National Institute for Health and Care Excellence

Draft for consultation

Kidney cancer: diagnosis and management

Economic model report for follow up and monitoring for previously treated renal cell carcinoma

NICE Guideline <NGXXX>

September 2025

Draft for Consultation

developed by health economic team

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

Funding
This economic analysis is being completed by the Guideline Development Team which receives funding from NICE

Contents

HE1 Introduction 5
HE1.1 Decision problem 5
HE2 Methods 6
HE2.1 Model overview 6
HE2.1.1 Population and comparators 6
HE2.1.2 Type of evaluation, time horizon, perspective, discount rate 6
HE2.2 Model structure 7
HE2.3 Model parameterisation 8
HE2.4 Parameters 9
HE2.4.1 Recurrences 9
HE2.4.2 Mortality 13
HE2.4.3 Resource use and costs 14
HE2.4.4 Quality of life 20
HE2.5 Sensitivity analyses 22
HE2.5.1 Deterministic sensitivity analyses 22
HE2.5.2 Probabilistic analysis 23
HE3 Results 24
HE3.1 Base-case analysis 24
HE3.1.1 Probabilistic analysis 24
HE3.1.2 Deterministic analysis 27
HE3.2 Sensitivity analysis 28
HE3.2.1 Deterministic sensitivity analysis 28
HE3.3 Discussion 31
HE3.3.1 Principal findings 31
HE3.3.2 Strengths of the analysis 32
HE3.3.3 Weaknesses of the analysis 32
HE3.3.4 Comparison with other CUAs 33
HE3.4 Conclusions 33
HE4 References 35

Appendices 37
Appendix A: AIC and BIC values for survival analysis 38
Appendix B: Summary of parameters 41

HE1 Introduction

HE1.1 Decision problem

An original cost-utility decision model was developed to assess the cost-effectiveness of different follow-up strategies for people who have been treated for localised or locally advanced renal cell carcinoma (RCC).

There is currently no consensus on follow-up strategies for patients treated for localised or locally advanced RCC. Follow-up is crucial for early detection of disease recurrence and the evaluation of long-term sequelae. The follow-up frequency is likely to depend on the recurrence rate, which varies by risk level. Tumours detected earlier are more likely to be asymptomatic and have a better prognosis than symptomatic ones. Therefore, there is a need to identify the most effective risk-stratified follow-up strategies to detect recurrence earlier and improve post-treatment outcomes for people receiving treatment for localised or locally advanced RCC.

The committee prioritised this review question for original economic modelling due to the expected high resource impact given the potentially large population size considered by this review, and the potential associated costs of monitoring people over several years. The results from an analysis of the RECUR database (Dabestani 2019b, Dabestani 2019c) indicated that increased imaging scans during follow up were not generally associated with improved survival benefits after recurrence for the overall population. However, the RECUR data was not initially analysed in this way for risk subgroups, but other risk-stratified analyses of the dataset suggested that certain strategies may be more effective at detecting asymptomatic recurrences than symptomatic recurrences.

Table HE001: Review questions

RQ F	Clinical and cost-effective follow-up strategies for monitoring long-term consequences of treatment and for early detection of recurrence or progression of the disease.

Table HE002: PICO for review question

Population	Adults (18 years or over) who have been treated for localised or locally advanced RCC
Intervention	Risk-stratified* follow-up protocols which might include: • Frequency of follow-up • Method of follow-up (type of imaging) * risk refers to risk of recurrence or death.
Comparator	Different risk stratified follow-up protocols compared to each other.
Outcomes	• Quality adjusted life years (QALYs) • Costs • Incremental cost-effectiveness ratios (ICERs) • Net health benefits (NHBs) • Net monetary benefits (NMBs),

HE2 Methods

HE2.1 Model overview

The objective of this model was to assess the cost-effectiveness of different follow-up strategies for people who have been treated for localised or locally advanced RCC. This model was a cost-utility analysis comparing outcomes of follow-up strategies over the patient's lifetime.

HE2.1.1 Population and comparators

Population

The population considered in the analysis was people who had previously undergone nephrectomy for treatment of localised or locally advanced RCC and had successful tumour removal. Clinical and resource use parameters in the model were informed by an analysis of the RECUR database (Dabestani 2019a, Dabestani 2019b, Dabestani 2019c; for a description of the study, see Section HE2.3), who enrolled patients with localised RCC of mean age 62.9 years.In RECUR, 76.1% of patients had clear cell RCC (ccRCC), 14.5% had papillary RCC, 7.0% had chromophobe RCC and 2.4% had other subtypes of RCC. Risk stratification of people in RECUR was based on their initial tumour characteristics using validated risk tools. These were the Leibovich (2003) and the UICC scoring system for clear cell and non-clear cell RCC, respectively. Overall, 19.2% of patients in RECUR were at high risk, 30.8% were at intermediate risk and 50% were at low risk, regardless of subtype of RCC.

Comparators

Our evaluation focuses on two distinct sets of comparisons for each risk group, which were based on those evaluated in the RECUR study where the median follow-up period was 61.9 (IQR: 51.9-74.2) months (Dabestani 2019). The comparisons were defined by 1) proportions of cross-sectional imaging (CSI) and 2) imaging frequency.

- Comparison 1: a high proportion of CSI versus a low proportion of CSI strategy ("high CSI" and "low CSI").
- Comparison 2: a low imaging frequency strategy versus a high imaging frequency strategy ("low imaging frequency" and "high imaging frequency").

The overall study imaging frequency was defined as the total number of imaging scans conducted during follow-up until recurrence or last follow-up, divided by the total years of follow-up in the RECUR study. The high imaging frequency group was defined by patients who received higher than the median number of scans in the RECUR database, while the low imaging frequency group was defined by patients who received lower than the median. The low CSI group was defined as less than 50% of an individual's total scans being CT or MRI. All RECUR institutes used their own follow-up protocols with varying intervals between each imaging.

HE2.1.2 Type of evaluation, time horizon, perspective, discount rate

A lifetime cost-utility analysis was conducted to reflect all important differences in costs and health outcomes between the interventions compared. Health outcomes were valued in terms of quality adjusted life years (QALYs) estimated by weighting the years of life remaining with a quality of life (utility) score, and the results were presented using incremental cost-effectiveness ratios (ICERs) that express the cost per QALY gained, net health benefit (NHB) that expresses the value of an intervention in health benefits and net monetary benefit (NMB) that expresses the value of an intervention in monetary terms.

This economic analysis was conducted from the UK NHS and personal social services (PSS) perspective. A lifetime horizon is used for the analysis, and a discount rate of 3.5% is applied to both costs and health outcomes. The cost year for the analysis was 2024. A threshold of £20,000 per QALY gained is used as the decision rule to assess the cost effectiveness of a strategy.

HE2.2 Model structure

A de-novo semi-Markov decision model was developed using the R language (version R 4.5.0), with a 1-month cycle length and a lifetime horizon of 25 years (until the cohort was no longer alive). Given the short cycle length, half-cycle correction is not applied in the model. The R language offers advantages in terms of flexibility, adaptability and data visualisation. In our model, it was necessary to conduct numerous survival analyses for different risk groups, and the R language can efficiently incorporate statistical analysis into the economic model. Additionally, with twelve individual strategies in the model, it is time saving to run repetitive tasks in the R language.

Recurrences were categorised into potentially curable (PC) recurrence and probably incurable (PI) recurrence in the RECUR database analysis. PC recurrences were defined as isolated local, solitary distant metastatic, or oligometastatic (three or fewer lesions at a single site). PI recurrences were defined as more than three lesions at a single site or dissemination to two or more sites. These two definitions were based on a clinical utility perspective and agreed upon by the RECUR consortium.

The model structure and transitions between different health states are illustrated in Figure HE001. This model consists of nine health states. All patients start from the disease-free health state following nephrectomy. They face a risk of PC or PI recurrence according to their risk group.

For each type of recurrence, patients may present as being symptomatic or non-symptomatic. The rate at which these occur is determined by the follow-up strategies and risk group. The probability of a recurrence being symptomatic was assumed to be constant over time (i.e. a recurrence occurring shortly after treatment has the same probability of being symptomatic as a recurrence occurring many years after treatment) and constant between PI and PC recurrences, as data was not reported in a more granular way to explore relaxing these assumptions.

Patients may either experience non-cancer death from the disease-free health state, or post-recurrence death (with both cancer and non-cancer death modelled together). This model structure was designed to utilize the best available evidence from the RECUR database analysis and avoid the need to explicitly model the evolution of undetected recurrences, for which evidence is not available or poor quality.

This model included costs associated with imaging scans, management of recurrence and administration. QALYs were accrued by weighting the time spent in a health state by the corresponding utility value for that state and adjusting for the utility losses (disutilities) due to the management of recurrence. Further information on costs and QALYs is provided in section HE2.4.3 and HE2.4.4

Table HE003: Modelled health states

Health state	Definition
Disease free	People who have previously received nephrectomy and had successful removal of their tumour.
Curable recurrence	Recurrence that is potentially curable, was defined as isolated local, solitary, and oligometastatic (three or fewer lesions at a single site) in the RECUR study.

Health state	Definition
Incurable recurrence	Recurrence that is probably incurable, was defined as more than three lesions at a single site or dissemination to two or more sites in the RECUR study.
Symptomatic recurrence	Present as being symptomatic for curable and incurable recurrence.
Asymptomatic recurrence	Present as being asymptomatic for curable and incurable recurrence.
Death	Either non-cancer death from the disease-free health state, or post-recurrence death.

Figure HE001 provides a schematic depiction of the model structure.

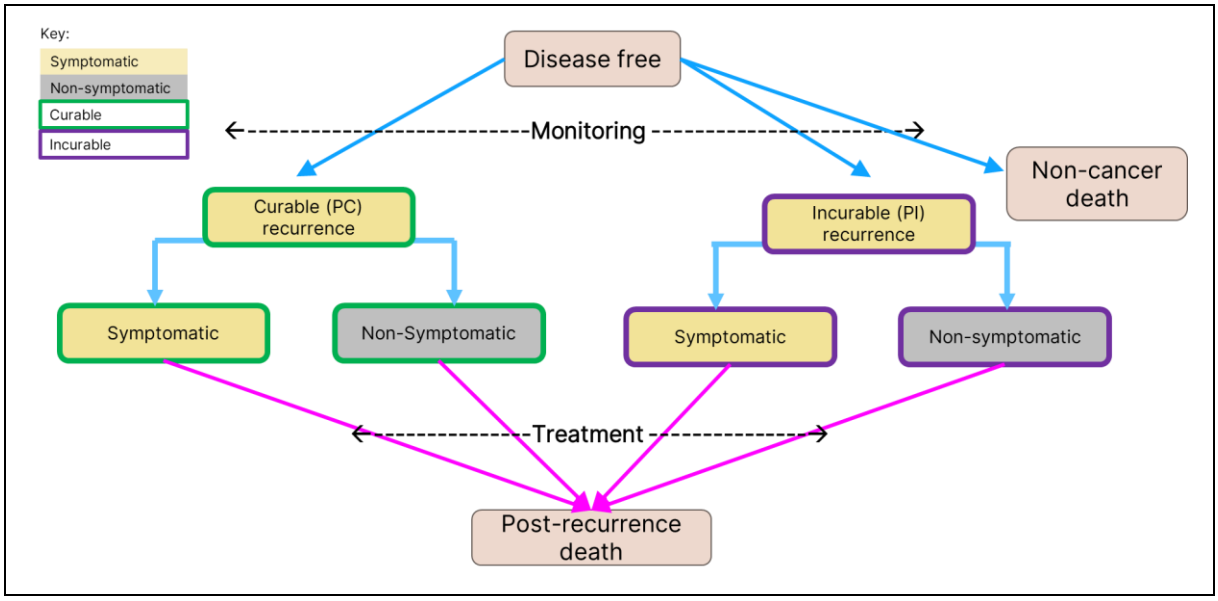


Figure HE001: Structure of original cost–utility model

HE2.3 Model parameterisation

Identifying sources of parameters

The primary sources for quality of life, resource use and cost parameters were the existing NICE RCC pathway model (TA964), the RECUR database analysis (Dabestani 2019a, Dabestani 2019b, Dabestani 2019c), other published economic studies and publicly available sources such as NHS Cost Collection (2024) and PSSRU (2024).

Clinical and resource use parameters in the model were informed by an analysis of the RECUR database (Dabestani 2019a, Dabestani 2019b, Dabestani 2019c), who enrolled 1,889 patients with localised RCC of mean age 62.9 years, from 12 centres in eight European countries, including the UK. The objective of RECUR study was to investigate the optimal follow-up imaging strategies for localised RCC and the associations with outcomes after detection of recurrence.

The risk-dependent probability of a detected recurrence being asymptomatic, based on imaging strategy, was identified and analysed in the effectiveness review, and was estimated from the RECUR database analysis. The time-dependent probabilities of incurable and curable recurrence rates for each risk group, and survival outcomes following for incurable and curable recurrences, are estimated from the RECUR database analysis, as this source

provided transition probabilities for health states that were consistent (with respect to the population and the health state definitions) with the effectiveness evidence for imaging strategies.

The committee's expert opinion was sought when data were not available. All assumptions made in the model have been validated by the committee.

A complete summary of all parameters used in the model are summarised in Appendix B:, including details of the distributions and parameters used in the probabilistic analysis.

HE2.4 Parameters

HE2.4.9 Recurrences

HE2.4.10 Rate of recurrence

Time-varying and risk-based cumulative rates of curable and incurable recurrence were estimated using data from the RECUR study (Dabestani 2019a). The RECUR study showed cumulative incidence of recurrence risk in PI and PC groups for low-, intermediate- and high risks according to the Leibovich score and accounted for competing risk of death. A breakdown of probability of recurrence by risk is shown in Table HE004.

Table HE004: Probability of recurrence by risk group

Recurrence type	Cumulative probability of recurrence
Curable recurrence: Low risk	1 year: 1.12% 5 years: 3.87% 10 years:28.82%
Curable recurrence: Intermediate risk	1 year: 1.44% 5 years: 9.91% 10 years: 22.96%
Curable recurrence: High risk	1 year: 10.50% 5 years: 24.03% 10 years: 35.96%
Incurable recurrence: Low risk	1 year: 0.43% 5 years: 2.45% 10 years: 3.94%
Incurable recurrence: Intermediate risk	1 year: 2.50% 5 years: 7.62% 10 years: 9.55%
Incurable recurrence: High risk	1 year: 14.34% 5 years: 22.62% 10 years: 23.36%

The survival analysis was conducted following the approach in the DSU technical support document. Kaplan-Meier (KM) curves of recurrence risk and overall survival were extracted from the RECUR study (Dabestani 2019a) and were digitized using WebPlotDigitizer, which is an open-source software to help extract numeric data from images. Because the graph presents the risk of recurrence as cumulative incidence which is an upward trend over time in the RECUR study, we inverted the data and graph so that it keeps consistent with the recurrence-free survival data in the clinical review and allowed us to reconstruct the pseudo individual patient data (IPD) in order to conduct the parametric survival analysis.

We then used the digitized KM curves as well as data on the number at risk and time interval to produce pseudo-IPD (with predicted survival times and censor times for each individual patient) for each risk group on a validated online platform which uses the Guyot algorithm for each plot (Enhanced Kaplan-Meier Curves). Parametric models were then fitted to the recreated KM plots for recurrence outcomes to make predictions during the observed period and to extrapolate beyond the observed period over the patient's lifetime. Six survival distributions were tested separately for each imaging strategy to choose the best fit model, these distributions include exponential, Weibull, gamma, Gompertz, log-logistic and log-normal.

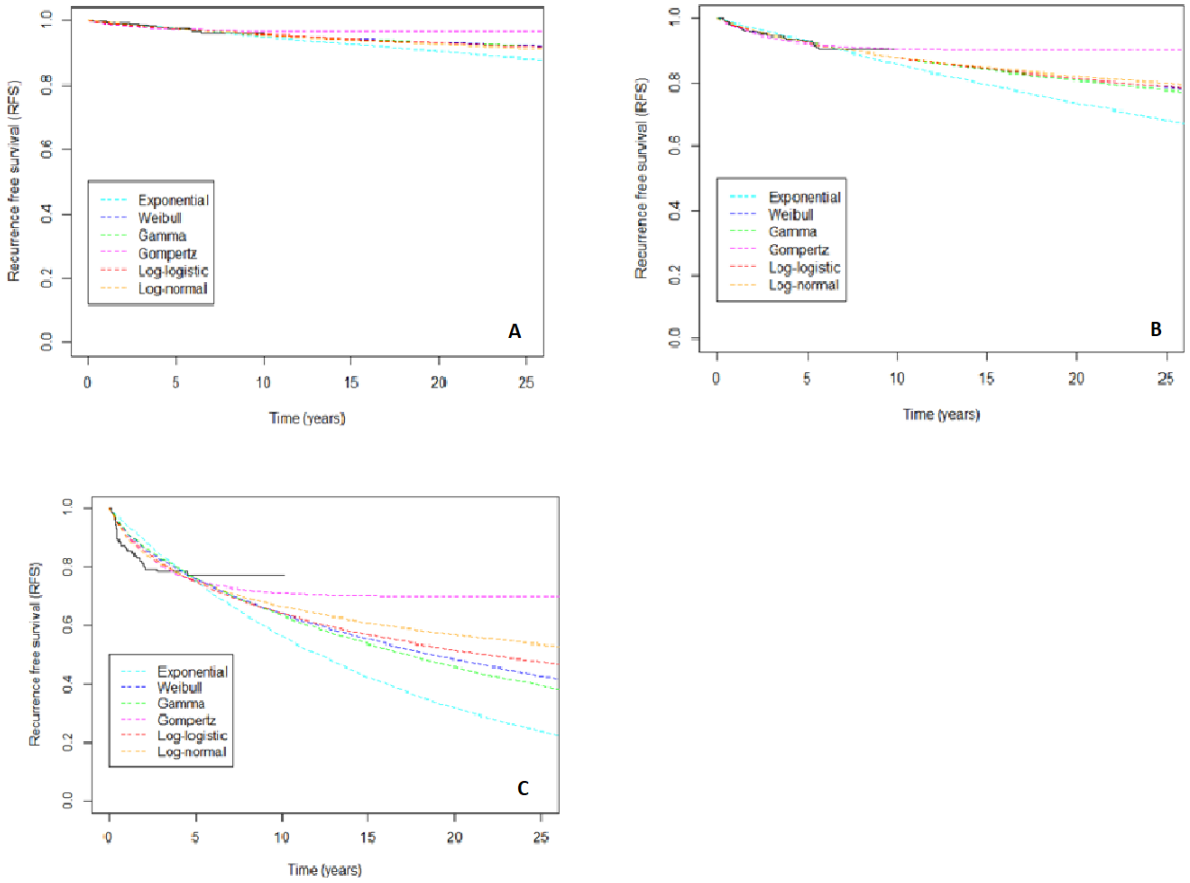
The selection of the survival model was based on statistical fit (AIC and BIC [Appendix A]), visual fit and clinical plausibility of survival predictions. We sought the committee's expert opinion to ensure the external validity of long-term extrapolations. The committee noted that people with probably incurable recurrence tend to have poor prognosis and are less likely to survive more than five years. A list of distributions selected for each risk group are shown in Table HE005 and plots of KM curves alongside extrapolations over the long term are shown in Figure HE002 and Figure HE003.

Table HE005: Survival model selection for each risk group

Outcome	Distribution
Incurable recurrence: low risk	Gompertz
Incurable recurrence: intermediate risk	Gompertz
Incurable recurrence: high risk	Gompertz
Curable recurrence: low risk	Exponential
Curable recurrence: intermediate risk	Gamma
Curable recurrence: high risk	Lognormal

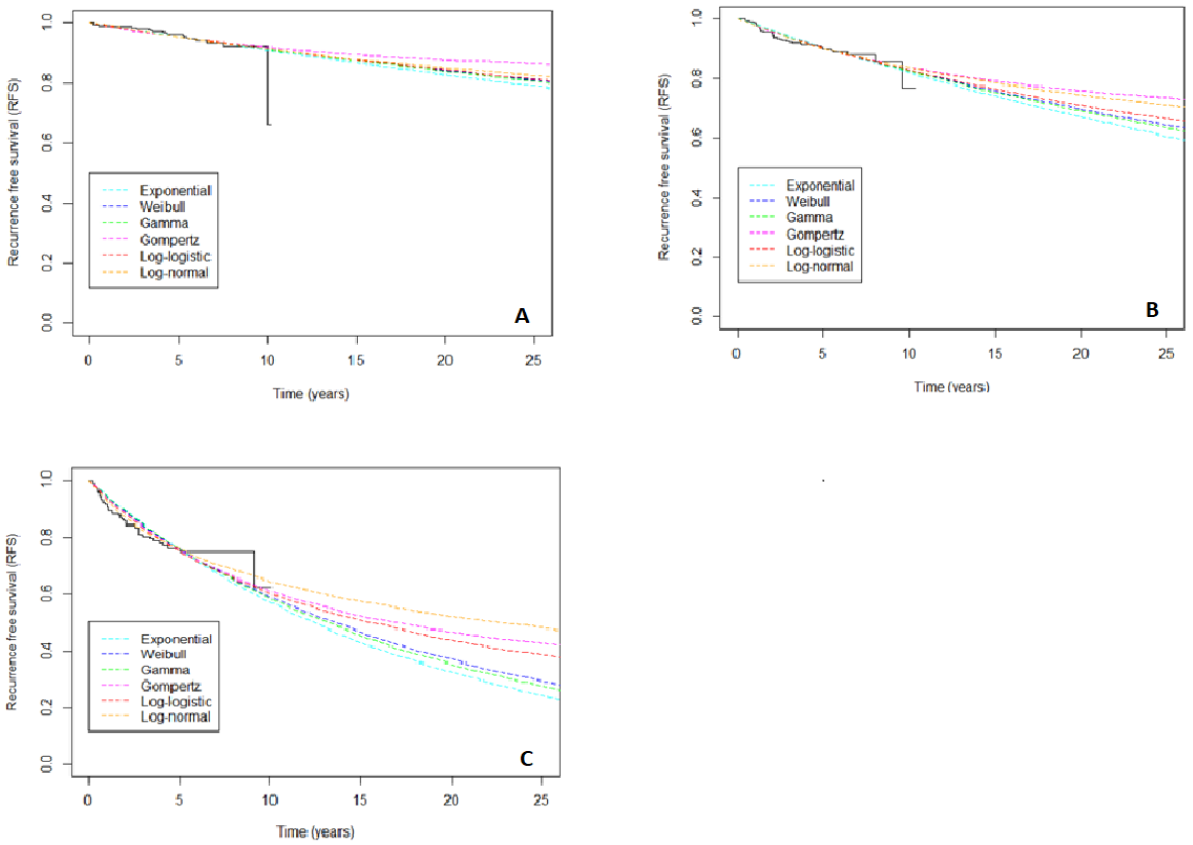
As shown in Figure HE002, the Gompertz distribution provides a good fit for low- and intermediate-risk PI recurrences, while recurrence-free survival curves generated using other parametric distributions deviate from the observed KM data reported in the RECUR database analysis. For the high-risk group, none of these distributions fit the observed data perfectly, yet Gompertz distribution offers a closer fit towards the end of the tail.

For PC recurrences, different parametric distributions are selected for each risk category. Specifically, exponential distribution is chosen for the low risk, gamma distribution for intermediate risk and lognormal for high risk, as depicted in Figure HE003.



A= low risk, B= intermediate risk, C=high risk.

Figure HE002: Kaplan-Meier curves of recurrence free survival with fitted survival curves for people with incurable recurrence



A= low risk, B= intermediate risk, C=high risk.

Figure HE003: Kaplan-Meier curves of recurrence free survival with fitted survival curves for people with PC recurrence

HE2.4.152 Probability of a detected recurrence being asymptomatic

The probability of a detected recurrence being symptomatic or non-symptomatic for each monitoring strategy was derived from the clinical review, and based on the RECUR database analysis (Dabestani 2019c) (Table HE006). Recurrences will occur in patients during follow up regardless of their monitoring schedule. However, early detection, while the tumour is non-symptomatic, has better survival outcomes and QALYs than symptomatic recurrences. In the low- and intermediate-risk groups, the high CSI and the high imaging frequency strategies had a greater probability of detecting a recurrence that was non-symptomatic, compared with the low CSI and the low imaging frequency strategies. The probability that a recurrence detected by a high-CSI strategy is non-symptomatic was lower than the low-CSI strategy, which is counter to expectations given the greater accuracy of CSI.

The committee considered that there was a clinically plausible rationale for different imaging strategies detecting recurrences earlier in their stage of development, while they are still asymptomatic, and this would lead to improved outcomes. However, the quality and certainty of the clinical evidence was assessed to be very low, and there were no statistically significant differences between follow-up strategies. This may have been due to the study design or to low patient numbers.

The point estimate of the probability of a detected recurrence being asymptomatic was used in the economic model base case analysis to provide an estimate of the base case ICER. In the probabilistic analysis, the probability of a detected recurrence being asymptomatic was sampled from the distribution estimated in the forest plot, to estimate the probability that a follow-up strategy is cost-effective.

Table HE006: Probability of a detected recurrence being asymptomatic

Follow-up strategy	Risk group	Probability of a detected recurrence being asymptomatic
Low CSI (<50%)	Low risk	50%
	Intermediate risk	62%
	High risk	68%
High CSI (>50%)	Low risk	71%
	Intermediate risk	71%
	High risk	58%
Low imaging frequency	Low risk	53%
	Intermediate risk	60%
	High risk	60%
High imaging frequency	Low risk	70%
	Intermediate risk	77%
	High risk	64%

HE2.4.2 Mortality

HE2.4.2.1 Disease-free mortality

The mortality rate for individuals in the disease-free state is derived from Lai 2023, a cost-effectiveness analysis of pembrolizumab for adjuvant treatment of RCC. In this analysis, the mortality rate for people in the disease-free health state is estimated from clinical trial KEYNOTE-564 using an exponential distribution, for people under routine surveillance transitioning to death. The weekly mortality rate was estimated in the study as 0.00006, and converted to a monthly mortality rate for this model.

HE2.4.2.2 Post-recurrence mortality

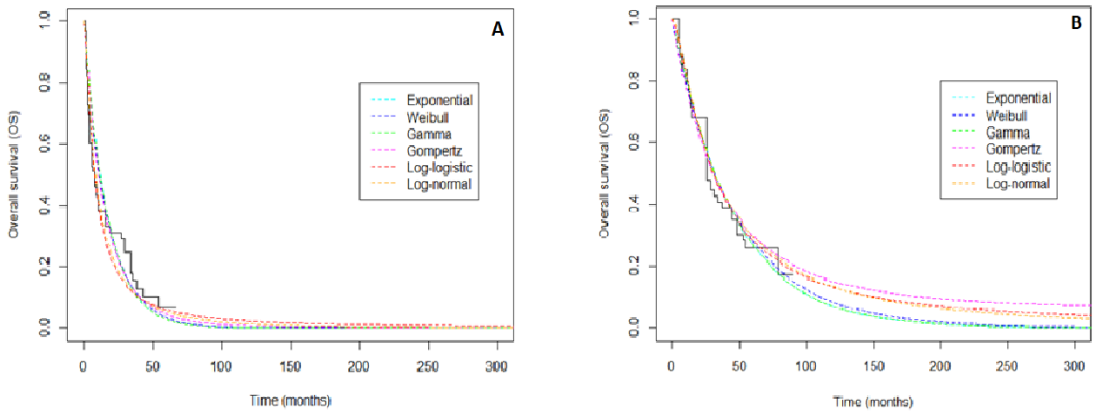
Time-varying rates of overall survival after recurrence were taken from the RECUR study (Dabestani 2019a) to capture differences between symptomatic and asymptomatic detection associated with curable and incurable recurrences. These rates capture both cancer and non-cancer related deaths.

The selected survival model is presented in Table HE007. The loglogistic distribution is chosen for overall survival (OS) following a symptomatic recurrence, and the Weibull distribution is chosen for OS following an asymptomatic recurrence. The selected survival models both fit well at the start of the curve, though slightly deviate as they progress, and eventually reach a plateau at the end (Figure HE004**Error! Reference source not found.** and Figure HE005).

Table HE007: Post-recurrence survival model selection for each risk group

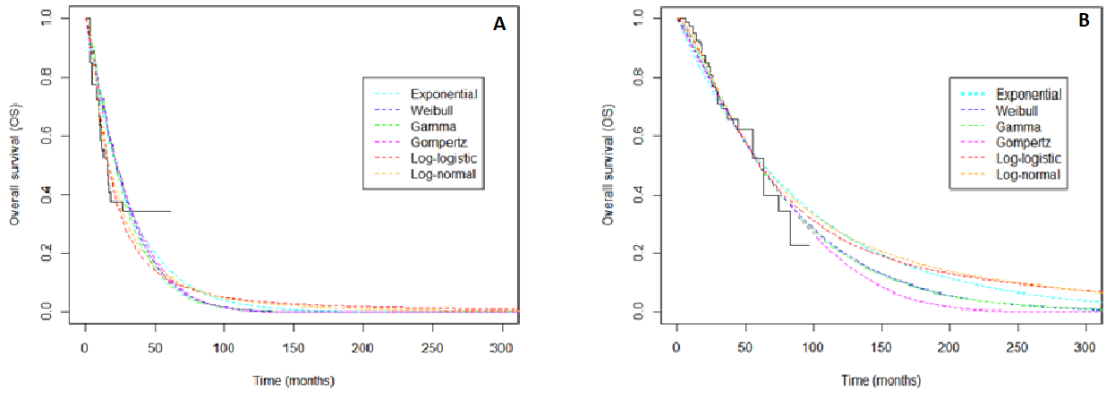
Outcome	Distribution
OS after incurable recurrence: symptomatic group	Log-logistic
OS after incurable recurrence: asymptomatic group	Weibull
OS after curable recurrence: symptomatic group	Log-logistic
OS after curable recurrence: asymptomatic group	Weibull

Plots of KM curves alongside extrapolations over the long term are shown in Figure HE004 and Figure HE005.



A=symptomatic recurrence, B=asymptomatic recurrence

Figure HE004: Kaplan-Meier curves and fitted survival curves for overall survival following an incurable recurrence



A=symptomatic recurrence, B=asymptomatic recurrence

Figure HE005: Kaplan-Meier curves and fitted survival curves for overall survival following a curable recurrence

HE2.4.3 Resource use and costs

Costs of monitoring and recurrence management were estimated using unit costs and resource use associated with each health state. Unit costs were estimated from published national sources, such as the BNF (accessed February 2025) for drug costs, NHS Cost Collection (2024) for hospital episode, outpatient and imaging costs, and PSSRU (2024) for staffing costs.

HE2.4.3.1 Intervention costs

The primary intervention cost incurred in the disease-free health state is the imaging cost. We confirmed the usage of imaging types in clinical practice with committee members. The committee acknowledged that there are some variations across NHS trusts, most people use CT CAP (chest, abdomen, and pelvis) or MRI depending on renal function, while chest X-rays and ultrasound (US) are rarely offered now based on the regional availability of imaging. Meanwhile, the GIRFT guideline recommends contrast CT only, or MRI and abdominal chest

CT without contrast. The imaging modalities modelled in this analysis are consistent with those used in the RECUR study and GIRFT guideline, including thoracic and abdominal CT, MRI, US and X-ray, so that there is consistency between the imaging effectiveness evidence and imaging costs.

The RECUR database analysis (Dabestani 2019a, Dabestani 2019c) only reports the total and median number of scans for different imaging types across three ccRCC risk groups, categorised by Leibovich score. The median number of scans per year in RECUR was 2.08 in the low-risk group, 2.41 in the intermediate-risk group, and 3.32 in the high-risk group (median total scans not reported) (Dabestani 2019a). To estimate the number of scans under different follow-up strategies being compared using data reported by RECUR (Dabestani 2019a), we firstly calculated the mean number of imaging scans and approximated the standard deviation of the mean from the reported interquartile range. Then we randomly simulated 10,000 estimates of total scans, using a gamma distribution. This enabled the calculation of the mean number of scans if the total fell above or below the median for the sampled population, in line with the definition of low and high frequency imaging.

Total scan costs (Table HE010) for each follow-up strategy in each risk category were calculated as a weighted average of the different types of imaging using the proportions in Table HE009 and their respective unit costs in Table HE013, based on the frequency of imaging in Table HE008. The costs of scans are applied as one-off costs at the start of the model.

In addition, people with RCC have a full blood count every 6 months for 2 years then annually until 5 years, as informed by the pembrolizumab NICE technology appraisal (TA830).

Table HE008: Total number of scans estimated for each strategy

Follow-up strategy	Risk group	Mean no. of scans
Low imaging frequency	Low risk	7.62
	Intermediate risk	6.87
	High risk	4.86
High imaging frequency	Low risk	14.34
	Intermediate risk	15.23
	High risk	12.05
CSI	Low risk	10.98
	Intermediate risk	11.09
	High risk	8.41

Table HE009: Proportion of different imaging types

Risk group	Type of imaging	Proportion of imaging
Imaging frequency: low risk	Thoracic CT	14.47%
	Abdominal CT	27.21%
	MRI	1.20%
	US	16.01%
	Xray	41.11%
Imaging frequency: intermediate risk	Thoracic CT	17.10%
	Abdominal CT	27.95%
	MRI	1.13%

Risk group	Type of imaging	Proportion of imaging
	US	16.56%
	Xray	37.25%
Imaging frequency: high risk	Thoracic CT	27.74%
	Abdominal CT	33.37%
	MRI	0.65%
	US	10.44%
	Xray	27.81%
Low CSI: low risk	Thoracic CT	9.32%
	Abdominal CT	24.18%
	MRI	1.04%
	US	17.94%
	Xray	47.52%
Low CSI: intermediate risk	Thoracic CT	10.25%
	Abdominal CT	21.30%
	MRI	0.77%
	US	19.99%
	Xray	47.69%
Low CSI: high risk	Thoracic CT	16.60%
	Abdominal CT	16.05%
	MRI	0.37%
	US	17.12%
	Xray	49.87%
High CSI: low risk	Thoracic CT	17.33%
	Abdominal CT	44.95%
	MRI	1.93%
	US	9.81%
	Xray	25.98%
High CSI: intermediate risk	Thoracic CT	22.20%
	Abdominal CT	46.13%
	MRI	1.67%
	US	8.86%
	Xray	21.14%
High CSI: high risk	Thoracic CT	42.79%
	Abdominal CT	41.37%
	MRI	0.94%
	US	3.81%
	Xray	11.08%

Table HE010: Total costs of scan

Follow-up strategy	Risk group	Total costs
	Low risk	£791

Follow-up strategy	Risk group	Total costs
Low imaging frequency	Intermediate risk	£716
	High risk	£536
High imaging frequency	Low risk	£1489
	Intermediate risk	£1587
	High risk	£1327
Low CSI	Low risk	£1109
	Intermediate risk	£1101
	High risk	£845
High CSI	Low risk	£1231
	Intermediate risk	£1260
	High risk	£999

HE2.4.322 Management of recurrence

Treatments for the management of recurrence was informed by the RECUR analysis (Dabestani 2019a), with the proportions of people requiring each type of intervention listed in Table HE011. **Error! Reference source not found.**It is not possible to distinguish between management of symptomatic and non-symptomatic recurrences, as it is not reported in the RECUR analysis in this way. Hence, the costs of managing recurrence (Table HE014) depend only on the curable status of a recurrence which drives how it is managed, not its symptoms. Patients could receive palliative treatment regardless of whether they had a curable or incurable recurrence, which comprised either systemic anti-cancer therapy [SACT], best supportive care [BSC] or observation. For people with incurable recurrence, they could also receive metastasectomy, followed by observation. People with curable recurrence could receive metastasectomy, SABR or ablation, followed by observation. The management of symptomatic and non-symptomatic recurrence is assumed to be the same and have identical management costs, as it is not the symptom status that is the main driver of the choice of management.

Table HE011: Resource use for the management of recurrence

Type of recurrence	Interventions	Proportion
Incurable	Metastasectomy	6%
	Palliative	70%
	Observation	25%
Curable	Receive curative intent treatment	53%
	Metastasectomy	*89%*
	Radiotherapy i.e. SABR	*7%*
	Ablative therapy	*4%*
	Receive non-curative treatment	47%
	Palliative	*64%*
	Observation	*36%*

Incurable recurrence

People undergoing metastasectomy incur a one-off cost at the start of the health state, calculated as a weighted average of the different types of surgery commonly used to treat RCC metastases, with the unit costs in Table HE013. They then receive the cost of observation, consisting of CT scan and visits to medical/clinical oncologist as in Table HE013. The committee assumed that people get observation visits every four months based on their clinical expertise.

For palliative care, we assume that 75% of people receive SACT, and this is applied as a one-off cost. The total cost of a SACT management strategy was calculated from the commercial in confidence outputs of the NICE RCC pathway model which was used for NICE TA964 by the external assessment group. Given the confidential nature of the data we cannot explicitly report the calculations, and instead present the aggregate cost of SACT used in our analysis in Table HE013. The costs used in this analysis are those of the entire strategy for each SACT option and include the full sequence of treatments and any associated management costs after starting SACT treatment, weighted by the estimated uptake of each therapy and based on the confidential access prices for the medicines. The therapies included were; sunitinib, pazopanib, tivozanib, cabozantinib, nivolumab+ipilimumab, avelumab+axitinib, lenvatinib+pembrolizumab, and cabozantinib+nivolumab.

The remaining 25% of palliative care patients are assumed to receive BSC, which includes monthly consultant and nurse visits (i.e. every 4 weeks), a one-off cost for two sessions of radiotherapy for bone pain management, and a one-off cost for pain medication applied at death.

Curable recurrence

The costs of metastasectomy and ablation are calculated as weighted averages of different types of procedures that are commonly used to treat RCC metastases and their respective unit costs (reported in Table HE013). People undergoing curative treatment incur a one-off cost which is made up of metastasectomy, SABR and ablation in the proportions in Table HE011 and Table HE012, followed by observation costs for each cycle onwards. For people who undergo noncurative treatment, the palliative treatment and observation costs are the same as those for people with incurable recurrence.

Table HE012: Proportion of different ablation types

Interventions	Proportion	Source
Radiofrequency ablation	20%	Rossi et al. (2021)
Cryoablation	60%	
Microwave ablation	20%	

Table HE013: Unit cost of healthcare resources

Resource	Unit costs (£)	Source
Single CT chest abdomen and pelvis scan	£123	NHS Cost Collection (2024). RD26z Computerised Tomography Scan of Three areas with contrast
Single MRI scan	£202	NHS Cost Collection (2024). RD05z Magnetic Resonance Imaging Scan of Two or Three areas with contrast
Single ultrasound scan	£53	NHS Cost Collection (2024). RD41z Ultrasound Scan with duration of less than 20 minutes with contrast
Single plain film x-ray	£101	NHS Cost Collection (2024). IMAGCDC_PF community diagnostic centres plain film

Resource	Unit costs (£)	Source
Single biopsy	£298	NHS Cost Collection (2024). Percutaneous needle biopsy of lesion of kidney 19 years and over outpatient
CT preparation for SABR therapy	£1,770	NHS Cost Collection (2024). SC41z preparation for intensity modulated radiation therapy with technical support
One fraction of SABR	£240	NHS Cost Collection (2024). SC22z deliver a fraction of treatment on a megavoltage machine
Systemic therapies after recurrence	£84,510	Calculated from NICE RCC pathway model (TA964)
Radiofrequency ablation	£1,960	NHS Cost Collection (2024). YL02z Standard Percutaneous Ablation of Lesion of Kidney
Cryoablation	£3,474	NHS Cost Collection (2024). YL01z Complex Percutaneous Ablation of Lesion of Kidney
Microwave ablation	£1,960	NHS Cost Collection (2024). YL02z Standard Percutaneous Ablation of Lesion of Kidney
Medical oncology appointment	£193	NHS Cost Collection (2024). Summary OP attendances 370 medical oncology
Clinical oncology appointment	£160	NHS Cost Collection (2024). Summary OP attendances 800 clinical oncology
Palliative radiotherapy for management of recurrence	£311	NHS Cost Collection (2024). SC31Z fraction of adaptive radiotherapy on a megavoltage machine total
Consultant outpatient follow up	£157	NHS Cost Collection (2024). WF01A 800 Consultant led clinical oncology service
Specialist nurse visit as BSC	£62	PSSRU (2024). Section 11.2.2 Nurse specialist Band 6 cost per working hour (including qualifications)
Pain medication as BSC per month	£159	BNF 1mg/1ml vial of morphine sulphate solution for infusion 5.24 per vial, 1mg/ml daily
Full blood count	£3	NHS Cost Collection (2024). 24 DAPS PATH05 haematology, total
Metastasectomy	£6,473	NHS Cost Collection (2024). 24 LB06J Kidney urinary tract or prostate neoplasms with interventions CC score 6-8
	£4,866	NHS Cost Collection (2024). LB06K Kidney urinary tract or prostate neoplasms with interventions CC score 4-5
	£5,228	NHS Cost Collection (2024). LB06L Kidney urinary tract or prostate neoplasms with interventions CC score 2-3
	£5,014	NHS Cost Collection (2024). LB06M Kidney urinary tract or prostate neoplasms with interventions CC score 0-1
	£6,774	NHS Cost Collection (2024). DZ17P Respiratory neoplasms with single intervention CC score 10+
	£4,826	NHS Cost Collection (2024). DZ17Q Respiratory neoplasms with single intervention CC score 6-9
	£4,160	NHS Cost Collection (2024). DZ17R Respiratory neoplasms with single intervention CC score 0-5

1

Table HE014: Costs of managing recurrences

Type of recurrence	Cycle	Costs
Incurable recurrence	1st month	£44,782
	Monthly cost onwards	£62
	Last month (near death)	£89
Curable recurrence	1st month	£32,664
	Monthly cost onwards	£84
	Last month (near death)	£84

HE2.434 Quality of life

In order to express outcomes in the form of QALYs, health states were linked to appropriate utility scores. Utility scores represent the health-related quality of life (HRQoL) associated with specific health states on a scale from 0 (death) to 1 (perfect health); they are estimated using preference-based measures that capture people's preferences on the HRQoL experienced in the health states under consideration.

Utility data was sourced from other published RCC models, including Florea et al.,2024, the NICE technology appraisal of adjuvant pembrolizumab (TA830) and the NICE RCC pathway pilot (TA964).

People with detected RCC were split into health states based on symptom presence and curability, namely, symptomatic incurable, non-symptomatic incurable, symptomatic curable and asymptomatic curable. Quality of life associated with each model health state was estimated based on the treatment that people received for each health state (Table HE011). The overall utility value (Table HE016) for the recurrence-based health states was estimated using the utility value for the treatment and the proportion of people in that health state receiving the treatment (as presented in Table HE011).

Utility losses associated with the management of recurrence with either ablation, radiotherapy or metastasectomy, as detailed in Table HE015Table HE015: Utility score for health events, were assumed to apply for one year. For people with symptomatic recurrences, these utility decrements were applied to the baseline utility (equivalent to the utility value in the disease-free state) during this time, and then the utility reverted to disease-free state level afterwards. For patients with an asymptomatic recurrence, the same approach is used except that mental health impact associated with being asymptomatic and untreated was incorporated into the baseline utility.

The committee highlighted that a patient knowing they have a recurrence has a significant impact on their mental health, especially if this recurrence is potentially incurable or lacks treatment options. They recommended that it was not appropriate to assume that an asymptomatic recurrence has the same QoL as people who are disease-free. Our model accounts for this by applying a decrement to reflect the mental health impact associated with asymptomatic, untreated recurrences. No mental health-related decrement was applied for symptomatic recurrences as the impact is expected to be implicitly captured in the treatment utility decrement for symptomatic treated recurrences, and in the BSC disutility for symptomatic untreated recurrences. For individuals with asymptomatic recurrence, whether incurable or receiving curable treatment, a utility loss associated with observation during the asymptomatic recurrence period is applied, which was assumed to last about 14.9 months (as estimated in the study Rini 2016) until symptoms develop and their quality-of-life declines. Afterwards, their quality of life reverts to those in the BSC health state.

The utility value for SACT from the RCC pathway model (TA964) reflects the distribution of types of treatment received and the time on each line of treatment, and incorporates the

impact of adverse events and progression over time. Weighted averages of life years in the model and QALYs gained were calculated from the pathway model results using NHS England uptake figures for the included therapies, and the average utility calculated by dividing the total QALY gains by the life years.

Table HE015: Utility score for health events

Health event	Utility	Approach	Source
Ablation	Disutility 0.02	Disutility associated with ablation was applied to the baseline disease free state	NICE TA830 for adjuvant pembrolizumab
Metastasectomy	Disutility 0.02	Disutility associated with metastasectomy was applied to the baseline disease free state	Assumed equivalent to ablation
Radiotherapy	Disutility 0.02	Disutility associated with radiotherapy was applied to the baseline disease free state	Assumed equivalent to ablation
BSC	Utility 0.482	Applies to people on BSC or observation (when symptomatic)	TA964 RCC pathway model
SACT	Utility 0.603	Applies to people on SACT	Estimated from TA964 RCC pathways model
Mental health impact	Disutility 0.01	Disutility associated with mental health was applied to the baseline disease free state. Applies to people on observation when non-symptomatic	Florea et al. 2024. Assume symptoms develop after 14.9 months (Rini 2016)

Table HE016: Utility score for health states

Health state	Utility value	Approach
Disease free	0.868	-
Incurable symptomatic recurrence	Utility in year 1: 0.572 Utility after year 1: 0.574	Year 1: Weighted average of utility associated with surgery, palliative care and observation. After Year 1: Weighted average of utility associated with disease-free, palliative care and observation.
Curable symptomatic recurrence	Utility in year 1: 0.703 Utility after year 1: 0.714	Year 1: Weighted average of utility associated with treatment, palliative care and observation. After Year 1: Weighted average of utility associated with disease-free, palliative care and observation.
Incurable non-symptomatic recurrence	Utility in year 1: 0.732 Utility after year 1 (before symptoms): 0.733 Utility after year 1 (after symptoms): 0.573	Year 1: Weighted average of utility associated with surgery, palliative care and observation, including mental health impact. After Year 1 (before symptoms): Weighted average of utility associated with disease-free, palliative care and observation, including mental health impact. After Year 1 (after symptoms): Weighted average of utility associated with disease-free

		and palliative care (with mental health impact) and observation (modelled as BSC).
Curable non-symptomatic recurrence	Utility in year 1: 0.795 Utility after year 1 (before symptoms): 0.806 Utility after year 1 (after symptoms): 0.714	Year 1: Weighted average of utility associated with treatment, palliative care and observation, including mental health impact. After Year 1 (before symptoms): Weighted average of utility associated with disease-free, palliative care and observation, including mental health impact. After Year 1 (after symptoms): Weighted average of utility associated with disease-free and palliative care (with mental health impact) and observation (modelled as BSC).

HE2.5 Sensitivity analyses

HE2.5.1 Deterministic sensitivity analyses

One-way deterministic sensitivity analyses (DSA) were undertaken to explore the impact of parameter uncertainty on the cost effectiveness result. The parameters explored are summarised below.

Transition probability

- Probability of a detected recurrence being asymptomatic (high imaging frequency): vary by +/-20%,
- Probability of a detected recurrence being asymptomatic (low imaging frequency): vary by +/-20%,
- Recurrence free survival, curable recurrence: Alternative survival curves (Gompertz and exponential for high-risk group, Gompertz for intermediate risk group, Gompertz for low-risk group),
- Recurrence free survival, incurable recurrence: Alternative survival curves (lognormal for high-risk group, lognormal for intermediate risk group, lognormal for low-risk group),
- Overall survival after asymptomatic incurable recurrence: Alternative survival curves (loglogistic for upper estimate, Gompertz for lower estimate),
- Overall survival after symptomatic incurable recurrence: Alternative survival curves (Weibull for upper estimate),
- Overall survival after asymptomatic curable recurrence: Alternative survival curves (Gompertz for lower estimate),
- Overall survival after symptomatic curable recurrence: Alternative survival curves (Weibull for lower estimate),

Cost value

- Total scan cost (high imaging frequency): vary by +/-20%,
- Total scan cost (low imaging frequency): vary by +/-20%,

Utility

- Disease free utility: vary by lower and upper bound of 95% confidence interval,
- BSC utility: vary by lower and upper bound of 95% confidence interval.

HE2.5.12 Probabilistic analysis

Probabilistic analysis was employed to estimate results for the base-case analysis. Model input parameters were assigned probability distributions rather than expressed as point estimates (which is the approach adopted in a deterministic analysis). We configured the models to perform probabilistic analysis to quantify uncertainty in the true values of input parameters. The PSA was run for 1,000 iterations. We specified probability distributions for all input variables (see Appendix B). We decided the type of distribution with reference to the properties of data of that type (for example, we use beta distributions for probabilities that are bounded between 0 and 1 and we use gamma distributions for cost parameters that cannot be negative). Where possible, we parameterised each distribution using dispersion data from the source from which the value was obtained; where no such data were available, we gave consideration to applying plausible ranges based on committee advice and the usual properties of similar data. Costs were varied by ±20% and utilities were varied by ±10% when no other information was available.

HE3 Results

HE3.1 Base-case analysis

HE3.1.1 Probabilistic analysis

Results of the probabilistic base case analysis are presented in Table HE017.

In all three risk groups, the strategy with a lower proportion of CSI had lower mean lifetime costs compared to a strategy with a higher proportion of CSI, due to higher costs of CT and MRI relative to ultrasound and X-ray. The total costs associated with each strategy over the patient lifetime are driven by the scan costs. In the low-risk and intermediate-risk groups, the low CSI strategies were also associated with lower mean lifetime QALYs, as their probabilities of a detected recurrence being asymptomatic were low. While the monitoring schedule does not influence the overall rate of recurrence, since recurrences will occur regardless of when patients are scanned, early detection of recurrences while the tumour still remains asymptomatic is associated with greater survival and QALYs than later detection of symptomatic recurrences. The high CSI strategy had a cost per QALY of £3,231 in the low-risk group and of £4,919 in the intermediate-risk group, suggesting that it is an effective use of NHS resources in these risk groups.

In the high-risk group, the low CSI strategy was associated with higher mean lifetime QALYs, as its probability of a detected recurrence being asymptomatic was higher, conversely to the probability in the low-risk and intermediate-risk groups. The analysis suggests that the low CSI strategy was the dominant strategy, and that it is the more effective use of NHS resources. This outcome appears counterintuitive, and underlying reasons have been discussed with the committee in HE3.3.3.

In all three risk groups, the low intensity imaging strategies had lower mean lifetime costs compared to the high intensity imaging strategies, due to a reduction in imaging costs. However, they are also associated with lower mean lifetime QALYs. The high intensity imaging strategy had a cost per QALY of £14,674 in the low-risk group, and £11,710 in the intermediate-risk group, suggesting that it is an effective use of NHS resources in these risk groups as interventions with an ICER of less than £20,000 per QALY gained are generally considered to be cost effective.

In the high-risk group, the cost per QALY was estimated to be £25,684. Interventions with ICERs between £20,000 and £30,000 require greater certainty in the analysis or consideration of uncaptured benefits. While the estimates of the probability of a detected recurrence being asymptomatic was not statistically significant in all risk groups, the point estimates favoured high imaging frequency in all groups. However, the risk ratio was greatest in the low-risk group and lowest in the high-risk group.

The probability of a strategy detecting a recurrence being asymptomatic was highly uncertain in all analyses, as they were based on small patient numbers and the quality of the evidence in relation to this review question was assessed as being very low. For the majority of estimates, these were not estimated as being statistically significant. The impact of that uncertainty is explored in a sensitivity analysis.

Table HE017: Probabilistic analysis results

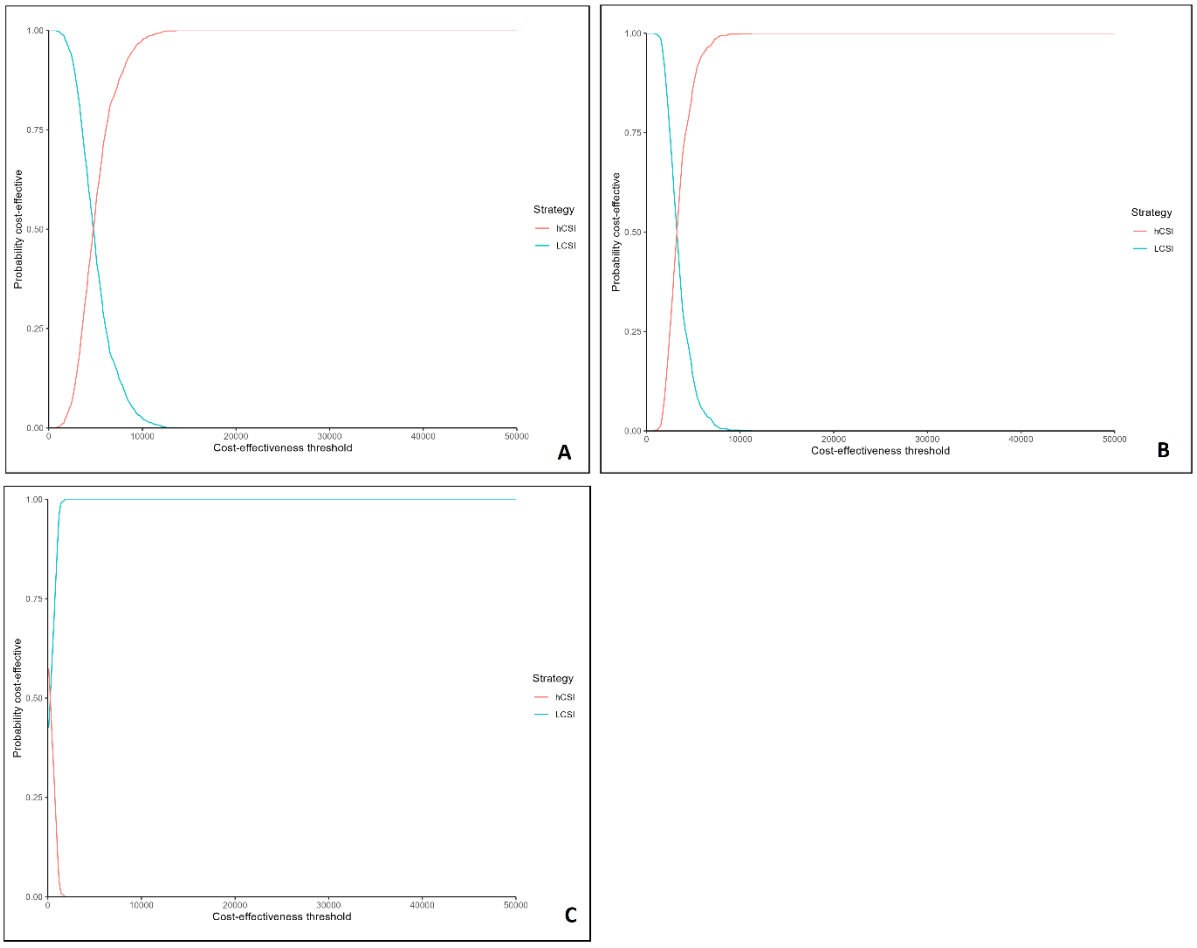
Strategy	Total cost (95% CI)	Total QALYs (95% CI)	NHB	Inc. NMB	ICER	Probability cost effective

Low-risk group						
Higher vs lower proportion cross-sectional imaging						
<50% CSI	£1801 (£1773, £1828)	12.81 (12.81, 12.82)	12.72	NA	-	-
>50% CSI	£1969 (£1938, £1999)	12.85 (12.84, 12.85)	12.75	£498	£5046	100%
Higher vs low intensity of imaging frequency						
Low intensity	£1484 (£1466, £1503)	12.81 (12.81, 12.81)	12.74	NA	-	-
High intensity	£2241 (£2219, £2264)	12.86 (12.86, 12.87)	12.75	£265	£14811	73%
Intermediate-risk group						
Higher vs lower cross-sectional imaging						
<50% CSI	£2858 (£2822, £2894)	10.51 (10.51, 10.52)	10.37	NA	-	-
>50% CSI	£3127 (£3086, £3168)	10.59 (10.59, 10.59)	10.43	£1,271	£3490	99%
Higher vs low intensity of imaging						
Low intensity	£2491 (£2471, £2511)	10.53 (10.53, 10.54)	10.41	NA	-	-
High intensity	£3441 (£3409, £3473)	10.61 (10.6, 10.61)	10.44	£583	£12398	85%
High-risk group						
Higher vs lower cross-sectional imaging						
<50% CSI	£2915 (£2883, £2947)	9.01 (9.00, 9.01)	8.86	NA	-	-
>50% CSI	£2910 (£2874, £2947)	8.90 (8.89, 8.90)	8.75	-£2,183	Dominated	0%
Higher vs low intensity of imaging						
Low intensity	£2479 (£2462, £2496)	8.91 (8.91, 8.92)	8.79	NA	-	-
High intensity	£3322 (£3286, £3359)	8.95 (8.95, 8.96)	8.79	-£48	£21208	47%

Cost effectiveness acceptability curves (CEACs) are presented in Figure HE006 and Figure HE00**7**.

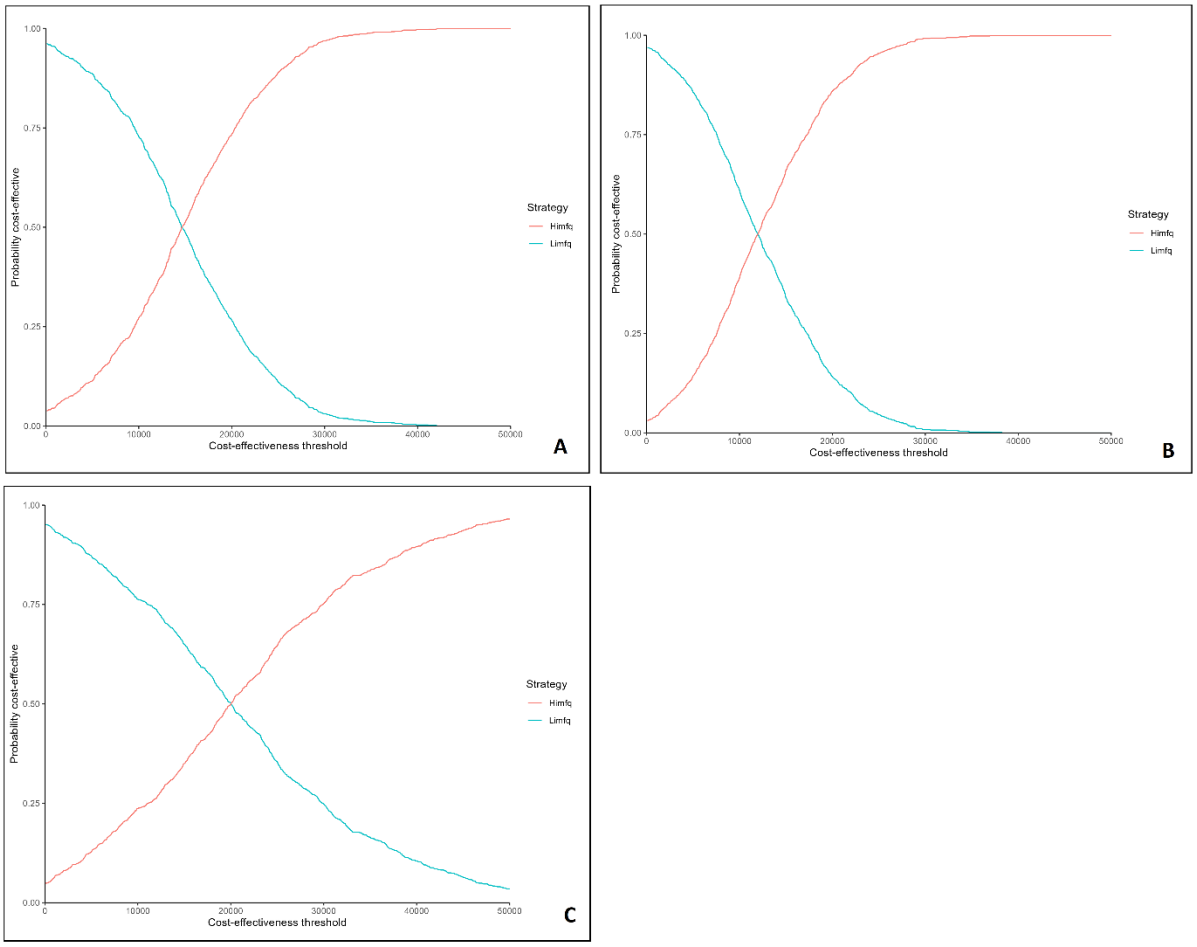
The probability that the high frequency imaging strategy is cost effective compared to the low frequency imaging strategy at a threshold of £20,000 per QALY is 73%, 85% and 47% in the low-, intermediate- and high-risk groups, respectively.

The probability that the high CSI strategy is cost effective compared to the low CSI strategy at a threshold of £20,000 per QALY is 100%, 99% and 0% in the low-, intermediate- and high-risk groups, respectively.



Red line: high CSI strategy, blue line: low CSI strategy. A: low-risk group, B: intermediate-risk group, C: high-risk group.

Figure HE006 Cost effectiveness acceptability curves for the proportion of CSI analysis



Red line: high imaging frequency strategy, blue line: low imaging frequency strategy. A: low-risk group, B: intermediate-risk group, C: high-risk group.

Figure HE007 Cost effectiveness acceptability curves for the imaging frequency analysis

HE3.162 Deterministic analysis

Results of the deterministic base-case cost effectiveness analysis are presented in Table HE018. The probabilistic analysis generated slightly higher QALYs for the high-risk group and slightly lower QALYs and higher costs for the intermediate-risk group than the deterministic analysis. The ICERs for each analysis were relatively consistent across the deterministic and the probabilistic analysis, leading to consistent conclusions of the analyses.

Table HE018: Deterministic cost–utility results

Strategy	Total cost	Total QALYs	NHB	Inc. NMB	ICER	Probability cost effective
Low-risk group						
Higher vs lower proportion cross-sectional imaging						
<50% CSI	£1,939	12.46	12.37	-	-	-
>50% CSI	£2,148	12.53	12.42	£1,082	£3,231	100%
Higher vs low intensity of imaging frequency						
Low intensity	£1,635	12.47	12.39	-	-	-
High intensity	£2,401	12.52	12.40	£278	£14,674	73%
Intermediate-risk group						
Higher vs lower cross-sectional imaging						
<50% CSI	£2,547	11.23	11.10	-	-	-
>50% CSI	£2,766	11.27	11.13	£670	£4,919	99%
Higher vs low intensity of imaging						
Low intensity	£2,150	11.22	11.11	-	-	-
High intensity	£3,133	11.3	11.14	£696	£11,710	85%
High-risk group						
Higher vs lower cross-sectional imaging						
<50% CSI	£3,241	8.14	7.98	-	-	-
>50% CSI	£3,284	8.06	7.89	-£1,665	Dominated	0%
Higher vs low intensity of imaging						
Low intensity	£2,844	8.08	7.93	-	-	-
High intensity	£3,677	8.11	7.92	-£184	£25,684	47%

HE3.2 Sensitivity analysis

HE3.2.1 Deterministic sensitivity analysis

Key parameters were varied in a one-way sensitivity analysis to demonstrate which parameters had the greatest influence on the cost effectiveness results. Tornado diagrams in Figure HE008 and Figure HE009 illustrate the ten parameters that had the greatest influence

on the cost effectiveness results in each analysis comparison. The impact on the results is presented as the change in incremental net monetary benefit (iNMB), where “lower iNMB” and “upper iNMB” refer to the results of the scenario using the lower and higher range of the parameter being explored, respectively.

In both analyses, the parameters that had the greatest influence on the cost effectiveness results were the probability that an imaging strategy detecting a recurrence being asymptomatic (compared to a symptomatic recurrence), the total cost of imaging, and the time to curable recurrence. Parameters relating to the management or evaluation of recurrences (such as overall survival following a recurrence, time until asymptomatic recurrences developed symptoms, BSC utility value, cost of SACT) had little impact on the cost effectiveness results.

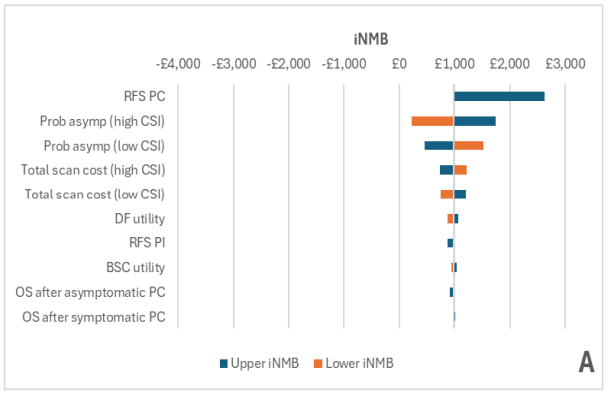
In the analysis comparing high proportion of CSI to low proportion of CSI, the high CSI strategy remained cost effective under all scenarios in the low-risk group.

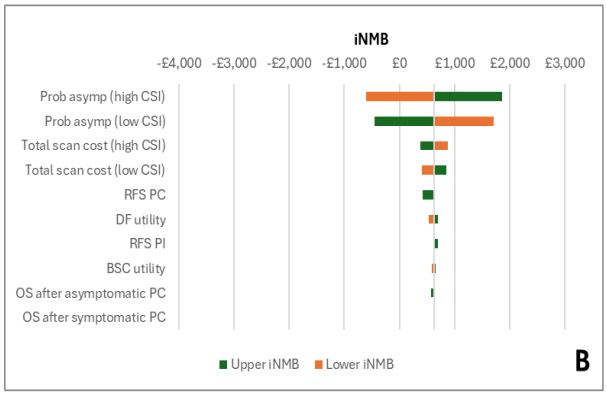
In the intermediate-risk group, the low CSI strategy became cost effective compared to the high CSI strategy under two alternative assumptions: when the probability that a detected recurrence was asymptomatic for the low CSI strategy increased by 20% from 0.62 to 0.74, or when the probability that a detected recurrence was asymptomatic for the high CSI strategy decreased by 20% from 0.71 to 0.57 (i.e. the low CSI strategy had a greater probability of detecting a recurrence while asymptomatic than the high CSI strategy).

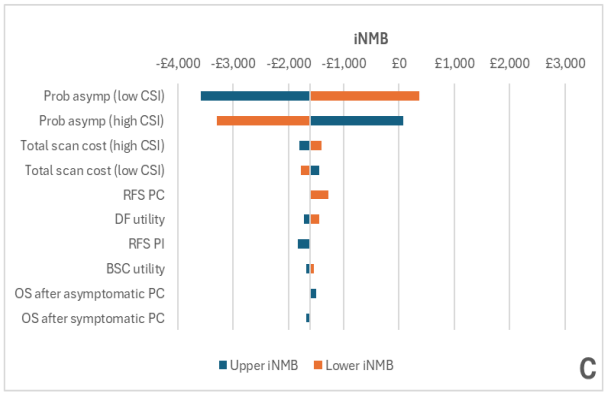
In the high-risk group, the high CSI imaging strategy became cost effective with a higher probability of detecting a recurrence while asymptomatic for the high CSI group or a lower probability for the low CSI group, compared with the base case.

Likewise, we varied key parameters such as the probability of a detected recurrence being asymptomatic and costs of imaging for the imaging strategy by 20% higher or lower than the corresponding base-case values for each risk group. In the analysis comparing high frequency of imaging to low frequency of imaging, the high imaging frequency strategy was cost effective in the base case analysis, but it became not cost effective when the high imaging frequency strategy had the lower probability or the low imaging frequency strategy had the higher probability of a detected recurrence being asymptomatic, or if the high imaging frequency strategy had the higher costs of imaging.

In the intermediate-risk group, the high imaging frequency strategy was cost effective in the base case analysis, but it became not cost effective when the high imaging frequency strategy had a lower probability or the low imaging frequency strategy had a higher probability of detecting asymptomatic recurrence. In the high-risk group, the high imaging frequency strategy was not cost effective in the base case analysis, but it became cost effective with a higher probability of detected recurrence being asymptomatic for the high imaging frequency group or a lower probability for the low imaging frequency group.



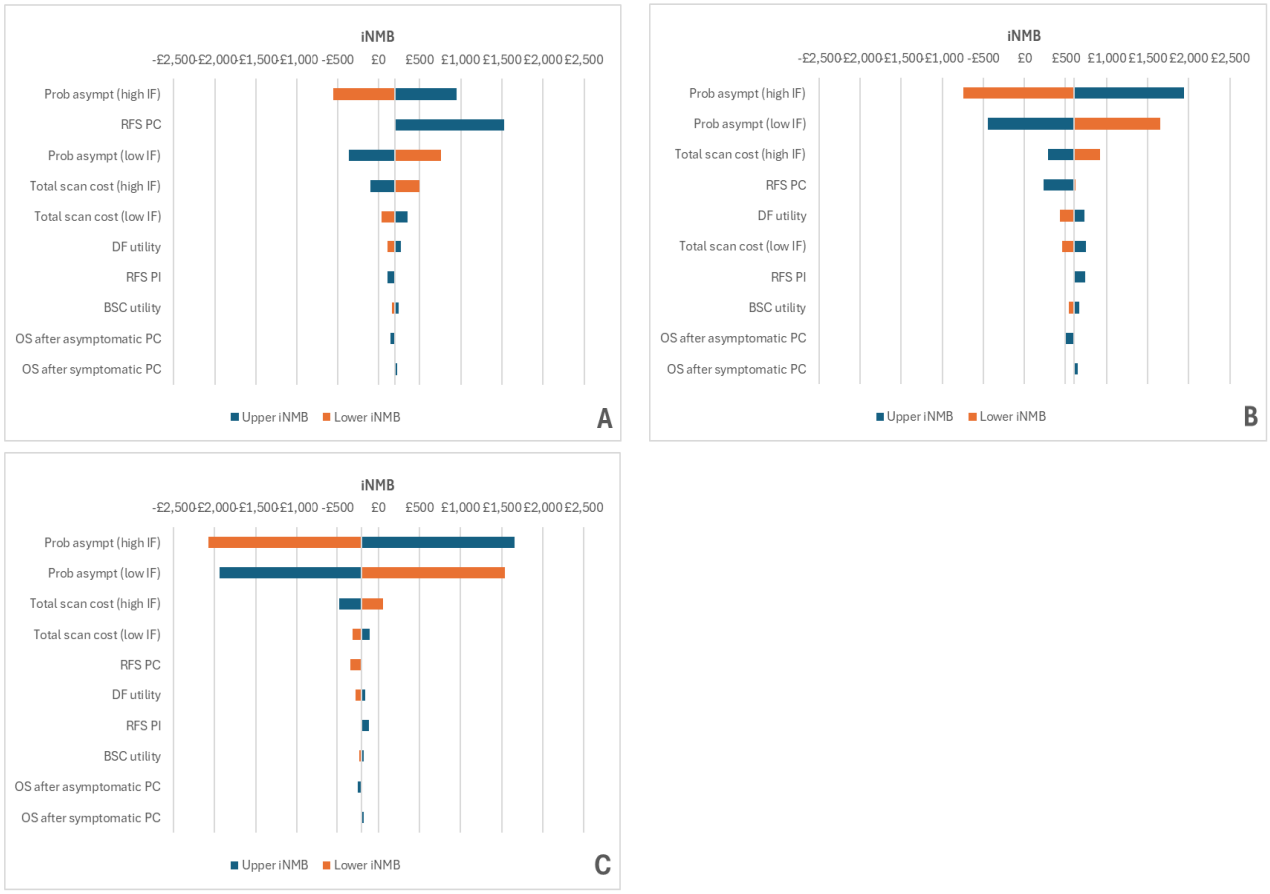




A = low-risk subgroup, B = intermediate-risk subgroup, C = high-risk subgroup.

Abbreviations: NMB = net monetary benefit, IF = imaging frequency, PC = potentially curable recurrence, DF = disease-free, RFS = recurrence free survival, PI = probably incurable recurrence, OS = overall survival. Upper iNMB refers to the iNMB when the higher value of the variable is applied; lower iNMB refers to the iNMB when the lower value of the variable is applied.
Interpretation: Tornado bars centre at the base case iNMB estimate for that risk group. NMB greater than 0 indicates the high CSI strategy is cost effective. iNMB estimated assuming a willingness to pay of £20,000 per QALY.

Figure HE008: Sensitivity analysis: high CSI vs low CSI imaging strategy



A = low-risk subgroup, B = intermediate-risk subgroup, C = high-risk subgroup.

Abbreviations: NMB = net monetary benefit, IF = imaging frequency, PC = potentially curable recurrence, DF = disease-free, RFS = recurrence free survival, PI = probably incurable recurrence, OS = overall survival. Upper iNMB refers to the iNMB when the higher value of the variable is applied; lower iNMB refers to the iNMB when the lower value of the variable is applied.
Interpretation: Tornado bars centre at the base case iNMB estimate for that risk group. NMB greater than 0 indicates the high CSI strategy is cost effective. iNMB estimated assuming a willingness to pay of £20,000 per QALY.

Figure HE009: Sensitivity analysis: high vs low intensity imaging frequency

HE3.3 Discussion

HE3.3.1 Principal findings

An original cost-utility analysis comparing a strategy with a high proportion of CSI, with a strategy with a low proportion of CSI found that for low-risk and intermediate-risk groups, the high CSI strategy is likely to be considered cost-effective at a threshold of £20,000 per QALY, with ICERs of £3,231 and £4,919, respectively. For the high-risk group, the high CSI strategy was associated with higher costs and lower QALYs than the low CSI strategy.

An original cost-utility analysis comparing a strategy with a high frequency of imaging with a strategy with a low frequency of imaging found that for low-risk and intermediate-risk groups, the high-intensity strategy is likely to be considered cost-effective at a threshold of £20,000 per QALY, with ICERs of £14,674 and £11,710, respectively. For the high-risk group, the high-intensity strategy had an ICER of £25,684 compared with the low-intensity strategy, which is less likely to be considered cost-effective at a threshold of £20,000 per QALY.

The total costs of each strategy were driven by the cost of imaging. The differences in outcomes (QALYs) were relatively small, with the majority of QALYs in the disease-free health state. In both analyses in all risk groups, the most influential parameter was the probability of a detected recurrence being asymptomatic, and changes in this parameter were the only scenarios where the conclusion of the economic analysis could change (i.e. an alternative strategy being cost effective).

HE3.3.2 Strengths of the analysis

A major strength of this analysis is that it allowed for comparisons of different follow-up strategies using the best available and most recent clinical evidence which includes some participants from the UK population. This analysis is the first economic study in the UK NHS setting in this research domain. All parameters used in the analyses were informed by published literature or assumptions and were validated by clinical experts to ensure alignment with current clinical practice. The uncertainty of parameters was also explored in sensitivity analysis to test the robustness of model results.

This analysis also highlights the benefits of early detection and treatment at the earliest possible stage, addressing the committee's concerns. It comprehensively captured all benefits associated with survival outcomes and quality of life, using evidence from the RECUR database analysis to compare asymptomatic tumours with symptomatic tumours as a reference point.

HE3.3.3 Weaknesses of the analysis

The main source of effectiveness evidence for follow-up strategies was from the RECUR database (Dabestani 2019a). The imaging strategies compared in RECUR were a "high proportion of CSI" strategy versus a "low proportion of CSI" strategy, and a "low frequency of scans" strategy versus a "high frequency of scans" strategy. These imaging strategies were considered to be relatively loosely defined, and so it was not possible to evaluate specific strategies, such as around which imaging modality to use, the duration of follow-up or specific frequencies per year. As such, the economic model can indicate what type of imaging strategy is likely to be cost effective, rather than any specific strategy. There was also no information about the optimal duration of monitoring.

The committee had concerns with the quality of the effectiveness evidence that was used to inform the economic model, which meant that the cost effectiveness results were also uncertain. RECUR is an observational database, and the methods of stratification of the sample by risk is unlikely to have removed the effects of confounding completely. Insufficient information was provided on what confounding variables it adjusted for. The follow-up times provided in the study were also categorised into three groups according to ranges of follow-up, meaning it was not possible to know the exact follow-up time. Dabestani et al. 2019c, 2019b did not account for participants with incomplete follow-up in their analyses and excluded participants with <4 years follow-up data. The evidence for the probability of a detected tumour being asymptomatic was not statistically significant, and it appears there was an error in the RECUR publication for this outcome due to inconsistencies in how it was reported. The point estimate was used in the economic model, and the impact of the uncertainty captured in the probabilistic analysis.

The effectiveness evidence also appeared to be counter intuitive in the high-risk group. For example, the probability that recurrence detected by a high CSI strategy is asymptomatic was lower than the low CSI strategy, which is counter to expectations given the greater accuracy of CSI. The committee suggested that this was because people in the high-risk group are more likely to require additional non-CSI scans (which are easier to access) beyond their follow up protocol if recurrence is suspected. In this case, the total number of CSI scans remains as per the protocol, but the total non-CSI scans increase. This results in a low CSI strategy with a higher total number of scans but similar numbers of CSI scans to the

high CSI strategy, which is more likely to detect early (non-symptomatic) recurrences. Another counterintuitive finding is that the probability that the high frequency imaging strategy being cost-effective compared to the low frequency imaging strategy did not follow a consistent trend; the probability is highest in the intermediate group and lowest in the high-risk group, whereas the probability of high CSI being cost-effective compared with low CSI strategy at a threshold of £20,000 per QALY shows a decreasing trend from the low to high-risk groups. The unexpected results was considered likely to be due to the issues with the underlying effectiveness evidence rather than any actual difference in effectiveness in this risk group.

The economic model accounted for a time-varying risk of recurrence in each risk group, which is used to support different durations and frequency of scans between the risk groups. In the low-risk group, there may an ongoing risk of recurrence beyond 5 years, although it is relatively small. In the high-risk group, it is commonly thought that the risk of recurrence is higher in the first five years after nephrectomy, after which it declines. This is supported by the RECUR data, which was used in the economic model. However, the committee highlighted other trials such as SORCE (Oza, 2022) where see some increase was still seen rather than a plateau in recurrence risk.

The RECUR study did not differentiate between symptomatic and non-symptomatic recurrences when reporting the types of management they receive. We assume that the curability of a recurrence drives the management of recurrence rather than the presence of symptoms. This means the management of symptomatic and non-symptomatic recurrence is the same and no additional cost savings occur.

A key limitation of the analysis was that the number and types of scans in each imaging strategy was not reported and had to be simulated for the economic model in order to estimate scan costs in each strategy. The median number of scans per year in RECUR was 2.08 in the low-risk group, 2.41 in the intermediate-risk group, and 3.32 in the high-risk group. The committee wished to consider a threshold analysis to determine the maximum number of scans in each risk group for a strategy to be cost effective. However, it was not possible to incorporate the analysis because the more precise relationship between scan frequency and scan type and effectiveness is not known.

Another limitation is that in RECUR study, the data was collected from people who had received treatment for localised RCC, whereas the population of interest in this research question includes both localised and locally advanced RCC. It is assumed that the effectiveness outcomes associated with locally advanced RCC may be different from those with localised RCC.

HE3.3.4 Comparison with other CUAs

We believe this is the first economic study comparing follow-up strategies (i.e. imaging frequency and proportion of CSI) for people with RCC in the UK. Without previously published CUAs addressing this question, there is a lack of a clear reference point for this analysis. Given the uncertainty in the results of the economic analysis due to the associated uncertainty in the effectiveness evidence, the committee elected to recommend considering a minimum imaging schedule based on the existing GIRFT guidelines, noting that the economic analysis supported the use of cross-sectional and more frequent imaging. These were developed by expert consensus given the lack of data and are already used in practice in many centres in the UK.

HE3.4 Conclusions

The economic results suggested that both high CSI and high imaging frequency are cost effective in the low- and intermediate-risk groups at a threshold of £20,000 per QALY. In the high-risk group, high CSI does not appear to be cost effective. However, all results are

subject to uncertainty due to limitations with the underlying clinical effectiveness data, such as the probability of asymptomatic recurrence, and further research is warranted to establish the benefits of different risk-stratified imaging strategies.

HE4 References

Dabestani, S., Beisland, C., Stewart, G. D., Bensalah, K., Gudmundsson, E., Lam, T. B., Gietzmann, W., Zakikhani, P., Marconi, L., Fernandéz-Pello, S., Monagas, S., Williams, S. P., Torbrand, C., Powles, T., Van Werkhoven, E., Meijer, R., Volpe, A., Staehler, M., Ljungberg, B., & Bex, A. (2019a). Long-term Outcomes of Follow-up for Initially Localised Clear Cell Renal Cell Carcinoma: RECUR Database Analysis. *European urology focus*, *5*(5), 857–866. https://doi.org/10.1016/j.euf.2018.02.010

Dabestani, S., Beisland, C., Stewart, G. D., Bensalah, K., Gudmundsson, E., Lam, T. B., Gietzmann, W., Zakikhani, P., Marconi, L., Fernandéz-Pello, S., Monagas, S., Williams, S. P., Torbrand, C., Powles, T., Van Werkhoven, E., Meijer, R., Volpe, A., Staehler, M., Ljungberg, B., & Bex, A. (2019b). Intensive Imaging-based Follow-up of Surgically Treated Localised Renal Cell Carcinoma Does Not Improve Post-recurrence Survival: Results from a European Multicentre Database (RECUR). *European urology*, *75*(2), 261–264. https://doi.org/10.1016/j.eururo.2018.10.007

Dabestani, S., Beisland, C., Stewart, G. D., Bensalah, K., Gudmundsson, E., Lam, T. B., Gietzmann, W., Zakikhani, P., Marconi, L., Fernandéz-Pello, S., Monagas, S., Williams, S. P., Powles, T., Van Werkhoven, E., Meijer, R., Volpe, A., Staehler, M., Ljungberg, B., & Bex, A. (2019c). Increased use of cross-sectional imaging for follow-up does not improve post-recurrence survival of surgically treated initially localized R.C.C.: results from a European multicenter database (R.E.C.U.R.). *Scandinavian journal of urology*, *53*(1), 14–20. https://doi.org/10.1080/21681805.2019.1588919

Enhanced Kaplan-Meier Curves. Available from: https://dominicmagirr.shinyapps.io/enhanceKM/

Florea, A., Zaric, G. S., Kang, Z., & Cool, D. W. (2024). Cost-Effectiveness Analysis Comparing Biopsy in Advance of Ablation with Concurrent Biopsy and Ablation for Small Renal Masses Measuring 1-3 cm. *Journal of vascular and interventional radiology : JVIR*, *35*(9), 1388–1396.e5. https://doi.org/10.1016/j.jvir.2024.05.008

Kaltenthaler E, Tappenden P, Paisley S, Squires H. NICE DSU technical support document 13: identifying and reviewing evidence to inform the conceptualisation and population of cost-effectiveness models. 2011. Available from www.nicedsu.org.uk

Lai, Y., Bensimon, A. G., Gao, E., Bhattacharya, R., Xu, R., Chevure, J., Imai, K., & Haas, N. B. (2023). Cost-Effectiveness Analysis of Pembrolizumab as an Adjuvant Treatment of Renal Cell Carcinoma Post-nephrectomy in the United States. *Clinical genitourinary cancer*, *21*(5), 612.e1–612.e11. https://doi.org/10.1016/j.clgc.2023.03.016

Latimer, N. NICE DSU Technical Support Document 14: Undertaking survival analysis for economic evaluations alongside clinical trials - extrapolation with patient-level data. 2011. Available from http://www.nicedsu.org.uk

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. https://doi.org/10.1002/cncr.11234

National Institute for Health and Care Excellence (NICE). Developing NICE guidelines: the manual. 2024. Available from: www.nice.org.uk/process/pmg20

National Institute for Health and Care Excellence (NICE). Pembrolizumab for adjuvant treatment of renal cell carcinoma TA830. Available from: https://www.nice.org.uk/guidance/ta830

National Institute for Health and Care Excellence (NICE). Cabozantinib with nivolumab for untreated advanced renal cell carcinoma TA964. Available from: https://www.nice.org.uk/guidance/TA964

National Institute for Health and Care Excellence (NICE). British National Formulary (BNF). Available from: https://bnf.nice.org.uk/

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

Personal Social Services Research Unit. Unit Costs of Health and Social Care 2024. Published online 2024. Available from: https://www.pssru.ac.uk/unitcostsreport/

Rini, B., Goddard, A., Knezevic, D., Maddala, T., Zhou, M., Aydin, H., Campbell, S., Elson, P., Koscielny, S., Lopatin, M., Svedman, C., Martini, J. F., Williams, J. A., Verkarre, V., Radulescu, C., Neuzillet, Y., Hemmerlé, I., Timsit, M. O., Tsiatis, A. C., Bonham, M., … Escudier, B. (2015). A 16-gene assay to predict recurrence after surgery in localised renal cell carcinoma: development and validation studies. *The Lancet. Oncology*, *16*(6), 676–685. https://doi.org/10.1016/S1470-2045(15)70167-1

Rossi, S. H., Klatte, T., Usher-Smith, J. A., Fife, K., Welsh, S. J., Dabestani, S., Bex, A., Nicol, D., Nathan, P., Stewart, G. D., & Wilson, E. C. F. (2021). A Decision Analysis Evaluating Screening for Kidney Cancer Using Focused Renal Ultrasound. *European urology focus*, *7*(2), 407–419. https://doi.org/10.1016/j.euf.2019.09.002

Zisman A, Pantuck AJ, Dorey F, et al. (2001). Improved prognostication of renal cell carcinoma using an integrated staging system. J Clin Oncol 19(6):1649-57. https://doi.org/10.1200/JCO.2001.19.6.1649

1 Appendices

Appendix A: AIC and BIC values for survival analysis

Table HE019: AIC value for recurrence free survival in PC recurrence

Distribution	Risk			
	Overall	High	Intermediate	Low
Exponential	1101.57	312.50	424.69	364.38
Weibull	1102.53	311.23	426.64	365.97
Gamma	1102.91	311.80	426.67	366.07
Gompertz	1101.96	306.23	425.39	362.67
Log-logistic	1099.89	309.74	426.16	366.32
Log-normal	1094.38	305.82	422.83	369.39

Table HE020: BIC value for recurrence free survival in PC recurrence

Distribution	Risk			
	Overall	High	Intermediate	Low
Exponential	1117.00	315.81	428.76	368.82
Weibull	1123.10	317.85	434.79	374.86
Gamma	1123.48	318.42	434.82	374.95
Gompertz	1122.53	312.86	433.54	371.55
Log-logistic	1120.46	316.37	434.31	375.21
Log-normal	1114.96	312.44	430.97	378.27

Table HE021: AIC value for recurrence free survival in PI recurrence

Distribution	Risk			
	Overall	High	Intermediate	Low
Exponential	870.56	310.91	343.57	216.08
Weibull	857.17	293.53	343.93	218.04
Gamma	859.35	295.23	344.07	218.04
Gompertz	846.37	269.95	341.14	218.00
Log-logistic	853.13	291.23	343.62	218.04
Log-normal	841.24	285.42	341.08	218.41

Table HE022: BIC value for recurrence free survival in PI recurrence

Distribution	Risk			
	Overall	High	Intermediate	Low
Exponential	885.99	314.23	347.64	220.52
Weibull	877.74	300.16	352.08	226.92
Gamma	879.92	301.85	352.21	226.92
Gompertz	866.94	276.58	349.29	226.89
Log-logistic	873.70	297.85	351.77	226.93
Log-normal	861.81	292.05	349.23	227.30

Table HE023: AIC value for overall survival in PI recurrence by symptoms

Distribution	Overall	Symptomatic	Asymptomatic
Exponential	919.24	416.19	503.05
Weibull	920.70	413.83	503.02
Gamma	921.24	415.69	501.72
Gompertz	919.02	411.19	505.04
Log-logistic	906.28	407.15	498.25
Log-normal	899.50	403.35	495.22

Table HE024: BIC value for overall survival in PI recurrence by symptoms

Distribution	Overall	Symptomatic	Asymptomatic
Exponential	925.33	418.38	505.54
Weibull	929.83	418.21	508.00
Gamma	930.37	420.07	506.70
Gompertz	928.15	415.57	510.02
Log-logistic	915.41	411.53	503.22
Log-normal	908.63	407.73	500.20

Table HE025: AIC value for overall survival in PC recurrence by symptoms

Distribution	Overall	Symptomatic	Asymptomatic
Exponential	625.61	214.91	410.70
Weibull	624.96	216.28	402.20
Gamma	622.75	216.82	401.28
Gompertz	626.49	210.03	406.06
Log-logistic	614.12	210.53	401.57
Log-normal	610.83	208.98	400.10

Table HE026: BIC value for overall survival in PC recurrence by symptoms

Distribution	Overall	Symptomatic	Asymptomatic
Exponential	631.36	216.63	413.20
Weibull	633.59	219.70	407.20
Gamma	631.38	220.25	406.28
Gompertz	635.12	213.46	411.05
Log-logistic	622.74	213.96	406.57
Log-normal	619.45	212.41	405.10

Appendix B: Summary of parameters

Parameter	Point estimate	Probabilistic analysis		Source
		Distribution	Parameters	
Probability of detecting non-symptomatic recurrence detection in each risk group for different follow-up strategy				
Low CSI: low risk	50%	Beta	n=15, N=30	Dabestani 2019c, clinical review
Low CSI: Intermediate risk	62%	Beta	n=32, N=52	Dabestani 2019c, clinical review
Low CSI: high risk	68%	Beta	n=30, N=44	Dabestani 2019c, clinical review
High CSI: low risk	71%	Beta	n=25, N=35	Dabestani 2019c, clinical review
High CSI: Intermediate risk	71%	Beta	n=40, N=56	Dabestani 2019c, clinical review
High CSI: high risk	58%	Beta	n=69, N=119	Dabestani 2019c, clinical review
Low imaging frequency: low risk	53%	Beta	n=17, N=32	Dabestani 2019c, clinical review
Low imaging frequency: Intermediate risk	60%	Beta	n=32, N=53	Dabestani 2019c, clinical review
Low imaging frequency: high risk	60%	Beta	n=45, N=75	Dabestani 2019c, clinical review
High imaging frequency: low risk	70%	Beta	n=23, N=33	Dabestani 2019c, clinical review
High imaging frequency: Intermediate risk	77%	Beta	n=30, N=39	Dabestani 2019c, clinical review
High imaging frequency: high risk	64%	Beta	n=54, N=84	Dabestani 2019c, clinical review
Probability				
PC pts who experienced another recurrence after curative intervention	18%	Beta	n=24, N=131	Dabestani 2019a
Disease free to death	0	Normal	SE=0.000004	Lai 2023
Resource use				
Number of scans used in different risk groups				
Low imaging frequency: low risk	7.62	Gamma	SE=2.56	Dabestani 2019a (estimated from simulated values)
Low imaging frequency: Intermediate risk	6.87	Gamma	SE=2.64	Dabestani 2019a (estimated from simulated values)
Low imaging frequency: high risk	4.86	Gamma	SE=1.99	Dabestani 2019a (estimated from simulated values)
High imaging frequency: low risk	14.34	Gamma	SE=3.36	Dabestani 2019a (estimated from simulated values)
High imaging frequency: Intermediate risk	15.23	Gamma	SE=4.45	Dabestani 2019a (estimated from simulated values)
High imaging frequency: high risk	12.05	Gamma	SE=4.76	Dabestani 2019a (estimated from simulated values)

Parameter	Point estimate	Probabilistic analysis		Source
		Distribution	Parameters	
CSI: low risk	10.98	Gamma	SE=4.31	Dabestani 2019a
CSI: intermediate risk	11.09	Gamma	SE=5.46	Dabestani 2019a
CSI: high risk	8.41	Gamma	SE=4.70	Dabestani 2019a
Proportion of different imaging types in each risk group for comparison on imaging frequency				
Low risk: Thoracic CT	14.47%	Dirichlet	n=1300, N=8986	Dabestani 2019a
Low risk: Abdominal CT	27.21%	Dirichlet	n=2445, N=8986	Dabestani 2019a
Low risk: MRI	1.20%	Dirichlet	n=108, N=8986	Dabestani 2019a
Low risk: US	16.01%	Dirichlet	n=1439, N=8986	Dabestani 2019a
Low risk: Xray	41.11%	Dirichlet	n=3694, N=8986	Dabestani 2019a
Intermediate risk: Thoracic CT	17.10%	Dirichlet	n=951, N=5560	Dabestani 2019a
Intermediate risk: Abdominal CT	27.95%	Dirichlet	n=1554, N=5560	Dabestani 2019a
Intermediate risk: MRI	1.13%	Dirichlet	n=63, N=5560	Dabestani 2019a
Intermediate risk: US	16.56%	Dirichlet	n=921, N=5560	Dabestani 2019a
Intermediate risk: Xray	37.25%	Dirichlet	n=2071, N=5560	Dabestani 2019a
High risk: Thoracic CT	27.74%	Dirichlet	n=773, N=2787	Dabestani 2019a
High risk: Abdominal CT	33.37%	Dirichlet	n=930, N=2787	Dabestani 2019a
High risk: MRI	0.65%	Dirichlet	n=18, N=2787	Dabestani 2019a
High risk: US	10.44%	Dirichlet	n=291, N=2787	Dabestani 2019a
High risk: Xray	27.81%	Dirichlet	n=775, N=2787	Dabestani 2019a
Proportion of different imaging types in each risk group for comparison on low CSI				
Low risk: Thoracic CT	9.32%	Dirichlet	n=607, N=6514	Dabestani 2019a (estimated from simulated values)
Low risk: Abdominal CT	24.18%	Dirichlet	n=1575, N=6514	Dabestani 2019a (estimated from simulated values)
Low risk: MRI	1.04%	Dirichlet	n=68, N=6514	Dabestani 2019a (estimated from simulated values)
Low risk: US	17.94%	Dirichlet	n=1169, N=6514	Dabestani 2019a (estimated from simulated values)
Low risk: Xray	47.52%	Dirichlet	n=3095, N=6514	Dabestani 2019a (estimated from simulated values)
Intermediate risk: Thoracic CT	10.25%	Dirichlet	n=488,	Dabestani 2019a (estimated from simulated values)

Parameter	Point estimate	Probabilistic analysis		Source
		Distribution	Parameters	
			N=4781	
Intermediate risk: Abdominal CT	21.30%	Dirichlet	n=1015, N=4781	Dabestani 2019a (estimated from simulated values)
Intermediate risk: MRI	0.77%	Dirichlet	n=37, N=4781	Dabestani 2019a (estimated from simulated values)
Intermediate risk: US	19.99%	Dirichlet	n=957, N=4781	Dabestani 2019a (estimated from simulated values)
Intermediate risk: Xray	47.69%	Dirichlet	n=2284, N=4781	Dabestani 2019a (estimated from simulated values)
High risk: Thoracic CT	16.60%	Dirichlet	n=281, N=1708	Dabestani 2019a (estimated from simulated values)
High risk: Abdominal CT	16.05%	Dirichlet	n=272, N=1708	Dabestani 2019a (estimated from simulated values)
High risk: MRI	0.37%	Dirichlet	n=6, N=1708	Dabestani 2019a (estimated from simulated values)
High risk: US	17.12%	Dirichlet	n=294, N=1708	Dabestani 2019a (estimated from simulated values)
High risk: Xray	49.87%	Dirichlet	n=855, N=1708	Dabestani 2019a (estimated from simulated values)
Proportion of different imaging types in each risk group for comparison on high CSI				
Low risk: Thoracic CT	17.33%	Dirichlet	n=1128, N=6514	Dabestani 2019a (estimated from simulated values)
Low risk: Abdominal CT	44.95%	Dirichlet	n=2926, N=6514	Dabestani 2019a (estimated from simulated values)
Low risk: MRI	1.93%	Dirichlet	n=126, N=6514	Dabestani 2019a (estimated from simulated values)
Low risk: US	9.81%	Dirichlet	n=640, N=6514	Dabestani 2019a (estimated from simulated values)
Low risk: Xray	25.98%	Dirichlet	n=1694, N=6514	Dabestani 2019a (estimated from simulated values)
Intermediate risk: Thoracic CT	22.20%	Dirichlet	n=1071, N=4781	Dabestani 2019a (estimated from simulated values)
Intermediate risk: Abdominal CT	46.13%	Dirichlet	n=2226, N=4781	Dabestani 2019a (estimated from simulated values)
Intermediate risk: MRI	1.67%	Dirichlet	n=81, N=4781	Dabestani 2019a (estimated from simulated values)
Intermediate risk: US	8.86%	Dirichlet	n=415, N=4781	Dabestani 2019a (estimated from simulated values)
Intermediate risk: Xray	21.14%	Dirichlet	n=989, N=4781	Dabestani 2019a (estimated from simulated values)
High risk: Thoracic CT	42.79%	Dirichlet	n=727, N=1708	Dabestani 2019a (estimated from simulated values)
High risk: Abdominal CT	41.37%	Dirichlet	n=703, N=1708	Dabestani 2019a (estimated from simulated values)
High risk: MRI	0.94%	Dirichlet	n=16, N=1708	Dabestani 2019a (estimated from simulated values)

Parameter	Point estimate	Probabilistic analysis		Source
		Distribution	Parameters	
High risk: US	3.81%	Dirichlet	n=67, N=1708	Dabestani 2019a (estimated from simulated values)
High risk: Xray	11.08%	Dirichlet	n=194, N=1708	Dabestani 2019a (estimated from simulated values)
Proportion of different interventions for the management of recurrence				
Probably incurable: metastasectomy	6%	Dirichlet	n=9, N=155	Dabestani 2019a
Probably incurable: palliative	70%	Dirichlet	n=108, N=155	Dabestani 2019a
Probably incurable: observation	25%	Dirichlet	n=38, N=155	Dabestani 2019a
Potentially curable: receive curative intent treatment	53%	Dirichlet	n=70, N=131	Dabestani 2019a
Potentially curable: receive non-curative treatment	47%	Dirichlet	n=61, N=131	Dabestani 2019a
Potentially curable: metastasectomy as curative intent treatment	89%	Dirichlet	n=62, N=70	Dabestani 2019a
Potentially curable: radiotherapy i.e. SABR as curative intent treatment	7%	Dirichlet	n=5, N=70	Dabestani 2019a
Potentially curable: ablative therapy as curative intent treatment	4%	Dirichlet	n=3, N=70	Dabestani 2019a
Potentially curable: palliative as noncurative treatment	64%	Dirichlet	n=39, N=61	Dabestani 2019a
Potentially curable: observation as noncurative treatment	36%	Dirichlet	n=22, N=61	Dabestani 2019a
Proportion of different ablation types, for people receiving ablation				
Radiofrequency ablation	20%	Dirichlet	n=20, N=100	Rossi 2021
Cryoablation	60%	Dirichlet	n=60, N=100	Rossi 2021
Microwave ablation	20%	Dirichlet	n=20, N=100	Rossi 2021
Costs				
Single CT chest abdomen and pelvis scan	123.03	Gamma	LCI=98.42, UCI=147.63	NHS Cost Collection (2024). RD26z Computerised Tomography Scan of Three areas with contrast

Parameter	Point estimate	Probabilistic analysis		Source
		Distribution	Parameters	
Single MRI scan	202.40	Gamma	LCI=161.92, UCI=242.88	NHS Cost Collection (2024). RD05z Magnetic Resonance Imaging Scan of Two or Three areas with contrast
Single ultrasound scan	53.32	Gamma	LCI=42.66, UCI=63.99	NHS Cost Collection (2024). RD41z Ultrasound Scan with duration of less than 20 minutes with contrast
Single plain film x-ray	101.10	Gamma	LCI=80.88, UCI=121.32	NHS Cost Collection (2024). IMAGCDC_PF community diagnostic centres plain film
Single biopsy	298.42	Gamma	LCI=238.73 UCI=358.10	NHS Cost Collection (2024). Percutaneous needle biopsy of lesion of kidney 19 years and over outpatient
CT preparation for SABR therapy	1770.46	Gamma	LCI=1416.37, UCI=2124.55	NHS Cost Collection (2024). SC41z preparation for intensity modulated radiation therapy with technical support
One fraction of SABR	239.83	Gamma	LCI=191.86, UCI=287.79	NHS Cost Collection (2024). SC22z deliver a fraction of treatment on a megavoltage machine
Systemic therapies after recurrence	84509.85	Gamma	LCI=67607.88, UCI=101411.82	Calculated from RCC pathway model (TA964)
Radiofrequency ablation	1960.46	Gamma	LCI=1568.37, UCI=2352.55	NHS Cost Collection (2024). YL02z Standard Percutaneous Ablation of Lesion of Kidney
Cryoablation	3474.14	Gamma	LCI=2779.31, UCI=4168.97	NHS Cost Collection (2024). YL01z Complex Percutaneous Ablation of Lesion of Kidney
Microwave ablation	1960.46	Gamma	LCI=1568.37 UCI=2352.55	NHS Cost Collection (2024). YL02z Standard Percutaneous Ablation of Lesion of Kidney
Medical oncology appointment	193.39	Gamma	LCI=154.71, UCI=232.07	NHS Cost Collection (2024). Summary OP attendances 370 medical oncology
Clinical oncology appointment	159.94	Gamma	LCI=127.95, UCI=191.92	NHS Cost Collection (2024). Summary OP attendances 800 clinical oncology
Palliative radiotherapy for management of recurrence	311.34	Gamma	LCI=249.07, UCI=373.61	NHS Cost Collection (2024). SC31Z fraction of adaptive radiotherapy on a megavoltage machine total
Consultant outpatient follow up	157.05	Gamma	LCI=125.64, UCI=188.46	NHS Cost Collection (2024). WF01A 800 Consultant led clinical oncology service
Specialist nurse visit as BSC	62.00	Gamma	LCI=49.60, UCI=74.40	PSSRU (2024). Section 11.2.2 Nurse specialist Band 6 cost per working hour (including qualifications)
Pain medication as BSC per month	159.49	Gamma	LCI=127.59, UCI=191.39	BNF 1mg/1ml vial of morphine sulphate solution for infusion 5.24 per vial, 1mg/ml daily
Full blood count for disease free	3.10	Gamma	LCI=2.48, UCI=3.71	NHS Cost Collection (2024). DAPS PATH05 haematology, total

Parameter	Point estimate	Probabilistic analysis		Source
		Distribution	Parameters	
Metastasectomy type 1	6473.07	Gamma	LCI=5178.46, UCI=7767.69	NHS Cost Collection (2024). LB06J Kidney urinary tract or prostate neoplasms with interventions CC score 6-8
Metastasectomy type 2	4865.59	Gamma	LCI=3892.47, UCI=5838.71	NHS Cost Collection (2024). LB06K Kidney urinary tract or prostate neoplasms with interventions CC score 4-5
Metastasectomy type 3	5228.32	Gamma	LCI=4182.65, UCI=6273.98	NHS Cost Collection (2024). LB06L Kidney urinary tract or prostate neoplasms with interventions CC score 2-3
Metastasectomy type 4	5013.96	Gamma	LCI=4011.17, UCI=6016.75	NHS Cost Collection (2024). LB06M Kidney urinary tract or prostate neoplasms with interventions CC score 0-1
Metastasectomy type 5	6774.33	Gamma	LCI=5419.47, UCI=8129.20	NHS Cost Collection (2024). DZ17P Respiratory neoplasms with single intervention CC score 10+
Metastasectomy type 6	4825.92	Gamma	LCI=3860.73, UCI=5791.10	NHS Cost Collection (2024). DZ17Q Respiratory neoplasms with single intervention CC score 6-9
Metastasectomy type 7	4160.46	Gamma	LCI=3328.37, UCI=4992.55	NHS Cost Collection (2024). DZ17R Respiratory neoplasms with single intervention CC score 0-5
Utility				
Disease free	0.868	Beta	SE=0.005	TA830 adjuvant pembrolizumab
BSC or observation (symptomatic)	0.482	Beta	SE=0.005	TA964 RCC pathways model
SACT	0.603	Beta	LCI=0.48, UCI=0.72	TA964 RCC pathways model
Disutility				
Ablation	0.02	Beta	LCI=0, UCI=0.03	TA830 adjuvant pembrolizumab
Metastasectomy	0.02	Beta	LCI=0, UCI=0.03	Assumed equivalent to ablation
Radiotherapy	0.02	Beta	LCI=0, UCI=0.03	Assumed equivalent to ablation
BSC or observation (asymptomatic)	0.01	Beta	LCI=0, UCI=0.03	Florea et al. 2024, assume symptoms develop after 14.9 months (Rini 2016)
Other				
Discount rate for costs	3.5%	NA	NA	NICE reference case
Discount rate for QALYs	3.5%	NA	NA	NICE reference case
Number of observation visits	0.25	NA	NA	Committee assumption
Proportion of BSC requiring palliative radiotherapy	12.36%	Beta	n=137, N=1108	Rossi 2021

Parameter	Point estimate	Probabilistic analysis		Source
		Distribution	Parameters	
Frequency of consultant follow up as BSC is once every 4 weeks	1	NA	NA	TA964 RCC pathways model
Frequency of specialist nurse follow up as BSC is once every 4 weeks	1	NA	NA	TA964 RCC pathways model
Proportion of individuals who get pain medication as BSC	1	NA	NA	Assumption
Proportion of pts who get BSC for the management of recurrences	25%	Dirichlet	n=25, N=100	Assumption
Proportion of pts who get SACT for the management of recurrences	75%	Dirichlet	n=75, N=100	Assumption
Frequency of full blood count _ once every 6 months	0.17	NA	NA	TA830 adjuvant pembrolizumab
Time asymptomatic before getting symptoms (in months) for probably incurable	14.9	Gamma	LCI=10.6, UCI=25	Rini 2016
Time asymptomatic before getting symptoms (in months) for probably curable	14.9	Gamma	LCI=10.6, UCI=25	Rini 2016

Abbreviations: n, number of events; N, total number of events; SE, standard error; NA, not applicable; LCI, lower bound of 95% confidence interval; UCI, upper bound of 95% confidence interval

1