yao, JiaXi; Liu, Li; Zheng, WenZhong; Hu, XiaoYi; Zhu, YanJun; Wang, Hang; Guo, JianMing; Serum Alpha1-Globulin as a Novel Prognostic Factor in Metastatic Renal Cell Carcinoma Treated with Tyrosine Kinase Inhibitors.; Targeted oncology; 2019; vol. 14 (no. 2); 187-195

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2009-2017
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	Adult patients with RCC who initiated first-line sunitinib or sorafenib systemic therapy for metastatic disease. All patients received radical, nephron-sparing, or cytoreductive surgery before systemic therapy
Exclusion criteria	Patients with incomplete data, loss of follow-up, medical history of glomerulonephritis or nephrotic syndrome, hepatic cirrhosis, chronic obstructive pulmonary disease, chronic infection, inflammatory bowel disease, and other malignancies.

Selection of cohort	Database or clinical registry Single centre
Description of interventions/ point in the pathway model is used	First-line sunitinib or sorafenib
Number of participants	N = 213 IMDC Favourable = 103 IMDC Intermediate = 58 IMDC Poor = 52
Length of follow-up	NR
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	This research was supported by grants from the National Natural Science Foundation of China (81772696, 81472376, and 81702496).
Additional comments	Univariate and multivariate Cox proportional hazards models were used to identify prognostic factors. The discriminatory abilities of the prognostic models were assessed with Harrell's C-index

Study arms

IMDC Favourable (N = 103)

IMDC Intermediate (N = 58)

IMDC Poor (N = 52)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 213)
% Female No of events	n = 53 ; % = 24.88
Age Median (IQR)	59 (52 to 65)
RCC subtypes - Clear cell RCC No of events	n = 185 ; % = 86.85
RCC subtypes - Non–clear cell RCC No of events	n = 28 ; % = 13.15
IMDC risk group - Favourable No of events	n = 103 ; % = 48.36
IMDC risk group - Intermediate No of events	n = 58 ; % = 27.23
IMDC risk group - Poor No of events	n = 52 ; % = 24.41

Outcomes

Survival

Outcome	IMDC Intermediate vs IMDC Favourable, N2 = 58, N1 = 103	IMDC Poor vs IMDC Favourable, N2 = 52, N1 = 103
Overall survival Hazard ratio/95% CI	1.16 (0.73 to 1.84)	2.15 (1.38 to 3.34)
Progression-free survival Hazard ratio/95% CI	0.87 (0.59 to 1.27)	1.19 (0.81 to 1.75)

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

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate
Overall Risk of bias and Applicability	Concerns for applicability	Low

Chrom, 2019

Bibliographic Reference	Chrom, Pawel; Zolnierek, Jakub; Bodnar, Lubomir; Stec, Rafal; Szczylik, Cezary; External validation of the systemic immune-inflammation index as a prognostic factor in metastatic renal cell carcinoma and its implementation within the international metastatic renal cell carcinoma database consortium model.; International journal of clinical oncology; 2019; vol. 24 (no. 5); 526-532

Study Characteristics

Study design	Retrospective cohort study
Study location	Poland
Study dates	2008-2016
Risk prediction model(s)	IMDC/Heng

Inclusion criteria	Patients diagnosed with mRCC of any histopathological subtype, the use of TKI as first-line systemic therapy for metastatic disease and the absence of other malignancies
Exclusion criteria	Patients who had received neoadjuvant, adjuvant or any investigational therapy
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Patients treated with TKI (sunitinib and pazopanib)
Number of participants	N = 502 IMDC Favourable = 203 IMDC Intermediate = 256 IMDC Poor = 43
Length of follow-up	Median was 52.5 months (95% CI 46.7–62.0 months)
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	None
Additional comments	The prognostic accuracy of the models was assessed separately for individual risk factors and the three risk groups using (1) concordance index, (2) Bayesian Information Criterion (BIC), (3) generalized R2, (4) calibration plot, (5) Integrated Discrimination Improvement (IDI) and (6) continuous Net Reclassification Index (cNRI). Concordance index is a measure of discrimination which is the ability of the model to separate patients with different outcomes.

Study arms

IMDC Favourable (N = 203)

IMDC Intermediate (N = 256)

IMDC Poor (N = 43)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 502)
% Female No of events	n = 163 ; % = 32.5
Age Median (IQR)	62 (22 to 88)
Nephrectomy status No of events	n = 502 ; % = 100
RCC subtypes - Clear cell RCC No of events	n = 486 ; % = 96.8
RCC subtypes - Other No of events	n = 16 ; % = 3.2
IMDC Criteria - IMDC Favourable No of events	n = 203 ; % = 40.4
IMDC Criteria - IMDC Intermediate No of events	n = 256 ; % = 51
IMDC Criteria - IMDC Poor No of events	n = 43 ; % = 8.6

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Low

Overall Risk of bias and Applicability	Concerns for applicability	Low

de Velasco, 2017

Bibliographic Reference	de Velasco, Guillermo; Culhane, Aedin C; Fay, Andre P; Hakimi, A Ari; Voss, Martin H; Tannir, Nizar M; Tamboli, Pheroze; Appleman, Leonard J; Bellmunt, Joaquim; Kimryn Rathmell, W; Albiges, Laurence; Hsieh, James J; Heng, Daniel Y C; Signoretti, Sabina; Choueiri, Toni K; Molecular Subtypes Improve Prognostic Value of International Metastatic Renal Cell Carcinoma Database Consortium Prognostic Model.; The oncologist; 2017; vol. 22 (no. 3); 286-292

Study Characteristics

Study design	Retrospective cohort study
Study location	US
Study dates	NR
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	Metastatic RCC (mRCC) patients
Exclusion criteria	NR
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	VEGF-targeted first-line therapy (Sunitinib, Pazopanib, Axitinib, Sorafenib, and Bevacizumab). Prognostic models were assessed before starting pharmacological therapy
Number of participants	N = 54 IMDC criteria IMDC - Favourable = 8

	IMDC - Intermediate = 35 IMDC - Poor = 11 MSKCC criteria MSKCC - Favourable = 8 MSKCC - Intermediate = 38 MSKCC - Poor = 8
Length of follow-up	NR
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	This study was supported by the Trust family, Loker Pinard, and Michael Brigham Funds for Kidney Cancer Research (to T.K. Choueiri) at the Dana-Farber Cancer Institute, the Dana-Farber/ Harvard Cancer Center Kidney Cancer Program and the DanaFarber/Harvard Cancer SEOM/CRIS Cancer Foundation (to G. de Velasco)
Additional comments	OS was calculated from the beginning of first-line targeted therapy to death of any cause. Cox proportional hazard models and likelihood ratio using OS were used to compare competing survival models. Uno's version of the concordance index (C-Index) was used to predict the final risk model.

Study arms

IMDC Favourable (N = 8)

IMDC Intermediate (N = 35)

IMDC Poor (N = 11)

MSKCC Favourable (N = 8)

MSKCC Intermediate (N = 38)

MSKCC Poor (N = 8)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 54)
% Female No of events	n = 17 ; % = 33.6
Age Median (IQR)	62 (39 to 84)
MSKCC Criteria - MSKCC - Favourable No of events	n = 8 ; % = 14.8
MSKCC Criteria - MSKCC - Intermediate No of events	n = 38 ; % = 70.3
MSKCC Criteria - MSKCC - Poor No of events	n = 8 ; % = 14.8
IMDC Criteria - IMDC - Favourable No of events	n = 8 ; % = 14.8
IMDC Criteria - IMDC - Intermediate No of events	n = 35 ; % = 64.8
IMDC Criteria - IMDC - Poor No of events	n = 11 ; % = 20.3

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate (*Lack of information around selection participants*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Derosa, 2019

Bibliographic Reference	Derosa, Lisa; Bayar, Mohamed Amine; Albiges, Laurence; Le Teuff, Gwenael; Escudier, Bernard; A new prognostic model for survival in second line for metastatic renal cell carcinoma: development and external validation.; Angiogenesis; 2019; vol. 22 (no. 3); 383-395

Study Characteristics

Study design	Retrospective cohort study
Study location	Discovery set: France Validation set: US, Argentina, Australia, Austria, Canada, Chile, China, Denmark, Finland, France, Germany, Hungary, Italy, Republic of Korea, Netherlands, Singapore, Spain, Sweden, Switzerland, UK
Study dates	Discovery set: January 2005 to December 2014 Validation set: clinical trials conducted between 2007 and 2016
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	Discovery set: People initially treated within approved clinical trials who received a second line targeted treatment, with VEGF inhibitor or mTOR inhibitor, after progressive disease on first-line targeted treatment Validation set: People who received first line treatment with sunitinib or bevacizumab, alone or in combination
Exclusion criteria	Discovery set: Patients who received cytokines as first-line therapy Validation set: All participants who received cytokines
Selection of cohort	Database or clinical registry

Description of interventions/ point in the pathway model is used	Discovery set: People who received a second line targeted treatment with VEGF inhibitor or mTOR inhibitor, after progressive disease on first-line targeted treatment Validation set: People receiving axitinib, sorafenib or temsirolimus following first-line treatment with sunitinib or bevacizumab alone or in combination
Number of participants	Discovery set: N = 222 Validation set: N = 947
Length of follow-up	Discovery set: median 49.4 months (IQR: 28.4 to 92.1) Validation set: median 16.3 months (IQR: 10.3 to 27.8)
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	Gustave Roussy Fondation Philanthropia and ESMO translational research fellowship
Additional comments	NA

Study arms

IMDC low risk (N = 20)

IMDC intermediate risk (N = 145)

IMDC poor risk (N = 57)

MSKCC low risk (N = 86)

MSKCC intermediate risk (N = 145)

MSKCC poor risk (N = 57)

Population characteristics

Study-level characteristics

Characteristic	Study (N =)
% Female Discovery set (n=222) Sample size	n = 56 ; % = 25.2
Age - Younger than 60 years Sample size	n = 107 ; % = 48.2
Age - 60 years or older Sample size	n = 115 ; % = 51.8
Nephrectomy status Discovery set (n=222) - prior nephrectomy Sample size	n = 207 ; % = 93.2
RCC subtypes - Clear cell Sample size	n = 197 ; % = 88.7
RCC subtypes - Non-clear cell Sample size	n = 25 ; % = 11.3
% Female Validation set (n=855) Sample size	n = 216 ; % = 25.3

Characteristic	Study (N =)
Age - Younger than 60 years Sample size	n = 395 ; % = 46.2
Age - 60 years and older Sample size	n = 460 ; % = 53.8
Nephrectomy status Validation set (n=855) - prior nephrectomy Sample size	n = 727 ; % = 85
RCC subtypes - Clear cell Sample size	n = 767 ; % = 90.6
RCC subtypes - Non-clear cell Sample size	n = 80 ; % = 9.4

Outcomes

Number of events - discovery set

Outcome	IMDC low risk, N = 20	IMDC intermediate risk, N = 145	IMDC poor risk, N = 57	MSKCC low risk, , N = 86	MSKCC intermediate risk, N = 135	MSKCC poor risk, N = 1
Mortality No of events	n = 9 ; % = 45	n = 114 ; % = 78.6	n = 53 ; % = 93	n = 60 ; % = 69.8	n = 115 ; % = 85.2	n = 1 ; % = 100

Mortality - Polarity - Lower values are better

Number of events - validation set

Outcome	IMDC low risk, N = 51	IMDC intermediate risk, N = 615	IMDC poor risk, N = 189	MSKCC low risk, N = 373	MSKCC intermediate risk, N = 476	MSKCC poor risk, N = 6
Mortality No of events	n = 18 ; % = 35.3	n = 286 ; % = 46.5	n = 151 ; % = 79.9	n = 139 ; % = 37.3	n = 310 ; % = 65.1	n = 6 ; % = 100

Mortality - Polarity - Lower values are better

Time-to-event - discovery set

Outcome	IMDC intermediate risk vs IMDC low risk, N2 = 145, N1 = 20	IMDC poor risk vs IMDC low risk, N2 = 57, N1 = 20	MSKCC intermediate risk vs MSKCC low risk, N2 = 135, N1 = 86	MSKCC poor risk vs MSKCC low risk, N2 = 1, N1 = 86
Overall survival Hazard ratio/95% CI	2.71 (1.37 to 5.38)	7.01 (3.4 to 14.43)	2.2 (1.59 to 3.03)	6.63 (0.9 to 48.7)

Time-to-event - validation set

Outcome	IMDC intermediate risk vs IMDC low risk, N2 = 615, N1 = 51	IMDC poor risk vs IMDC low risk, N2 = 189, N1 = 51	MSKCC intermediate risk vs MSKCC low risk, N2 = 476, N1 = 373	MSKCC poor risk vs MSKCC low risk, N2 = 6, N1 = 373
Overall survival Hazard ratio/95% CI	1.47 (0.91 to 2.37)	5.65 (3.45 to 9.26)	2.33 (1.91 to 2.85)	8.51 (3.68 to 19.53)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(There was missing data in the validation cohort, and they study did not report a measure of calibration for the models of interest.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Fiala, 2020

Bibliographic Reference	Fiala, Ondrej; Finek, Jindrich; Poprach, Alexandr; Melichar, Bohuslav; Kopecky, Jindrich; Zemanova, Milada; Kopeckova, Katerina; Mlcoch, Tomas; Dolezal, Tomas; Capkova, Lenka; Buchler, Tomas; Outcomes According to MSKCC Risk Score with Focus on the Intermediate-Risk Group in Metastatic Renal Cell Carcinoma Patients Treated with First-Line

Sunitinib: A Retrospective Analysis of 2390 Patients.; Cancers; 2020; vol. 12 (no. 4)

Study Characteristics

Study design	Retrospective cohort study
Outcome(s) of interest	
Study location	Czech Republic
Study dates	May 2006 to January 2018
Risk prediction model(s)	MSKCC
Inclusion criteria	• Adult metastatic renal cell carcinoma • treated with first-line sunitinib.
Exclusion criteria	• Received prior chemotherapy or cytokines prior to sunitinib.
Selection of cohort	Database or clinical registry Renal cell carcinoma information system (RENIS) registry
Description of interventions/ point in the pathway model is used	First-line sunitinib. Sunitinib administered orally at the standard approved dosing using disease progression, toxicity or patient refusal.
Number of participants and recruitment methods	N=2390 Data obtained from the RENIS registry which includes metastatic renal cell carcinoma patients who have been treated with targeted therapy.
Description of cohorts	All metastatic
Length of follow-up	PFS: 10.6 (95% CI 9.9–11.5) months OS: 28.5 (95% CI 26.3–30.5) months
Follow-up schedule	Physical examination and routine laboratory tests performed at least every 6 weeks. CT performed every 3 to 4 months during treatment.

Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	Not industry funded
Additional comments	Univariable Cox proportional hazard models were used to evaluate the effect of risk factors on survival measures.

Study arms

MSKCC favourable (N = 806)

MSKCC intermediate (N = 1450)

MSKCC poor (N = 134)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 2390)
% Female Sample size	n = 667 ; % = 27.9
Age Custom value	Median 60.3
RCC subtypes - Clear cell Sample size	n = 2262 ; % = 94.6
RCC subtypes - Papillary Sample size	n = 109 ; % = 4.5
RCC subtypes - Chromophobe Sample size	n = 9 ; % = 0.4
RCC subtypes - Bellini duct Sample size	n = 6 ; % = 0.3
RCC subtypes - Oncocytoma	n = 2 ; % = 0.1

Characteristic	Study (N = 2390)
Sample size	
RCC subtypes - Unknown Sample size	n = 2 ; % = 0.1

Outcomes

MSKCC

Outcome	MSKCC intermediate vs MSKCC favourable, N2 = 1450, N1 = 806	MSKCC poor vs MSKCC favourable, N2 = 134, N1 = 806
Overall survival Hazard ratio/95% CI	1.64 (1.46 to 1.85)	4.11 (3.27 to 5.16)
Progression-free survival Hazard ratio/95% CI	1.52 (1.38 to 1.68)	3.01 (2.45 to 3.69)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(18.5% of participants were not evaluable, however no description regarding how this data was handled. No information on calibration.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Fujita, 2024

Bibliographic Reference	Fujita, Kazutoshi; Matsushita, Yuto; Toyoda, Shingo; Kojima, Takahiro; Yamashita, Shimpei; Taniguchi, Hisanori; Monji, Keisuke; Ishiyama, Ryo; Tatarano, Shuichi; Masui, Kimihiko; Nakamura, Eijiro; Kaneko, Tomoyuki; Kitano, Goshi; Motoshima, Takanobu; Shiraishi; Kira, Satoru; Murashima, Takaya; Hara, Hiroaki; Matsumura; Nishiyama, Naotaka; Miyake, Hideaki; Kitamura, Hiroshi; Uemura, Hirotsugu; The efficacy of second-line tyrosine kinase inhibitor for patients with metastatic non-clear cell renal cell carcinoma following first-line immune-oncology combination therapy.; World journal of urology; 2024; vol. 42 (no. 1); 536

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	2018 to 2022
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	People with advanced non-clear cell RCC who underwent second-line TKI therapy following IO combination therapy.
Exclusion criteria	People who did not receive second-line therapy and those diagnosed with clear cell RCC
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Second-line TKI therapy following IO combination therapy.
Number of participants	n=52
Length of follow-up	Median follow-up 20 months (range 1 to 30 months)
Follow-up schedule	Not reported
Outcome(s) of interest	Overall survival Progression-free survival Hazard ratio
Source of funding	Not reported
Additional comments	NA

Study arms

IMDC - intermediate (N = 33)

IMDC - poor (N = 19)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 52)
% Female Sample size	n = 17 ; % = 32.7
Age Range	24 to 84
Age Median (IQR)	67.5 (*NR* to *NR*)
RCC subtypes Sample size	n = NA ; % = NA
RCC subtypes - Papillary Sample size	n = 20 ; % = 38
RCC subtypes - Unclassified Sample size	n = 16 ; % = 30
RCC subtypes - MiT family translocation Sample size	n = 6 ; % = 12
RCC subtypes - Chromophobe Sample size	n = 4 ; % = 8
RCC subtypes - Others Sample size	n = 6 ; % = 12
RCC subtypes - Presence of sarcomatoid component Sample size	n = 7 ; % = 13

Characteristic	Study (N = 52)
Metastases location Sample size	n = NA ; % = NA
Metastases location - Lymph node Sample size	n = 28 ; % = 53
Metastases location - Lung Sample size	n = 24 ; % = 46
Metastases location - Bone Sample size	n = 20 ; % = 37
Metastases location - Liver Sample size	n = 9 ; % = 17
Metastases location - Brain Sample size	n = 2 ; % = 4

Outcomes

Time-to-event outcomes

Outcome	IMDC - poor vs IMDC - intermediate, N2 = , N1 =
Progression-free survival Hazard ratio/95% CI	1.98 (1.02 to 3.82)
Overall survival Hazard ratio/95% CI	2.74 (1.15 to 6.52)

Critical appraisal - PROBAST tool

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(Insufficient number of outcome events and no method of calibration reported. There was also no definition provided for outcome measures.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Giridhar, 2017

Bibliographic Reference	Giridhar, Karthik V; Sosa, Carlos P; Hillman, David W; Sanhueza, Cristobal; Dalpiaz, Candace L; Costello, Brian A; Quevedo, Fernando J; Pitot, Henry C; Dronca, Roxana S; Ertz, Donna; Cheville, John C; Donkena, Krishna Vanaja; Kohli, Manish; Whole Blood mRNA Expression-Based Prognosis of Metastatic Renal Cell Carcinoma.; International journal of molecular sciences; 2017; vol. 18 (no. 11)

Study Characteristics

Study design	Retrospective cohort study
Study location	USA
Study dates	October 2011 to May 2015
Risk prediction model(s)	MSKCC
Inclusion criteria	Metastatic renal cell carcinoma
Exclusion criteria	Not specified
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	First-line treatment
Number of participants	N = 47 MSKCC Favourable = 31 MSKCC Intermediate = 12 MSKCC Poor = 4

Length of follow-up	Median (range): 3.6 years (0.06-4.12)
Outcome(s) of interest	Overall survival
Source of funding	This work was supported by Development funds provided by the Roger Thrun WHR Inc. group for research in advanced kidney cancer. No funds were received to cover the costs to publish in open access
Additional comments	Cox proportional hazard regression and Kaplan–Meier analysis were performed using the MSKCC prognostic model to assess their associations with OS

Study arms

MSKCC Favourable (N = 31)

MSKCC Intermediate (N = 12)

MSKCC Poor (N = 4)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 47)
% Female No of events	n = 34 ; % = 72.3
Age Median (IQR)	66.4 (62.5 to 75.4)
RCC subtypes - Clear cell RCC No of events	n = 47 ; % = 100
MSKCC score - Favourable No of events	n = 31 ; % = 66
MSKCC score - Intermediate	n = 12 ; % = 26

Characteristic	Study (N = 47)
No of events	
MSKCC score - Poor No of events	n = 4 ; % = 8

Outcomes

Survival

Outcome	MSKCC Favourable, N = 31	MSKCC Intermediate, N = 12	MSKCC Poor, = 4
Overall survival No of events	n = 15 ; % = 48.4	n = 6 ; % = 50	n = 4 ; % = 100

Overall survival - Polarity - Higher values are better

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High (*There were insufficient outcome events and a lack of information around how missing data was handled*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Gu, 2017

Bibliographic Reference	Gu, Weijie; Wu, Junlong; Liu, Xiaohang; Zhang, Hailiang; Shi, Guohai; Zhu, Yao; Ye, Dingwei; Early skeletal muscle loss during target therapy is a prognostic biomarker in metastatic renal cell carcinoma patients.; Scientific reports; 2017; vol. 7 (no. 1); 7587

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2008-2014

Risk prediction model(s)	IMDC/Heng
Inclusion criteria	Clear cell carcinoma; Eastern Cooperative Oncology Group (ECOG) performance status of 0–1; treated with targeted therapy for >3 months; treatment charts recording weight and height available; patients in a clinically stable condition without severe comorbidities; and no limitations on food access or intake
Exclusion criteria	Loss to follow-up or no abdominal CT scan at either baseline or after 3–4 months of targeted therapy.
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	Patients were treated with tyrosine kinase inhibitors and mTOR inhibitors (sunitinib, sorafenib, pazopanib, fabitinib, axtinib, and everolimus)
Number of participants	N = 101 IMDC Favourable = 26 IMDC Intermediate = 68 IMDC Poor = 7
Length of follow-up	Median 30.8 months (95% CI: 24.1–37.4 months)
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	The work was supported by the National Natural Science Foundation of China (grant number 81370073) and Shanghai Science and Technology Development Funds (grant number 16QA1401100).
Additional comments	Univariate and multivariate Cox proportional hazards models were used to test for associations between the investigated variables and PFS and OS

Study arms

IMDC - Favourable (N = 26)

IMDC - Intermediate (N = 68)

IMDC - Poor (N = 7)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 101)
% Female No of events	n = 36 ; % = 35.6
IMDC Score - IMDC - Favourable No of events	n = 26 ; % = 25.7
IMDC Score - IMDC - Intermediate No of events	n = 68 ; % = 67.3
IMDC Score - IMDC - Poor No of events	n = 7 ; % = 7

Outcomes

Survival

Outcome	IMDC - Intermediate vs IMDC - Favourable, N2 = 68, N1 = 26	IMDC - Poor vs IMDC - Favourable, N2 = 7, N1 = 26
Overall survival Hazard ratio/95% CI	4.9 (1.93 to 12.44)	11.36 (3.2 to 40.31)
Progression-free survival Hazard ratio/95% CI	3.08 (1.44 to 6.58)	4.92 (1.58 to 15.31)

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

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Guida, 2024

Bibliographic Reference	Guida, Annalisa; Gili, Alessio; Mosillo, Claudia; Maruzzo, Marco; Lai, Eleonora; Pierantoni, Francesco; Bimbatti, Davide; Basso, Umberto; Fornarini, Giuseppe; Rebuzzi, Sara Elena; Calabro, Fabio; Cerbone, Linda; Caserta, Claudia; Sirgiovanni, Grazia; Serafin, Debora; Caffo, Orazio; Scagliarini, Sarah; Bracarda, Sergio; Efficacy and Safety of Pembrolizumab plus Axitinib combination for Metastatic Renal Cell Carcinoma in a Real-World Scenario: Data From the Prospective ProPAXI Study.; Clinical genitourinary cancer; 2024; vol. 22 (no. 6); 102225

Study Characteristics

Study design	Prospective cohort study
Study location	Italy
Study dates	2020 to 2023
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	People with histologically confirmed diagnosis of RCC and radiologically or histologically confirmed metastatic disease.
Exclusion criteria	People with secondary tumour and one participant lost to follow-up.
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First-line pembrolizumab/axitinib

Number of participants	n=172
Length of follow-up	Median follow-up 19.3 months (range 1.3 to 34.5)
Follow-up schedule	Not reported
Outcome(s) of interest	Overall survival Progression-free survival Hazard ratio
Source of funding	Not reported
Additional comments	NA

Study arms

IMDC - favourable (N = 32)

IMDC - intermediate (N = 106)

IMDC - poor (N = 32)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 170)
% Female Sample size	n = 35 ; % = 32.3
Age Range	33 to 86
Age Median (IQR)	62 (NR to NR)
Nephrectomy status Sample size	n = NA ; % = NA

Characteristic	Study (N = 170)
Nephrectomy status - Curative nephrectomy Sample size	n = 71 ; % = 41.8
Nephrectomy status - Cytoreductive nephrectomy Sample size	n = 24 ; % = 14
Nephrectomy status - Deferred nephrectomy Sample size	n = 4 ; % = 3.4
RCC subtypes Sample size	n = NA ; % = NA
RCC subtypes - Clear cell Sample size	n = 141 ; % = 82.9
RCC subtypes - Non-clear cell Sample size	n = 29 ; % = 17.1
Metastases location Sample size	n = NA ; % = NA
Metastases location - Lung Sample size	n = 106 ; % = 62.4
Metastases location - Nodes Sample size	n = 80 ; % = 47.1
Metastases location - Bone Sample size	n = 66 ; % = 38.8
Metastases location - Liver Sample size	n = 29 ; % = 17.1
Metastases location - Pancreas Sample size	n = 11 ; % = 6.5
Metastases location - Brain Sample size	n = 12 ; % = 7.6

Outcomes

Time-to-event outcomes

Outcome	IMDC - intermediate vs IMDC - favourable, N2 = 106, N1 = 32	IMDC - poor vs IMDC - favourable, N2 = 32, N1 = 32
Progression-free survival Hazard ratio/95% CI	1.71 (0.87 to 3.37)	1.98 (0.9 to 4.36)
Overall survival Hazard ratio/95% CI	3.55 (1.09 to 11.6)	5.7 (1.64 to 19.6)

Critical appraisal - PROBAST tool

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(No measure of calibration reported)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Hara, 2025

Bibliographic Reference	Hara, Takuto; Ueki, Hideto; Okamura, Yasuyoshi; Bando, Yukari; Suzuki, Kotaro; Terakawa, Tomoaki; Chiba, Koji; Hyodo, Yoji; Teishima, Jun; Miyake, Hideaki; Comparative prognostic value of tumor volume in IOIO and IOTKI treatment for metastatic renal cancer.; Urologic oncology; 2025; vol. 43 (no. 1); 63e19-63e27

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	October 2014 to February 2024
Risk prediction model(s)	IMDC/Heng

Inclusion criteria	People diagnosed with mRCC who received either IOIO or IOTKI treatment and had available clinical and imaging data from Kobe University Hospital and 5 affiliated hospitals.
Exclusion criteria	People without target lesions
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First-line combination therapy with dual immune checkpoint inhibitors
Number of participants	n=99
Description of cohorts	
Length of follow-up	Median follow-up 29.5 months (range 1.6 to 102.7)
Follow-up schedule	Not reported
Outcome(s) of interest	Overall survival Progression-free survival Hazard ratio
Source of funding	Not reported

Study arms

IMDC - intermediate (N = 60)

Outcome data reported for dual immune checkpoint inhibitor (IOIO) therapy arm only

IMDC - poor (N = 39)

Outcome data reported for dual immune checkpoint inhibitor (IOIO) therapy arm only

Population characteristics

Study-level characteristics

Characteristic	Study (N = 99)
% Female Sample size	n = 21 ; % = 21.2
Age Range	30 to 84
Age Median (IQR)	70 (NR to NR)
Nephrectomy status Sample size	n = 58 ; % = 58.6
RCC subtypes Sample size	n = NA ; % = NA
RCC subtypes - Clear cell Sample size	n = 75 ; % = 75.8
RCC subtypes - Non–clear cell Sample size	n = 58 ; % = 58.6
Metastases location Sample size	n = NA ; % = NA
Metastases location - Liver Sample size	n = 14 ; % = 14.1

Characteristic	Study (N = 99)
Metastases location - Bone Sample size	n = 38 ; % = 38.4
Metastases location - Lymph node Sample size	n = 46 ; % = 46.5

Outcomes

Time-to-event

Outcome	IMDC - poor vs IMDC - intermediate, N2 = 39, N1 = 60
Progression-free survival Hazard ratio/95% CI	2.21 (1.35 to 3.63)
Overall survival Hazard ratio/95% CI	2.77 (1.53 to 5.04)

Critical appraisal - PROBAST tool

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(Determination of outcome was unclear and a measure of calibration was not reported.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Kikuta, 2025

Bibliographic Reference	Kikuta, Masato; Naito, Sei; Osawa, Takahiro; Numakura, Kazuyuki; Narisawa, Takafumi; Takai, Yuki; Yagi, Mayu; Sekine, Yuya; Tokairin, Ojiro; Shinohara, Nobuo; Habuchi, Tomonori; Tsuchiya, Norihiko; Real-world short-term outcomes and treatment regimen comparisons in patients with metastatic renal cell carcinoma treated with first-line immune combinations.; BMC cancer; 2025; vol. 25 (no. 1); 117

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	August 2015 to July 2023
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	People who were clinically diagnosed with RCC and treated with immune combinations.
Exclusion criteria	• No metastatic lesions • Inability to evaluate IMDC risk • Use of immunotherapy combination as sequential therapy
Selection of cohort	Database or clinical registry
Description of interventions/ point in the pathway model is used	First-line treatment with either immune-oncologic drug doublet or immune-oncologic drug tyrosine kinase inhibitor combinations
Number of participants	n=172
Length of follow-up	Median follow-up: 15.8 months (IQR 6.5 to 30.2)
Follow-up schedule	Not reported
Outcome(s) of interest	Overall survival Progression-free survival Hazard ratio
Source of funding	None
Additional comments	Unclear whether HR analysis was univariate or multivariate People with favourable IMDC risk were excluded from analysis as there were only 3 participants in the IO-IO group

Study arms

IOIO - IMDC intermediate (N = 51)

IOIO - IMDC poor (N = 54)

IO-TKI - IMDC intermediate (N = 31)

IO-TKI - IMDC poor (N = 12)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 172)
% Female Sample size	n = 38 ; % = 22.1
Age Median (IQR)	68 (64 to 73)
Nephrectomy status Sample size	n = NA ; % = NA
Nephrectomy status - Yes Sample size	n = 89 ; % = 51.1
Nephrectomy status - No Sample size	n = 83 ; % = 48.9
RCC subtypes Sample size	n = NA ; % = NA
RCC subtypes - Clear cell Sample size	n = 142 ; % = 82.6
RCC subtypes - Non-clear cell/undetectable Sample size	n = 30 ; % = 17.4
Metastases location Sample size	n = NA ; % = NA

Characteristic	Study (N = 172)
Metastases location - Bone Sample size	n = 55 ; % = 32
Metastases location - Liver Sample size	n = 26 ; % = 15.2
Metastases location - Brain Sample size	n = 16 ; % = 9.3
Metastases location - Lymph node Sample size	n = 67 ; % = 40

Outcomes

Time-to-event outcomes

Outcome	IOIO - IMDC intermediate vs IOIO - IMDC poor, N2 = 51, N1 = 54	IO-TKI - IMDC intermediate vs IO-TKI - IMDC poor, N2 = 31, N1 = 12
Progression-free survival Hazard ratio/95% CI	1.8 (1.13 to 2.89)	2.68 (0.95 to 7.52)
Overall survival Hazard ratio/95% CI	2.05 (1.07 to 3.92)	10.8 (1.89 to 61.5)

Critical appraisal - PROBAST tool

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(A method of calibration was not reported. For the outcome of OS there were an insufficient number of events.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Kim, 2019a

Bibliographic Reference	Kim, Jung Kwon; Kim, Sung Han; Song, Mi Kyung; Joo, Jungnam; Seo, Seong Il; Kwak, Cheol; Jeong, Chang Wook; Song, Cheryn; Hwang, Eu Chang; Seo, Ill Young; Lee, Hakmin; Hong, Sung-Hoo; Park, Jae Young; Chung, Jinsoo; Application of the International Metastatic Renal Cell Carcinoma Database Consortium and Memorial Sloan Kettering Cancer Center Risk Models in Patients with Metastatic Non-Clear Cell Renal Cell Carcinoma: A Multi-Institutional Retrospective Study Using the Korean Metastatic Renal Cell Carcinoma Registry.; Cancer research and treatment; 2019; vol. 51 (no. 2); 758-768

Study Characteristics

Study design	Retrospective cohort study
Study location	Korea
Study dates	2001 to 2016
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	• Metastatic renal cell carcinoma • non-clear cell
Exclusion criteria	Not specified
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First-line targeted therapy: • vascular endothelial growth factor-tyrosine kinase inhibitors [VEGT-TKIs] • mammalian target of rapamycin inhibitors [mTORi]) or cytokines Model used at the start of first-line therapy.
Number of participants	N=156
Length of follow-up	For first-line progression free survival: median 5 months

Follow-up schedule	Not specified
Outcome(s) of interest	Model discrimination (C-stats) Progression-free survival
Source of funding	Not industry funded, grant support
Additional comments	NA

Population characteristics

Study-level characteristics

Characteristic	Study (N = 156)
% Female Sample size	n = 48 ; % = 31
Age Median (IQR)	57 (46 to 67)
Nephrectomy status - Cytoreductive nephrectomy Sample size	n = 93 ; % = 59.6
RCC subtypes - Papillary Sample size	n = 93 ; % = 59.6
RCC subtypes - Chromophobe Sample size	n = 20 ; % = 12.8
RCC subtypes - Collecting duct Sample size	n = 18 ; % = 11.5
RCC subtypes - Unclassified Sample size	n = 16 ; % = 10.3
RCC subtypes - Xp11.2 translocation Sample size	n = 9 ; % = 5.8
Metastases location - Lung Sample size	n = 71 ; % = 46.1

Characteristic	Study (N = 156)
Metastases location - Liver Sample size	n = 41 ; % = 26.6
Metastases location - Lymph nodes Sample size	n = 82 ; % = 53.3
Metastases location - Bone Sample size	n = 66 ; % = 42.9
Metastases location - Brain Sample size	n = 5 ; % = 3.3

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(No information on number of participants with the outcome. No information on whether all participants enrolled were included and no model performance measures.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Kim, 2018b

Bibliographic Reference	Kim, Myung Soo; Chung, Ho Seok; Hwang, Eu Chang; Jung, Seung Il; Kwon, Dong Deuk; Hwang, Jun Eul; Bae, Woo Kyun; Park, Jae Young; Jeong, Chang Wook; Kwak, Cheol; Song, Cheryn; Seo, Seong Il; Byun, Seok-Soo; Hong, Sung-Hoo; Chung, Jinsoo; Efficacy of First-Line Targeted Therapy in Real-World Korean Patients with Metastatic Renal Cell Carcinoma: Focus on Sunitinib and Pazopanib.; Journal of Korean medical science; 2018; vol. 33 (no. 51); e325

Study Characteristics

Study design	Retrospective cohort study
Study location	Korea
Study dates	2012 to 2016

Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	• metastatic renal cell carcinoma • treated with first-line systemic tyrosine kinase inhibitor (TKI) therapy (sunitinib (SU) or pazopanib (PZ))
Exclusion criteria	Not specified
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Each drug was administered at a standard dose: • SU at 50 mg daily for 4 weeks, followed by 2 weeks off drug per treatment cycle • PZ at 800 mg daily continuously Model used at baseline - start of first-line treatment
Number of participants	N=554
Length of follow-up	Median 16.4 months (95% confidence interval [CI], 14.7–17.8; interquartile range [IQR], 8.3–31.3)
Follow-up schedule	Not specified
Outcome(s) of interest	Overall survival
Source of funding	Not industry funded, grant supported
Additional comments	PFS and OS were analysed using Kaplan-Meier methods and log-rank tests. Univariate Cox proportional hazards regression analyses were performed to assess the association between baseline parameters and PFS or OS.

Study arms

Heng risk criteria - good (N = 114)

Heng risk criteria - intermediate (N = 345)

Heng risk criteria - poor (N = 90)

Heng risk criteria - unknown (N = 5)

MSKCC risk group good (N = 121)

MSKCC risk group intermediate (N = 356)

MSKCC risk group poor (N = 72)

MSKCC risk group unknown (N = 5)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 554)
% Female Sample size	n = 119 ; % = 21.5
Age - SU group Median (IQR)	59 (52 to 67)
Age - PZ group Median (IQR)	64 (55 to 72)
Nephrectomy status - Nephrectomy Sample size	n = 252 ; % = 45.4
Nephrectomy status - Metastasectomy Sample size	n = 142 ; % = 25.6
Metastases location - Lung Sample size	n = 403 ; % = 73
Metastases location - Liver Sample size	n = 63 ; % = 11

Characteristic	Study (N = 554)
Metastases location - Lymph node Sample size	n = 192 ; % = 35
Metastases location - Bone Sample size	n = 141 ; % = 25
Metastases location - Brain Sample size	n = 36 ; % = 6
Metastases location - Other Sample size	n = 147 ; % = 27

Outcomes

MSKCC

Outcome	MSKCC risk group intermediate vs MSKCC risk group good, N2 = 356, N1 = 121	MSKCC risk group poor vs MSKCC risk group good, N2 = 72, N1 = 121
Overall survival Hazard ratio/95% CI	1.93 (1.27 to 2.94)	5.34 (3.26 to 8.76)

Heng

Outcome	Heng risk criteria - intermediate vs Heng risk criteria - good, N2 = 345, N1 = 114	Heng risk criteria - poor vs Heng risk criteria - good, N2 = 90, N1 = 114
Overall survival Hazard ratio/95% CI	1.99 (1.28 to 3.09)	7.21 (4.43 to 11.7)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate *(No information on whether all participants enrolled were included. No performance measures evaluated.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Kim, 2019b

Bibliographic Reference	Kim, Sung Han; Kim, Jung Kwon; Park, Eun Young; Joo, Jungnam; Lee, Kang Hyun; Seo, Ho Kyung; Joung, Jae Young; Chung, Jinsoo; Liver metastasis and Heng risk are prognostic factors in patients with non-nephrectomized synchronous metastatic renal cell carcinoma treated with systemic therapy.; PloS one; 2019; vol. 14 (no. 2); e0211105

Study Characteristics

Study design	Retrospective cohort study
Study location	Korea
Study dates	2002-2005
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	Patients with mRCC with naïve, unresectable primary renal lesions who did not undergo nephrectomy
Exclusion criteria	Patients who had no eligible follow-up computed tomography (CT) imaging results during first-line systemic therapy or CT images from the last follow-up before discontinuation of treatment, discontinued systemic therapy owing to adverse side effects, refused therapy, had a past history of invasive surgical or local treatment for RCC (including nephrectomy, embolisation, and radiation therapy), had bilateral RCCs, had incomplete information regarding a past history of treatment for RCC, or had a history of mTOR inhibitor-targeted treatment were excluded
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	Patients who received VEGF-targeted therapy (either sunitinib, sorafenib or pazopanib). The prognostic model was used before systemic therapy

Number of participants	N = 70
Length of follow-up	Median follow-up period of 30.9 (6.0–30.9) months
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	This study was supported by the Research and Institute of National Cancer Center Grant (No. 1710290-2) to JC.
Additional comments	Univariable and multivariable analyses were performed using the Cox proportional hazards model to investigate the potential prognostic factors for PFS and OS

Study arms

Favourable + intermediate risk (N = 44)

Poor risk (N = 26)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 70)
% Female No of events	n = 15 ; % = 21.4
Age Mean (SD)	58.77 (11.89)
RCC subtypes - Clear cell RCC No of events	n = 57 ; % = 81.4
RCC subtypes - Unclassified No of events	n = 13 ; % = 18.6
Metastases location - Lung No of events	n = 54 ; % = 77.1

Characteristic	Study (N = 70)
Metastases location - Liver No of events	n = 16 ; % = 22.9
Metastases location - Lymph nodes No of events	n = 26 ; % = 37.1
Metastases location - Bone No of events	n = 22 ; % = 31.4
Metastases location - Brain No of events	n = 8 ; % = 11.4

Outcomes

Survival

Outcome	Poor risk vs Favourable + intermediate risk, N2 = 44, N1 = 26
Overall survival Hazard ratio/95% CI	2.63 (1.54 to 4.47)
Progression-free survival Hazard ratio/95% CI	2.05 (1.2 to 3.48)

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

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate (*Lack of information around analysis*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Ko, 2015

Bibliographic Reference	Ko, Jenny J; Xie, Wanling; Kroeger, Nils; Lee, Jae-Lyun; Rini, Brian I; Knox, Jennifer J; Bjarnason, Georg A; Srinivas, Sandy; Pal, Sumanta K; Yuasa, Takeshi; Smoragiewicz, Martin; Donskov, Frede; Kanesvaran, Ravindran; Wood, Lori; Ernst, D Scott; Agarwal, Neeraj; Vaishampayan, Ulka N; Rha, Sun-Young; Choueiri, Toni K; Heng, Daniel Y C; The International Metastatic Renal Cell Carcinoma Database Consortium model as a prognostic tool in patients with metastatic renal cell carcinoma previously treated with first-line targeted therapy: a population-based study.; The Lancet. Oncology; 2015; vol. 16 (no. 3); 293-300

Study Characteristics

Study design	Retrospective cohort study
Study location	Canada, USA, Greece, Japan, Singapore, South Korea, and Denmark
Study dates	2005 to 2012
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	• Patients who received second-line targeted therapy (anti-VEGF drug or mTOR inhibitor).
Exclusion criteria	• Treatment information on prognostic factors at initiation of second-line therapy not recorded.
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Second-line targeted therapy with either an anti-VEGT drug or an mTOR inhibitor. Model used at the initiation of second-line therapy.
Number of participants	N=1021
Description of cohorts	
Length of follow-up	Median follow-up in alive patients was 12.6 months (IQR 5.3–23.2) after the initiation of second-line therapy.
Follow-up schedule	Not specified

Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	Authors received some funding from industry
Additional comments	Cox regression analyses to assess the statistical association between overall survival and the six factors included in the IMDC prognostic model, and calculated hazard ratios (HR) with 95% CIs.

Study arms

IMDC favourable (N = 76)

IMDC intermediate (N = 529)

IMDC poor (N = 261)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 1021)
% Female Sample size	n = 260 ; % = 25
Age - <60 years at start of second-line therapy Sample size	n = 455 ; % = 45
Age - 60 or over at the start of second-line therapy Sample size	n = 566 ; % = 55
Nephrectomy status - Previous nephrectomy Sample size	n = 863 ; % = 85
Nephrectomy status - No previous nephrectomy Sample size	n = 157 ; % = 15

Outcomes

IMDC

Outcome	IMDC intermediate vs IMDC favourable, , N2 = 529, N1 = 76	IMDC poor vs IMDC favourable, N2 = 261, N1 = 76
Overall survival Hazard ratio/95% CI	1.89 (1.33 to 2.68)	5.73 (3.99 to 8.23)

Critical appraisal - PROBAST tool

Analysis	Overall risk of bias for analysis domain	Low
Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Kroeger, 2013

Bibliographic Reference	Kroeger, Nils; Xie, Wanling; Lee, Jae-Lyn; Bjarnason, Georg A; Knox, Jennifer J; Mackenzie, Mary J; Wood, Lori; Srinivas, Sandy; Vaishamayan, Ulka N; Rha, Sun-Young; Pal, Sumanta K; Yuasa, Takeshi; Donskov, Frede; Agarwal, Neeraj; Kollmannsberger, Christian K; Tan, Min-Han; North, Scott A; Rini, Brian I; Choueiri, Toni K; Heng, Daniel Y C; Metastatic non-clear cell renal cell carcinoma treated with targeted therapy agents: characterization of survival outcome and application of the International mRCC Database Consortium criteria.; Cancer; 2013; vol. 119 (no. 16); 2999-3006

Study Characteristics

Study design	Retrospective cohort study
Study location	20 academic centres from Canada, USA, Japan, South Korea, Singapore, and Denmark
Study dates	2008-2012
Risk prediction model(s)	IMDC/Heng MSKCC

Inclusion criteria	Patients who have received first-line targeted therapy between 2003 and 2012
Exclusion criteria	Patients with unknown histological subtypes and unknown treatment initiation date
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First-line targeted therapy, which includes anti-VEGF therapy, Sutent, Sorafenib, Axitinib, Bevacizumab, Pazopanib, and Tivozanib
Number of participants	N = 2215 Patients with clear cell RCC = 1963 Patients with non-clear cell RCC = 252 IMDC Favourable (nccRCC) = 29 IMDC Intermediate (nccRCC) = 127 IMDC Poor (nccRCC) = 66 IMDC Favourable (ccRCC) = 337 IMDC Intermediate (ccRCC) = 972 IMDC Poor (ccRCC) = 463
Length of follow-up	Median follow-up in alive patients was 22.3 months (IQR: 10.8-38.4 months)
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	None
Additional comments	It was applied the IMDC Model (presence/absence of the six pre-determined prognostic factors to determine the favourable, intermediate and poor risk groups) to nccRCC patients using Cox regression. Concordance indices (C-

	Index) were computed in order to test the predictive accuracy of the IMDC prognostic model

Study arms

IMDC Favourable (nccRCC patients) (N = 29)

IMDC Intermediate (nccRCC patients) (N = 127)

IMDC Poor (nccRCC patients) (N = 66)

IMDC Favourable (ccRCC patients) (N = 337)

IMDC Intermediate (ccRCC patients) (N = 972)

IMDC Poor (ccRCC patients) (N = 463)

Population characteristics

Study-level characteristics

Characteristic	Study (N =)
% Female No of events	n = 573 ; % = 26
Nephrectomy status - Prior Nephrectomy No of events	n = 1790 ; % = 80.9
RCC subtypes - Clear cell RCC No of events	n = 1963 ; % = 88.6
RCC subtypes - Non–clear cell RCC No of events	n = 252 ; % = 11.4

Outcomes

Survival

Outcome	IMDC Intermediate (nccRCC patients) vs IMDC Favourable (nccRCC patients), , N2 = 127, N1 = 29	IMDC Poor (nccRCC patients) vs IMDC Favourable (nccRCC patients), , N2 = 66, N1 = 29
Overall survival Hazard ratio/95% CI	1.97 (1.13 to 3.42)	5.69 (3.2 to 10.1)

Overall survival - Polarity - Higher values are better

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High (Not all enrolled participants were included in the analysis and it was judged unlikely that missing data were handled appropriately.)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Laukhtina, 2020

Bibliographic Reference	Laukhtina, Ekaterina; Pradere, Benjamin; D Andrea, David; Rosiello, Giuseppe; Luzzago, Stefano; Pecoraro, Angela; Palumbo, Carlotta; Knipper, Sophie; Karakiewicz, Pierre I; Margulis, Vitaly; Quhal, Fahad; Sari Motlagh, Reza; Mostafaei, Hadi; Mori, Keiichiro; Kimura, Shoji; Enikeev, Dmitry; Shariat, Shahrokh F; Association of preoperative serum De Ritis ratio with oncological outcomes in patients treated with cytoreductive nephrectomy for metastatic renal cell carcinoma.; Urologic oncology; 2020; vol. 38 (no. 12); 936e7-936e14

Study Characteristics

Study design	Retrospective cohort study
Study location	Tertiary centres in the United States and Europe
Study dates	NR

Risk prediction model(s)	IMDC/Heng
Inclusion criteria	Patients treated with cytoreductive nephrectomy
Exclusion criteria	Patients with other malignant primary tumours mRCC, except those with concomitant haematological disorders and chronic liver diseases (hepatitis, liver cirrhosis, and severe fatty liver disease) within the last 12 months
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Cytoreductive nephrectomy
Number of participants	N = 613 IMDC Favourable = 186 IMDC Intermediate = 343 IMDC Poor = 84
Length of follow-up	Median follow-up was 31 (IQR 16−58) months
Outcome(s) of interest	Overall survival
Source of funding	NR
Additional comments	The risk of survival was expressed as hazard ratios (HR) and 95% confidence intervals (95% CI)

Study arms

IMDC Favourable (N = 186)

IMDC Intermediate (N = 343)

IMDC Poor (N = 84)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 613)
% Female No of events	n = 185 ; % = 30
Age Median (IQR)	57 (50 to 64)
Nephrectomy status - Cytoreductive nephrectomy No of events	n = 613 ; % = 100
RCC subtypes - Clear cell RCC No of events	n = 584 ; % = 95
RCC subtypes - Other No of events	n = 29 ; % = 5
Metastases location - Adrenal glands No of events	n = 112 ; % = 18
Metastases location - Bones No of events	n = 181 ; % = 30
Metastases location - Brain No of events	n = 20 ; % = 3.3
Metastases location - Liver No of events	n = 41 ; % = 6.7
Metastases location - Lung	n = 415 ; % = 68

Characteristic	Study (N = 613)
No of events	
Metastases location - Lymph nodes No of events	n = 138 ; % = 22.5
Metastases location - Other No of events	n = 38 ; % = 6.2

Outcomes

Survival

Outcome	IMDC Intermediate vs IMDC Favourable, N2 = 343, N1 = 186	IMDC Poor vs IMDC Favourable, N2 = 84, N1 = 186
Overall survival Hazard ratio/p value	1.19 (0.09)	1.52 (0.01)

Overall survival - Polarity - Higher values are better

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Lee, 2017

Bibliographic Reference	Lee H; Kim YJ; Hwang EC; Kang SH; Hong SH; Chung J; Kwon TG; Kwak C; Kim HH; Oh JJ; Lee SC; Hong SK; Lee SE; Byun SS; ; Preoperative cholesterol level as a new independent predictive factor of survival in patients with metastatic renal cell carcinoma treated with cyto-reductive nephrectomy.; BMC cancer; 2017; vol. 17 (no. 1)

Study Characteristics

Study design	Retrospective cohort study
Study location	South Korea

Study dates	Not reported
Prognostic model(s)	IMDC/Heng
Inclusion criteria	People diagnosed with mRCC and initially treated with nephrectomy
Exclusion criteria	People who received neoadjuvant therapy, other malignancy, and incomplete information
Selection of cohort	Database or clinical registry
Description of interventions/ point in the pathway model is used	Cytoreductive nephrectomy following nephrectomy
Number of participants	N=244
Length of follow-up	Median follow-up 13 months (IQR 6.0 to 26.5)
Follow-up schedule	Follow-up protocols varied slightly among institutions or physicians but usually included 3 month intervals after surgery.
Outcome(s) of interest	Overall survival Hazard ratio
Source of funding	No specific funding or financial support for study
Additional comments	NA

Study arms

IMDC Low risk (N = NR)

IMDC Intermediate risk (N = NR)

IMDC High risk (N = NR)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 244)
Age Median (IQR)	59 (52 to 68)
RCC subtypes Sample size	n = NA ; % = NA
RCC subtypes - Clear cell Sample size	n = 213 ; % = 87.3
RCC subtypes - Papillary Sample size	n = 13 ; % = 5.3
RCC subtypes - Chromophobe Sample size	n = 4 ; % = 1.6
RCC subtypes - Collecting duct Sample size	n = 5 ; % = 2
RCC subtypes - Unclassified Sample size	n = 9 ; % = 3.7
Metastases location Sample size	n = NA ; % = NA
Metastases location - Lung Sample size	n = 78 ; % = 32
Metastases location - Liver Sample size	n = 7 ; % = 2.7
Metastases location - Bone Sample size	n = 24 ; % = 9.8
Metastases location - Non-regional LNI Sample size	n = 2 ; % = 1
Metastases location - Adrenal gland	n = 8 ; % = 3.3

Characteristic	Study (N = 244)
Sample size	
Metastases location - Multiple metastasis Sample size	n = 10 ; % = 4.1
% Male Sample size	n = 185 ; % = 75.8

Outcomes

Time-to-event

Outcome	IMDC Intermediate risk vs IMDC Low risk, N2 = NR, N1 = NR	IMDC High risk vs IMDC Low risk, N2 = NR, N1 = NR
Overall survival Hazard ratio/95% CI	1.19 (0.72 to 1.96)	1.81 (1 to 3.27)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(A measure of calibration and discrimination was not reported and there was no information around whether follow-up differed between different IMDC risk categories.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Li, 2020

Bibliographic Reference	Li, Tao; Li, Heng; Xie, Sheng; Tan, Yan; Xie, Zi-Ping; Li, Wen-Yi; Ai, Fen; Lactate Dehydrogenase-to-Lymphocyte Ratio Represents a Powerful Prognostic Tool of Metastatic Renal Cell Carcinoma Patients Treated with Tyrosine Kinase Inhibitors.; Pathology oncology research : POR; 2020; vol. 26 (no. 2); 1319-1324

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	January 2010 December 2017
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	• Metastatic renal cell carcinoma • first-line tyrosine kinase inhibitors (TKIs)
Exclusion criteria	• Immunodeficiency including HIV positive • other malignancies diagnosed during the observation period • insufficient data • history of other treatments such as neoadjuvant, adjuvant or any investigational therapy before TKIs.
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	Tyrosine kinase inhibitors. Model used at the start of pathway.
Number of participants and recruitment methods	N=355
Length of follow-up	Median progression-free survival: 14.2 months (95% CI 12.1–17.2) Median overall survival: 32.7 months (95% CI 27.1–36.4)
Follow-up schedule	Not specified
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	Health and Family Planning Commission of Wuhan Municipality
Additional comments	Survival were calculated using the Kaplan-Meier method and compared with the log-rank test. Clinicopathological characteristics on OS and PFS were evaluated by univariate analysis,

Study arms

IMDC good (N = 142)

IMDC intermediate (N = 181)

IMDC poor (N = 32)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 355)
% Female Sample size	n = 103 ; % = 29
Age Custom value	Median 62 years, range 23 to 87
RCC subtypes - Clear cell Sample size	n = 315 ; % = 89

Outcomes

IMDC

Outcome	IMDC intermediate vs IMDC good, N2 = 181, N1 = 142	IMDC poor vs IMDC good, N2 = 32, N1 = 142
Progression-free survival Hazard ratio/95% CI	1.43 (1.09 to 1.87)	5.09 (3.39 to 7.66)
Overall survival Hazard ratio/95% CI	1.99 (1.41 to 2.8)	11.12 (6.95 to 17.8)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate *(No information on model performance measures)*

Overall Risk of bias and Applicability	Concerns for applicability	Low

Lin, 2018

Bibliographic Reference	Lin, Zhiyuan; Liu, Li; Xia, Yu; Chen, Xiang; Xiong, Ying; Qu, Yang; Wang, Jiajun; Bai, Qi; Guo, Jianming; Xu, Jiejie; Tumor infiltrating CD19+ B lymphocytes predict prognostic and therapeutic benefits in metastatic renal cell carcinoma patients treated with tyrosine kinase inhibitors.; Oncoimmunology; 2018; vol. 7 (no. 10); e1477461

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	March 2005 to June 2014
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	• Diagnosis of metastatic renal cell carcinoma • no other malignancy history • treatment with sunitinib or sorafenib as first line systemic therapy • available fixed tumour tissue.
Exclusion criteria	• Lack of tissue sample • tumour necrosis area greater than 80% • received prior systemic therapy • loss of follow-up.
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	Sunitinib or sorafenib. First-line therapy, model used at start of pathway.
Number of participants and recruitment methods	N=108
Length of follow-up	Medians 23.35 months, range 1.1–92.6 months

Follow-up schedule	Not specified
Outcome(s) of interest	Overall survival Progression-free survival
Additional comments	Univariate Cox proportional hazard models were applied to evaluate the hazard ratio and 95% confidence interval.

Study arms

IMDC favourable (N = 23)

IMDC intermediate (N = 58)

IMDC poor (N = 27)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 108)
% Female Sample size	n = 32 ; % = 29.6
Age - 59 or less Sample size	n = 54 ; % = 50
Age - over 59 Sample size	n = 54 ; % = 50
RCC subtypes - Clear cell Sample size	n = 87 ; % = 80.6
RCC subtypes - Non-clear cell Sample size	n = 21 ; % = 19.4

Outcomes

IMDC

Outcome	IMDC intermediate vs IMDC favourable, N2 = 58, N1 = 23	IMDC poor vs IMDC favourable, N2 = 27, N1 = 23
Overall survival Hazard ratio/95% CI	1.19 (0.66 to 2.17)	4.32 (2.05 to 9.1)
Progression-free survival Hazard ratio/95% CI	0.87 (0.49 to 1.55)	2.27 (1.1 to 4.69)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate *(No information on performance measures.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Lolli, 2016

Bibliographic Reference	Lolli, Cristian; Basso, Umberto; Derosa, Lisa; Scarpi, Emanuela; Sava, Teodoro; Santoni, Matteo; Crabb, Simon J; Massari, Francesco; Aieta, Michele; Conteduca, Vincenza; Maruzzo, Marco; La Russa, Francesca; Wheater, Matthew; Berardi, Rossana; Galli, Luca; De Giorgi, Ugo; Systemic immune-inflammation index predicts the clinical outcome in patients with metastatic renal cell cancer treated with sunitinib.; Oncotarget; 2016; vol. 7 (no. 34); 54564-54571

Study Characteristics

Study design	Retrospective cohort study
Study location	Italy
Study dates	2006 to 2014
Risk prediction model(s)	IMDC/Heng MSKCC

Inclusion criteria	• Unresectable or metastatic renal cell carcinoma • first-line treatment with sunitinib.
Exclusion criteria	• History of treatments other that sunitinib.
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First-line treatment with sunitinib. Initial dose of 50 mg a day - 4 weeks on 2 weeks off. Model used before treatment.
Number of participants	N=335
Length of follow-up	Median 49 months (range 1 to 102)
Follow-up schedule	Patients evaluated at each cycle for possible toxicities, with a clinical examination and blood test. CT scan done at baseline and every 3 months during treatment.
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	No funding
Additional comments	Kaplan-Meier method used to estimate PFS and OS. Log-rank test and Cox proportional hazard regression were used to test for differences between groups.

Study arms

MSKCC good (N = 98)

MSKCC intermediate (N = 199)

MSKCC poor (N = 38)

IMDC good (N = 117)

IMDC intermediate (N = 176)

IMDC poor (N = 42)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 335)
% Female Sample size	n = 97 ; % = 29
Age Custom value	Median: 63, range 27-88
RCC subtypes - Clear cell Sample size	n = 315 ; % = 94
RCC subtypes - Papillary Sample size	n = 14 ; % = 4.2
RCC subtypes - Others Sample size	n = 6 ; % = 1.8

Outcomes

MSKCC

Outcome	MSKCC intermediate vs MSKCC good, N2 = 199, N1 = 98	MSKCC poor vs MSKCC good, N2 = 38, N1 = 98
Progression-free survival Hazard ratio/95% CI	1.48 (1.12 to 1.97)	2 (1.29 to 3.09)
Overall survival Hazard ratio/95% CI	2.44 (1.68 to 3.55)	4.04 (2.39 to 6.82)

IMDC

Outcome	IMDC intermediate vs IMDC good, N2 = 176, N1 = 117	IMDC poor vs IMDC good, N2 = 42, N1 = 117
Progression-free survival Hazard ratio/95% CI	1.43 (1.09 to 1.87)	5.09 (3.39 to 7.66)
Overall survival Hazard ratio/95% CI	1.99 (1.41 to 2.8)	11.12 (6.95 to 17.8)

Event data

Outcome	MSKCC good, N = 98	MSKCC intermediate, N = 199	MSKCC poor, N = 38	IMDC good , , N = 117	IMDC intermediate, N = 176	IMDC poor, N = 42
Progression-free survival No of events	n = 70	n = 161	n = 29	n = 84	n = 139	n = 37
Overall survival No of events	n = 35	n = 134	n = 24	n = 48	n = 109	n = 36

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(No information on whether all participants enrolled were included, and no information on model performance measures)*
Overall Risk of bias and Applicability	Concerns for applicability	Unclear *(Population a mixed of unresectable and metastatic. Proportions are not reported.)*

Lu, 2016

Bibliographic Reference	Lu, Xiaolin; Gu, Weijie; Zhang, Hailiang; Zhu, Yao; Shi, Guohai; Ye, Dingwei; Oligometastatic state predicts a favorable outcome for renal cell carcinoma patients with bone metastasis under the treatment of sunitinib.; Oncotarget; 2016; vol. 7 (no. 18); 26879-87

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2008-2015
Risk prediction model(s)	MSKCC
Inclusion criteria	Patients with RCC bone metastasis treated with sunitinib
Exclusion criteria	NR
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	Sunitinib, 50 mg/day; 4 weeks on and 2 weeks off
Number of participants	N = 67 MSKCC Favourable = 33

	MSKCC Intermediate = 31 MSKCC Poor = 1
Length of follow-up	NR
Follow-up schedule	NR
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	NR
Additional comments	Survival curves were constructed using the Kaplan–Meier method, with log-rank tests used to assess the differences between the groups. Adjusted hazard ratio (HR) with 95% confidence intervals (95% CIs) was calculated using Cox proportional hazards models. Harrell's c-index was used to evaluate the predictive accuracy of Cox proportional hazards models which is analogous to the area under the receiver operating characteristic curve for censored data

Study arms

MSKCC Favourable (N = 33)

MSKCC Intermediate + Poor (N = 34)

Population characteristics

Study-level characteristics

Characteristic	**Study (N = 67)**
% Female No of events	n = 16 ; % = 33.9
Age - ≥58 No of events	n = 37 ; % = 55.2
Age - <58 No of events	n = 30 ; % = 44.8
Nephrectomy status	n = 67 ; % = 100

Characteristic	Study (N = 67)
No of events	
RCC subtypes - Clear cell RCC No of events	n = 59 ; % = 88.1
RCC subtypes - Other No of events	n = 8 ; % = 11.9
Metastases location - Lung No of events	n = 42 ; % = 56
Metastases location - Liver No of events	n = 8 ; % = 10.7
Metastases location - Lymph nodes No of events	n = 13 ; % = 17.3
Metastases location - Brain No of events	n = 2 ; % = 2.7
Metastases location - Other No of events	n = 10 ; % = 13.3
MSKCC score - Favourable No of events	n = 33 ; % = 49.3
MSKCC score - Intermediate No of events	n = 31 ; % = 46.3
MSKCC score - Poor No of events	n = 1 ; % = 4.4

Outcomes

Survival

Outcome	MSKCC Intermediate + Poor vs MSKCC Favourable, N2 = 34, N1 = 33
Overall survival	2.25 (1.26 to 4.02)

Outcome	MSKCC Intermediate + Poor vs MSKCC Favourable, N2 = 34, N1 = 33
Hazard ratio/95% CI	

Overall survival - Polarity - Higher values are better

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate (*Lack of information around whether participants with missing data were handled appropriately.*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Marchioni, 2021

Bibliographic Reference	Marchioni, Michele; Kriegmair, Maximilian; Heck, Mathias; Amiel, Thomas; Porpiglia, Francesco; Ceccucci, Enrico; Campi, Riccardo; Minervini, Andrea; Mari, Andrea; Van Bruwaene, Siska; Linares, Estefania; Hevia, Vital; Musquera, Mireia; D'Anna, Mauricio; Derweesh, Ithaar; Bradshaw, Aaron; Autorino, Riccardo; Guruli, Georgi; Veccia, Alessandro; Roussel, Eduard; Albersen, Maarten; Pavan, Nicola; Claps, Francesco; Antonelli, Alessandro; Palumbo, Carlotta; Klatte, Tobias; Erdem, Selcuk; Mir, Maria Carmen; Development of a Novel Risk Score to Select the Optimal Candidate for Cytoreductive Nephrectomy Among Patients with Metastatic Renal Cell Carcinoma. Results from a Multi-institutional Registry (REMARCC).; European urology oncology; 2021; vol. 4 (no. 2); 256-263

Study Characteristics

Study design	Retrospective cohort study
Study location	North America and Europe
Study dates	2005 to 2019
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	• Patients who underwent cytoreductive nephrectomy • only those who underwent CN after 2005 were included as this date is accepted initiation of target therapies

	• patients with data about vital status and follow-up.
Exclusion criteria	Not specified
Selection of cohort	Database or clinical registry
Description of interventions/ point in the pathway model is used	Participants underwent cytoreductive nephrectomy as first-line. Model used pre-treatment.
Number of participants	N=519
Length of follow-up	Median: 18.1 months (IQR: 5.9–39.7)
Follow-up schedule	Not specified
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	No funding
Additional comments	Univariate Cox proportional hazard regression models were performed to test the main predictors of overall mortality.

Population characteristics

Study-level characteristics

Characteristic	**Study (N = 519)**
% Female Sample size	n = 149 ; % = 29
Age Median (IQR)	63 (55 to 70)
RCC subtypes - Clear cell Sample size	n = 340 ; % = 65

Characteristic	Study (N = 519)
RCC subtypes - Non-clear cell Sample size	n = 82 ; % = 16
RCC subtypes - Unknown Sample size	n = 97 ; % = 19
Metastases location - Bone Sample size	n = 74 ; % = 14
Metastases location - Brain Sample size	n = 31 ; % = 6
Metastases location - Liver Sample size	n = 51 ; % = 10
Metastases location - Lung Sample size	n = 273 ; % = 53
Metastases location - Mediastinal lymph nodes Sample size	n = 54 ; % = 10

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate *(No information on model performance measures.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Matsushita, 2024

Bibliographic Reference	Matsushita, Yuto; Kojima, Takahiro; Osawa, Takahiro; Sazuka, Tomokazu; Hatakeyama, Shingo; Goto, Keisuke; Numakura, Kazuyuki; Yamana, Kazutoshi; Kandori, Shuya; Fujita, Kazutoshi; Ueda, Kosuke; Tanaka, Hajime; Tomida, Ryotaro; Kurahashi, Toshifumi; Bando, Yukari; Nishiyama, Naotaka; Kimura, Takahiro; Yamashita, Shimpei; Kitamura, Hiroshi; Miyake, Hideaki; Prognostic outcomes in patients with metastatic renal cell carcinoma receiving second-line treatment with tyrosine kinase inhibitor following first-line immune-oncology combination therapy.;

International journal of urology : official journal of the Japanese Urological Association; 2024; vol. 31 (no. 5); 526-533

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	2018-2022
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	Patients who were diagnosed with mRCC and treated with first-line immune-oncology combination therapy, followed by second-line TKI therapy
Exclusion criteria	NR
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	The second-line therapy assessed were Cabozantinib, Axitinib, Pazopanib, Sunitinib, and Sorafenib
Number of participants	N = 243 IMDC Score Favourable = 27 Intermediate = 141 Poor = 75 MSKCC Score Favourable = 76 Intermediate = 125 Poor = 42
Follow-up schedule	NR

Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	No external funding was received for this study.
Additional comments	The prognostic impact of clinicopathological factors was assessed by univariate analyses using the Cox proportional hazards regression model. The c-index was calculated, and the decision curve analyses were performed to compare the accuracy and feasibility of the risk prediction models, as previously described.

Study arms

IMDC Favourable + Intermediate (N = 168)

IMDC Poor (N = 75)

MSKCC Favourable + Intermediate (N = 201)

MSKCC Poor (N = 42)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 243)
% Female No of events	n = 57 ; % = 23.5
RCC subtypes - Clear cell RCC No of events	n = 182 ; % = 74.9
RCC subtypes - Non–clear cell RCC No of events	n = 53 ; % = 21.8
RCC subtypes - Unknown No of events	n = 8 ; % = 3.3
Metastases location - Lung No of events	n = 169 ; % = 69.5

Characteristic	Study (N = 243)
Metastases location - Liver No of events	n = 49 ; % = 20.2
Metastases location - Bone No of events	n = 93 ; % = 37.9
Metastases location - Brain No of events	n = 14 ; % = 5.8
IMDC Score - Favourite No of events	n = 27 ; % = 11.1
IMDC Score - Intermediate No of events	n = 141 ; % = 58
IMDC Score - Poor No of events	n = 75 ; % = 30.9
MSKCC score - Favourable No of events	n = 76 ; % = 31.3
MSKCC score - Intermediate No of events	n = 125 ; % = 51.4
MSKCC score - Poor No of events	n = 42 ; % = 17.3

Outcomes

IMDC

Outcome	IMDC Poor vs IMDC Favourable + Intermediate, N2 = 75, N1 = 168
Progression-free survival Hazard ratio/95% CI	2.07 (1.48 to 2.88)
Overall survival Hazard ratio/95% CI	2.65 (1.76 to 4)

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

MSKCC

Outcome	MSKCC Poor vs MSKCC Favourable + Intermediate, N2 = 42, N1 = 201
Progression-free survival Hazard ratio/95% CI	2.31 (1.57 to 3.39)
Overall survival Hazard ratio/95% CI	2.84 (1.79 to 4.5)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Miyake, 2014

Bibliographic Reference	Miyake, Hideaki; Miyazaki, Akira; Harada, Ken-Ichi; Fujisawa, Masato; Assessment of efficacy, safety and quality of life of 110 patients treated with sunitinib as first-line therapy for metastatic renal cell carcinoma: experience in real-world clinical practice in Japan.; Medical oncology (Northwood, London, England); 2014; vol. 31 (no. 6); 978

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	September 2008 to October 2013
Risk prediction model(s)	MSKCC
Inclusion criteria	People with mRCC who were treated with sunitinib as first-line therapy
Exclusion criteria	Not reported

Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	First-line therapy with sunitinib
Number of participants	N=110
Length of follow-up	Median 19 months (range 3 to 63 months)
Follow-up schedule	Tumour measurements were generally performed by CT before and every 12 weeks after the initiation of treatment with sunitinib.
Outcome(s) of interest	Progression-free survival
Source of funding	Not reported
Additional comments	The prognostic significance of certain parameters was assessed using the Cox proportional hazards regression model. The study also reported the outcome of OS, however, it was judged likely that there was overlap with Miyazake 2015, and therefore only PFS was extracted.

Study arms

MSKCC poor risk (N = 26)

MSKCC favourable and intermediate risk (N = 84)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 110)
% Female Sample size	n = 24 ; % = 21.8
Age Range	37 to 85

Characteristic	Study (N = 110)
Age Median (IQR)	62.5 (*NR* to *NR*)
Nephrectomy status Prior nephrectomy Sample size	n = 99 ; % = 90
RCC subtypes - Clear cell Sample size	n = 96 ; % = 87.3
RCC subtypes - Non–clear cell Sample size	n = 14 ; % = 12.8
Metastases location - Lung Sample size	n = 64 ; % = 58.2
Metastases location - Lymph node Sample size	n = 32 ; % = 29.1
Metastases location - Bone Sample size	n = 31 ; % = 28.2
Metastases location - Liver Sample size	n = 17 ; % = 15.5
Metastases location - Brain Sample size	n = 10 ; % = 9.1

Outcomes

Time-to-event

Outcome	MSKCC poor risk vs MSKCC favourable and intermediate risk, N2 = 26, N1 = 84
Progression-free survival Reported as HR (p-value). 95% CIs calculated by analyst Hazard ratio/p value	3.89 (0.001)

Outcome	MSKCC poor risk vs MSKCC favourable and intermediate risk, N2 = 26, N1 = 84
Progression-free survival Reported as HR (p-value). 95% CIs calculated by analyst Hazard ratio/95% CI	3.89 (1.74 to 8.71)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(No measure of calibration or discrimination was reported.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Miyazaki, 2015

Bibliographic Reference	Miyazaki, Akira; Miyake, Hideaki; Harada, Ken-Ichi; Inoue, Taka-Aki; Fujisawa, Masato; Prognostic outcome in patients treated with tyrosine kinase inhibitors as first-line molecular-targeted therapy for metastatic renal cell carcinoma: Experience in real-world clinical practice in Japan.; Molecular and clinical oncology; 2015; vol. 3 (no. 3); 601-606

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	April 2008 to September 2013
Risk prediction model(s)	MSKCC
Inclusion criteria	People with pathologically diagnosed mRCC who were TKI naïve and treated with either sorafenib or sunitinib as first-line molecular targeted therapy for ≥2 months
Exclusion criteria	Not reported
Selection of cohort	Single centre

Description of interventions/ point in the pathway model is used	Participants received sorafenib or sunitinib as first-line molecular targeted therapy
Number of participants	N=271
Length of follow-up	Median 19 months (range 2-64 months)
Follow-up schedule	Tumour measurements were performed by CT prior to and every 12 weeks following TKI introduction
Outcome(s) of interest	Overall survival
Source of funding	Not reported
Additional comments	The prognostic significance of certain factors was assessed using the Cox proportional hazards regression model.

Study arms

MSKCC poor risk (N = 44)

MSKCC favourable or intermediate risk (N = 227)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 271)
% Female Sample size	n = 56 ; % = 20.7
Age - 65 years and younger Sample size	n = 126 ; % = 46.5
Age - Older than 65 years Sample size	n = 145 ; % = 53.5

Characteristic	Study (N = 271)
Nephrectomy status Not treated by radical nephrectomy Sample size	n = 26 ; % = 9.6
RCC subtypes - Clear cell Sample size	n = 231 ; % = 85.2
RCC subtypes - Other Sample size	n = 40 ; % = 14.8
Metastases location - Lung Sample size	n = 177 ; % = 65.3
Metastases location - Lymph node Sample size	n = 69 ; % = 25.5
Metastases location - Bone Sample size	n = 55 ; % = 20.3
Metastases location - Liver Sample size	n = 31 ; % = 11.4
Metastases location - Brain Sample size	n = 21 ; % = 7.7

Outcomes

Time-to-event

Outcome	MSKCC poor risk vs MSKCC favourable or intermediate risk, N2 = 44, N1 = 227
Overall survival Reported as HR (p-value). 95% CIs calculated by analyst Hazard ratio/p value	4.31 (0.001)
Overall survival Reported as HR (p-value). 95% CIs calculated by analyst Hazard ratio/95% CI	4.31 (1.81 to 10.26)

Event outcomes

Outcome	MSKCC poor risk, N = 44	MSKCC favourable or intermediate risk, N = 227
Mortality No of events	n = 34 ; % = 27	n = 92 ; % = 83

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(No measure of discrimination or calibration was reported)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Miyake, 2016a

Bibliographic Reference	Miyake, Hideaki; Miyazaki, Akira; Imai, Satoshi; Harada, Ken-Ichi; Fujisawa, Masato; Early Tumor Shrinkage Under Treatment with First-line Tyrosine Kinase Inhibitors as a Predictor of Overall Survival in Patients with Metastatic Renal Cell Carcinoma: a Retrospective Multi-Institutional Study in Japan.; Targeted oncology; 2016; vol. 11 (no. 2); 175-82

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	April 2011 to December 2014
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	• Metastatic renal cell carcinoma • treated with sunitinib and sorafenib for at least 3 months as first-line molecular-targeted therapy.
Exclusion criteria	Not specified
Selection of cohort	Multicentre

Description of interventions/ point in the pathway model is used	First-line molecular-targeted therapy with sunitinib and sorafenib. All patients initially received either sunitinib 50 mg once daily in repeated 6-week cycles (4 weeks on, 2 weeks off) or sorafenib 400 mg twice daily continuously. Model used at baseline before initiation of treatment.
Number of participants	N=185
Length of follow-up	OS: Median 33.6 months
Follow-up schedule	Tumour measurements were conducted by CT before and approximately every 12 weeks after initiation of treatment.
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	None received
Additional comments	Impact of clinicopathological factors were analysed by univariate analysed using Cox proportional hazards regression model

Study arms

MSKCC favourable (N = 59)

MSKCC intermediate (N = 91)

MSKCC poor (N = 35)

IMDC/Heng favourable (N = 44)

IMDC/Heng intermediate (N = 107)

IMDC/Heng poor (N = 34)

MSKCC favourable + intermediate (N = 150)

IMDC/Heng favourable + intermediate (N = 151)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 185)
% Female Sample size	n = 44 ; % = 23.8
Age Custom value	Median 62, Range (37-88)
Nephrectomy status - Prior nephrectomy Sample size	n = 171 ; % = 92.4
RCC subtypes - Clear cell Sample size	n = 159 ; % = 85.9
RCC subtypes - Others Sample size	n = 26 ; % = 14.1
Metastases location - Lung Sample size	n = 113 ; % = 61.1
Metastases location - Lymph node Sample size	n = 52 ; % = 28.1

Characteristic	Study (N = 185)
Metastases location - Bone Sample size	n = 50 ; % = 27
Metastases location - Liver Sample size	n = 29 ; % = 15.7
Metastases location - Brain Sample size	n = 18 ; % = 9.7

Outcomes

MSKCC

Outcome	MSKCC poor vs MSKCC favourable + intermediate, N2 = 35, N1 = 150
Overall survival Hazard ratio/95% CI	3.45 (1.33 to 8.73)

IMDC/Heng

Outcome	IMDC/Heng poor vs IMDC/Heng favourable + intermediate, N2 = 34, N1 = 151
Overall survival Hazard ratio/95% CI	1.87 (0.92 to 2.98)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(Not enough information provided on whether all participants enrolled were included in the analysis. Not mention of model performance measures.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Miyake, 2016b

Bibliographic Reference	Miyake, Hideaki; Harada, Ken-Ichi; Ozono, Seiichiro; Fujisawa, Masato; Prognostic Significance of Early Tumor Shrinkage Under Second-Line Targeted Therapy for Metastatic Renal Cell Carcinoma: A Retrospective Multi-Institutional Study in Japan.; Molecular diagnosis & therapy; 2016; vol. 20 (no. 4); 385-92

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	April 2011 to December 2014
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	People with mRCC who received second-line molecular targeted therapy for at least 3 months after progression on first-line targeted therapy . People who received immunotherapy using interferon-alpha and/or interleukin-2 before first-line therapy were also eligible.
Exclusion criteria	Not reported
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Second-line therapy with either sunitinib, sorafenib or temsirolimus.
Number of participants	N = 271
Length of follow-up	70 months
Follow-up schedule	Not reported
Outcome(s) of interest	Overall survival
Source of funding	The study received no direct or indirect industry or pharmaceutical company support.

Study arms

IMDC favourable and intermediate risk (N = 194)

IMDC poor risk (N = 77)

MSKCC favourable and intermediate risk (N = 201)

MSKCC poor risk (N = 70)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 271)
% Female Sample size	n = 70 ; % = 25.8
Age Range	37 to 82
Age Median (IQR)	61 (*NR* to *NR*)
Nephrectomy status Prior nephrectomy Sample size	n = 252 ; % = 93
RCC subtypes - Clear cell Sample size	n = 235 ; % = 86.7
RCC subtypes - Others Sample size	n = 36 ; % = 13.3
Metastases location - Lung Sample size	n = 183 ; % = 67.5
Metastases location - Lymph node Sample size	n = 79 ; % = 29.2
Metastases location - Bone Sample size	n = 79 ; % = 29.2

Characteristic	Study (N = 271)
Metastases location - Liver Sample size	n = 33 ; % = 12.2
Metastases location - Brain Sample size	n = 20 ; % = 7.4

Outcomes

Time-to-event

Outcome	IMDC poor risk vs IMDC favourable and intermediate risk, N2 = 77, N1 = 194	MSKCC poor risk vs MSKCC favourable and intermediate risk, N2 = 70, N1 = 201
Overall survival Hazard ratio/95% CI	1.89 (0.88 to 2.79)	3.41 (1.33 to 9.43)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(The study did not report a measure of calibration or discrimination)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Miyake, 2017

Bibliographic Reference	Miyake, Hideaki; Harada, Ken-Ichi; Ozono, Seiichiro; Fujisawa, Masato; Assessment of Efficacy, Safety, and Quality of Life of 124 Patients Treated With Axitinib as Second-Line Therapy for Metastatic Renal-Cell Carcinoma: Experience in Real-World Clinical Practice in Japan.; Clinical genitourinary cancer; 2017; vol. 15 (no. 1); 122-128

Study Characteristics

Study design	Retrospective cohort study

Study location	Japan
Study dates	August 2012 and September 2015
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	People with mRCC who received axitanib as a second-line therapy after the failure of first-line systemic therapy.
Exclusion criteria	Not reported
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	Second-line treatment with axitanib (participants had received sunitinib, sorafenib, temsirolimus, and cytokine therapy, in the first-line setting)
Number of participants	N = 124
Length of follow-up	41 months
Follow-up schedule	Tumour measurements were generally performed by computed tomography before and every 6 to 12 weeks after the initiation of treatment with axitinib.
Outcome(s) of interest	Progression-free survival
Source of funding	Not reported
Additional comments	Study reports OS, however, this was not extracted as it was judged that there could be overlap between Miyake 2016b and Miyake 2017, and OS outcomes were from Miyake 2016b

Study arms

IMDC favourable and intermediate risk (N = 92)

IMDC poor risk (N = 32)

MSKCC favourable and intermediate risk (N = 93)

MSKCC poor risk (N = 31)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 124)
% Female Sample size	n = 32 ; % = 25.8
Age Range	37 to 81
Age Median (IQR)	63 (*NR* to *NR*)
Nephrectomy status Prior nephrectomy Sample size	n = 114 ; % = 91.9
RCC subtypes - Clear cell Sample size	n = 110 ; % = 88.7
RCC subtypes - Non–clear cell Sample size	n = 14 ; % = 11.3
Metastases location - Lung Sample size	n = 84 ; % = 67.7
Metastases location - Lymph node Sample size	n = 36 ; % = 29
Metastases location - Bone Sample size	n = 34 ; % = 27.4

Characteristic	Study (N = 124)
Metastases location - Liver Sample size	n = 16 ; % = 12.9
Metastases location - Brain Sample size	n = 8 ; % = 6.5

Outcomes

Time-to-event

Outcome	IMDC poor risk vs IMDC favourable and intermediate risk, N2 = 32, N1 = 92	MSKCC poor risk vs MSKCC favourable and intermediate risk, N2 = 31, N1 = 93
Progression-free survival Hazard ratio/p value	1.89 (0.12)	3.53 (0.0087)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(The study did not report a measure of calibration or discrimination)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Ning, 2022

Bibliographic Reference	Ning, Kang; Li, Zhen; Liu, Huiming; Tian, Xi; Wang, Jun; Wu, Yi; Xiong, Longbin; Zou, Xiangpeng; Peng, Yulu; Zhou, Zhaohui; Zhou, Fangjian; Yu, Chunping; Luo, Junhang; Zhang, Hailiang; Dong, Pei; Zhang, Zhiling; Perirenal Fat Thickness Significantly Associated with Prognosis of Metastatic Renal Cell Cancer Patients Receiving Anti-VEGF Therapy.; Nutrients; 2022; vol. 14 (no. 16)

Study Characteristics

Study design	Retrospective cohort study

Study location	China
Study dates	May 2008 to September 2020
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	• Metastatic renal cell carcinoma • receiving first-line anti-VEGF therapy.
Exclusion criteria	• No CT scan for body composition • less than 1 year follow-up.
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Treated with sunitanib, axitinib, pazopanib, sorafenib, and bevacizumab. Model used pretreatment. Model include the time from diagnosis to treatment of less than 1 year.
Number of participants	N=358
Length of follow-up	Median OS: 22 (IQR 13 - 17) Median PFS: 9.1 (IQR 4.8 - 16.1)
Follow-up schedule	Not specified
Outcome(s) of interest	Model discrimination (C-stats) Overall survival Progression-free survival
Source of funding	Not industry funded
Additional comments	Model fit was measure by the concordance index.

Population characteristics

Study-level characteristics

Characteristic	Study (N = 358)
% Female Sample size	n = 91 ; % = 25
Age Median (IQR)	56 (48 to 64)
Nephrectomy status - Had nephrectomy Sample size	n = 289 ; % = 80.7
Metastases location - Lung Sample size	n = 170 ; % = 47.5
Metastases location - Bone Sample size	n = 102 ; % = 28.5
Metastases location - Liver Sample size	n = 37 ; % = 10.3
Metastases location - Adrenal gland Sample size	n = 37 ; % = 10.3
Metastases location - Lymph node Sample size	n = 168 ; % = 46.9

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate *(No information on model performance measures)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Rebuzzi, 2022

Bibliographic Reference	Rebuzzi, S E; Signori, A; Buti, S; Banna, G L; Murianni, V; Damassi, A; Maruzzo, M; Giannarelli, D; Tortora, G; Galli, L; Rizzo, M; De Giorgi, U; Antonuzzo, L; Bracarda, S; Carteni, G; Atzori, F; Tamberi, S; Procopio, G; Fratino, L; Lo Re, G; Santoni, M; Baldessari, C; Astone, A; Calabro, F; Brunelli, M; Porta, C; Rescigno, P; Basso, U; Fornarini, G; Validation of the Meet-URO score in patients with metastatic renal cell carcinoma receiving first-line nivolumab and ipilimumab in the Italian Expanded Access Program.; ESMO open; 2022; vol. 7 (no. 6); 100634

Study Characteristics

Study design	Retrospective cohort study
Study location	Italy
Study dates	April and October 2019
Risk prediction model(s)	IMDC/Heng Meet-URO
Inclusion criteria	Adults with metastatic clear cell or non-clear cell RCC and IMDC intermediate/poor risk who had received at least one cycle of nivolumab plus ipilimumab.
Exclusion criteria	Patients with IMDC favourable disease
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	Nivolumab plus ipilimumab was administered intravenously at 3 mg/kg and 1 mg/kg, respectively, every 3 weeks for four doses, followed by maintenance nivolumab at a flat dose of 240 mg every 2 weeks or 480 mg every 4 weeks. Prognostic model was applied before starting pharmacologic therapy
Number of participants	N = 306 IMDC Intermediate = 206 IMDC Poor = 100
Length of follow-up	Median of 12.2 months (IQR: 4.7-17.3 months)
Outcome(s) of interest	Overall survival Progression-free survival

Source of funding	None declared
Additional comments	The Meet-URO score was calibrated using a calibration plot that compared estimated and observed OS probabilities at 1 year.

Study arms

IMDC Intermediate (N = 206)

IMDC poor (N = 100)

Meet-URO group 2 (N = 89)

Meet-URO group 3 (N = 88)

Meet-URO group 4 (N = 101)

Meet-URO group 5 (N = 28)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 306)
% Female No of events	n = 78 ; % = 25.5
Age Median (IQR)	62.2 (24 to 87)
Nephrectomy status - Yes No of events	n = 200 ; % = 65.4
Nephrectomy status - No No of events	n = 106 ; % = 34.6
RCC subtypes - Clear cell RCC No of events	n = 255 ; % = 83.3
RCC subtypes - Non–clear cell RCC No of events	n = 48 ; % = 15.7

Characteristic	Study (N = 306)
RCC subtypes - Missing No of events	n = 3 ; % = 1
Metastases location - Bone No of events	n = 96 ; % = 31.4
Metastases location - Liver No of events	n = 250 ; % = 81.7
IMDC - Intermediate No of events	n = 206 ; % = 67.3
IMDC - Poor No of events	n = 100 ; % = 32.7

Outcomes

IMDC

Outcome	IMDC poor vs IMDC Intermediate, N2 = 100, N1 = 206
Overall survival Hazard ratio/95% CI	3.45 (2.4 to 4.96)
Progression-free survival Hazard ratio/95% CI	1.9 (1.43 to 2.52)

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

Meet-URO

Outcome	Meet-URO group 3 vs Meet-URO group 2, N2 = 88, N1 = 89	Meet-URO group 4 vs Meet-URO group 2, N2 = 101, N1 = 89	Meet-URO group 5 vs Meet-URO group 2, N2 = 28, N1 = 89
Progression-free survival Hazard ratio/95% CI	2.05 (1.37 to 3.04)	2.77 (1.88 to 4.08)	6.56 (3.97 to 10.82)
Overall survival	3.09 (1.54 to 6.19)	6.07 (3.16 to 11.67)	16.03 (7.74 to 33.21)

Outcome	Meet-URO group 3 vs Meet-URO group 2, N2 = 88, N1 = 89	Meet-URO group 4 vs Meet-URO group 2, N2 = 101, N1 = 89	Meet-URO group 5 vs Meet-URO group 2, N2 = 28, N1 = 89
Hazard ratio/95% CI			

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High (*Participants with missing data were not handled appropriately*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Rini, 2019

Bibliographic Reference	Rini BI; Plimack ER; Stus V; Gafanov R; Hawkins R; Nosov D; Pouliot F; Alekseev B; Soulières D; Melichar B; Vynnychenko I; Kryzhanivska A; Bondarenko I; Azevedo SJ; Borchiellini D; Szczylik C; Markus M; McDermott RS; Bedke J; Tartas S; Chang YH; Tamada S; Shou Q; Perini RF; Chen M; Atkins MB; Powles T; ; Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma.; The New England journal of medicine; 2019; vol. 380 (no. 12)

Study Characteristics

Study design	Randomised controlled trial
Study location	Brazil, Canada, Czech Republic, France, Germany, Hungary, Ireland, Japan, Poland, Russia, South Korea, Spain, Taiwan, Ukraine, UK, US
Study dates	2016 to 2018
Prognostic model(s)	IMDC/Heng
Inclusion criteria	• Aged 18 years or older • Newly diagnosed or recurrent stage IV clear cell RCC • No previous systemic therapy for advanced disease • Karnofsky performance-status score of 70 or more • At least one measurable lesion as evaluated according to RECIST
Exclusion criteria	• Symptomatic central nervous system metastases • Active auto-immune disease • Poorly controlled hypertension

	• Ischaemic cardiovascular event or New York Association class III or IV congestive heart failure within 1 year before screening • Receiving systemic immunosuppressive treatment
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	1st line treatment with pembrolizumab + axitinib or sunitinib
Number of participants	N=861
Length of follow-up	Median follow-up: 12.8 months
Follow-up schedule	Tumour imaging was performed at baseline and 12 weeks and then every 6 weeks through week 54 and every 12 weeks thereafter. People were contacted for assessment of survival every 12 weeks during follow-up.
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	Merck Sharp and Dohme
Additional comments	NA

Study arms

Pembrolizumab + Axitinib (N = 432)

Sunitinib (N = 429)

IMDC Favourable risk (N = 269)

IMDC Intermediate risk (N = 484)

IMDC Poor risk (N = 108)

Population characteristics

Arm-level characteristics

Characteristic	Pembrolizumab + Axitinib (N = 432)	Sunitinib (N = 429)
Age Range	30 to 89	26 to 90
Age Median (IQR)	62 (NA to NA)	61 (NA to NA)
Nephrectomy status Previous nephrectomy Sample size	n = 357 ; % = 82.6	n = 358 ; % = 83.4
Metastases location Sample size	n = NA ; % = NA	n = NA ; % = NA
Metastases location - Lung Sample size	n = 312 ; % = 72.2	n = 309 ; % = 72
Metastases location - Lymph node Sample size	n = 199 ; % = 46.1	n = 197 ; % = 45.9
Metastases location - Bone Sample size	n = 103 ; % = 23.8	n = 103 ; % = 24
Metastases location - Adrenal gland Sample size	n = 67 ; % = 15.5	n = 76 ; % = 17.7
Metastases location - Liver Sample size	n = 66 ; % = 15.3	n = 71 ; % = 16.6
Number of organs with metastases Sample size	n = NA ; % = NA	n = NA ; % = NA
Number of organs with metastases - 1 site Sample size	n = 114 ; % = 26.4	n = 96 ; % = 22.4

Characteristic	Pembrolizumab + Axitinib (N = 432)	Sunitinib (N = 429)
Number of organs with metastases - 2 or more sites Sample size	n = 315 ; % = 72.9	n = 331 ; % = 77.2
% Male Sample size	n = 308 ; % = 71.3	n = 320 ; % = 74.6

Outcomes

Number of events

Outcome	Pembrolizumab + Axitinib, N = 432	Sunitinib, N = 429	IMDC Favourable risk, N = 269	IMDC Intermediate risk, N = 484	IMDC Poor risk, N = 108
Overall survival (Deaths) Sample size	n = NA ; % = NA	n = NA ; % = NA	n = 17 ; % = 6.3	n = 93 ; % = 19.2	n = 46 ; % = 42.6
Progression-free survival (disease progression or death) Sample size	n = NA ; % = NA	n = NA ; % = NA	n = 90 ; % = 33.5	n = 232 ; % = 47.9	n = 73 ; % = 67.6

Overall survival (Deaths) - Polarity - Lower values are better
Progression-free survival (disease progression or death) - Polarity - Lower values are better

Critical appraisal - PROBAST tool

Section	Question	Answer
Overall Risk of bias and Applicability	Risk of bias	High *(No measure of calibration or discrimination)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Schuttke, 2024

Bibliographic Reference	Schuttke, Vayda; Kusiek, Cathrin; Fuessel, Susanne; Thomas, Christian; Buerk, Bjoern Thorben; Erdmann, Kati; Early kinetics of C-reactive protein as prognosticator for survival in a real-world cohort of patients with metastatic renal cell cancer under first-line therapy with immune checkpoint inhibitors.; Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico; 2024; vol. 26 (no. 5); 1117-1128

Study Characteristics

Study design	Retrospective cohort study
Study location	Germany
Study dates	2019-2022
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	mRCC patients who initiated immune checkpoint inhibitors-based 1L therapy
Exclusion criteria	Patients with missing clinical or C-reactive protein data
Selection of cohort	Database or clinical registry Single centre
Description of interventions/ point in the pathway model is used	1st line checkpoint inhibitors therapy (ipilimumab/nivolumab)
Number of participants	N = 61 IMDC Favourable = 8 IMDC Intermediate = 29 IMDC Poor = 24
Length of follow-up	Median (range): 12.4 (1.2–41.1)
Outcome(s) of interest	Overall survival

	Progression-free survival
Source of funding	Open Access funding enabled and organized by Projekt DEAL
Additional comments	PFS and OS were determined by the Kaplan-Meier method and differences between groups were assessed using the log-rank test. Survival rates were calculated from life tables. Univariate and multivariate Cox regression analyses were performed to identify prognostic factors for PFS and OS

Study arms

Favourable + Intermediate (N = 37)

Poor (N = 24)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 61)
% Female No of events	n = 18 ; % = 29.5
Age Median (IQR)	65 (47 to 82)
Nephrectomy status - Yes No of events	n = 39 ; % = 63.9
Nephrectomy status - No No of events	n = 22 ; % = 36.1
RCC subtypes - Clear cell RCC No of events	n = 56 ; % = 91.8
Metastatic organs at 1L - Single No of events	n = 15 ; % = 24.6
Metastatic organs at 1L - Multiple No of events	n = 46 ; % = 75.4

Outcomes

Survival

Outcome	Poor vs Favourable + Intermediate, N2 = 37, N1 = 24
Progression-free survival Hazard ratio/95% CI	1.35 (0.65 to 2.79)
Overall survival Hazard ratio/95% CI	3.04 (1.2 to 7.67)

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

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate (*Lack of information around how missing data were handled.*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Shin, 2021

Bibliographic Reference	Shin, Dongrul; Jeong, Chang Wook; Song, Cheryn; Kang, Minyong; Seo, Seong Il; Kim, Jung Kwon; Lee, Hakmin; Chung, Jinsoo; Hong, Sung-Hoo; Hwang, Eu Chang; Kwak, Cheol; Park, Jae Young; Prognostic factors for overall survival in patients with clear cell metastatic renal cell carcinoma: Model development and external validation with Memorial Sloan Kettering Cancer Center model and the international metastatic renal cell carcinoma database consortium model.; Medicine; 2021; vol. 100 (no. 31); e26826

Study Characteristics

Study design	Retrospective cohort study
Study location	Korea
Study dates	July 2000 to July 2017
Risk prediction model(s)	IMDC/Heng MSKCC

Inclusion criteria	• Metastatic renal cell carcinoma • received a single targeted therapy agent, including tyrosine kinase inhibitor or mammalian target of rapamycin inhibitor as first-line.
Exclusion criteria	• Patients who received immunotherapy as first-line treatment.
Selection of cohort	Database or clinical registry Korean Renal Cancer Study Group (KRoCS) database
Description of interventions/ point in the pathway model is used	Single targeted therapy agent, including tyrosine kinase inhibitor or mammalian target of rapamycin inhibitor as their first-line treatment. Model used at start of treatment.
Number of participants	KRoCS model developing cohort: N=619 External validation cohort: N=171
Length of follow-up	Model developing cohort: median 36 months (IQR, 8.2 to 61 months)
Follow-up schedule	Not specified
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	Not specified
Additional comments	Cox proportional hazards regression performed and concordance index calculated.

Study arms

Model development cohort (N = 619)

External validation cohort (N = 171)

Population characteristics

Arm-level characteristics

Characteristic	Model development cohort (N = 619)	External validation cohort (N = 171)
% Female Sample size	n = 134 ; % = 21.6	n = 37 ; % = 21.6
Age Mean (SD)	59.5 (11.4)	58.4 (11.6)
Nephrectomy status - Prior nephrectomy Sample size	n = 524 ; % = 84.7	n = 136 ; % = 79.5
Metastases location - Lung Sample size	n = 441 ; % = 71.2	n = 127 ; % = 74
Metastases location - Lymph node Sample size	n = 233 ; % = 37.6	n = 79 ; % = 46.2
Metastases location - Bone Sample size	n = 185 ; % = 29.9	n = 50 ; % = 29.2
Metastases location - Liver Sample size	n = 81 ; % = 13.1	n = 32 ; % = 18.7
Metastases location - Brain Sample size	n = 50 ; % = 8	n = 14 ; % = 8.2
Metastases location - Others Sample size	n = 148 ; % = 23.9	n = 46 ; % = 26.9

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(Fewer than 50 events per cohort. No model performance measure reported.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Smith, 2013

Bibliographic Reference	Smith, Andrew D; Shah, Shetal N; Rini, Brian I; Lieber, Michael L; Remer, Erick M; Utilizing pre-therapy clinical schema and initial CT changes to predict progression-free survival in patients with metastatic renal cell carcinoma on VEGF-targeted therapy: a preliminary analysis.; Urologic oncology; 2013; vol. 31 (no. 7); 1283-91

Study Characteristics

Study design	Retrospective cohort study
Study location	USA
Study dates	January 2000 to December 2007
Risk prediction model(s)	MSKCC
Inclusion criteria	• Pathology-proven metastatic renal cell carcinoma • pure clear cell • measurable disease • treated with first-line VEGF-targeted therapy with either sorafenib or sunitinib.
Exclusion criteria	• Brain metastases • unmeasurable disease • off-therapy for any reason, other than progressive disease, • off therapy for more than 1 week during an on-therapy portion of the protocol within the first year of therapy • patients without progressive disease if they had less than 1 year of clinical or imaging follow-up.
Selection of cohort	Single centre

Description of interventions/ point in the pathway model is used	Continuous daily oral therapy with 400 mg BID of sorafenib or repeated 6-week cycles of daily oral therapy with 50 mg sunitinib for 4 weeks followed by 2 weeks off-therapy. Model used at the start of treatment.
Number of participants	N=82
Length of follow-up	Median PFS: 17 months
Follow-up schedule	Not specified
Outcome(s) of interest	Progression-free survival
Source of funding	Not specified
Additional comments	Sensitivity and specificity were calculated for predicting a good clinical response (PFS 1 year or more) for the lowest risk group, and predicting early progression (PFS <1) for the highest risk group. Correctly predicting PFS for 1 year or more. Lowest risk group: Sensitivity: 52%% Specificity: 87% Correctly predicting time to PFS <1 year Highest risk group: Sensitivity: 20% Specificity: 100%

Population characteristics

Study-level characteristics

Characteristic	Study (N = 82)
% Female Sample size	n = 16 ; % = 20

Characteristic	Study (N = 82)
Age Custom value	Median (range): 63 (35 to 79)
Nephrectomy status - Prior nephrectomy Sample size	n = 76 ; % = 93
RCC subtypes - Clear cell Sample size	n = 72 ; % = 88
RCC subtypes - Mixed with clear cell Sample size	n = 10 ; % = 12
Metastases location - Lungs Sample size	n = 54 ; % = 66
Metastases location - Liver Sample size	n = 12 ; % = 15
Metastases location - Bone Sample size	n = 22 ; % = 27
Metastases location - Brain Sample size	n = 6 ; % = 7

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(Unclear for high risk group > 1 year. High risk for low risk less than 1 year as number of events fewer than 50.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Soerensen, 2016

Bibliographic Reference	Soerensen, Anne V; Geertsen, Poul F; Christensen, Ib J; Hermann, Gregers G; Jensen, Niels V; Fode, Kirsten; Petersen, Astrid; Sandin, Rickard; Donskov, Frede; A five-factor biomarker profile obtained week 4-

12 of treatment for improved prognostication in metastatic renal cell carcinoma: Results from DARENCA study 2.; Acta oncologica (Stockholm, Sweden); 2016; vol. 55 (no. 3); 341-8

Study Characteristics

Study design	Retrospective cohort study
Study location	Denmark
Study dates	January 2006 to December 2010
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	People who received TKI (sorafenib and sunitinib) or interleukin-2 (IL2)-based immunotherapy as a first-line treatment.
Exclusion criteria	Not reported
Selection of cohort	Database or clinical registry
Description of interventions/ point in the pathway model is used	First line TKI (sorafenib and sunitinib) or interleukin-2 (IL2)-based immunotherapy.
Number of participants	N= 735
Length of follow-up	Median follow-up 50.2 months (range 1.9 to 81.8)
Follow-up schedule	Blood pressure (BP) and blood samples (BS) were measured on day 1 in each cycle for the first 12-week on treatment (week 4–12).
Outcome(s) of interest	Model discrimination (C-stats) Overall survival
Source of funding	Pfizer; Axel Muusfeldts fund; Christian Larsen and judge Ellen Larsens fund; Else and Mogens Wedell-Wedellsborgs Fund; Timber merchant Johannes Fogs Fund; Svend H.A. Schroeder and wife Ketty K. Larsen Fund; Novartis grant and the Department of Oncology and Research Fund at Herlev University Hospital
Additional comments	NA

Study arms

IMDC Favourable risk (N = 71)

IMDC Intermediate risk (N = 322)

IMDC Poor risk (N = 197)

Population characteristics

Study-level characteristics

Characteristic	Study (N =)
% Female Sample size	n = 180 ; % = 70
Age Median (IQR)	63 (57 to 69)
Nephrectomy status Sample size	n = 451 ; % = 61
RCC subtypes - Clear cell Sample size	n = 606 ; % = 82
RCC subtypes - Non-clear cell Sample size	n = 118 ; % = 16
RCC subtypes - NA Sample size	n = 11 ; % = 1
Metastases location - CNS Sample size	n = 52 ; % = 7
Metastases location - Liver Sample size	n = 156 ; % = 21

Outcomes

Time-to-event

Outcome	IMDC Intermediate risk vs IMDC Favourable risk, N2 = 322, N1 = 71	IMDC Poor risk vs IMDC Favourable risk, N2 = 197, N1 = 71
Overall survival Hazard ratio/95% CI	1.67 (1.2 to 2.34)	3.62 (2.55 to 5.13)

Overall survival - Polarity - Lower values are better

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(No measure of calibration was reported)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Tamura, 2021

Bibliographic Reference	Tamura, Keita; Ando, Ryosuke; Takahara, Kiyoshi; Ito, Toshiki; Kanao, Kent; Yasui, Takahiro; Shiroki, Ryoichi; Miyake, Hideaki; Development of novel ACN (albumin, C-reactive protein and neutrophil-to-lymphocyte ratio) prognostication model for patients with metastatic renal cell carcinoma receiving first-line molecular-targeted therapy.; Urologic oncology; 2021; vol. 39 (no. 1); 78e1-78e8

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	January 2008 to November 2018
Risk prediction model(s)	IMDC/Heng MSKCC

Inclusion criteria	People with mRCC who were treated with 1st line molecular targeted therapy
Exclusion criteria	Not reported
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	1st line therapy: treatments included axitinib, everolimus, pazopanib, sorafenib, sunitinib, and temsirolimus.
Number of participants	N = 325
Length of follow-up	Median 19 months (IQR 8 to 40 months)
Follow-up schedule	Tumour measurements were carried out with computed tomography every 12 weeks following the introduction of first-line targeted agents.
Outcome(s) of interest	Model discrimination (C-stats) Overall survival Mortality
Source of funding	Not reported

Study arms

MSKCC Favourable risk (N = 49)

MSKCC Intermediate risk (N = 205)

MSKCC Poor risk (N = 71)

IMDC Favourable risk (N = 50)

IMDC Intermediate risk (N = 198)

IMDC Poor risk (N = 77)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 325)
% Female Sample size	n = 76 ; % = 23.4
Age Median (IQR)	67 (60 to 74)
Nephrectomy status Received previous nephrectomy Sample size	n = 263 ; % = 80.9
RCC subtypes - Clear cell Sample size	n = 275 ; % = 84.6
RCC subtypes - Non-clear cell Sample size	n = 50 ; % = 15.4

Outcomes

Number of events

Outcome	MSKCC Favourable risk, N = 49	MSKCC Intermediate risk, N = 205	MSKCC Poor risk, N = 71	IMDC Favourable risk, N = 50	IMDC Intermediate risk, N = 198	IMDC Poor risk, N = 77
Mortality (number of deaths) No of events	n = 12 ; % = 24.5	n = 104 ; % = 50.7	n = 51 ; % = 71.8	n = 12 ; % = 24	n = 97 ; % = 49	n = 58 ; % = 75.3

Mortality (number of deaths) - Polarity - Lower values are better

Time-to-event outcomes

Outcome	MSKCC Intermediate risk vs MSKCC Favourable risk, N2 = 205, N1 = 49	MSKCC Poor risk vs MSKCC Favourable risk, N2 = 71, N1 = 49	IMDC Intermediate risk vs IMDC Favourable risk, N2 = 198, N1 = 50	IMDC Poor risk vs IMDC Favourable risk, N2 = 77, N1 = 50
Overall survival Hazard ratio/95% CI	2.31 (1.27 to 4.21)	6.06 (3.22 to 11.4)	2.27 (1.24 to 4.14)	6.09 (3.26 to 11.4)

Overall survival - Polarity - Lower values are better

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(A measure of calibration was not reported.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Tanaka, 2016

Bibliographic Reference	Tanaka, Nobuyuki; Mizuno, Ryuichi; Ito, Keiichi; Shirotake, Suguru; Yasumizu, Yota; Masunaga, Ayako; Ito, Yujiro; Miyazaki, Yasumasa;

Hagiwara, Masayuki; Kanao, Kent; Mikami, Shuji; Nakagawa, Ken; Momma, Tetsuo; Masuda, Takeshi; Asano, Tomohiko; Oyama, Masafumi; Oya, Mototsugu; External Validation of the MSKCC and IMDC Risk Models in Patients Treated with Targeted Therapy as a First-line and Subsequent Second-line Treatment: A Japanese Multi-institutional Study.; European urology focus; 2016; vol. 2 (no. 3); 303-309

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	NR
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	People who received first-line targeted therapy, either anti-VEGF targeted drugs or mTOR inhibitors, for mRCC [this included patients with prior immunotherapy receiving targeted therapy as a second-line treatment in their clinical course]
Exclusion criteria	People treated with targeted therapy in a presurgical setting for non-metastatic disease and people with incomplete treatment data.
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First-line targeted therapy with either anti-VEGF targeted drugs or mTOR inhibitors, or second-line targeted therapy if participants had received immunotherapy as part of their treatment.
Number of participants	First line: N = 312 Progressed to 2nd line where model was reassessed: N=168
Length of follow-up	1st line: Median 18.1 months (IQR 8.7 to 32.0) 2nd line: Median 12.7 months (IQR: 5.9–23.8)
Follow-up schedule	Participants were followed every 2–4 weeks during the administration of any targeted therapy. Follow-up consisted of history, physical examination, routine blood work, and chest radiography. Radiographic evaluations of computed tomography (CT) were generally performed every 3 months; additional CTs and elective bone scans were performed when clinically indicated.

Outcome(s) of interest	Overall survival
Source of funding	Ministry of Education, Culture, Sports, Science, and Technology of Japan.
Additional comments	NA

Study arms

Favourable MSKCC 1st line (N = 63)

Intermediate MSKCC 1st line (N = 174)

Poor MSKCC 1st line (N = 46)

Favourable IMDC 1st line (N = 61)

Intermediate IMDC 1st line (N = 152)

Poor IMDC 1st line (N = 64)

Favourable MSKCC 2nd line (N = 47)

Intermediate MSKCC 2nd line (N = 78)

Poor MSKCC 2nd line (N = 32)

Favourable IMDC 2nd line (N = 23)

Intermediate IMDC 2nd line (N = 102)

Poor IMDC 2nd line (N = 26)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 312)
% Female 1st line Sample size	n = 87 ; % = 28

Characteristic	Study (N = 312)
Age (years) 1st line Median (IQR)	66 (59 to 73)
Nephrectomy status 1st line - prior nephrectomy Sample size	n = 232 ; % = 74.6
RCC subtypes - Clear cell Sample size	n = 238 ; % = 76.5
RCC subtypes - Non–clear cell Sample size	n = 27 ; % = 8.7
RCC subtypes - Unknown Sample size	n = 46 ; % = 14.8
% Female 2nd line Sample size	n = 47 ; % = 28
Age (years) 2nd line Median (IQR)	65 (58 to 72)
Nephrectomy status 2nd line - prior nephrectomy Sample size	n = 125 ; % = 74.4
RCC subtypes - Clear cell Sample size	n = 132 ; % = 78.6
RCC subtypes - Non–clear cell Sample size	n = 16 ; % = 9.5
RCC subtypes - Unknown Sample size	n = 20 ; % = 11.9

Outcomes

Overall survival

Outcome	Favourable MSKCC 1st line, N = 63	Intermediate MSKCC 1st line, N = 174	Poor MSKCC 1st line, N = 46	Favourable IMDC 1st line, N = 61	Intermediate IMDC 1st line, N = 152	Poor IMDC 1st line, N = 64	Favourable MSKCC 2nd line, N = 47	Intermediate MSKCC 2nd line, N = 78	Poor MSKCC 2nd line, N = 32	Favourable IMDC 2nd line, N = 23	Intermediate IMDC 2nd line, N = 102	Poor IMDC 2nd line, N = 26
Overall survival at 3 years - first-line SACT Reported as 3-year OS rates in percentage [number of events calculated by analyst] No of events	n = 48 ; % = 76.2	n = 81 ; % = 46.7	n = 6 ; % = 13.4	n = 47 ; % = 77.3	n = 73 ; % = 47.9	n = 10 ; % = 15.6	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Overall Survival at	*NR*	*NR*	*NR*	*NR data*	*NR*	*NR*	n = 38 ; % = 80.9	n = 56 ; % = 71.4	n = 10 ; % = 31.7	n = 21 ; % = 90.5	n = 72 ; % = 70.6	n = 6 ; % =

Outcome	Favourable MSKCC 1st line, N = 63	Intermediate MSKCC 1st line, N = 174	Poor MSKCC 1st line, N = 46	Favourable IMDC 1st line, N = 61	Intermediate IMDC 1st line, N = 152	Poor IMDC 1st line, N = 64	Favourable MSKCC 2nd line, N = 47	Intermediate MSKCC 2nd line, N = 78	Poor MSKCC 2nd line, N = 32	Favourable IMDC 2nd line, N = 23	Intermediate IMDC 2nd line, N = 102	Poor IMDC 2nd line, N = 26
1 year Reported as 1-year OS rates in percentage [number of events calculated by analyst] Sample size												24.6
Mortality at 3 years Calculated from survival events by analyst	n = 15 ; % = 23.8	n = 93 ; % = 53.4	n = 40 ; % = 87	n = 14 ; % = 23	n = 79 ; % = 52	n = 54 ; % = 84.4	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*

Outcome	Favourable MSKCC 1st line, N = 63	Intermediate MSKCC 1st line, N = 174	Poor MSKCC 1st line, N = 46	Favourable IMDC 1st line, N = 61	Intermediate IMDC 1st line, N = 152	Poor IMDC 1st line, N = 64	Favourable MSKCC 2nd line, N = 47	Intermediate MSKCC 2nd line, N = 78	Poor MSKCC 2nd line, N = 32	Favourable IMDC 2nd line, N = 23	Intermediate IMDC 2nd line, N = 102	Poor IMDC 2nd line, N = 26
No of events												
Mortality at 1 year Calculated from survival events by analyst No of events	*NR*	*NR*	*NR*	*NR*	*NR*	*empty data*	n = 9 ; % = 19.1	n = 22 ; % = 28.2	n = 22 ; % = 68.8	n = 2 ; % = 8.7	n = 30 ; % = 29.4	n = 20 ; % = 76.9

Overall survival at 3 years - first-line SACT - Polarity - Higher values are better
Mortality at 3 years - Polarity - Lower values are better
Mortality at 1 year - Polarity - Lower values are better

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Low
Overall Risk of bias and Applicability	Concerns for applicability	Low

Toyoda, 2024

Bibliographic Reference	Toyoda, Shingo; Fukuokaya, Wataru; Mori, Keiichiro; Kawada, Tatsushi; Katayama, Satoshi; Nishimura, Shingo; Maenosono, Ryoichi; Tsujino,

Takuya; Adachi, Takahiro; Hirasawa, Yosuke; Saruta, Masanobu; Komura, Kazumasa; Nukaya, Takuhisa; Yanagisawa, Takafumi; Takahara, Kiyoshi; Hashimoto, Takeshi; Azuma, Haruhito; Ohno, Yoshio; Shiroki, Ryoichi; Araki, Motoo; Kimura, Takahiro; Fujita, Kazutoshi; Clinical outcomes and prognostic factors in metastatic nonclear cell renal cell carcinoma treated with immuno-oncology combination therapy.; Japanese journal of clinical oncology; 2024; vol. 54 (no. 12); 1336-1342

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	January 2018 to August 2023
Risk prediction model(s)	IMDC/Heng
Inclusion criteria	People with mRCC treated with ICI-based combination therapy with non-clear cell RCC
Exclusion criteria	• People with no tissue diagnosis or no description • People with clear cell RCC
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	First-line treatment with IO-based combination therapy
Number of participants	n=75
Length of follow-up	Not reported
Follow-up schedule	Every 2 to 3 months from the start of IO combination therapy
Outcome(s) of interest	Overall survival Progression-free survival Hazard ratio

Source of funding	None
Additional comments	NA

Study arms

IMDC - poor (N = 26)

IMDC - favourable/intermediate (N = 49)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 75)
% Female Sample size	n = 18 ; % = 24
Age Range	27 to 87
Age Median (IQR)	65 (NR to NR)
RCC subtypes Sample size	n = NA ; % = NA
RCC subtypes - Papillary Sample size	n = 29 ; % = 38.6
RCC subtypes - Unclassified Sample size	n = 13 ; % = 17.3
RCC subtypes - HD-related Sample size	n = 3 ; % = 4
RCC subtypes - MiT family translocation Sample size	n = 1 ; % = 1.3

Characteristic	Study (N = 75)
RCC subtypes - Chromophobe Sample size	n = 1 ; % = 1.3
RCC subtypes - Others Sample size	n = 28 ; % = 37.3
RCC subtypes - Presence of sarcomatoid component Sample size	n = 10 ; % = 13.3
Metastases location Sample size	n = NA ; % = NA
Metastases location - Lung Sample size	n = 31 ; % = 41.3
Metastases location - Bone Sample size	n = 17 ; % = 22.6
Metastases location - Liver Sample size	n = 13 ; % = 17.3
Metastases location - Brain Sample size	n = 2 ; % = 2.6
Metastases location - Lymph node Sample size	n = 43 ; % = 57.3

Outcomes

Time-to-event outcomes

Outcome	IMDC - poor vs IMDC - favourable/intermediate, N2 = 26, N1 = 49
Progression-free survival Hazard ratio/95% CI	1.14 (0.61 to 2.15)
Overall survival Hazard ratio/95% CI	3.17 (1.48 to 6.77)

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(Lack of reporting around number of outcome events and no measure of calibrations.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Ueda, 2018

Bibliographic Reference	Ueda, Kosuke; Suekane, Shigetaka; Hirano, Taishi; Ogasawara, Naoyuki; Chikui, Katsuaki; Uemura, Keiichiro; Nakiri, Makoto; Nishihara, Kiyoaki; Matsuo, Mitsunori; Igawa, Tsukasa; Efficacy of Axitinib as Second-line Treatment in Locally Advanced and Metastatic Renal Cell Carcinoma.; Anticancer research; 2018; vol. 38 (no. 9); 5387-5392

Study Characteristics

Study design	Retrospective cohort study
Study location	Japan
Study dates	November 2012 to March 2017
Risk prediction model(s)	IMDC/Heng MSKCC
Inclusion criteria	People with locally advanced and metastatic RCC who received at least one dose of axitinib as second-line therapy after the failure of first-line TKI [Baseline characteristics showed that all participants had at least one organ with metastasis]
Exclusion criteria	Not reported
Selection of cohort	Single centre
Description of interventions/ point in the pathway	Second-line treatment with axitinib

model is used	
Number of participants	N = 35
Length of follow-up	Not reported
Follow-up schedule	Radiological evaluations were performed for all patients by computed tomography. Tumour response was evaluated as best response according to the Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1. Early tumour response on the first-follow up CT was evaluated at 4-12 weeks after the introduction of axitinib and a 10% decrease in diameter of the tumour was used as the cut-off value.
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	Not reported
Additional comments	NA

Study arms

IMDC favourable + intermediate risk (N = 29)

IMDC poor risk (N = 6)

MSKCC favourable + intermediate risk (N = 30)

MSKCC poor risk (N = 5)

Population characteristics

Study-level characteristics

Characteristic	**Study (N = 35)**
% Female Sample size	n = 9 ; % = 25.7
Age Range	40 to 78

Characteristic	Study (N = 35)
Age Median (IQR)	66 (*NR* to *NR*)
Nephrectomy status Prior nephrectomy Sample size	n = 26 ; % = 74.3
RCC subtypes - Clear cell RCC Sample size	n = 22 ; % = 62.9
RCC subtypes - non-clear cell RCC Sample size	n = 5 ; % = 14.3
RCC subtypes - Unknown Sample size	n = 8 ; % = 22.9
Metastases location - Lung Sample size	n = 21
Metastases location - Bone Sample size	n = 11 ; % = 31.4
Metastases location - Liver Sample size	n = 4 ; % = 11.4

Outcomes

Time-to-event outcomes

Outcome	IMDC poor risk vs IMDC favourable + intermediate risk, N2 = 6, N1 = 28	MSKCC poor risk vs MSKCC favourable + intermediate risk, N2 = 5, N1 = 30
Overall survival Hazard ratio/95% CI	7.27 (2.34 to 21.37)	5.39 (1.64 to 15.84)
Progression-free survival	1.48 (0.54 to 3.44)	1.08 (0.36 to 2.63)

Outcome	IMDC poor risk vs IMDC favourable + intermediate risk, N2 = 6, N1 = 28	MSKCC poor risk vs MSKCC favourable + intermediate risk, N2 = 5, N1 = 30
Hazard ratio/95% CI		

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High *(Insufficient number of outcome events and no measure of calibration or discrimination.)*
Overall Risk of bias and Applicability	Concerns for applicability	Low

Voss, 2018

Bibliographic Reference	Voss, Martin H; Reising, Albert; Cheng, Yuan; Patel, Parul; Marker, Mahtab; Kuo, Fengshen; Chan, Timothy A; Choueiri, Toni K; Hsieh, James J; Hakimi, A Ari; Motzer, Robert J; Genomically annotated risk model for advanced renal-cell carcinoma: a retrospective cohort study.; The Lancet. Oncology; 2018; vol. 19 (no. 12); 1688-1698

Study Characteristics

Study design	Retrospective cohort study
Study location	US
Study dates	COMPARZ trial: 2008-2011 RECORD-3 trial: 2009-2011
Risk prediction model(s)	MSKCC
Inclusion criteria	**COMPARZ trial** Patients aged ≥18 years, who had advanced or metastatic renal-cell carcinoma with a clear cell histologic component, had not received systemic treatment previously, measurable disease according to the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines, a Karnofsky performance-status score of at least 70, adequate organ function.

	RECORD-3 trial Patients aged ≥18 years, who had measurable clear cell or non–clear cell mRCC, with or without nephrectomy, no prior systemic therapy; a Karnofsky performance status of 70% or greater; adequate hematologic, liver, and kidney function; and normal left ventricular ejection fraction
Exclusion criteria	**COMPARZ trial** Brain metastases, poorly controlled hypertension, and cardiac, and vascular conditions within 6 months before screening. **RECORD-3 trial** Patients with brain metastases
Selection of cohort	Multicentre
Description of interventions/ point in the pathway model is used	COMPARZ trial was conducted to compare first-line pazopanib versus sunitinib RECORD-3 trial was conducted to compare first-line everolimus followed by sunitinib at progression with the standard sequence of first-line sunitinib followed by everolimus in patients with metastatic renal cell carcinoma.
Number of participants	COMPARZ trial N = 927 RECORD-3 trial N = 471
Length of follow-up	Not reported
Follow-up schedule	Not reported
Outcome(s) of interest	Model discrimination (C-stats) Overall survival Progression-free survival
Source of funding	The study was designed by academic investigators and representatives of the funder, who were involved in data collection, data analyses, data interpretation, and writing of the report. All authors had full access to the data and contributed to the development and approval of the manuscript.

	The corresponding author had full access to the data throughout the study and had final responsibility for the decision to submit for publication
Additional comments	Harrell's concordance index (C-index) was used to test discrimination for overall survival and progression-free survival in the original and new MSKCC risk models

Study arms

COMPARZ total (N = 927)

RECORD-3 total (N = 471)

Population characteristics

Arm-level characteristics

Characteristic	COMPARZ total (N = 927)	RECORD-3 total (N = 471)
% Female No of events	n = 256 ; % = 28	n = 129 ; % = 27
Age Mean (95% CI)	62 (18 to 88)	62 (20 to 89)
Nephrectomy status - Previous nephrectomy No of events	n = 779 ; % = 84	n = 471 ; % = 100
RCC subtypes - Clear cell RCC No of events	n = 927 ; % = 100	n = 402 ; % = 85.4
RCC subtypes - Non–clear cell RCC No of events	n = 0 ; % = 0	n = 66 ; % = 14
RCC subtypes - Missing No of events	n = 0 ; % = 0	n = 3 ; % = 0.6
Number of metastatic sites - ≤2 metastatic sites at baseline No of events	n = 603 ; % = 65	n = 262 ; % = 56

Characteristic	COMPARZ total (N = 927)	RECORD-3 total (N = 471)
Number of metastatic sites - ≤2 metastatic sites at baseline No of events	n = 324 ; % = 35	n = 209 ; % = 44
MSKCC risk group - Favourable No of events	n = 212 ; % = 24	n = 140 ; % = 30
MSKCC risk group - Intermediate No of events	n = 508 ; % = 58	n = 264 ; % = 56
MSKCC risk group - Poor No of events	n = 157 ; % = 18	n = 67 ; % = 14
MSKCC risk group - Unknown No of events	n = 50	n = 0

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	Moderate (*Lack of information around the number of outcome events.*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Yao, 2018

Bibliographic Reference	Yao, Jia-Xi; Chen, Xiang; Xi, Wei; Zhu, Yan-Jun; Wang, Hang; Hu, Xiao-Yi; Guo, Jian-Ming; Immunoscore System for Predicting Clinical Outcome of Metastatic Renal Cell Carcinoma Patients Treated with Tyrosine Kinase Inhibitors.; Journal of Cancer; 2018; vol. 9 (no. 22); 4099-4107

Study Characteristics

Study design	Retrospective cohort study
Study location	China
Study dates	2007-2017

Risk prediction model(s)	IMDC/Heng
Inclusion criteria	Patients with mRCC who received VEGF-TKI as first-line treatment
Exclusion criteria	NR
Selection of cohort	Single centre
Description of interventions/ point in the pathway model is used	VEGF-TKI as first-line treatment (Sunitinib or Sorafenib)
Number of participants and recruitment methods	N = 218
Length of follow-up	60 months
Follow-up schedule	NR
Outcome(s) of interest	Overall survival Progression-free survival
Source of funding	This study was funded by grants from the National Natural Science Foundation of China (81772696, 81472376).
Additional comments	Univariate and multivariate analyses were done with the Cox proportional hazards regression model to determine whether the immunoscore system had predictive value.

Study arms

IMDC Favourable (N = 37)

IMDC Intermediate (N = 143)

IMDC Poor (N = 38)

Population characteristics

Study-level characteristics

Characteristic	Study (N = 218)
% Female No of events	n = 58 ; % = 26.61
Age Median (IQR)	59 (52 to 65)
RCC subtypes - Clear cell RCC No of events	n = 187 ; % = 85.78
RCC subtypes - Non–clear cell RCC No of events	n = 31 ; % = 14.22

Outcomes

Survival

Outcome	IMDC Intermediate vs IMDC Favourable, N2 = 143, N1 = 37	IMDC Favourable vs IMDC Poor, N2 = 38, N1 = 37
Overall survival Hazard ratio/95% CI	1.38 (0.76 to 2.51)	3.53 (1.83 to 6.81)
Progression-free survival Hazard ratio/95% CI	0.98 (0.61 to 1.56)	1.75 (0.99 to 3.08)

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

Critical appraisal - PROBAST tool

Overall Risk of bias and Applicability	Risk of bias	High (*Lack of clarity around inclusion and exclusion criteria, whether missing data were handled appropriately, and whether relevant model performance measures were evaluated appropriately.*)
Overall Risk of bias and Applicability	Concerns for applicability	Low

Appendix E – Forest plots

Cytoreductive nephrectomy

IMDC

Figure 2: IMDC: overall survival - c-statistic; cytoreductive nephrectomy, mixed subtype

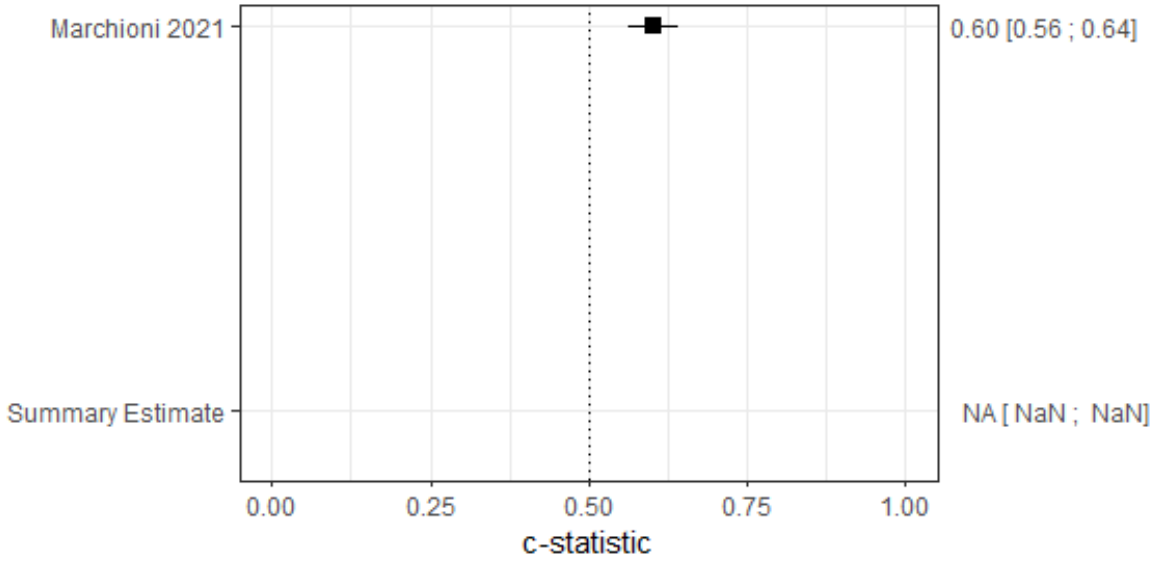


Figure 3: IMDC poor risk vs favourable risk: overall survival - Hazard ratio; no SACT

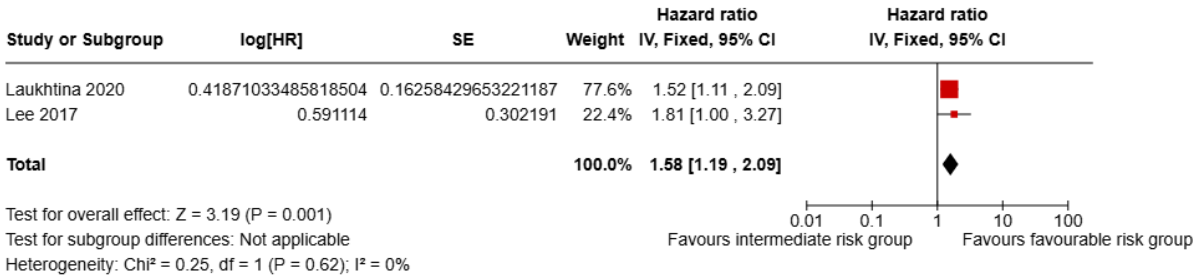
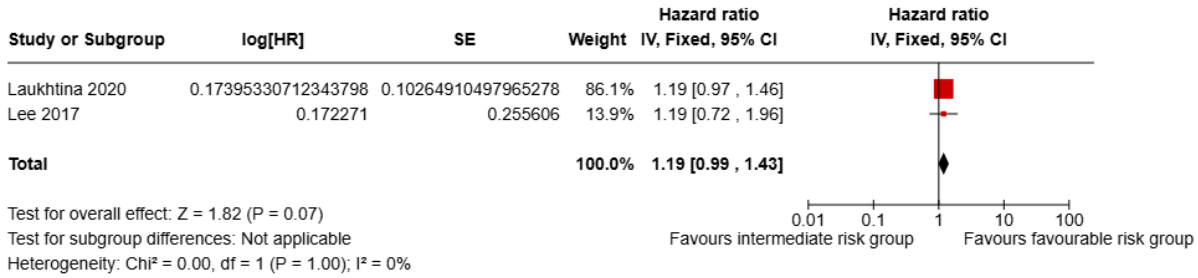
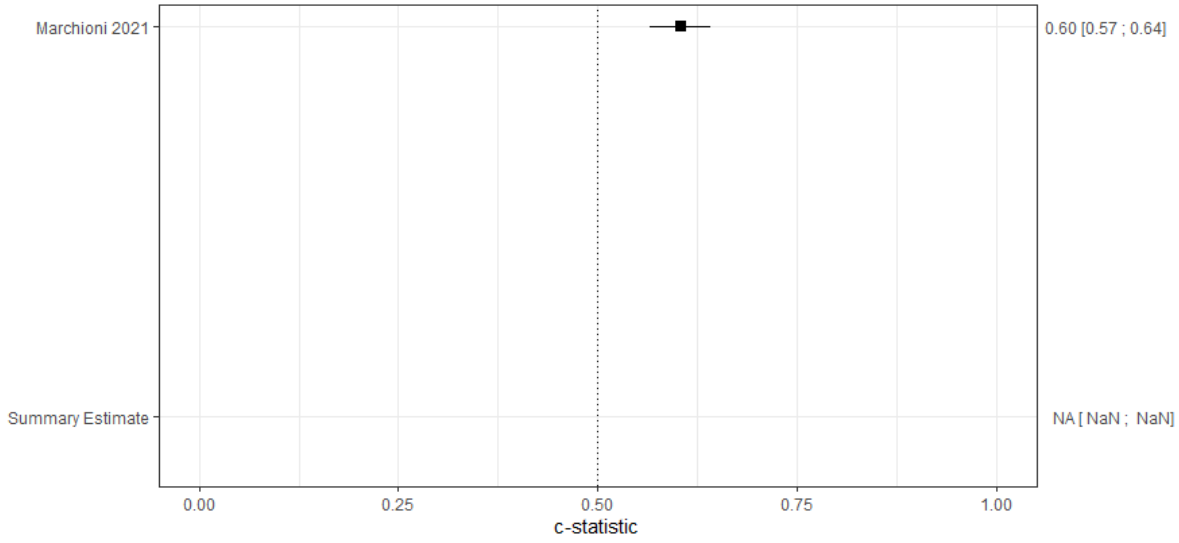


Figure 4: IMDC intermediate risk vs favourable risk: overall survival - Hazard ratio; no SACT



MSKCC

Figure 5: MSKCC: overall survival - c-statistic; cytoreductive nephrectomy, mixed subtype



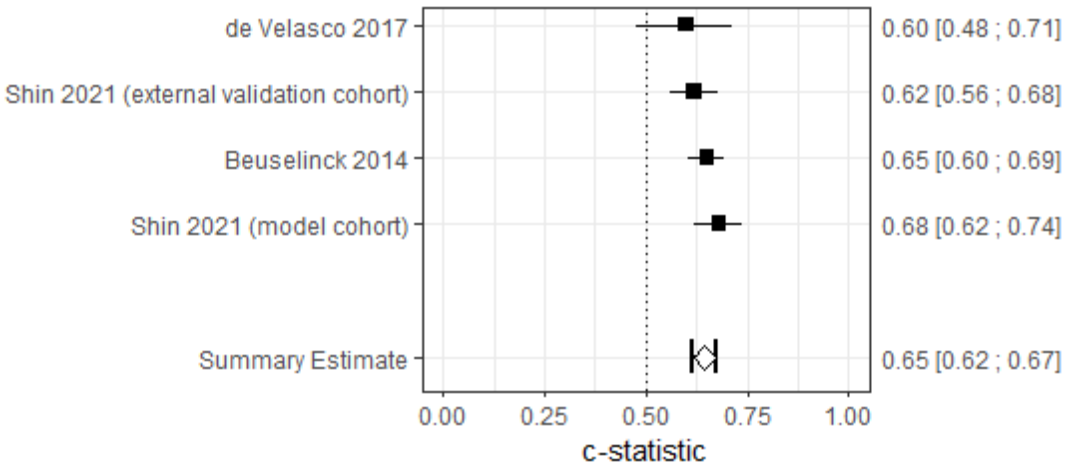
Meet-URO

No evidence was identified for this model in this treatment line.

First-line SACT

IMDC

Figure 6: IMDC: overall survival - c-statistic; first-line SACT, clear cell, FE



I^2: 0.00%

Figure 7: IMDC: progression-free survival - c-statistic; first-line SACT, clear cell

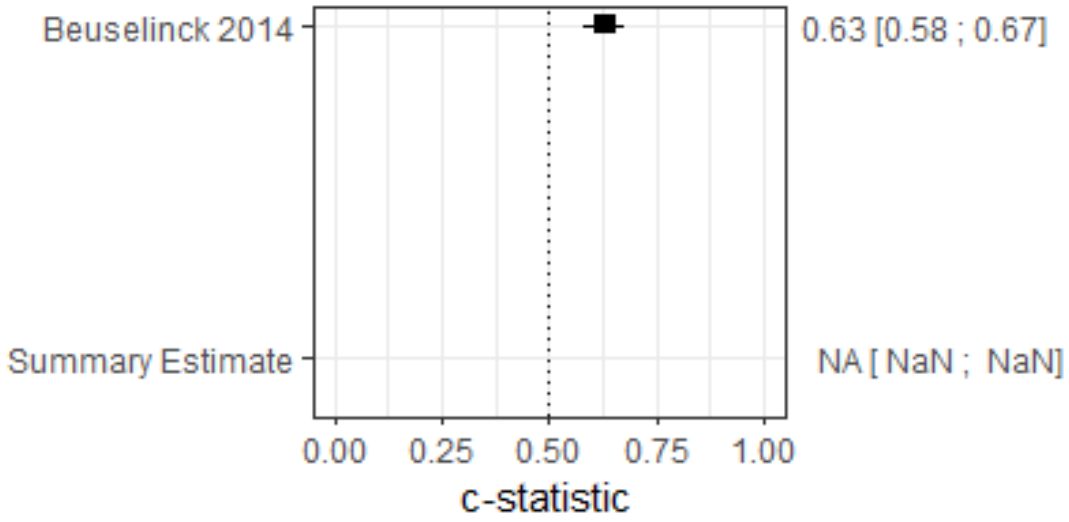
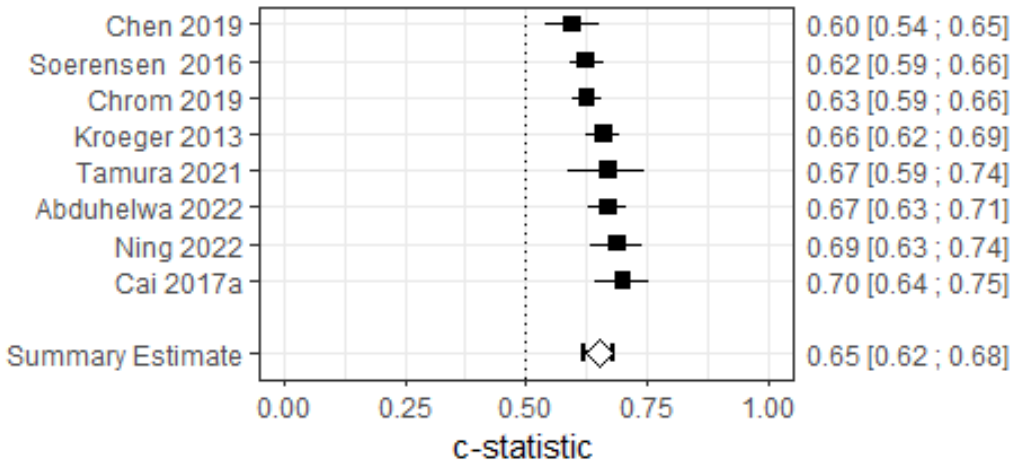
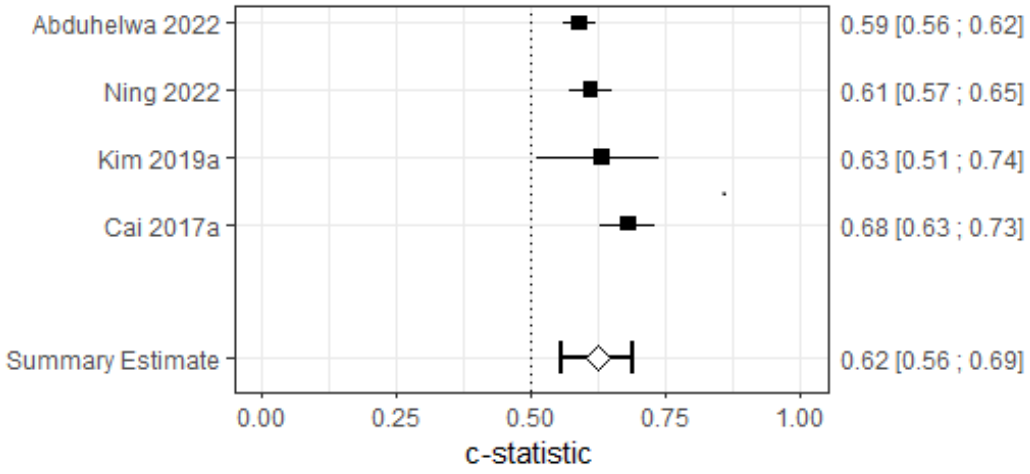


Figure 8: IMDC: overall survival - c-statistic; first-line SACT, mixed subtypes, RE



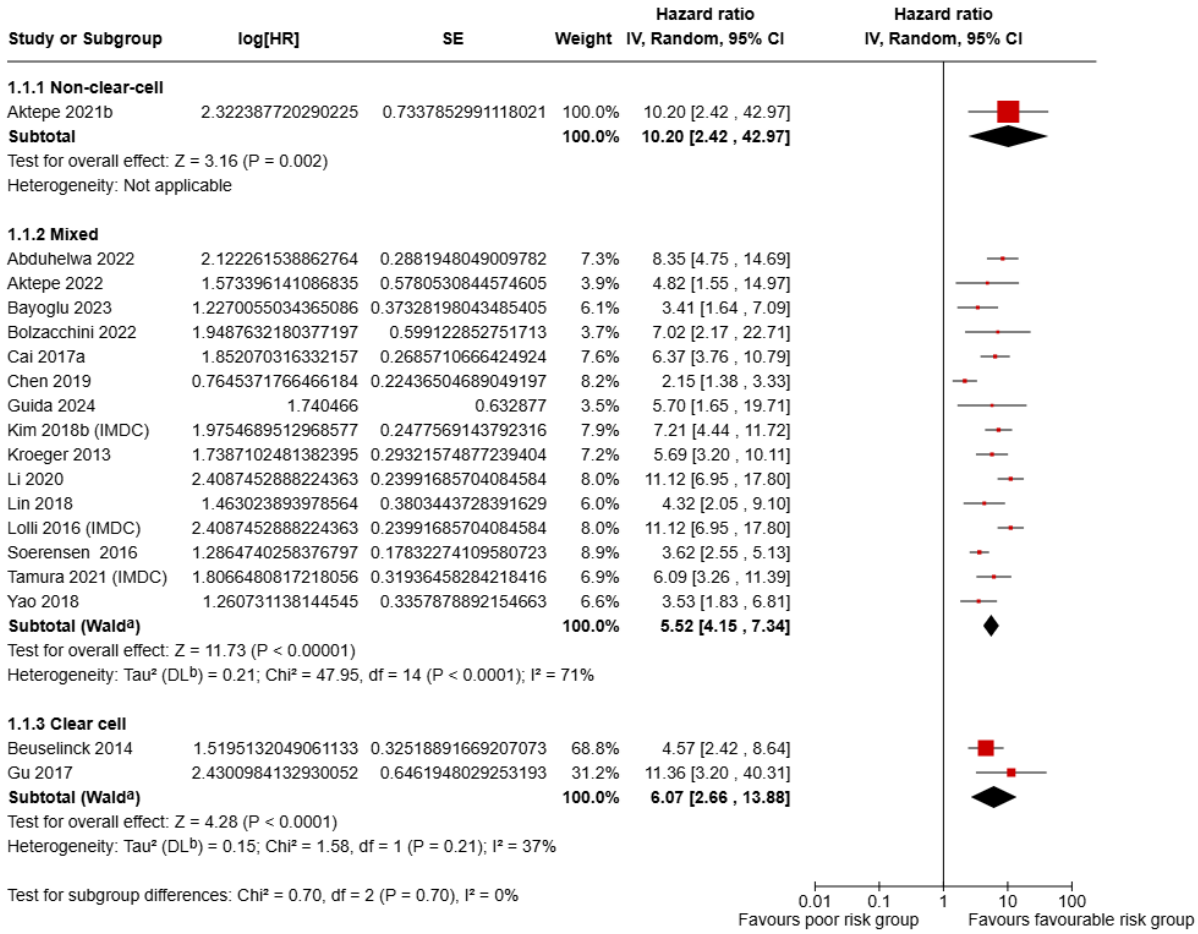
I^2: 52.05%

Figure 9: IMDC: progression-free survival - c-statistic; first-line SACT, mixed subtypes, RE



I^2: 67.67%

Figure 10: IMDC poor risk vs favourable risk: overall survival - Hazard ratio; first-line SACT

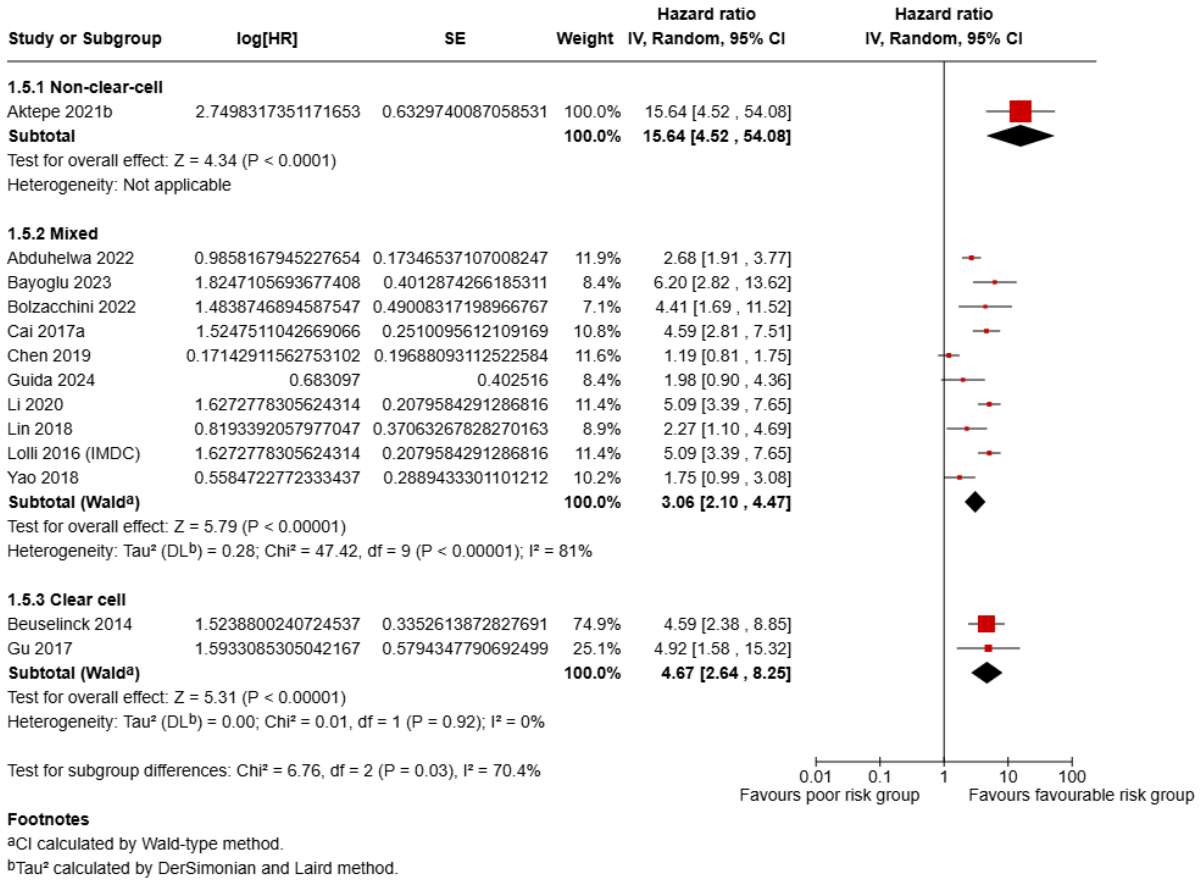


Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Figure 11: IMDC poor risk vs favourable risk: progression-free survival - Hazard ratio; first-line SACT

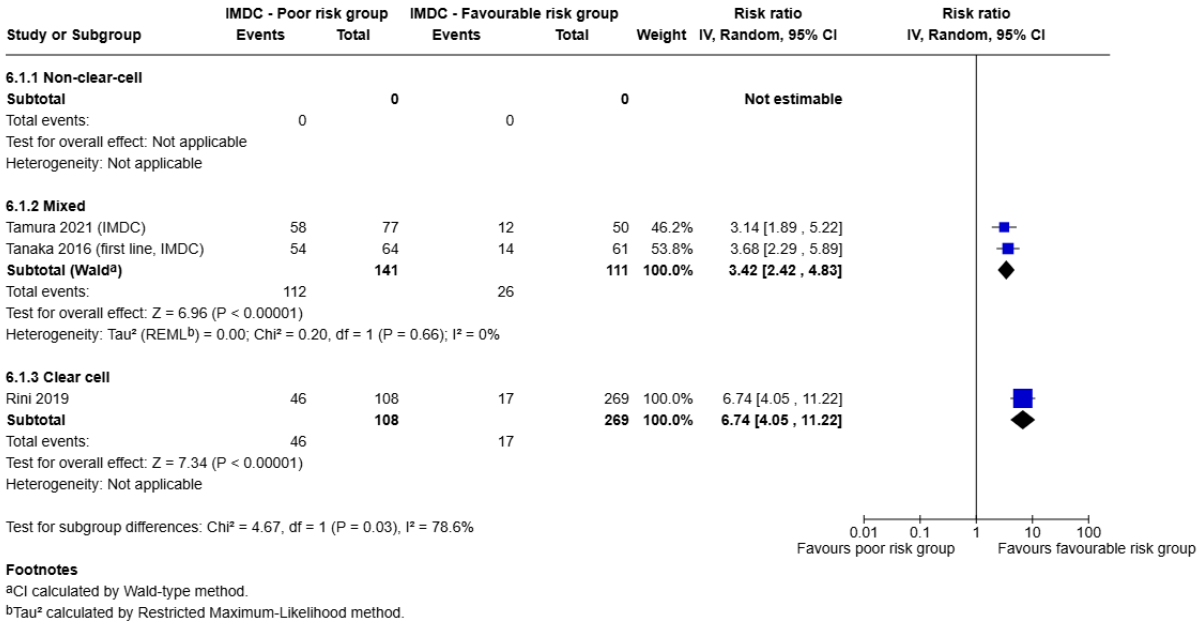


Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Figure 12: IMDC poor risk vs favourable risk: overall survival - Risk ratio; first-line SACT



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 13: IMDC poor risk vs favourable risk: progression-free survival - Risk ratio; first-line SACT, clear cell RCC

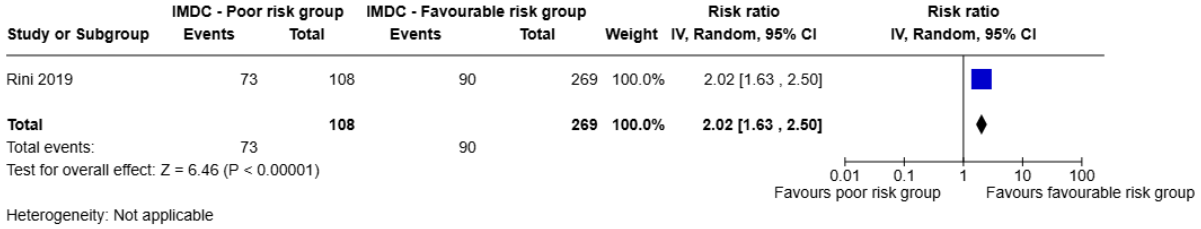
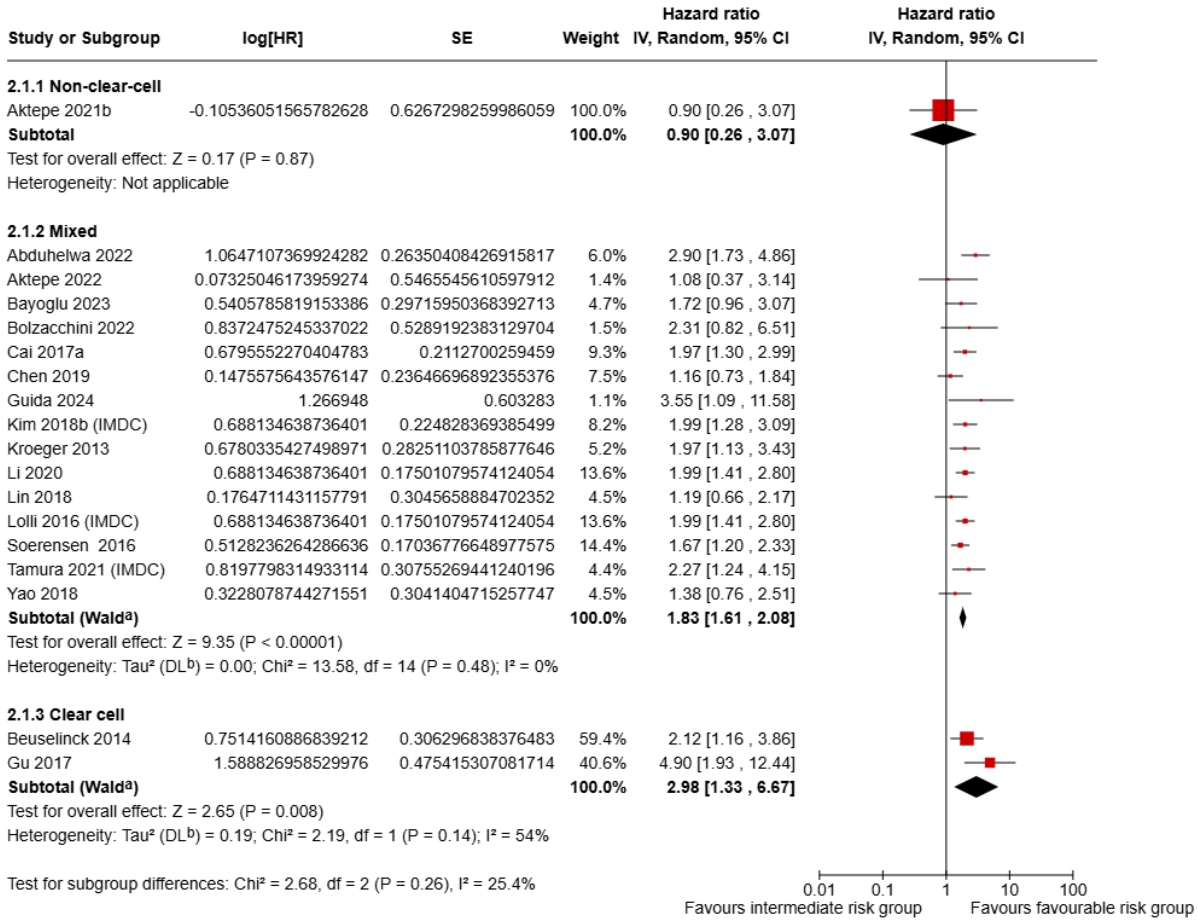


Figure 14: IMDC intermediate risk vs favourable risk: overall survival - Hazard ratio; first-line SACT

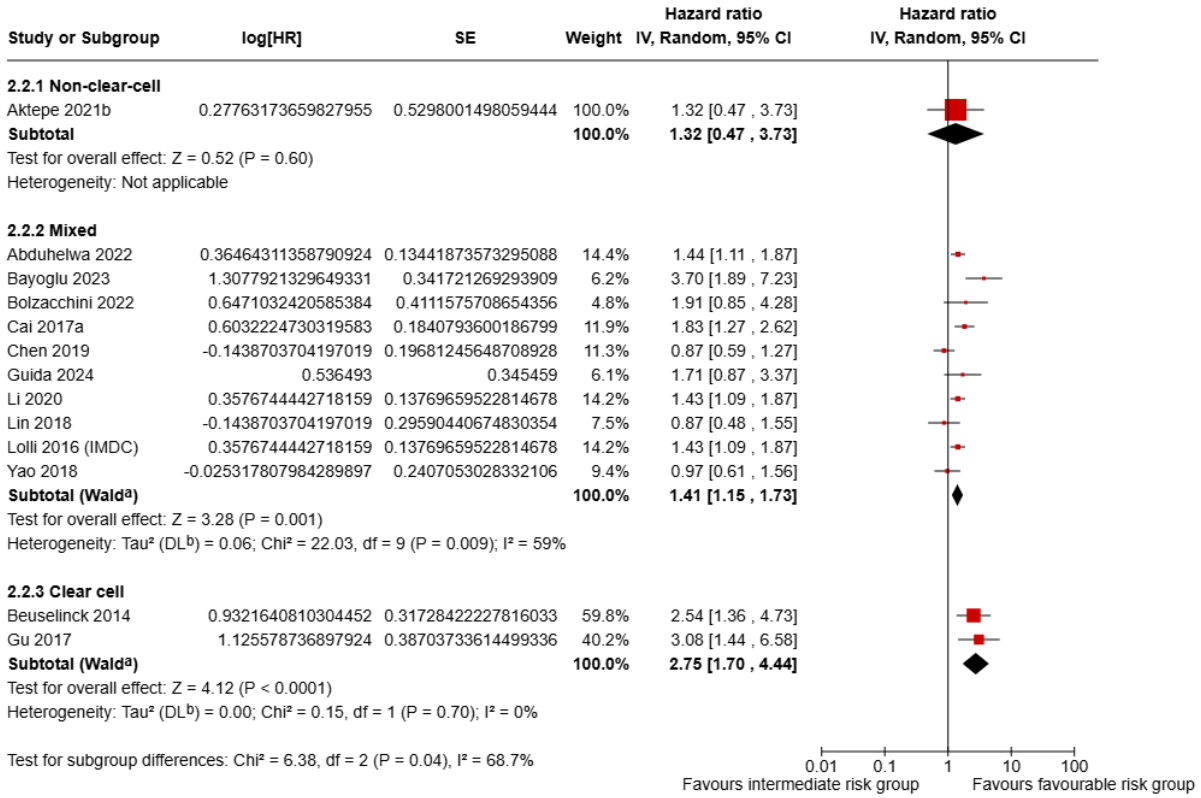


Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Figure 15: IMDC intermediate risk vs favourable risk: progression-free survival - Hazard ratio; first-line SACT



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Figure 16: IMDC intermediate risk vs favourable risk: overall survival - Risk ratio; first-line SACT

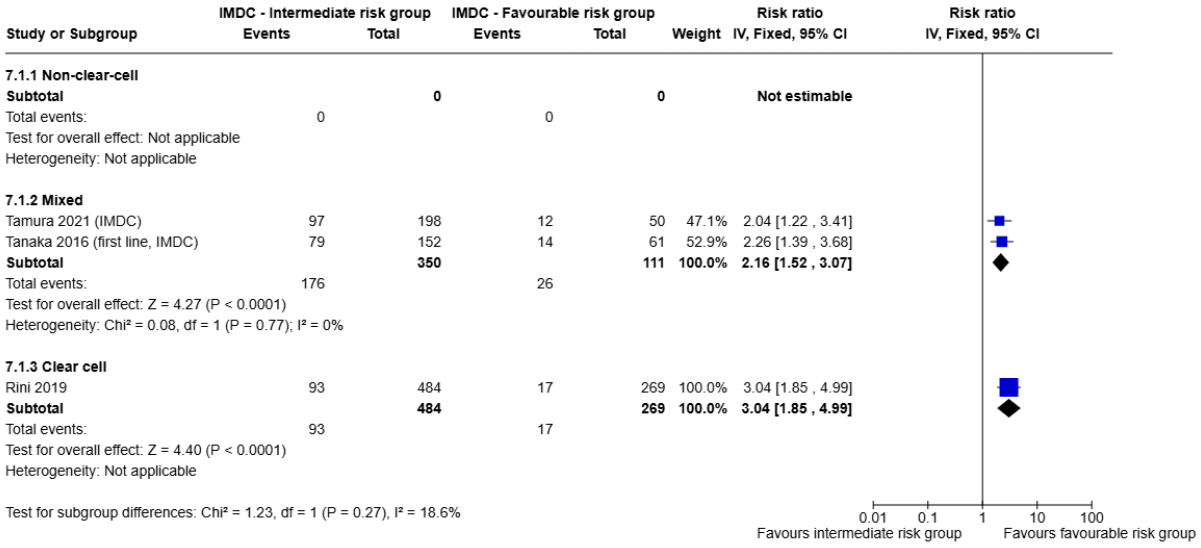


Figure 17: IMDC intermediate risk vs favourable risk: progression-free survival - Risk ratio; first-line SACT, clear cell RCC

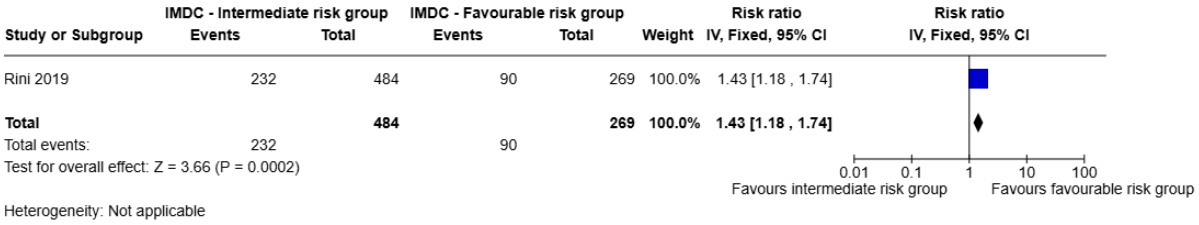


Figure 18: IMDC poor risk vs intermediate risk: overall survival - Hazard ratio; first-line SACT, mixed RCC subtypes

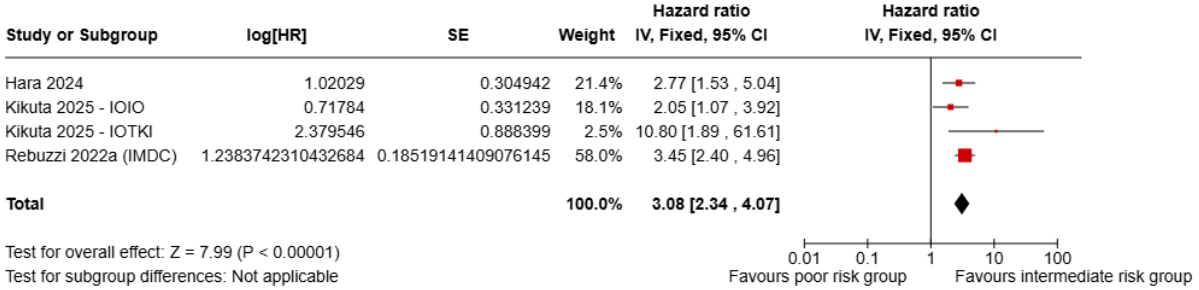


Figure 19: IMDC poor risk vs intermediate risk: progression-free survival - Hazard ratio; first-line SACT, mixed RCC subtypes

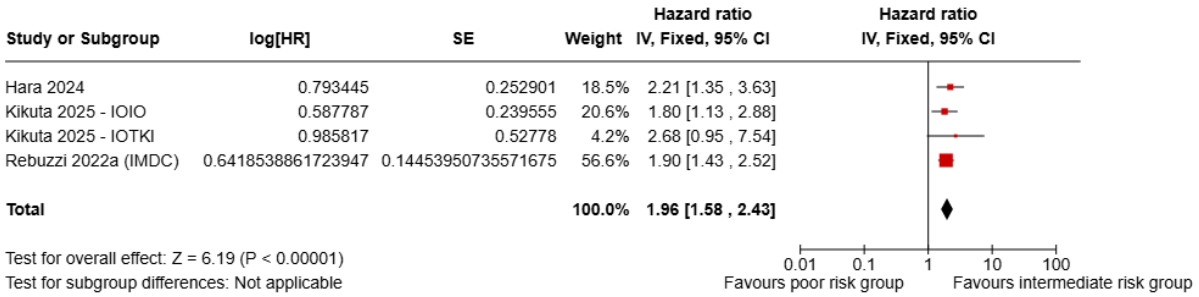


Figure 20: IMDC poor risk vs intermediate risk: overall survival - Risk ratio; first-line SACT

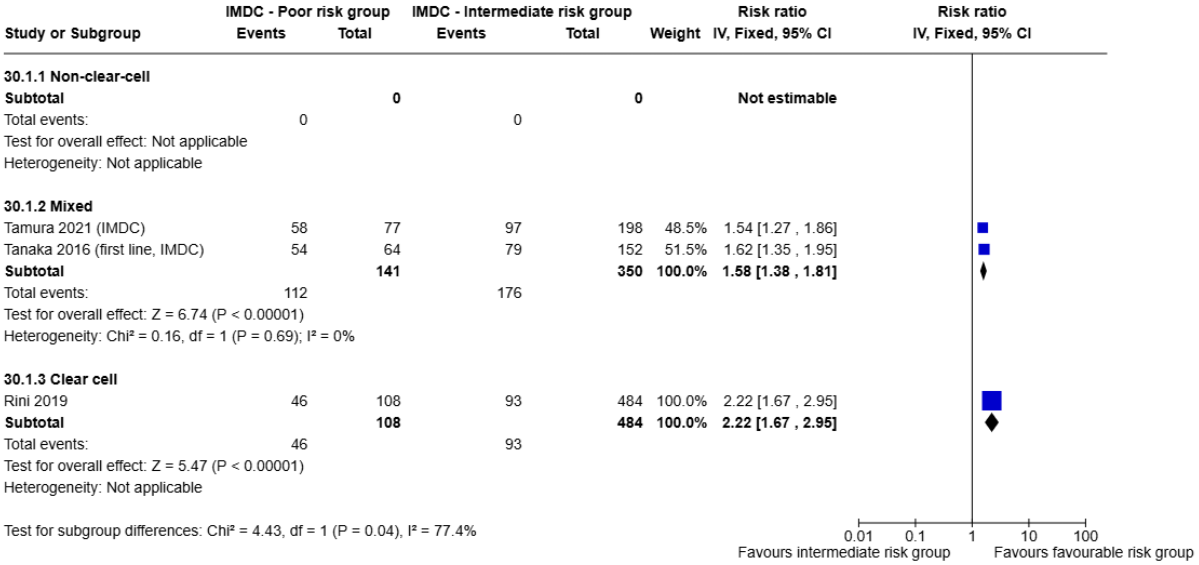


Figure 21: IMDC poor risk vs intermediate risk: progression-free survival - Risk ratio; first-line SACT - clear cell RCC

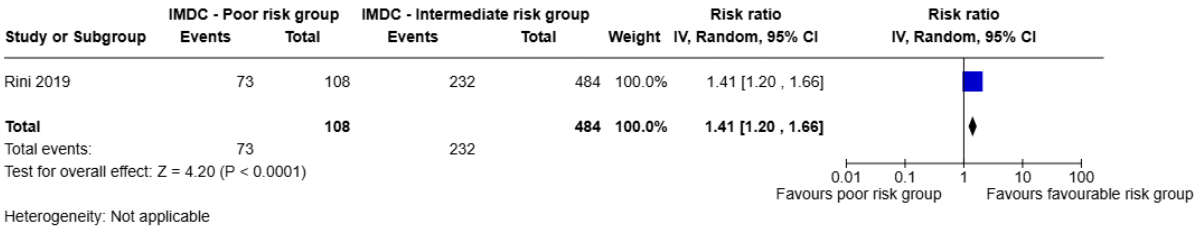


Figure 22: IMDC poor risk vs favourable + intermediate risk: overall survival - Hazard ratio; first-line SACT

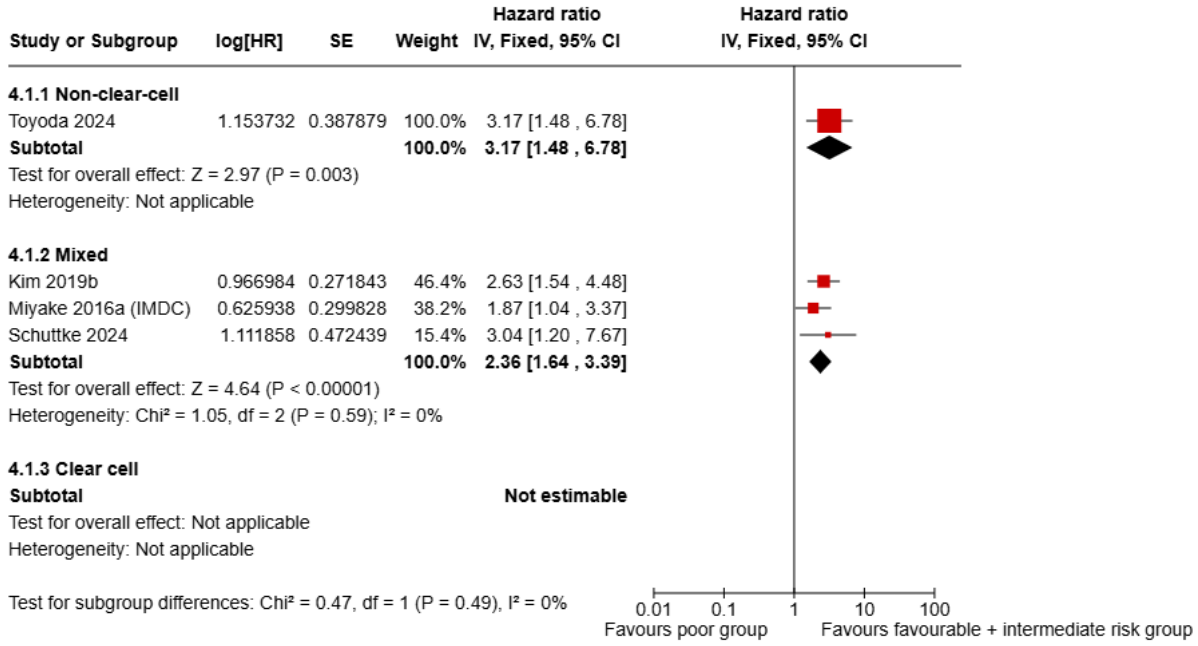
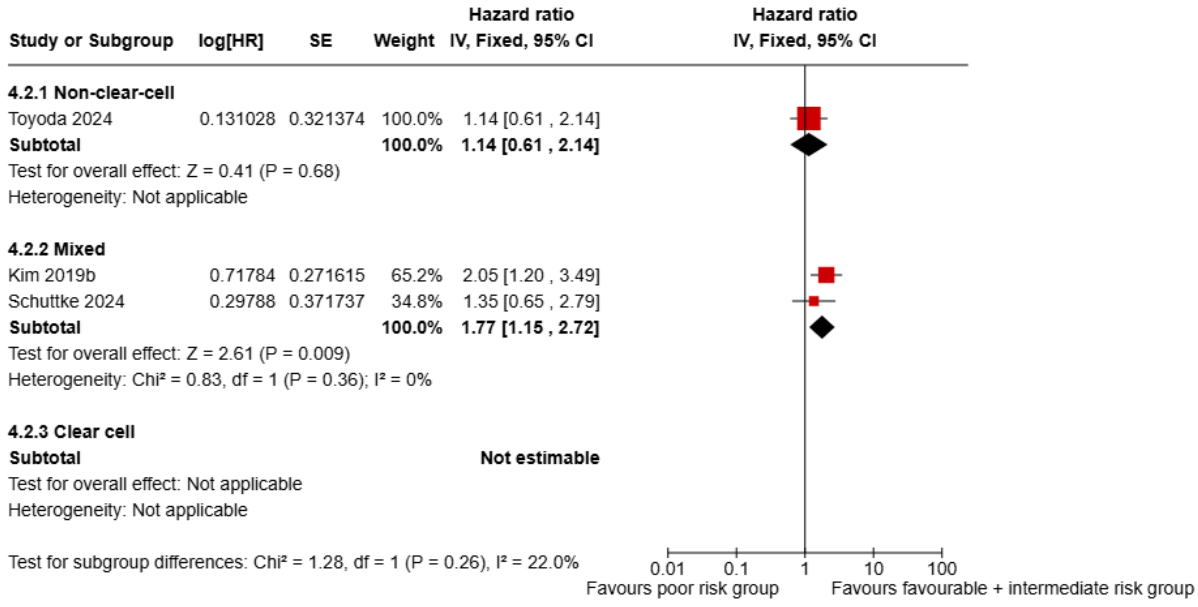
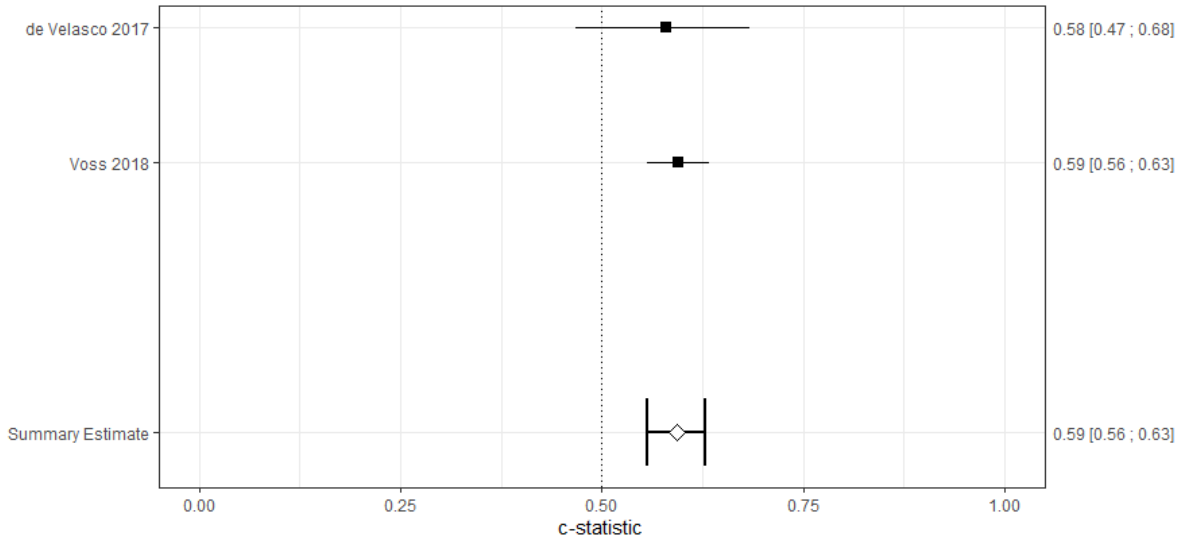


Figure 23: IMDC poor risk vs favourable + intermediate risk : progression-free survival - Hazard ratio; first-line SACT, mixed RCC subtypes



MSKCC

Figure 24: MSKCC: overall survival - c-statistic; first-line SACT, clear cell, FE



I^2 = 0.00%

Figure 25: MSKCC: progression-free survival - c-statistic; first-line SACT, clear cell

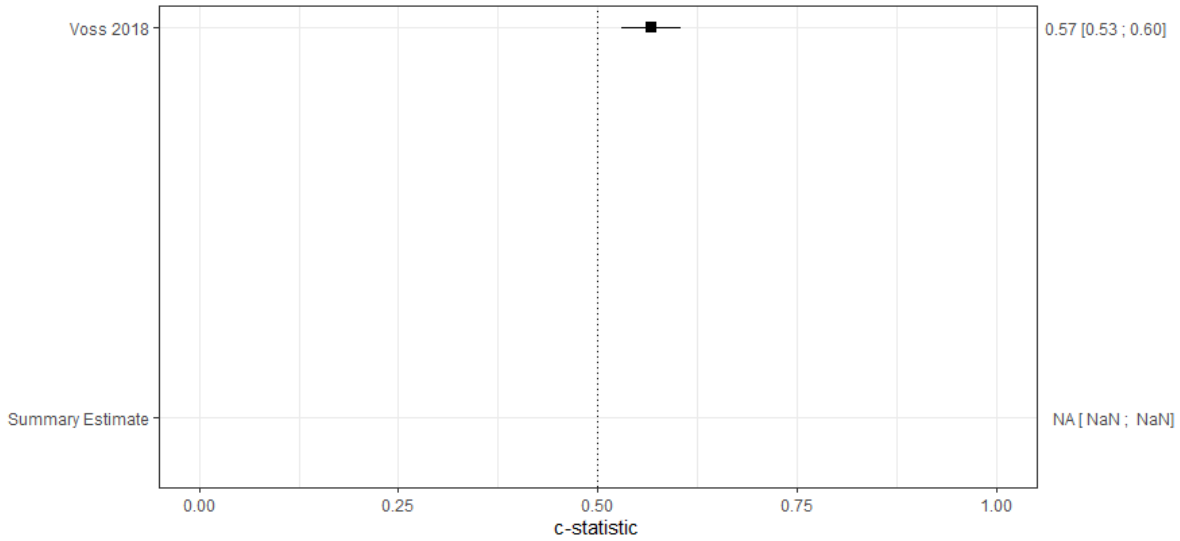
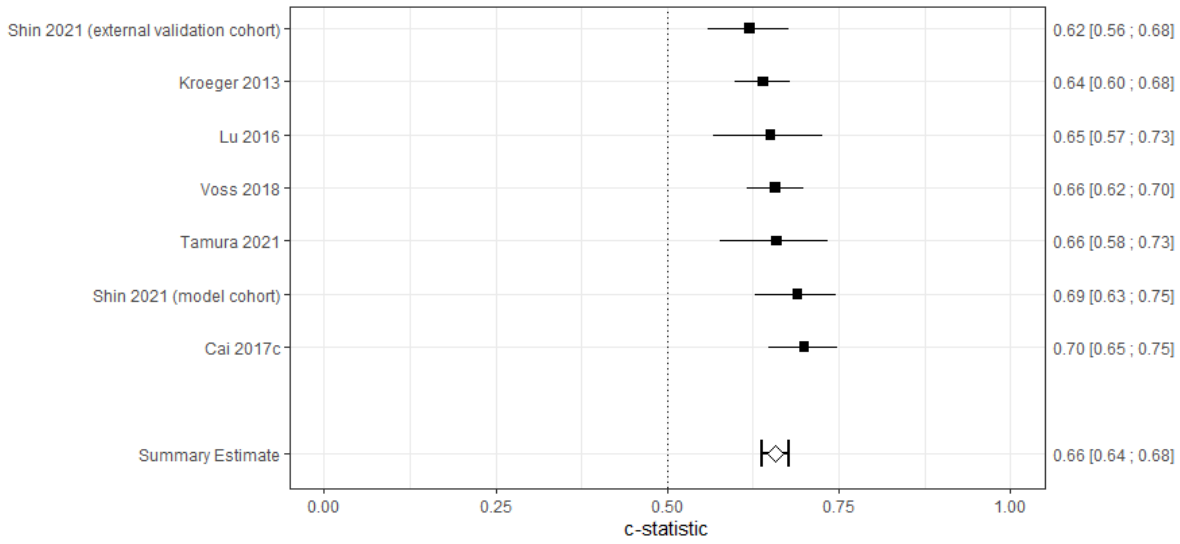
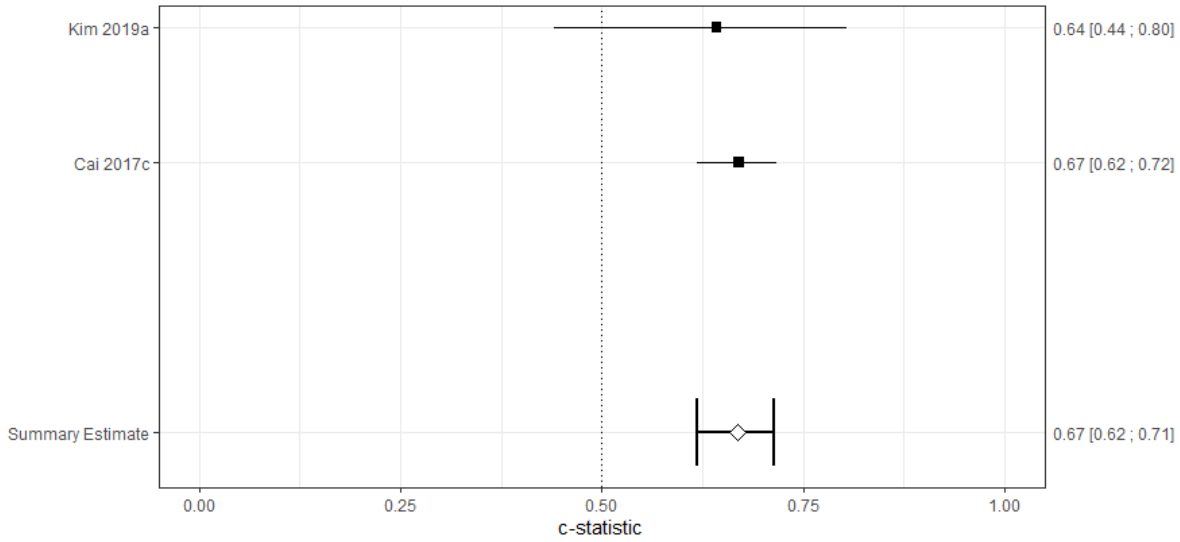


Figure 26: MSKCC: overall survival - c-statistic; first-line SACT, mixed subtype, FE



I^2 = 3.97

Figure 27: MSKCC: progression-free survival - c-statistic; first-line SACT, mixed subtype, FE



I^2 = 0.00%

Figure 28: MSKCC poor risk vs favourable risk: overall survival - Hazard ratio; first-line SACT, mixed subtype

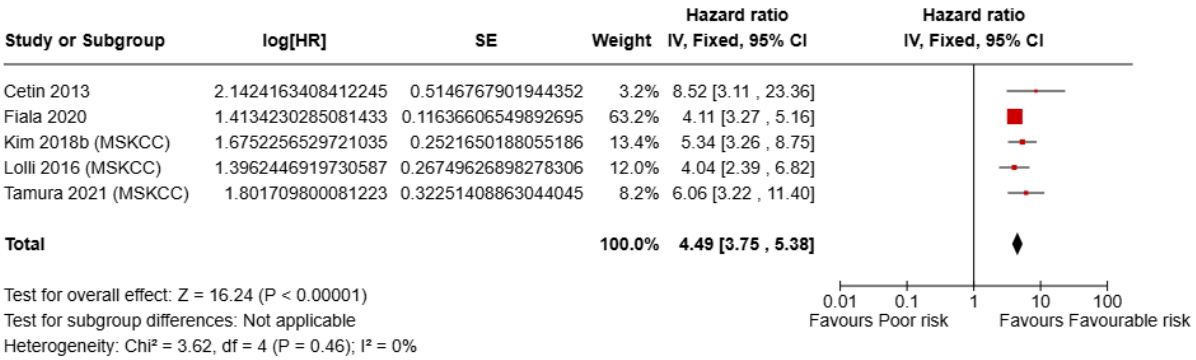


Figure 29: MSKCC poor risk vs favourable risk: progression-free survival - Hazard ratio; first-line SACT, mixed subtype

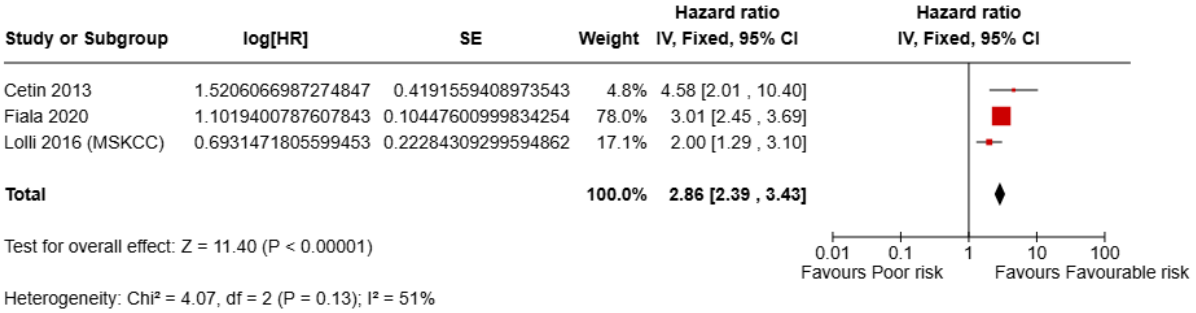
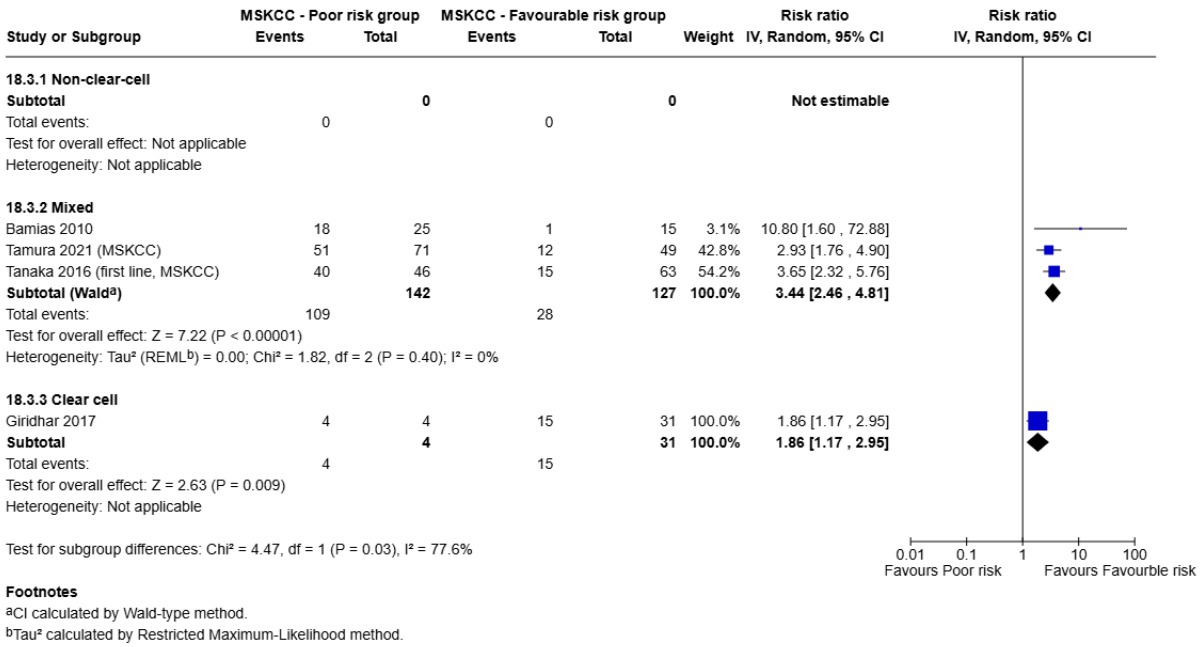


Figure 30: MSKCC poor risk vs favourable risk: overall survival - Risk ratio; first-line SACT



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 31: MSKCC intermediate risk vs favourable risk: overall survival - Hazard ratio; first-line SACT, mixed subtype

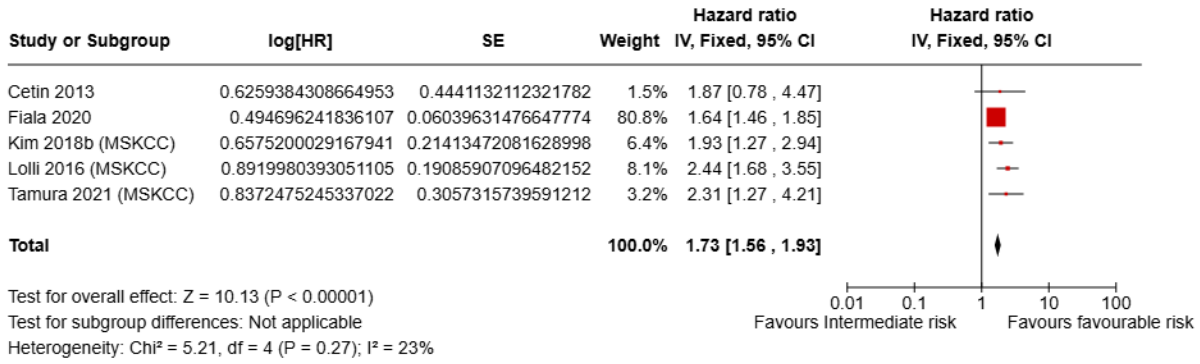


Figure 32: MSKCC intermediate risk vs favourable risk: progression-free survival - Hazard ratio; first-line SACT, mixed subtype

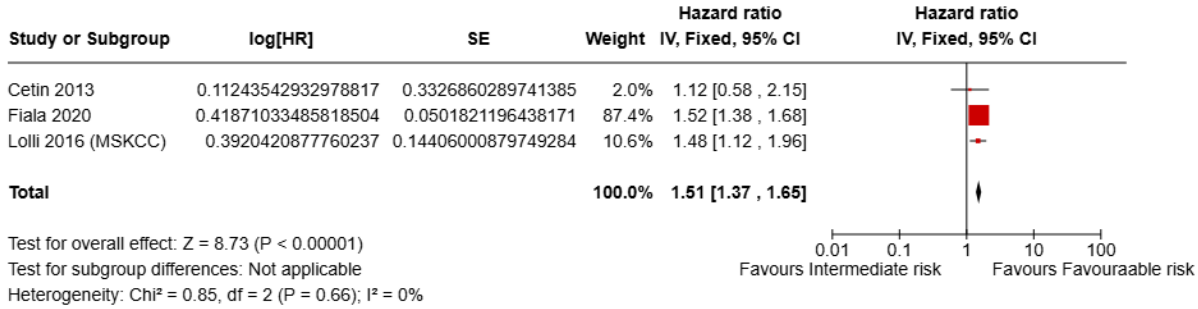
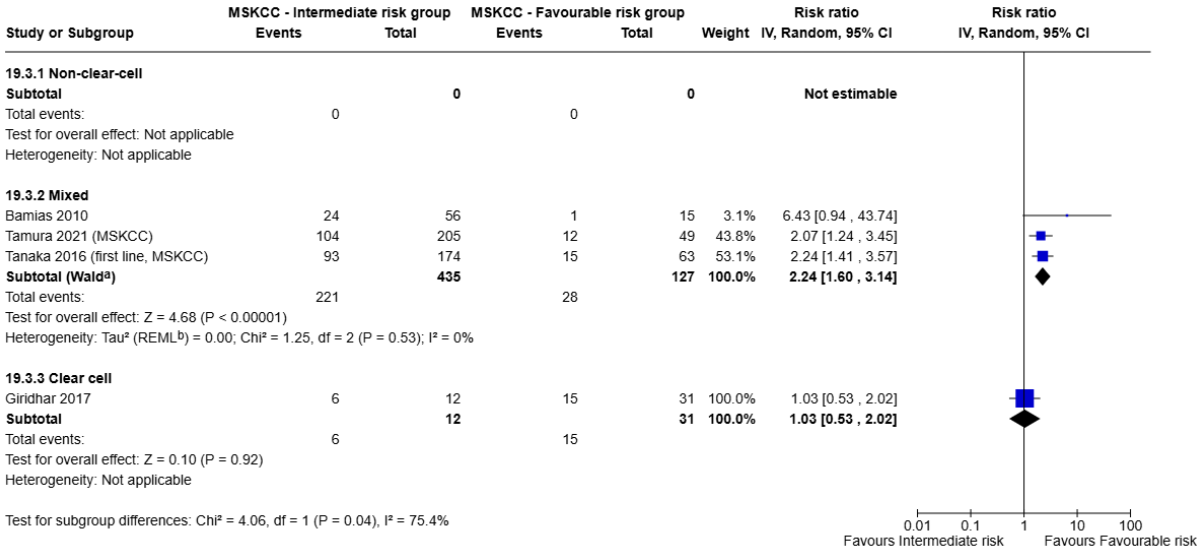


Figure 33: MSKCC intermediate risk vs favourable risk: overall survival - Risk ratio; first-line SACT



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 34: MSKCC poor risk vs intermediate risk: overall survival - Risk ratio; first-line SACT

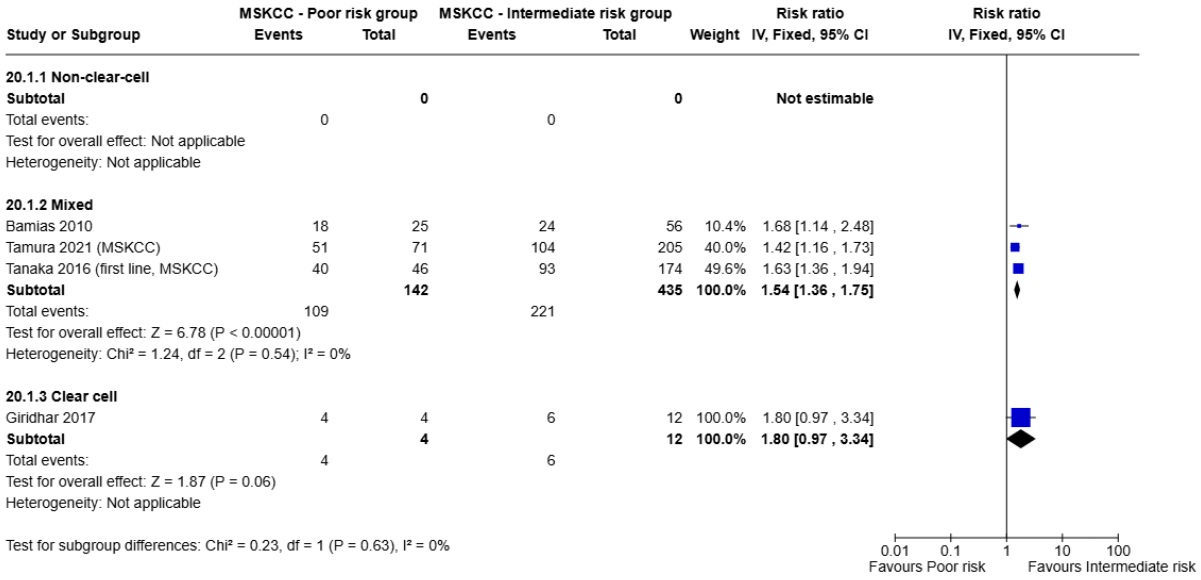


Figure 35: MSKCC poor risk vs intermediate risk: progression-free survival - Risk ratio; first-line SACT, clear cell RCC

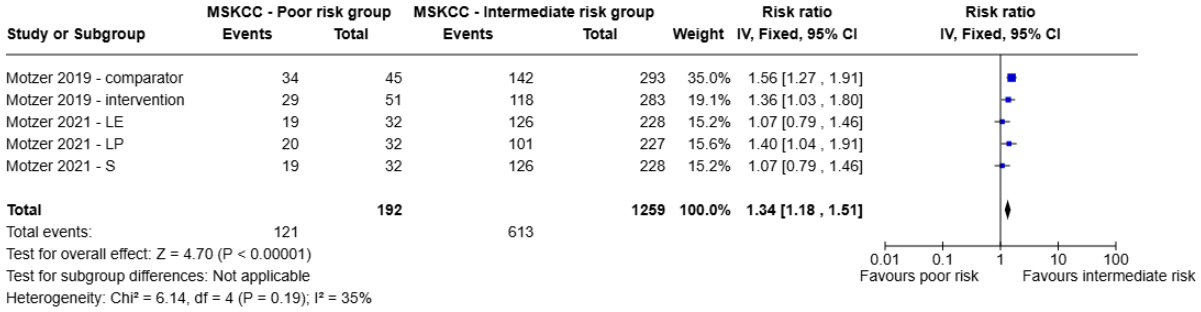
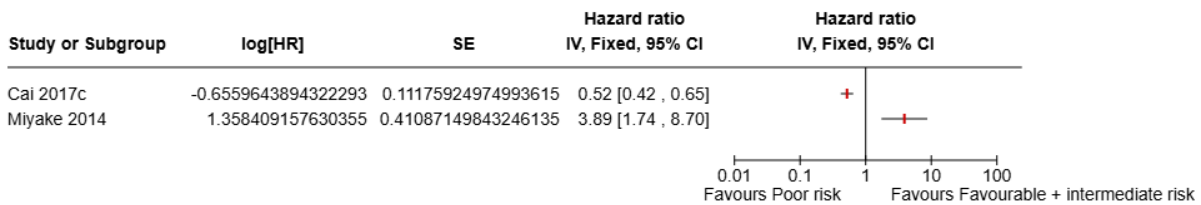
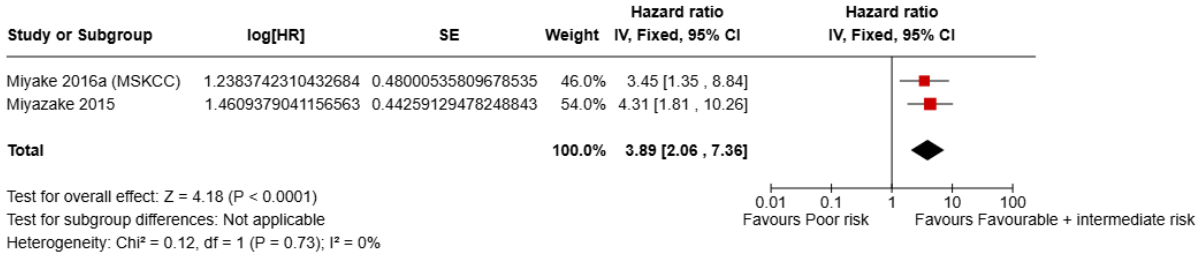


Figure 36: MSKCC poor risk vs favourable + intermediate risk: progression-free survival - Hazard ratio; first-line SACT, mixed subtypes



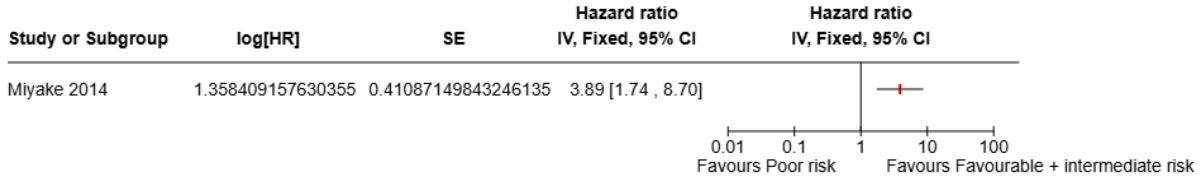
Evidence could not be pooled as I^2 was above 80%.

Figure 37: MSKCC poor risk vs favourable + intermediate risk: overall survival - Hazard ratio; first-line SACT, mixed subtypes [Sensitivity analysis removing Cai 2017c]



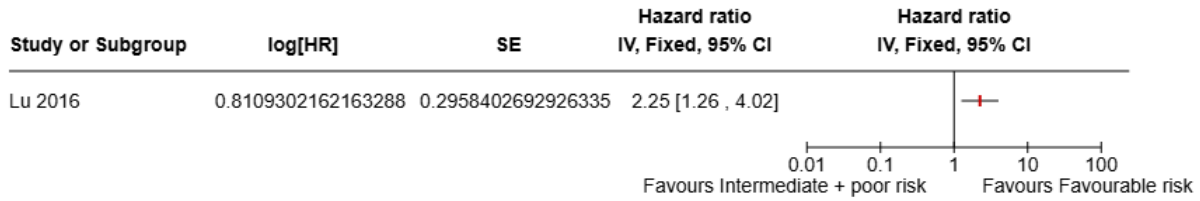
Data from Cai 2017c was removed as the reported hazard ratios favoured the poor-risk subgroup. Including the data from Cai 2017c introduced a high degree of heterogeneity, and it was judged likely that there was an error in the reporting of the results in this study.

Figure 38: MSKCC poor risk vs favourable + intermediate risk: progression-free survival - Hazard ratio; first-line SACT, mixed subtypes [Sensitivity analysis removing Cai 2017c]



Data from Cai 2017c was removed as the reported hazard ratios favoured the poor-risk subgroup. Including the data from Cai 2017c 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 39: MSKCC intermediate + poor risk vs favourable risk: overall survival - Hazard ratio; first-line SACT, mixed subtypes



Meet-URO

Figure 40: Meet-URO Score 5 vs Score 2: overall survival - Hazard ratio; first-line SACT, mixed subtypes

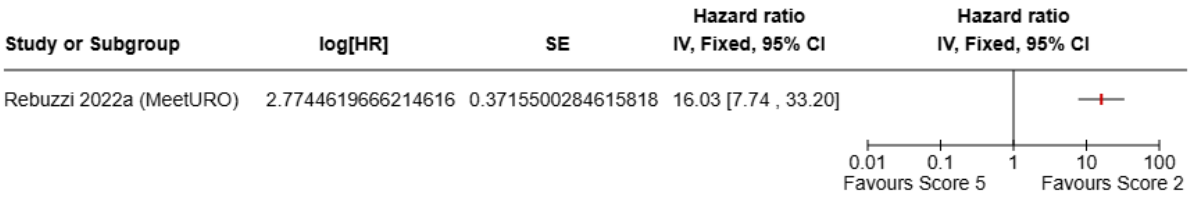


Figure 41: Meet-URO Score 5 vs Score 2: progression-free survival - Hazard ratio; first-line SACT, mixed subtypes

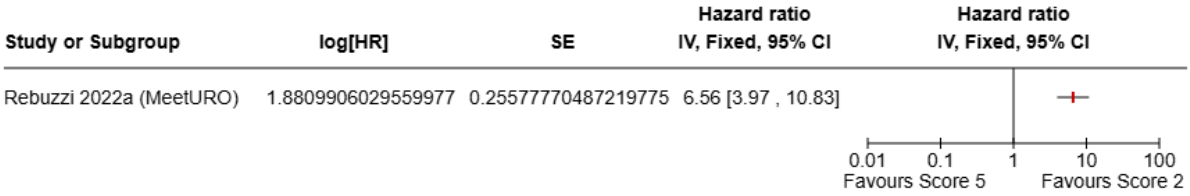


Figure 42: Meet-URO Score 4 vs Score 2: overall survival - Hazard ratio; first-line SACT, mixed subtypes

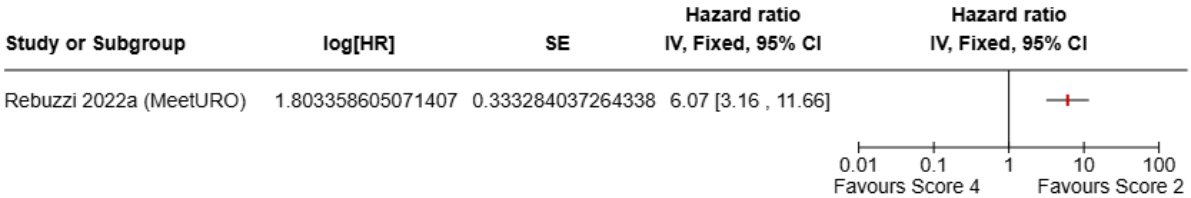


Figure 43: Meet-URO Score 4 vs Score 2: progression-free survival - Hazard ratio; first-line SACT, mixed subtypes

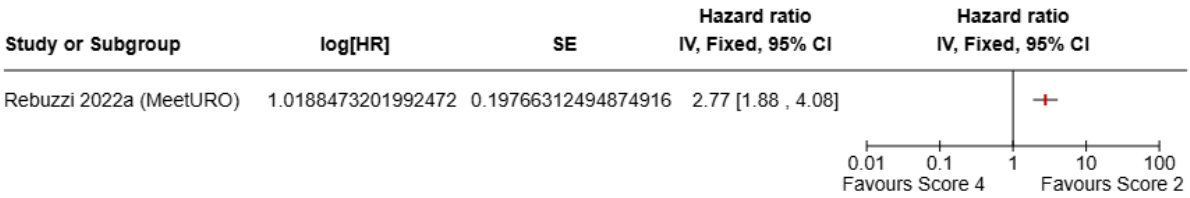


Figure 44: Meet-URO Score 3 vs Score 2: overall survival - Hazard ratio; first-line SACT, mixed subtypes

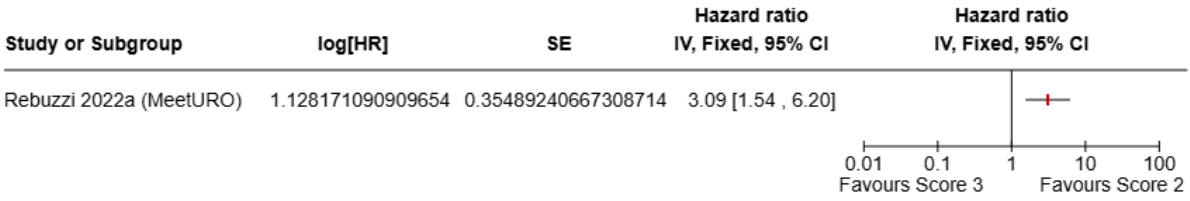
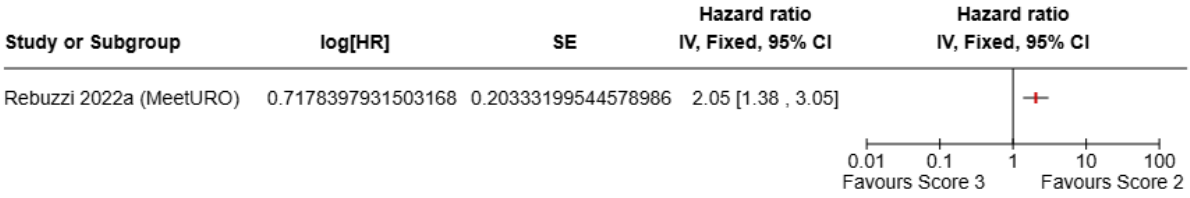


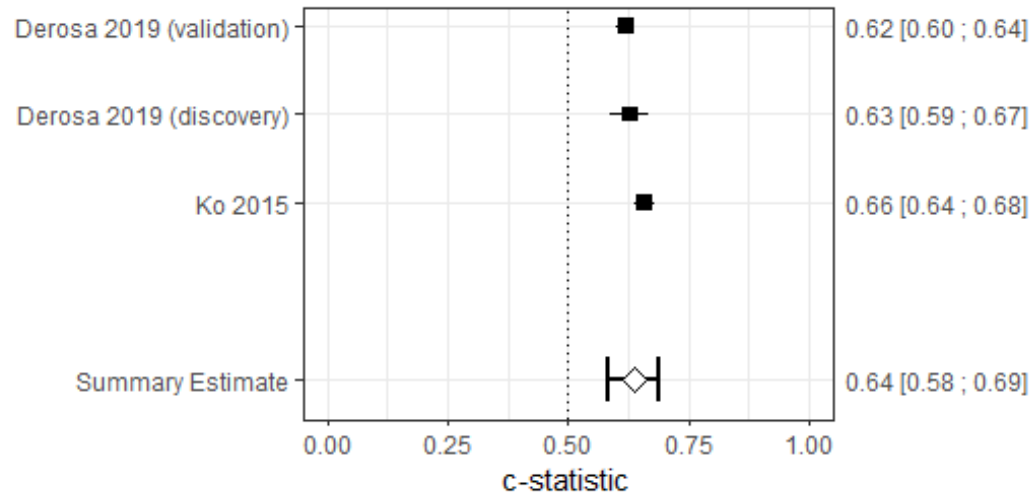
Figure 45: Meet-URO Score 3 vs Score 2: progression-free survival - Hazard ratio; first-line SACT, mixed subtypes



Second-line SACT

IMDC

Figure 46: IMDC: overall survival - c-statistic; second-line SACT, mixed subtype, RE



I^2: 74.67%

Figure 47: IMDC poor risk vs favourable risk: overall survival - Hazard ratio; second-line SACT, mixed subtypes

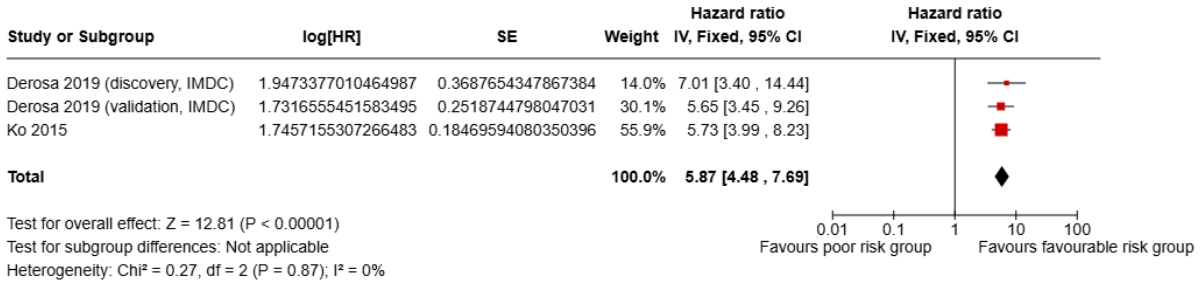


Figure 48: IMDC poor risk vs favourable risk: overall survival - Risk ratio; second-line SACT, mixed subtypes

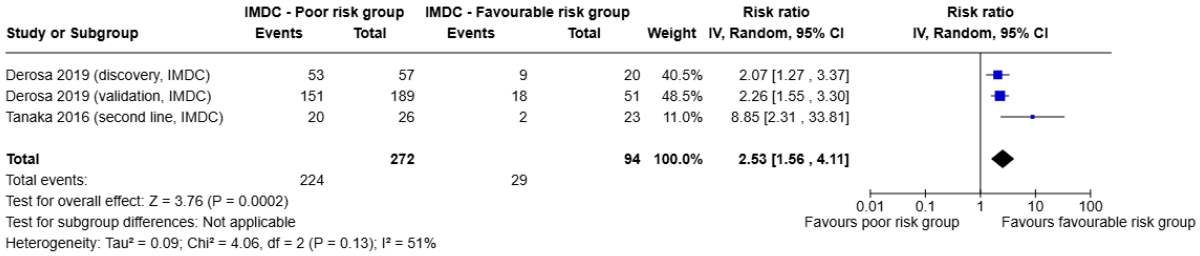


Figure 49: IMDC intermediate risk vs favourable risk: overall survival - Hazard ratio; second-line SACT, mixed subtypes

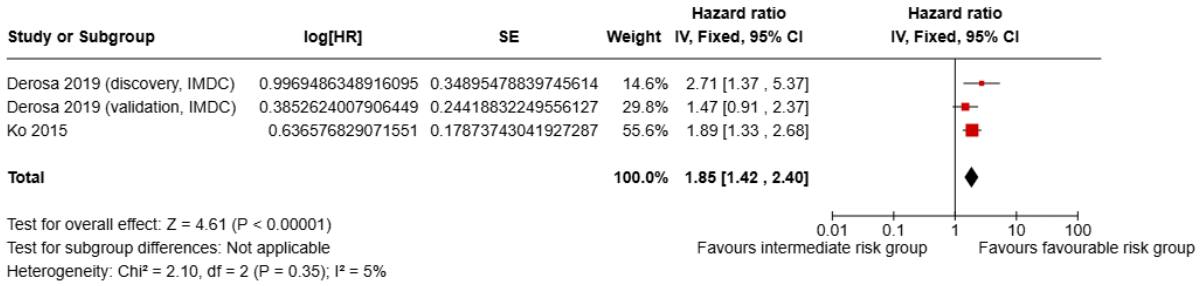


Figure 50: IMDC intermediate risk vs favourable risk: overall survival - Risk ratio; second-line SACT, mixed subtypes

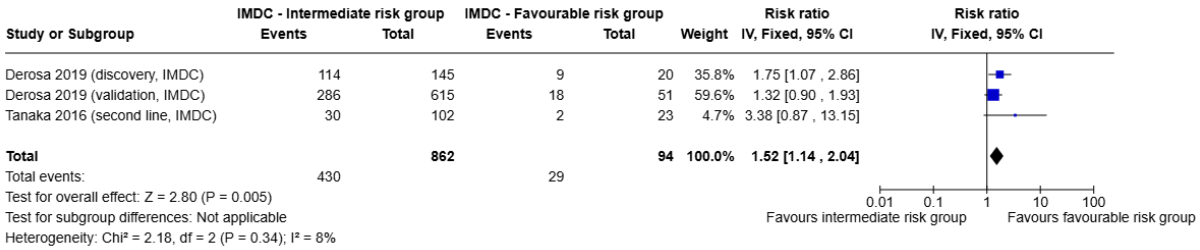


Figure 51: IMDC poor risk vs favourable + intermediate risk : overall survival - Hazard ratio; second-line SACT, mixed subtypes

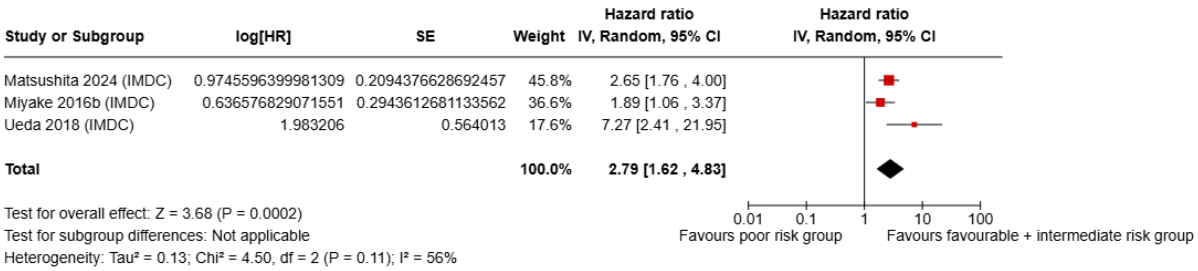


Figure 52: IMDC poor risk vs favourable + intermediate risk : progression-free survival - Hazard ratio; second-line SACT, mixed subtypes

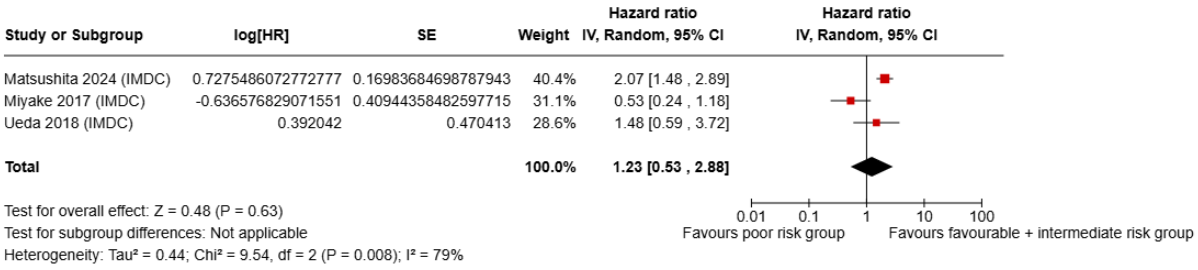


Figure 53: IMDC poor risk vs intermediate risk: overall survival - Hazard ratio; second-line SACT, non-clear cell RCC

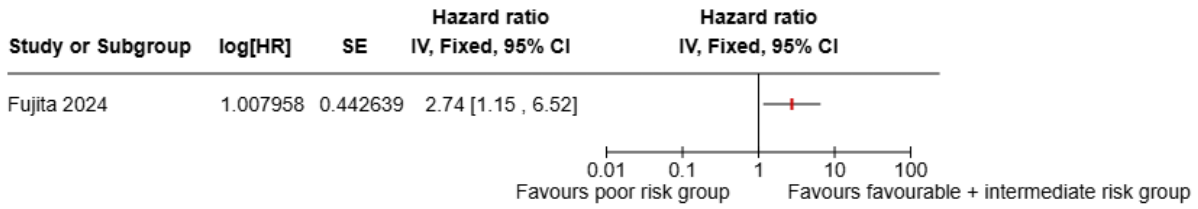
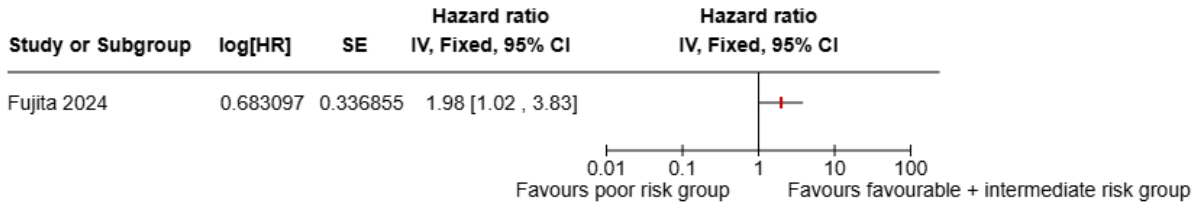
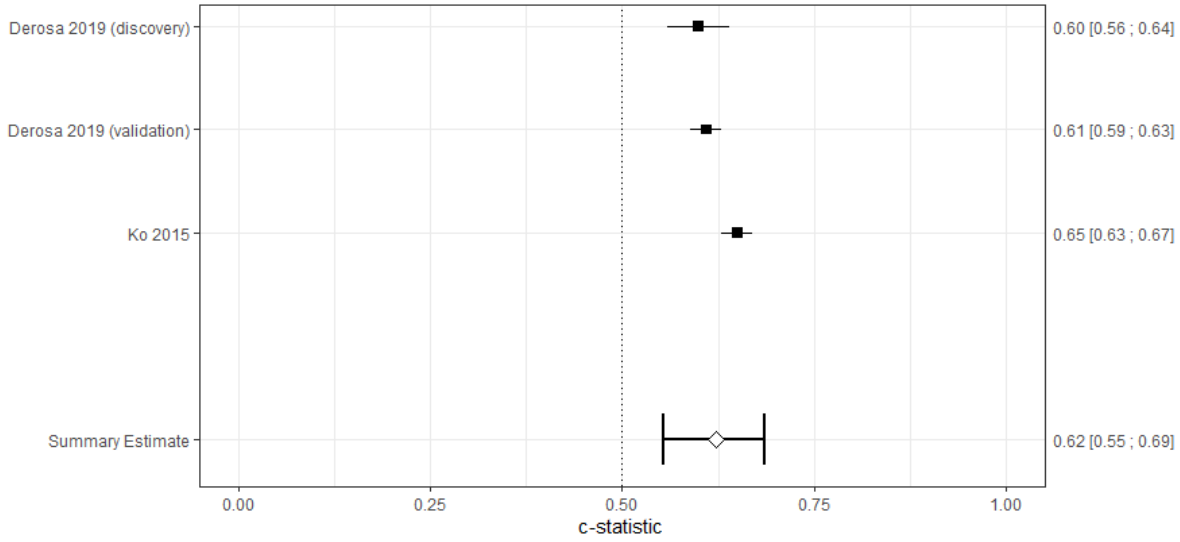


Figure 54: IMDC poor risk vs intermediate risk: progression-free survival - Hazard ratio; second-line SACT, non-clear cell RCC



MSKCC

Figure 55: MSKCC: overall survival - c-statistic; second-line SACT, mixed subtype, RE



I^2 = 79.18%

Figure 56: MSKCC poor risk vs favourable risk: overall survival - Hazard ratio; second-line SACT, mixed subtypes

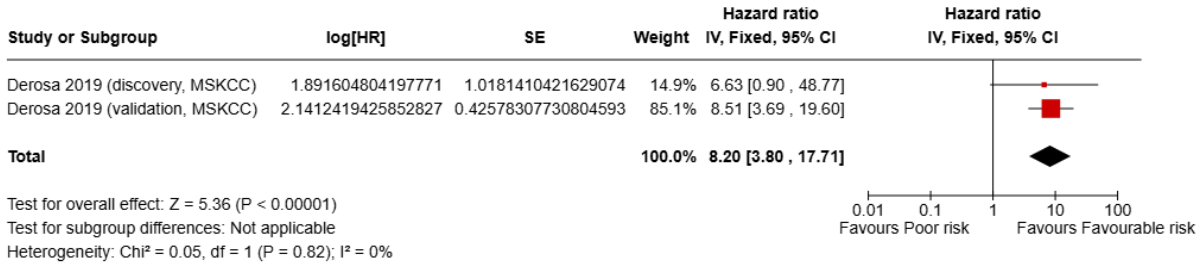


Figure 57: MSKCC poor risk vs favourable risk: overall survival - Risk ratio; second-line SACT, mixed subtypes

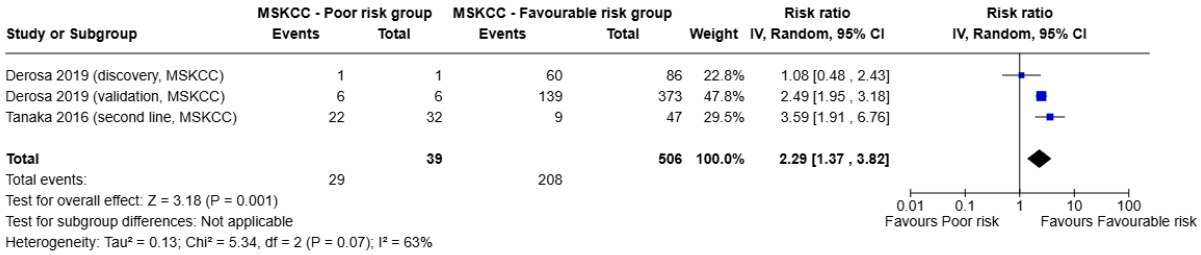


Figure 58: MSKCC intermediate risk vs favourable risk: overall survival - Hazard ratio; second-line SACT, mixed subtypes

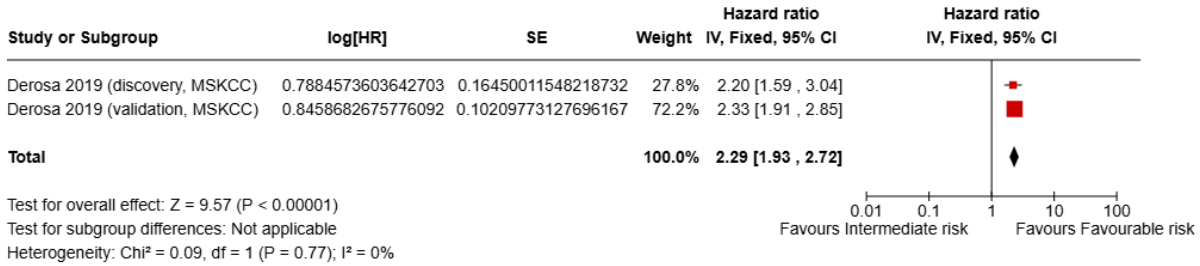
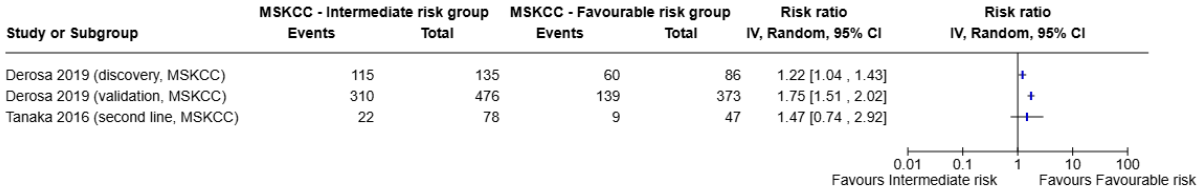


Figure 59: MSKCC intermediate risk vs favourable risk: overall survival - Risk ratio; second-line SACT, mixed subtypes



Evidence could not be pooled as I^2 was above 80%.

Figure 60: MSKCC poor risk vs intermediate risk: overall survival - Risk ratio; second-line SACT, mixed subtypes

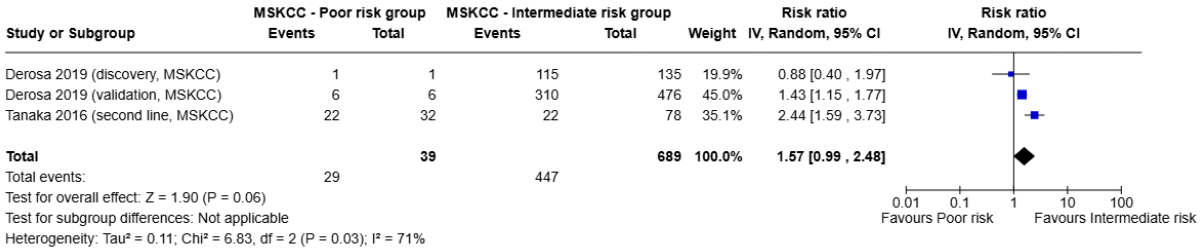


Figure 61: MSKCC poor risk vs favourable + intermediate risk: overall survival - Hazard ratio; second-line SACT, mixed subtypes

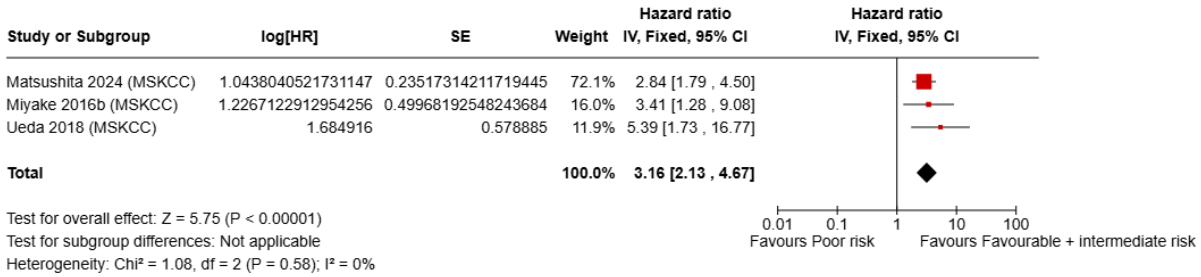
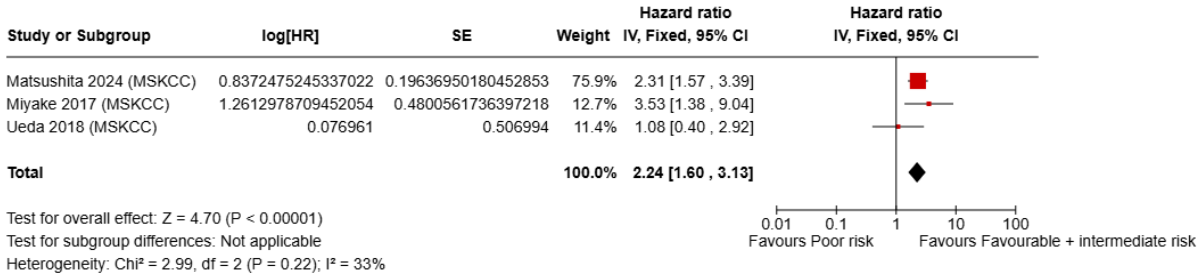


Figure 62: MSKCC poor risk vs favourable + intermediate risk: progression-free survival - Hazard ratio; second-line SACT, mixed subtypes



Meet-URO

No evidence was identified for this model in this treatment line.

Subsequent-line SACT

No evidence identified for this treatment line.

Appendix F – GRADE

Prior to cytoreductive nephrectomy

IMDC

Table 17: Clinical evidence profile (C-statistics): IMDC model, cytoreductive nephrectomy, mixed RCC subtypes

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Overall survival in people with mixed RCC treated with cytoreductive nephrectomy, follow-up time of 18.1 months								
1 (Marchioni 2021)	Retrospective cohort	519	0.60 (0.56, 0.64)	Serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded as study was at moderate 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 18: Clinical evidence profile (Hazard ratio): IMDC model poor risk vs favourable risk; cytoreductive nephrectomy, no SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs favourable risk - for prediction of overall survival at cytoreductive nephrectomy, no SACT for mixed RCC subtypes, median 22 months follow-up								
2 (Laukhtina 2020, Lee 2017)	Retrospective cohort	514	1.58 (1.19, 2.09)	Not serious	Not serious	Not serious	Not serious	High

Table 19: Clinical evidence profile (Hazard ratio): IMDC model intermediate risk vs favourable risk; cytoreductive nephrectomy, no SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – intermediate risk vs favourable risk - for prediction of overall survival at cytoreductive nephrectomy, no SACT for mixed RCC subtypes, median 22 months follow-up								
2 (Laukhtina 2020, Lee 2017)	Retrospective cohort	773	1.19 (0.99, 1.43)	Not serious	Not serious	Not serious	Serious[a]	Moderate

a. Downgraded once as 95% confidence interval crossed the line of no effect

MSKCC

Table 20: Clinical evidence profile (C-statistics): MSKCC model, cytoreductive nephrectomy, mixed RCC subtypes

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model for prediction of overall survival in people with clear cell RCC at treatment with cytoreductive nephrectomy, median 18.1 months follow-up								
1 (Marchioni 2021)	Retrospective cohort	519	0.60 (0.57, 0.64)	Serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded once as study at moderate risk of bias
b. Downgraded once as single study
c. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Meet-URO

No evidence was identified for this model in this treatment line.

Prior to first-line SACT

IMDC

Table 21: Clinical evidence profile (C-statistics): IMDC model, first-line SACT, clear cell RCC subtype

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Overall survival in people with clear cell RCC, treated with first-line SACT, median follow-up 36 months								
3 (Beuselinck 2014; de Velasco 2017; Shin 2021 (model cohort); Shin 2021 (external validation cohort))	Retrospective cohort	1,044	0.65 (0.62, 0.67)	Very serious[a]	Not serious	Not serious	Not serious	Low
Progression-free survival in people with clear cell RCC, treated with first-line SACT and median follow-up of 67 months								
1 (Beuselinck 2024)	Retrospective cohort	200	0.63 (0.58, 0.67)	Very serious[b]	Not serious	Serious[c]	Very serious[d]	Very low

a. Downgraded twice as >50% of the weight of the meta-analysis came from studies at high risk of bias
b. Downgraded twice as study at high risk of bias
c. Downgraded once as single study
d. Downgraded twice as sample size < 500 and 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Table 22: Clinical evidence profile (C-statistics): IMDC model, first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Overall survival in people with mixed RCC subtype treated with first-line SACT, median follow-up 22 months								
8 (Abduhelwa 2022; Cai 2017a; Chen 2019; Chrom 2019; Kroeger 2013; Ning 2022; Soerensen 2016; Tamura 2021)	Retrospective cohort	5,053	0.65 (0.62, 0.68)	Very serious[a]	Not serious	Serious[b]	Not serious	Very low
Progression-free survival in people with mixed RCC subtype at treatment with first-line SACT, median follow-up 14.05 months								
4 (Abduhelwa 2022; Cai 2017a; Kim 2019a; Ning 2022)	Retrospective cohort	1,219	0.62 (0.56, 0.69)	Very serious[a]	Not serious	Very serious[c]	Serious[d]	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 I^2 was between 40% and 60%
c. Downgraded twice as I^2 was greater than 60%
d. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Table 23: Clinical evidence profile (Hazard ratios): IMDC model poor risk vs favourable risk; first-line SACT, non-clear cell RCC subtype

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs favourable risk - for prediction of overall survival at first-line SACT for non-clear cell RCC subtype, median 21 months follow-up								
1 (Aktepe 2021b)	Retrospective cohort	25	10.20 (2.42, 42.97)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
IMDC model – poor risk vs favourable risk - for prediction of progression-free survival at first-line SACT for non-clear cell RCC subtype, median 21 months follow-up								
1 (Aktepe 2021b)	Retrospective cohort	25	15.64 (4.52, 54.08)	Very serious[a]	Not serious	Serious[b]	Serious[c]	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 single study
c. Downgraded once as sample size < 500

Table 24: Clinical evidence profile (Hazard ratios): IMDC model poor risk vs favourable risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs favourable risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median follow-up 22.3 months								
15 (Abuhelwa 2022; Aktepe 2022; Bayoglu 2023; Bolzacchini 2022; Cai 2017a; Chen	Retrospective cohort	2,645	5.52 (4.15, 7.34)	Very serious[a]	Not serious	Very serious[b]	Not serious	Very low

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
2019; Guida 2024; Kim 2018b (IMDC); Kroeger 2013; Li 2020; Lin 2018; Lolli 2016 (IMDC); Soerense 2016; Tamura 2021; Yao 2018)								
IMDC model – poor risk vs favourable risk - for prediction of progression-free survival at first-line SACT for mixed RCC subtypes, median follow-up ranged between 14.2 and 60 months								
1 (Abduhelwa 2022)	Retrospective cohort	210	2.68 (1.91, 3.77)	Very serious[c]	Not serious	Very serious[d]	Not serious	Very low
1 (Bayoglu 2023)	Retrospective cohort	94	6.20 (2.82, 13.62)					
1 (Bolzacchini 2022)	Retrospective cohort	25	4.41 (1.69, 11.52)					
1 (Cai 2017a)	Retrospective cohort	109	4.59 (2.81, 7.51)					
1 (Chen 2019)	Retrospective cohort	155	1.19 (0.81, 1.75)					
1 (Guida 2024)	Retrospective cohort	64	1.98 (0.90, 4.36)					
1 (Li 2020)	Retrospective cohort	174	5.09 (3.39, 7.65)					

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
1 (Lin 2018)	Retrospective cohort	50	2.27 (1.10, 4.69)					
1 (Lolli 2016) (IMDC)	Retrospective cohort	159	5.09 (3.39, 7.65)					
1 (Yao 2018)	Retrospective cohort	75	1.75 (0.99, 3.08)					

a. Downgraded twice as >50% of the weight of the meta-analysis came from studies at high risk of bias
b. Downgraded twice as I^2<60%
c. Downgraded twice as >50% of the population weight came from studies at high risk of bias
d. Downgraded twice as I^2 > 80%, however, point estimates did not cross the line of no effect

Table 25: Clinical evidence profile (Risk ratio): IMDC model poor risk vs favourable risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs favourable risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, follow-up ranged between 18.1 and 19 months								
2 (Tamura 2021 (IMDC); Tanaka 2016 (first line, IMDC))	Retrospective cohort	252	3.42 (2.42, 4.83)	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 oncer as sample size < 500

Table 26: Clinical evidence profile (Hazard ratios): IMDC model poor risk vs favourable risk; first-line SACT, clear cell RCC subtype

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs favourable risk - for prediction of overall survival at first-line SACT for clear cell RCC, median follow-up ranged between 30.8 and 67 months								
2 (Beuselinck 2014; Gu 2017)	Retrospective cohort	123	6.07 (2.66, 13.88)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low
IMDC model – poor risk vs favourable risk - for prediction of progression-free survival at first-line SACT for clear cell RCC, median follow-up ranged between 30.8 and 67 months								
2 (Beuselinck 2014; Gu 2017)	Retrospective cohort	123	4.67 (2.64, 8.25)	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 27: Clinical evidence profile (Risk ratio): IMDC model poor risk vs favourable risk; first-line SACT, clear cell RCC

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs favourable risk - for prediction of overall survival at first-line SACT for clear cell RCC subtypes, median follow-up 12.8 months								
1 (Rini 2019)	Retrospective cohort	377	6.74 (4.05, 11.22)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
IMDC model – poor risk vs favourable risk - for prediction of progression-free survival at first-line SACT for clear cell RCC subtypes, median follow-up 12.8 months								
1 (Rini 2019)	Retrospective cohort	377	2.02 (1.63, 2.50)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded twice as study at high risk of bias

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
b. Downgraded once as single study c. Downgraded once as sample size < 500								

Table 28: Clinical evidence profile (Hazard ratios): IMDC model intermediate risk vs favourable risk; first-line SACT, non-clear cell RCC subtype

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – intermediate risk vs favourable risk - for prediction of overall survival at first-line SACT for non-clear cell RCC subtype, median 21 months follow-up								
1 (Aktepe 2021b)	Retrospective cohort	26	0.90 (0.26, 3.97)	Very serious[a]	Not serious	Serious[b]	Very serious[c]	Very low
IMDC model – intermediate risk vs favourable risk - for prediction of progression-free survival at first-line SACT for non-clear cell RCC subtype, median 21 months follow-up								
1 (Aktepe 2021b)	Retrospective cohort	26	1.32 (0.47, 3.73)	Very serious[a]	Not serious	Serious[b]	Very serious[c]	Very low
a. Downgraded once as study at high risk of bias b. Downgraded once as single study c. Downgraded once as sample size < 500 and 95% confidence interval crossed the line of no effect								

Table 29: Clinical evidence profile (Hazard ratios): IMDC model intermediate risk vs favourable risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – intermediate risk vs favourable risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median follow-up 22.15 months								
15 (Abduhelwa 2022; Aktepe 2022; Bayoglu 2023; Bolzacchini 2022; Cai 2017a; Chen 2019; Guida 2024; Kim 2018b (IMDC); Kroeger 2013; Li 2020; Lin 2018; Lolli 2016 (IMDC); Soerense 2016; Tamura 2021; Yao 2018)	Retrospective cohort	4,653	1.83 (1.61, 2.08)	Very serious[a]	Not serious	Not serious	Not serious	Low
IMDC model – intermediate vs favourable risk - for prediction of progression-free survival at first-line SACT for mixed RCC subtypes, median follow-up 22.7 months								
10 (Abduhelwa 2022; Bayoglu 2023; Bolzacchini 2022; Cai	Retrospective cohort	2,031	1.41 (1.15, 1.73)	Very serious[a]	Not serious	Very serious[b]	Not serious	Very low

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
2017a; Chen 2019; Guida 2024; Li 2020; Lin 2018; Lolli 2016 (IMDC); Yao 2018)								

a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias
b. Downgraded twice as I^2 > 60%

Table 30: Clinical evidence profile (Risk ratio): IMDC model intermediate risk vs favourable risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – intermediate risk vs favourable risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median follow-up 18.6 months								
2 (Tamura 2021 (IMDC); Tanaka 2016 (first line, IMDC))	Retrospective cohort	461	2.16 (1.52, 3.07)	Very serious[a]	Not serious	Not serious	Serious[b]	Very ow

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 31: Clinical evidence profile (Hazard ratios): IMDC model intermediate risk vs favourable risk; first-line SACT, clear cell RCC subtype

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – intermediate risk vs favourable risk - for prediction of overall survival at first-line SACT for clear cell RCC subtype, median follow-up 48.9 months								
2 (Beuselinck 2014; Gu 2017)	Retrospective cohort	229	2.98 (1.33, 6.67)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
IMDC model – poor risk vs favourable risk - for prediction of progression-free survival at first-line SACT for clear cell RCC, median follow-up 48.9 months								
2 (Beuselinck 2014; Gu 2017)	Retrospective cohort	229	2.75 (1.70, 4.44)	Very serious[a]	Not serious	Not serious	Serious[c]	Very low

a. Downgraded once as 50% of the weight in a meta-analysis came from studies at high risk of bias
b. Downgraded once as I^2 was between 40% and 60%
c. Downgraded once as sample size < 500

Table 32: Clinical evidence profile (Risk ratio): IMDC model intermediate risk vs favourable risk; first-line SACT, clear cell RCC

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – intermediate risk vs favourable risk - for prediction of overall survival at first-line SACT for clear cell RCC subtypes, median follow-up 12.8 months								
1 (Rini 2019)	Retrospective cohort	753	3.04 (1.85, 4.98)	Very serious[a]	Not serious	Serious[b]	Not serious	Very low
IMDC model – intermediate risk vs favourable risk - for prediction of progression-free survival at first-line SACT for clear cell RCC subtypes, median follow-up 12.8 months								

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
1 (Rini 2019)	Retrospective cohort	753	1.43 (1.18, 1.74)	Very serious[a]	Not serious	Serious[b]	Not serious	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 single study

Table 33: Clinical evidence profile (Hazard ratios): IMDC model poor risk vs intermediate risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs intermediate risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 12.2 months follow-up								
3 (Hara 2024; Kikuta 2025 – IOIO; Kikuta 2025 – IOTKI; Rebuzzi 2022)	Retrospective cohort	553	3.08 (2.34, 4.07)	Serious[a]	Not serious	Not serious	Not serious	Moderate
IMDC model – poor risk vs intermediate risk - for prediction of progression-free survival at first-line SACT for mixed RCC subtypes, median 12.2 months follow-up								
3 (Hara 2024; Kikuta 2025 – IOIO; Kikuta 2025 – IOTKI; Rebuzzi 2022)	Retrospective cohort	553	1.96 (1.58, 2.43)	Serious[a]	Not serious	Not serious	Not serious	Moderate

a. Downgraded once as >50% of the weight in a meta-analysis came from studies at moderate or high risk of bias

Table 34: Clinical evidence profile (Risk ratio): IMDC model poor risk vs intermediate risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs intermediate risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median follow-up 18.6 months								
2 (Tamura 2021 (IMDC); Tanaka 2016 (first line, IMDC))	Retrospective cohort	491	1.58 (1.38, 1.81)	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 35: Clinical evidence profile (Risk ratio): IMDC model poor risk vs intermediate risk; first-line SACT, clear cell RCC

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs intermediate risk - for prediction of overall survival at first-line SACT for clear cell RCC subtypes, median follow-up 12.8 months								
1 (Rini 2019)	Retrospective cohort	592	2.22 (1.67, 2.95)	Very serious[a]	Not serious	Serious[b]	Not serious	Very low
IMDC model – poor risk vs intermediate risk - for prediction of progression-free survival at first-line SACT for clear cell RCC subtypes, median follow-up 12.8 months								
1 (Rini 2019)	Retrospective cohort	592	1.41 (1.20, 1.66)	Very serious[a]	Not serious	Serious[b]	Not serious	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 single study								

Table 36: Clinical evidence profile (Hazard ratio): IMDC model poor risk vs favourable + intermediate risk; first-line SACT, non-clear cell RCC

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs favourable + intermediate risk - for prediction of overall survival at first-line SACT for non-clear cell RCC, median follow-up not reported								
1 (Toyoda 2024)	Retrospective cohort	75	3.17 (1.48, 6.78)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
IMDC model – poor risk vs favourable + intermediate risk - for prediction of progression-free survival at first-line SACT for non-clear cell RCC, median follow-up not reported								
1 (Toyoda 2024)	Retrospective cohort	75	1.14 (0.61, 2.14)	Very serious[a]	Not serious	Serious[b]	Very serious[d]	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 single study
c. Downgraded once as ample size <500
d. 95% confidence interval crossed the non-effect line and sample size <500

Table 37: Clinical evidence profile (Hazard ratios): IMDC model poor risk vs favourable + intermediate risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – favourable + intermediate risk vs poor risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median follow-up 30.9 months								
3 (Kim 2019b; Miyake 2016a (IMDC); Schuttke 2024)	Retrospective cohort	402	2.36 (1.64, 3.39)	Very serious[a]	Not serious	Not serious	Serious[b]	Very low

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – favourable + intermediate risk vs poor risk - for prediction of progression-free survival at first-line SACT for mixed RCC subtypes, median follow-up 21.7 months								
2 (Kim 2019b; Schuttke 2024)	Retrospective cohort	131	1.77 (1.15, 2.79)	Serious[c]	Not serious	Not serious	Serious[b]	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
c. Downgraded once as >50% of the weight in a meta-analysis came from studies at moderate or high risk of bias

MSKCC

Table 38:Clinical evidence profile (C-statistics): MSKCC model, first-line SACT, clear cell RCC subtypes

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model for prediction of overall survival in people with clear cell RCC at treatment with first-line SACT, follow-up time not reported								
2 (de Velasco 2017, Voss 2018)	Retrospective cohort	981	0.59 (0.56, 0.63)	Serious[a]	Not serious	Not serious	Serious[b]	Low
MSKCC model for prediction of progression-free survival in people with clear cell RCC at treatment with first-line SACT, follow-up time not reported								
1 (Voss 2018)	Retrospective cohort	927	0.57 (0.53, 0.60)	Serious[a]	Not serious	Serious[c]	Serious[b]	Very low

a. Downgraded once as >50% of the population weight across the studies came from studies at some moderate risk of bias
b. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy
c. Downgraded once as single study

Table 39: Clinical evidence profile (C-statistics): MSKCC model, first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model for prediction of overall survival in people with mixed RCC subtype at treatment with first-line SACT, median 29.15 months follow-up								
7 (Cai 2017c, Kroeger 2013, Lu 2016, Shin 2021 (external validation cohort), Shin 2021 (model cohort), Tamura 2021, Voss 2018)	Retrospective cohort	4,052	0.66 (0.64, 0.68)	Very serious[a]	Not serious	Not serious	Not serious	Low
MSKCC model for prediction of progression-free survival in people with mixed RCC subtype at treatment with first-line SACT, median 5 months follow-up								
2 (Cai 2017c Kim 2019a)	Retrospective cohort	340	0.67 (0.62, 0.71)	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 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Table 40: Clinical evidence profile (Hazard ratios): MSKCC model poor risk vs favourable risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs favourable risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 19 months follow-up								
5 (Cetin 2013, Fiala 2020, Kim	Retrospective cohort	1,361	4.49 (3.75, 5.38)	Very serious[a]	Not serious	Not serious	Not serious	Low

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
2018b, Lolli 2016, Tamura 2021)								
MSKCC model – poor risk vs favourable risk - for prediction of progression-free survival at first-line SACT for mixed RCC subtypes, median 15 months follow-up								
3 (Cetin 2013, Fiala 2020, Lolli 2016)	Retrospective cohort	1,124	2.86 (2.39, 3.43)	Very serious[a]	Not serious	Serious[b]	Not serious	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 I^2 40-60%								

Table 41: Clinical evidence profile (Risk ratios): MSKCC model poor risk vs favourable risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs favourable risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 18.1 months follow-up								
3 (Bamias 2010, Tamura 2021, Tanaka 2016)	Retrospective cohort	269	3.44 (2.46, 4.81)	Not serious	Not serious	Not serious	Serious[a]	Moderate
a. Downgraded once as sample size < 500								

Table 42: Clinical evidence profile (Risk ratios): MSKCC model poor risk vs favourable risk; first-line SACT, clear cell RCC

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs favourable risk - for prediction of overall survival at first-line SACT for clear cell RCC, median 43.2 months follow-up								
1 (Giridhar 2017)	Retrospective cohort	35	1.86 (1.17, 2.95)	Very serious[a]	Not serious	Serious[b]	Serious[c]	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 single study
c. Downgraded once as sample size < 500

Table 43: Clinical evidence profile (Hazard ratios): MSKCC model intermediate risk vs favourable risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – intermediate risk vs favourable risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 19 months follow-up								
5 (Cetin 2013, Fiala 2020, Kim 2018b, Lolli 2016, Tamura 2021)	Retrospective cohort	3,232	1.73 (1.56, 1.93)	Very serious[a]	Not serious	Not serious	Not serious	Low
MSKCC model – intermediate risk vs favourable risk - for prediction of progression-free survival at first-line SACT for mixed RCC subtypes, median 15 months follow-up								
3 (Cetin 2013, Fiala 2020, Lolli 2016)	Retrospective cohort	1,904	1.51, (1.37, 1.65)	Very serious[a]	Not serious	Not serious	Not serious	Low

a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias

Table 44: Clinical evidence profile (Risk ratios): MSKCC model intermediate risk vs favourable risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – intermediate risk vs favourable risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 18.1 months follow-up								
3 (Bamias 2010, Tamura 2021, Tanaka 2016)	Retrospective cohort	577	2.24 (1.60, 3.14)	Not serious	Not serious	Not serious	Not serious	High

Table 45: Clinical evidence profile (Risk ratios): MSKCC model intermediate risk vs favourable risk; first-line SACT, clear cell RCC

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – intermediate risk vs favourable risk - for prediction of overall survival at first-line SACT for clear cell RCC, median 43.2 months follow-up								
1 (Giridhar 2017)	Retrospective cohort	43	1.03 (0.53, 2.02)	Very serious[a]	Not serious	Serious[b]	Very serious[c]	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 single study
c. Downgraded twice as 95% confidence intervals cross the line of no effect and sample size <500

Table 46: Clinical evidence profile (Risk ratios): MSKCC model poor risk vs intermediate risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs intermediate risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 18.1 months follow-up								
3 (Bamias 2010, Tamura 2021, Tanaka 2016)	Retrospective cohort	577	1.54 (1.36, 1.75)	Very serious[a]	Not serious	Not serious	Not serious	Low
a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias								

Table 47: Clinical evidence profile (Risk ratios): MSKCC model poor risk vs intermediate risk; first-line SACT, clear cell RCC

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs intermediate risk - for prediction of overall survival at first-line SACT for clear cell RCC, median 43.2 months follow-up								
1 (Giridhar 2017)	Retrospective cohort	16	1.80 (0.97, 3.34)	Very serious[a]	Not serious	Serious[b]	Very serious[c]	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 single study c. Downgraded twice as 95% confidence intervals cross the line of no effect and sample size <500								

Table 48: Clinical evidence profile (Hazard ratios): MSKCC model poor risk vs favourable + intermediate risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs favourable + intermediate risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 26.3 months follow-up								
1 (Cai 2017c)	Retrospective cohort	184	0.52 (0.42, 0.65)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low
1 (Miyake 2016a)	Retrospective cohort	185	3.45 (1.35, 8.84)					
1 (Miyazake 2015)	Retrospective cohort	271	4.31 (1.81, 10.26)					
MSKCC model – poor risk vs favourable + intermediate risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 19 months follow-up								
1 (Cai 2017c)	Retrospective cohort	184	0.52 (0.42, 0.65)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low
1 (Miyake 2014)	Retrospective cohort	110	3.89 (1.74, 8.70)					
MSKCC model – poor risk vs favourable + intermediate risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes [Excluding Cai 2017c], median 26.3 months follow-up								
2 (Miyake 2016a, Miyazake 2015)	Retrospective cohort	456	3.89 (2.06, 7.36)	Very serious[d]	Not serious	Not serious	Serious[e]	Very low
MSKCC model – poor risk vs favourable + intermediate risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes [Excluding Cai 2017c], median 19 months follow-up								

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
1 (Miyake 2014)	Retrospective cohort	110	3.89 (1.74, 8.70)	Very serious[d]	Not serious	Serious[f]	Serious[e]	Very low

a. Downgraded twice as >50% of the population weight came from studies at high risk of bias
b. Downgraded twice as pooled I^2 was above 80% and the point estimates spanned the line of no effect
c. Downgraded once as 95% confidence intervals crossed the line of no effect
d. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias
e. Downgraded once as sample size < 500
f. Downgraded once as single study

Table 49: Clinical evidence profile (Hazard ratios): MSKCC model intermediate + poor risk vs favourable risk; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – intermediate + poor risk vs favourable risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, follow-up not reported								
1 (Lu 2016)	Retrospective cohort	67	2.25 (1.26, 4.02)	Serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded once as study at moderate risk of bias
b. Downgraded once as single study
c. Downgraded once as sample size < 500

Meet-URO

Table 50: Clinical evidence profile (Hazard ratios): Meet-URO model score 5 vs score 2; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – score 5 vs score 2 for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 12.2 months follow-up								
1 (Rebuzzi 2022a)	Retrospective cohort	117	16.03 (7.74, 33.20)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
MSKCC model – score 5 vs score 2 for prediction of progression-free survival at first-line SACT for mixed RCC subtypes, median 12.2 months follow-up								
1 (Rebuzzi 2022a)	Retrospective cohort	117	6.56 (3.97, 10.83)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded twice as study at high risk of bias
b. Downgraded once as single study
c. Downgraded once as sample size < 500

Table 51: Clinical evidence profile (Hazard ratios): Meet-URO model score 4 vs score 2; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – score 4 vs score 2 for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 12.2 months follow-up								
1 (Rebuzzi 2022a)	Retrospective cohort	190	6.07 (3.16, 11.66)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
MSKCC model – score 4 vs score 2 for prediction of progression-free survival at first-line SACT for mixed RCC subtypes, median 12.2 months follow-up								
1 (Rebuzzi 2022a)	Retrospective cohort	190	2.77 (1.88, 4.08)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low

a. Downgraded twice as study at high risk of bias

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
b. Downgraded once as single study c. Downgraded once as sample size < 500								

Table 52: Clinical evidence profile (Hazard ratios): Meet-URO model score 3 vs score 2; first-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – score 3 vs score 2 for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 12.2 months follow-up								
1 (Rebuzzi 2022a)	Retrospective cohort	177	3.09 (1.54, 6.20)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
MSKCC model – score 3 vs score 2 for prediction of progression-free survival at first-line SACT for mixed RCC subtypes, median 12.2 months follow-up								
1 (Rebuzzi 2022a)	Retrospective cohort	177	2.05 (1.38, 3.05)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
a. Downgraded twice as study at high risk of bias b. Downgraded once as single study c. Downgraded once as sample size < 500								

Prior to second-line SACT

IMDC

Table 53: Clinical evidence profile (C-statistics): IMDC model, second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Overall survival in people with mixed RCC subtype treated with second-line SACT, median 2 years follow-up								
2 (Derosa 2019 (discovery); Derosa 2019 (validation); Ko 2015)	Retrospective cohort	2,190	0.64 (0.58, 0.69)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low

a. Downgraded twice as 50% of the weight in a meta-analysis came from studies at high risk of bias
b. Downgraded twice as I^2 was greater than 60%
c. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy

Table 54: Clinical evidence profile (Hazard ratio): IMDC model poor risk vs favourable risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs favourable risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median follow-up 16.3 months								
2 (Derosa 2019 (discovery, IMDC)	Retrospective cohort	654	5.87 (4.48, 7.69)	Very serious[a]	Not serious	Not serious	Not serious	Low

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Derosa 2019 (validation, IMDC) Ko 2015)								
a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias								

Table 55: Clinical evidence profile (Risk ratio): IMDC model poor risk vs favourable risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs favourable risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median follow-up 16.3 months								
2 (Derosa 2019 (discovery) Derosa 2019 (validation) Tanaka 2016 (second-line))	Retrospective cohort	366	2.53 (1.56, 4.11)	Very serious[a]	Not serious	Serious[b, c]	Not serious	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 I^2 between 40% and 60% c. Downgraded once as sample size < 500								

Table 56: Clinical evidence profile (Hazard ratio): IMDC model intermediate risk vs favourable risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – intermediate risk vs favourable risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median follow-up 16.3 months								
2 (Derosa 2019 (discovery, IMDC) Derosa 2019 (validation, IMDC) Ko 2015)	Retrospective cohort	1,436	1.85 (1.42, 2.40)	Very serious[a]	Not serious	Not serious	Not serious	Low

a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias

Table 57: Clinical evidence profile (Risk ratio): IMDC model intermediate risk vs favourable risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – intermediate risk vs favourable risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median follow-up 16.3 months								
2 (Derosa 2019 (discovery) Derosa 2019 (validation) Tanaka 2016 (second-line))	Retrospective cohort	956	1.52 (1.14, 2.04)	Very serious[a]	Not serious	Not serious	Not serious	Moderate

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
a. Downgraded twice as 50% of the weight in a meta-analysis came from studies at high risk of bias								

Table 58: Clinical evidence profile (Hazard ratios): IMDC model favourable + intermediate risk vs poor risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – favourable + intermediate risk vs poor risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median 70 months follow-up								
3 (Matsushita 2024 (IMDC); Miyake 2016b (IMDC); Ueda 2018)	Retrospective cohort	549	2.79 (1.62, 4.83)	Very serious[a]	Not serious	Serious[b]	Not serious	Very low
IMDC model – favourable + intermediate risk vs poor risk - for prediction of progression-free survival at second-line SACT for mixed RCC subtypes, median 70 months follow-up								
3 (Matsushita 2024 (IMDC); Miyake 2017; Ueda 2018)	Retrospective cohort	402	1.23 (0.53, 2.88)	Very serious[a]	Not serious	Very serious[c]	Serious[d]	Very low
a. Downgraded twice as 50% of the population weight came from studies at high risk of bias b. Downgraded once as I^2 was between 40% and 60% c. Downgraded twice as I^2 was greater than 60% d. Downgraded twice as sample size < 500 and 95% confidence intervals crossed the line of no effect								

Table 59: Clinical evidence profile (Hazard ratio): IMDC model poor risk vs intermediate risk; second-line SACT, non-clear cell RCC

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
IMDC model – poor risk vs intermediate risk - for prediction of overall survival at second-line SACT for non-clear cell RCC, median 20 months follow-up								
1 (Fujita 2024)	Retrospective cohort	52	2.74 (1.15, 6.52)	Very serious[a]	Not serious	Serious[b]	Serious[c]	Very low
IMDC model – poor risk vs intermediate risk - for prediction of progression-free survival at second-line SACT for non-clear cell RCC, median 20 months follow-up								
1 (Fujita 2024)	Retrospective cohort	52	1.98 (1.02, 3.83)	Very serious[a]	Not serious	Serious[b]	Serious[c]	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 single study
c. Downgraded once as sample size <500

MSKCC

Table 60: Clinical evidence profile (C-statistics): MSKCC model, second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model for prediction of overall survival in people with mixed RCC subtype at treatment with second-line SACT, median 36 months follow-up								
2 (Derosa 2019 (discovery), Derosa 2019 (validation), Ko 2015)	Retrospective cohort	2,190	0.62 (0.55, 0.69)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low

No. of studies	Study design	Sample size	C-statistic (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias b. Downgraded twice as I^2 >60% c. Downgraded once as 95% confidence interval crossed 2 categories of c-statistic classification accuracy								

Table 61: Clinical evidence profile (Hazard ratios): MSKCC model poor risk vs favourable risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs favourable risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median 32.9 months follow-up								
1 (Derosa 2019 (discovery) Derosa 2019 (validation))	Retrospective cohort	525	8.20 (3.80, 17.71)	Very serious[a]	Not serious	Not serious	Not serious	Low
a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias								

Table 62: Clinical evidence profile (Risk ratios): MSKCC model poor risk vs favourable risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs favourable risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median 16.3 months follow-up								
2 (Derosa 2019 (discovery), Derosa 2019 (validation), Tanaka 2016)	Retrospective cohort	545	2.29 (1.37, 3.82)	Very serious[a]	Not serious	Very serious[b]	Not serious	Very low

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias b. Downgraded twice as I^2 > 60%								

Table 63: Clinical evidence profile (Hazard ratios): MSKCC model intermediate risk vs favourable risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – intermediate risk vs favourable risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median 32.9 months follow-up								
1 (Derosa 2019 (discovery) Derosa 2019 (validation))	Retrospective cohort	1,070	2.29 (1.93, 2.72)	Very serious[a]	Not serious	Not serious	Not serious	Low
a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias								

Table 64: Clinical evidence profile (Risk ratios): MSKCC model intermediate risk vs favourable risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – intermediate risk vs favourable risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median 16.3 months follow-up								
1 (Derosa 2019) (discovery)	Retrospective cohort	221	1.22 (1.04, 1.43)	Very serious[a]	Not serious	Very serious[b]	Not serious	Very low

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
1 (Derosa 2019) (validation)	Retrospective cohort	849	1.75 (1.51, 2.02)					
1 (Tanaka 2016)	Retrospective cohort	125	1.47 (0.74, 2.92)					

a. Downgraded twice as >50% of the population weight came from studies at high risk of bias
b. Downgraded twice as pooled I^2 was above 80% and the point estimates spanned the line of no effect

Table 65: Clinical evidence profile (Risk ratios): MSKCC model poor risk vs intermediate risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Risk ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs intermediate risk - for prediction of overall survival at first-line SACT for mixed RCC subtypes, median 16.3 months follow-up								
2 (Derosa 2019 (discovery), Derosa 2019 (validation), Tanaka 2016)	Retrospective cohort	728	1.57 (0.99, 2.48)	Very serious[a]	Not serious	Very serious[b]	Serious[c]	Very low

a. Downgraded twice as >50% of the weight in a meta-analysis came from studies at high risk of bias
b. Downgraded twice as I^2 > 60%
c. Downgraded once as 95% confidence intervals crossed the line of no effect

Table 66: Clinical evidence profile (Hazard ratios): MSKCC model poor risk vs favourable + intermediate risk; second-line SACT, mixed RCC subtypes

No. of studies	Study design	Sample size	Hazard ratio (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
MSKCC model – poor risk vs favourable + intermediate risk - for prediction of overall survival at second-line SACT for mixed RCC subtypes, median 70 months follow-up								
3 (Matsushita 2024, Miyake 2016b, Ueda 2018)	Retrospective cohort	549	3.16 (2.13, 4.67)	Not serious	Not serious	Not serious	Not serious	High
MSKCC model – poor risk vs favourable + intermediate risk - for prediction of progression-free survival at second-line SACT for mixed RCC subtypes, median 70 months follow-up								
3 (Matsushita 2024, Miyake 2017, Ueda 2018)	Retrospective cohort	402	2.24 (1.60, 3.13)	Not serious	Not serious	Not serious	Serious[a]	Moderate

a. Downgraded once as sample size < 500

Meet-URO

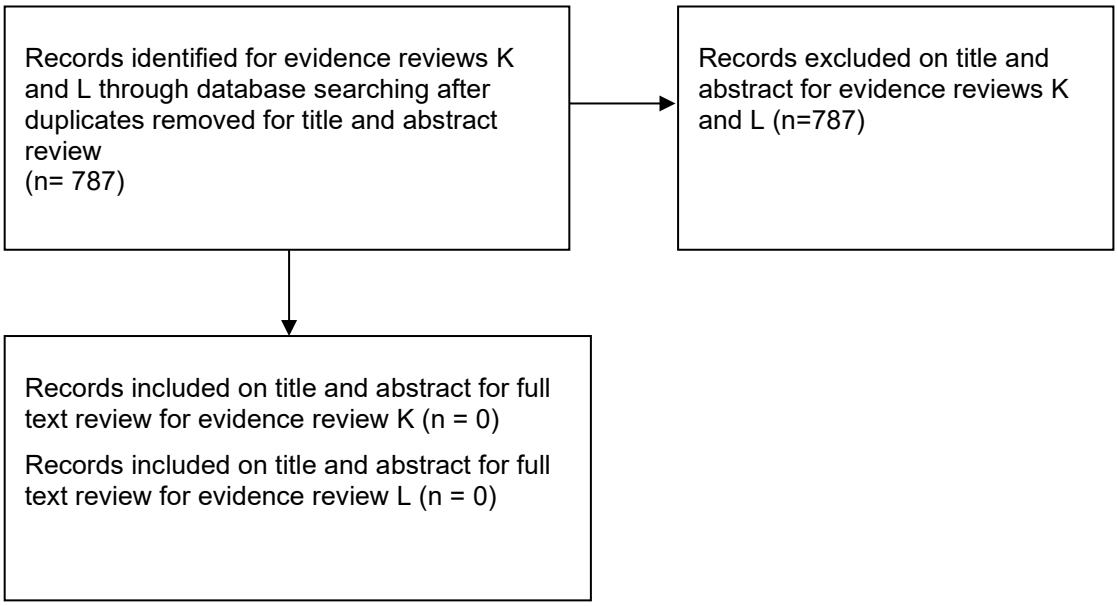
No evidence was identified for this model in this treatment line.

Prior to subsequent-line SACT

No evidence identified for this treatment line

Appendix G – Economic evidence study selection

Figure 63: 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 67: Excluded studies

Study	Reason for exclusion
Abdelaziz, LA, Taha, HF, Ali, MM et al. (2020) Tolerability and outcome of sunitinib by giving 4/2 schedule versus 2/1 schedule in metastatic renal cell carcinoma patients: a prospective randomized multi-centric Egyptian study. Contemporary oncology (Poznan, Poland) 24(4): 221-228	- Not a relevant study design RCT
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
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	- Exclude - Study reported the outcome as median

renal cancer and malignant melanoma. Cancer Biomarkers 38(3): 367-377	- 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)
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	- Exclude - Study didn't assess a prognostic model of interest

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	
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 Carcinoma?. Urologia internationalis 105(78): 666-673	- Data only reported for multivariate analysis
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, Powles T, Burotto M et al. (2021) Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell	- Not a relevant study design RCT

Carcinoma. The New England journal of medicine 384(9): 829-841	
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
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
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 preoperative imaging: a practical and useful prognostic parameter for papillary renal cell carcinoma. European radiology 31(6): 3745-3753	- Does not separate out metastatic and non-metastatic participants
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	- Study does not contain a relevant outcome

Renal Cell Carcinoma. European Urology Focus 2(2): 197-203	
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 metastases arising from advanced renal cell carcinoma. Cancer 126suppl9: 2079-2085	- Data not reported in an extractable format
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 FBXO11 expression in patients with clear cell renal cell carcinoma. BMC cancer 19(1): 534	- C statistic without SE / 95% CI ("parked" studies code) 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:	- Exclude - Study didn't assess a prognostic model of interest

retrospective analysis of 675 cases. European urology 41(2): 190-8	
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
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	- Does not report data by specific treatment line

by cytoreductive nephrectomy. International journal of clinical oncology 23(3): 539-546	
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
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 Networks: An Immunotherapy Case Study in Patients With Metastatic Renal Cell Carcinoma. JCO clinical cancer informatics 5: 326-337	- Exclude - Outcome reported as AUC
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	- Exclude - Outcome reported as AUC

study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 27(34): 5794-9	
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 prognostic model: a population-based study. The Lancet. Oncology 14(2): 141-8	- Does not report data by specific treatment line
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	- Exclude - Study doesn't report an outcome of interest

Tyrosine Kinase Inhibitor Monotherapy for Advanced Renal Cell Carcinoma. Anticancer research 45(1): 379-386	
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 Real-World Study. Medicina (Kaunas, Lithuania) 60(7)	- Exclude - Study doesn't report an outcome of interest
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	- Judged likely that there was overlap between databases in other included study Kim 2018 included due to larger sample size

tyrosine kinase inhibitor therapy for metastatic renal cell carcinoma. International journal of urology : official journal of the Japanese Urological Association 25(6): 596-603	
Karakiewicz, Pierre I, Briganti, Alberto, Chun, Felix K-H et al. (2007) Multi-institutional validation of a new renal cancer-specific survival nomogram. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 25(11): 1316-22	- Study does not contain a relevant outcome
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	- Exclude - Study didn't assess a prognostic model of interest

official journal of the American Association for Cancer Research 10(16): 5464-71	
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
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	- Data not reported in an extractable format

Multicenter Retrospective Study. Clinical genitourinary cancer 17(5): e1080-e1089	
Konishi, Sakae, Hatakeyama, Shingo, Tanaka, Toshiaki et al. (2019) C-reactive protein/albumin ratio is a predictive factor for prognosis in patients with metastatic renal cell carcinoma. International journal of urology : official journal of the Japanese Urological Association 26(10): 992-998	- Study does not contain a relevant outcome Multivariable analysis only
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
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 Classification by Concordance Index. Korean journal of urology 52(8): 524-30	- Exclude - Study didn't assess a prognostic model of interest
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	- Exclude - Study didn't assess a prognostic model of interest

cell carcinoma. Frontiers in oncology 12: 982833	
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 carcinoma. World journal of urology 43(1): 45	- C statistic without SE / 95% CI ("parked" studies code)
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	- Exclude - Study didn't assess a prognostic model of interest

experimental biology and medicine 176(3): 363-368	
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, Zhengfang, Zang, Maolin, Li, Kaiyue et al. (2024) The immunotherapy-based combination associated score as a robust predictor for outcome and response to combination of immunotherapy and VEGF inhibitors in renal cell carcinoma. Computers in biology and medicine 182: 109210	- Not a relevant study design RCT
Liu, Zheng, Liu, Yidong, Xu, Le et al. (2015) P2X7 receptor predicts postoperative cancer-specific survival of patients with clear-cell renal cell carcinoma. Cancer science 106(9): 1224-31	- C statistic without SE / 95% CI ("parked" studies code) TNM, UISS, SSIGN c index, 6.2% metastatic
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	- C statistic without SE / 95% CI ("parked" studies code)

Surgically Treated Papillary Renal Cell Carcinoma. Technology in cancer research & treatment 24: 15330338251329848	
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
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	- Data not reported for model of interest

Liver to IMDC Criteria in Patients With Metastatic Renal Cell Carcinoma: A Validation Study. Clinical genitourinary cancer 19(1): 32-40	
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
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	- Data only reported for multivariate analysis

oncology (Northwood, London, England) 34(4): 47	
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 comparing 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 R, Alekseev B, Rha SY et al. (2021) Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. The New England journal of medicine 384(14): 1289-1300	- Not a relevant study design RCT
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
Motzer RJ, Penkov K, Haanen J et al. (2019) Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. The New England journal of medicine 380(12): 1103-1115	- Not a relevant study design RCT
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 analysis of the Meet-URO 15 study. Frontiers in oncology 14: 1307635	- Exclude - prognostic model report the result from multivariate analysis
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	- C statistic without SE / 95% CI ("parked" studies code)

Japanese metastatic renal cell carcinoma patients in the targeted therapy era. International journal of clinical oncology 26(10): 1947-1954	- 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 international journal of pathology 476(3): 409-418	- Exclude - Study didn't assess a prognostic model of interest
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	- C statistic without SE / 95% CI ("parked" studies code)

cytoreductive nephrectomy in patients with primary metastatic renal cell carcinoma: A multicenter retrospective study. Urologic oncology 39(12): 836e11-836e17	
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 clear-cell renal cell carcinoma. Cancer science 106(5): 592-7	- C statistic without SE / 95% CI ("parked" studies code)
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	- Exclude - Study didn't assess a prognostic model of interest

in human renal cell carcinoma. Acta Oncologica 52(1): 159-165	
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 the European Society for Medical Oncology 27(4): 706-11	- Exclude - Results reported in non-extractable format
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-free, cancer-specific and overall survival in a European renal cell carcinoma single-centre series. BJU international 111(4ptb): e191-5	- Exclude - Study didn't assess a prognostic model of interest
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
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	- Exclude - study does not contain a relevant outcome

renal cancer. BJU international 101(8): 959-63	
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 patients treated with nivolumab. Urologic oncology 39(4): 239e17-239e25	- Data only reported for multivariate analysis - C statistic without SE / 95% CI ("parked" studies code)
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	- Data only reported for multivariate analysis

large cancer centre. European journal of cancer (Oxford, England : 1990) 107: 79-85	
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 comparing 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
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	- 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

carcinoma treated with targeted therapy. Targeted oncology 10(4): 517-22	
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 tumor behavior and growth. Journal of surgical oncology 84(3): 166-72	- Exclude - Study used the TNM 1997 system to classify the stages
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 comparing 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)
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	- C statistic without SE / 95% CI ("parked" studies code)

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	
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)
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	- Data only reported for multivariate analysis

to Risk Stratification Systems in Metastatic Renal Cell Carcinoma Patients?. Journal of the College of Physicians and Surgeons--Pakistan : JCPSP 32(11): 1425-1429	
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 survival in metastatic renal cell cancer patients. European urology 62(4): 685-95	- Exclude - Outcome reported as AUC
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
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
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 immunohistochemistry & molecular morphology : AIMM 33(1): 22-28	- Exclude - Study reported the HR without comparing it with a reference group/breaking it down into categories
Yao, C., Feng, B., Li, S. et al. (2024) Predicting postoperative prognosis in clear cell renal cell carcinoma using a multiphase	- Exclude - Prognostic model compares all 3 at once

CT-based deep learning model. Abdominal Radiology	
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 comparing 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 comparing 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 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	- TNM 2002 - 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
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 clinical factors can most accurately predict survival, risk of disease progression, or response to treatment across a broad population with different characteristics (for example, ethnicity and sex) who have metastatic renal cell carcinoma?

K1.1.1 Why this is important

The available evidence on using the IMDC, MSKCC and Meet-URO models to predict survival in adults with metastatic RCC is limited in terms of it mostly coming from clear cell RCC. Furthermore, the available evidence was of low quality. Thus, considering the limited availability and low quality of evidence on using risk prediction models, it is important to develop additional research to identify which tools/biomarkers/factors can more accurately predict survival, disease progression and response to treatment in a broad population.

K1.1.2 Rationale for research recommendation

Table 68: Rationale for research recommendation

Importance to 'patients' or the population	There is limited evidence on the use of risk prediction tools to predict survival in metastatic RCC. This information is important to guide treatment choices and for the quality of life of individuals.
Relevance to NICE guidance	Risk prediction models such as IMDC, MSKCC and Meet-URO were considered in this guideline and there is limited data on the ability of these risk prediction models to discriminate risk groups to predict survival. The data available indicates that these tools are not very good at stratifying risk.
Relevance to the NHS	The outcome could affect resource allocation enabling the NHS to optimise care delivery and support services according to patient needs
National priorities	Low
Current evidence base	Limited and low-quality evidence on the use of risk prediction tools to predict survival in metastatic RCC.
Equality considerations	None known

K1.1.3 Modified PICO table

Table 69: Modified PICO table

Population	Adults with metastatic renal cell carcinoma
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)
Outcome	• Overall survival • Progression-free survival • Tumour response
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