National Institute for Health and Care Excellence

DIAGNOSTICS ASSESSMENT PROGRAMME

Evidence overview

Point-of-care creatinine tests to assess kidney function before CT imaging with intravenous contrast

This overview summarises the key issues for the diagnostics advisory committee's consideration. This document is intended to be read with NICE's final scope for the assessment and the diagnostics assessment report. A glossary of terms is in appendix B.

1 Background

1.1 Introduction

The purpose of this assessment is to evaluate the clinical and cost effectiveness of point-of-care (POC) creatinine tests to assess kidney function. These tests are for people who need non-emergency contrast-enhanced CT imaging and who do not have a recent serum creatinine measurement.

Intravenous iodine-based contrast agents used in CT imaging can cause acute kidney injury (AKI), particularly in people who are at high risk and those with known kidney dysfunction. Measuring creatinine levels can show whether the kidneys are working properly, and if there is a risk of kidney injury from using contrast agents. If patients do not have a recent creatinine measurement, their imaging could be delayed while a test is processed in the laboratory, or it may be cancelled and rescheduled.

If the person is thought to be at low risk of kidney injury, they might be given the contrast agent, risking kidney injury. Sometimes, to avoid the risk of

kidney injury, people may have unenhanced imaging, which is less accurate than contrast-enhanced imaging. This can negatively affect clinical decisions about treatment and could mean further tests are needed to confirm a diagnosis.

POC creatinine tests allow rapid measurement of creatinine levels, which can be used to calculate the estimated glomerular filtration rate (eGFR). Creatinine and eGFR can show if the kidneys are working properly. Using them in outpatient appointments in the radiology department could reduce the incidence of delayed or cancelled scans, minimise the risk of kidney injury and improve patients' experiences. Provisional recommendations on these technologies will be made by the diagnostics advisory committee at the committee meeting on 22 May 2019.

1.2 Scope of the assessment

Table 1 Scope of the assessment

Decision question	Does point-of-care creatinine testing before outpatient CT imaging with intravenous contrast represent a clinically- and cost-effective use of NHS resources?
Populations	Adults who need non-emergency intravenous contrast for a CT scan done in an outpatient appointment and who do not have a recent* creatinine measurement. When data allow, the following subgroups may be considered: • people with known existing kidney disease • people at high risk of acute kidney injury (AKI). *Recent is defined as within 3 months for people who have a low risk of kidney injury, and within 7 days for people with cardiorenal syndrome, an acute disease or an acute deterioration of a chronic disease.
Interventions	• Nova StatSensor (Nova Biomedical) • i-STAT Alinity (Abbott) • ABL90 FLEX PLUS (Radiometer) • ABL800 FLEX (Radiometer) • epoc Blood Analysis System (Siemens Healthineers) • Piccolo Xpress (Abaxis) • Dri-chem NX500 (Fujifilm)
Comparators	1. Non-urgent laboratory-based serum creatinine measurement: (a) Jaffe method; (b) enzymatic method. 2. Urgent laboratory-based serum creatinine measurement: (a) Jaffe method; (b) enzymatic method. 3. No testing, clinical judgement alone.

Healthcare setting	Secondary care (radiology department).
Outcomes	Intermediate measures for consideration may include: • diagnostic accuracy of point-of-care (POC) creatinine tests compared with laboratory-based creatinine tests (based on either creatinine or estimated glomerular filtration rate [eGFR]) • agreement between POC creatinine tests and laboratory-based creatinine tests (based on either creatinine or eGFR) • test failure rates • number of delayed, or cancelled and rescheduled scans • volume of intravenous contrast material used • number of unenhanced scans • number of hospital admissions • hospital length of stay.
	Clinical outcomes for consideration may include: • AKI (either post-contrast or contrast-induced) • fall in baseline eGFR or rise in baseline creatinine • temporary renal replacement therapy • new onset chronic kidney disease of stage 3 or worse • end-stage renal disease with the need for renal replacement therapy • mortality.
	Patient-reported outcomes for consideration may include: • health-related quality of life.
	Costs will be considered from an NHS and personal social services perspective. Costs for consideration may include: • costs of testing • set up and support costs for POC testing • staff time and training • phlebotomy appointments for blood sampling • cost of imaging and associated costs (such as contrast agents, intravenous hydration) • cost of follow-up imaging or other testing • cost of cancelled or delayed CT scans • costs associated with treating kidney disease • cost associated with treating the underlying clinical condition.
	The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.

Time horizon	The time horizon for estimating clinical and cost effectiveness should be long enough to reflect any differences in costs or outcomes between the technologies being compared.

Further details including descriptions of the interventions, comparators, care pathway and outcomes can be found in the final scope.

2 The evidence

This section summarises data from the diagnostics assessment report compiled by the external assessment group (EAG).

2.1 Clinical effectiveness

The EAG systematically reviewed:

- studies that compared the results of point-of-care (POC) creatinine tests with laboratory-based tests to assess kidney function in any non-emergency setting
- studies that reported clinical or implementation outcomes of POC creatinine tests to assess kidney function before CT imaging in a non-emergency, outpatient setting.

Details of the methodology used start on page 27 of the diagnostics assessment report.

The NICE scope was restricted to POC creatinine devices that report estimated glomerular filtration rate (eGFR). However, to maximise the relevant evidence in the review of test accuracy, studies on older versions of the devices that do not report eGFR were identified. These studies were included when clinical and technical advice suggested that the device was sufficiently similar to the version of the device in the scope (table 2). For studies reporting clinical or implementation outcomes, any POC creatinine device used in a radiology or imaging department setting was eligible.

Table 2 POC devices eligible for the test accuracy systematic review

Manufacturer and devices	Device format	Parameters measured	Sample volume	Analysis time	eGFR equation used
Nova Biomedical StatSensor	Handheld	Creatinine only	1.2 microlitres	30 seconds	MDRD, Cockcroft-Gault, Schwartz and Counahan-Barratt
Related models: StatSensor-i, StatSensor Xpress-i. All models allow offset adjustment of results; StatSensor and StatSensor-i also allow slope adjustment.					
Abbott i-STAT Alinity	Handheld	Multiple parameters	65 microlitres	2 minutes	MDRD
Related models: iSTAT 1, many studies simply state “iSTAT”.					
Radiometer ABL90 FLEX PLUS	Portable	19 parameters	65 microlitres	35 seconds	CKD-EPI, MDRD and Schwartz
ABL800 FLEX	Table-top	18 parameters	125 to 250 microlitres	1 minute	CKD-EPI and MDRD
Related models: ABL 827, ABL 837.					
Siemens Healthineers Epoc Blood Analysis System	Handheld	11 parameters on one test card	92 microlitres	Less than 1 minute	CKD-EPI, MDRD and Schwartz
Abaxis Piccolo Xpress	Table-top	Multiple parameters	100 microlitres	Less than 14 minutes	MDRD
Fujifilm Dri-chem NX500	Table-top	Multiple parameters	1 microlitres	5 minutes	Expected
Abbreviations: CKD-EPI, chronic kidney disease epidemiology; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease.					

There were 54 studies in the review. Of those, 12 studies reported diagnostic accuracy data for eGFR, 7 studies reported diagnostic accuracy data for serum creatinine, 50 studies presented data on correlation or measurement bias between a POC device and a laboratory reference test, and 6 studies reported data on workflow or clinical outcomes. Results of the systematic review start on page 34 of the diagnostics assessment report.

The quality of studies reporting diagnostic accuracy data for eGFR measurements was assessed using the modified QUADAS-2 tool. The quality of other studies in the review was not assessed formally because these studies were not directly used in the quantitative synthesis or economic analyses.

Studies reporting measurement bias or correlation outcomes in relation to creatinine or eGFR

There were 50 studies including data on correlation or bias between a POC device and a laboratory reference test. Overall, results from the StatSensor studies showed wide variation in the size and direction of measurement bias. StatSensor devices can be adjusted to correct for any bias seen, to align the POC device results with those from local laboratory methods. Only 2 StatSensor studies reported using an offset adjustment for measurement bias. Although potentially important measurement bias was found in some studies of i-STAT and ABL devices, the concordance of results for these devices was generally better than for the StatSensor devices. Few studies were available on the epoc and Piccolo Xpress devices.

There were 3 studies identified that compared different types of POC creatinine devices. Of these, 2 studies compared StatSensor, i-STAT and ABL800 FLEX devices. Both studies found that the ABL800 FLEX had the strongest agreement with laboratory serum creatinine, followed by the i-STAT and then StatSensor. There was 1 study comparing an ABL827 device with an i-STAT. It concluded that creatinine results from both devices correlated well with laboratory serum creatinine.

In some studies, the EAG noted that measurement bias increased at higher creatinine levels. This might have implications for care decisions made about people at higher risk of kidney damage. Details on the result of studies reporting measurement bias or correlation outcomes can be found starting on page 37 of the diagnostics assessment report.

Studies reporting diagnostic accuracy based on serum creatinine thresholds

Of the studies reviewed, 7 reported diagnostic accuracy data relating to creatinine thresholds. All were of StatSensor POC devices and most used a Jaffe method for the laboratory reference standard. Most of the studies showed overestimation of creatinine by StatSensor, but 1 study reported that some StatSensor devices might underestimate creatinine. Details on the results of studies reporting diagnostic accuracy based on serum creatinine thresholds start on page 50 of the diagnostics assessment report.

Studies reporting diagnostic accuracy based on eGFR thresholds

There were 12 studies reporting diagnostic accuracy data relating to eGFR thresholds; 9 published papers and 3 conference abstracts. Sample sizes ranged from 50 to 2,042 patients. Studies were of different devices, with some studies assessing more than 1 device. There were 7 studies that looked at iSTAT; 7 studies assessed a StatSensor device; 3 included a Radiometer POC device (ABL8009 or ABL827), 2 studies assessed 3 POC devices (ABL, iSTAT and StatSensor) and 1 study looked at 2 devices (ABL and iSTAT). There were no studies of ABL90 FLEX PLUS, Dri-chem NX500, epoc Blood Analysis System and Piccolo Xpress. The eGFR equations used in the studies varied, with only 3 studies using CKD-EPI.

All but 1 blood sample types used in StatSensor studies were capillary, however, most iSTAT studies used venous samples. None of the studies compared the accuracy of a single device using 2 different sample types. There were 3 StatSensor and 2 iSTAT studies that used an adjustment function to correct for any measurement bias seen between the POC test results and laboratory test results derived from the study sample. Adjusted and unadjusted results were reported in all 3 StatSensor studies, but only adjusted results were presented in the 2 iSTAT studies. Most studies used an enzymatic method as the laboratory reference, but the Jaffe method was used in 2 studies and the reference method was not reported in 1 study. Details on

the results of studies reporting diagnostic accuracy based on eGFR thresholds start on page 53 of the diagnostics assessment report.

Risk of bias assessment

There were 6 studies at low risk across all risk of bias areas, including 2 studies of ABL800, 3 studies of i-STAT and 3 studies of StatSensor. The other 6 studies had at least 1 domain at unclear or high risk of bias. Risks of bias related to how the adjustment function to correct for measurement bias was applied; patient selection; the use of different modification of diet in renal disease (MDRD) eGFR equations between the POC test and laboratory reference test; and the use of a Jaffe method for the laboratory reference test (compared with an enzymatic method for the POC test).

Only 2 studies had low concerns about the applicability of results across all domains, including 1 study of ABL800, i-STAT and StatSensor, and 1 study of i-STAT. The most common applicability concern was the use of eGFR threshold; 3 studies used an eGFR cut-off of 60 ml/min/1.73 m^2 or above. Several studies included disease-specific populations, therefore their applicability to a broader population of outpatients referred for CT without a recent eGFR may be limited.

Overall, 2 studies were at low risk of bias and had low applicability concerns across all domains assessed. These were 1 study that evaluated ABL800, i-STAT and StatSensor (Snaith et al. 2018) and 1 of i-STAT only (Snaith et al. 2019). Details on the risk of bias assessment can be found starting on page 35 of the diagnostics assessment report.

Quantitative analysis

Probability of being in each eGFR category

The probabilities of being in each eGFR category were calculated from the number of people in each category reported by all included studies (that is, regardless of the device assessed). The pooled probabilities of being in each

of the 4 categories are in table 3. Most studies only included a few people in category 1 (eGFR less than 30 ml/min/1.73 m^2) and more people in higher eGFR categories. However, Shephard et al. 2010 included mostly patients with renal conditions who therefore had a higher probability of being in category 1 than other studies (33% compared with 0 to 4%). Excluding this study slightly reduced the pooled probability of being in category 1.

Table 3 Estimated probabilities of being in each eGFR category

Category	eGFR (ml/min/1.73 m^2)	All data		Shephard 2010 removed	
		Median	95%CrI	Median	95%CrI
1	0 to 29	0.014	(0.011, 0.017)	0.009	(0.007, 0.012)
2	30 to 44	0.051	(0.039, 0.064)	0.051	(0.039, 0.064)
3	45 to 59	0.143	(0.127, 0.159)	0.143	(0.127, 0.159)
4	60 or higher	0.792	(0.780, 0.803)	0.797	(0.785, 0.808)
Abbreviation: CrI, credible interval					

Probability of classification by POC device in each laboratory-defined eGFR category (main analysis)

There were 7 studies with data for the analysis of StatSensor devices, 5 studies provided data for the analysis of iSTAT devices and 3 studies provided data for the analysis of ABL devices. The pooled probabilities of having a classification by a POC device in each eGFR category (*k*) and in each laboratory-defined eGFR category (*j*), are given in table 4. The iSTAT and ABL devices have higher median probabilities of correct classification in each of the 3 lowest categories (p[1,1], p[2,2], p[3,3]) compared with the StatSensor. StatSensor was particularly poor at correctly classifying category 3 (eGFR 45 to 59 ml/min/1.73 m^2). However, there is considerable uncertainty in these probabilities for all devices.

Table 4 Estimated probabilities of being classified in each eGFR category by POC device (main analysis)

p[j,k]	StatSensor		iStat		ABL (Radiometer)	
	Median	95%CrI	Median	95%CrI	Median	95%CrI
p[1,1]	0.74	(0.61, 0.85)	0.85	(0.69, 0.94)	0.87	(0.75, 0.95)
p[1,2]	0.18	(0.08, 0.30)	0.04	(0.00, 0.18)	0.03	(0.00, 0.14)
p[1,3]	0.03	(0.00, 0.12)	0.04	(0.00, 0.18)	0.03	(0.00, 0.14)
p[1,4]	0.04	(0.01, 0.11)	0.04	(0.00, 0.16)	0.04	(0.00, 0.15)
p[2,1]	0.09	(0.03, 0.19)	0.10	(0.04, 0.21)	0.02	(0.00, 0.11)
p[2,2]	0.57	(0.42, 0.71)	0.77	(0.64, 0.87)	0.78	(0.61, 0.90)
p[2,3]	0.22	(0.12, 0.36)	0.10	(0.04, 0.21)	0.15	(0.05, 0.29)
p[2,4]	0.10	(0.03, 0.24)	0.01	(0.00, 0.06)	0.03	(0.00, 0.15)
p[3,1]	0.01	(0.00, 0.03)	0.01	(0.00, 0.05)	0.02	(0.00, 0.08)
p[3,2]	0.14	(0.09, 0.20)	0.10	(0.04, 0.17)	0.06	(0.01, 0.16)
p[3,3]	0.25	(0.16, 0.34)	0.81	(0.72, 0.88)	0.74	(0.62, 0.85)
p[3,4]	0.60	(0.51, 0.69)	0.08	(0.04, 0.13)	0.17	(0.09, 0.26)
p[4,1]	0.00	(0.00, 0.01)	0.00	(0.00, 0.01)	0.00	(0.00, 0.01)
p[4,2]	0.00	(0.00, 0.01)	0.01	(0.00, 0.02)	0.00	(0.00, 0.01)
p[4,3]	0.06	(0.04, 0.08)	0.08	(0.06, 0.10)	0.01	(0.00, 0.01)
p[4,4]	0.94	(0.91, 0.95)	0.91	(0.89, 0.93)	0.99	(0.98, 0.99)

eGFR categories (ml/min/1.73 m^2): 1 = 0 to 29; 2 = 30 to 44, 3 = 45 to 59; 4 = 60 or higher.
Abbreviations: CrI, credible interval.

Probability of classification by POC device in each laboratory-defined eGFR category (additional analyses)

The EAG did 2 additional analyses to assess the effect of removing studies with limited applicability to clinical practice in the NHS.

- StatSensor devices allow a user-specified adjustment if systematic measurement bias is identified. An additional analysis including the adjusted data reported by Korpi-Steiner et al. 2009 and Shephard et al. 2010 was done. The Inoue et al. 2017 study was not included in this analysis because the reported adjustment could not be replicated in NHS practice. Results are presented in table 5.

- Only 2 studies used the CKD-EPI equation to calculate eGFR, all others used the MDRD equation. Of these studies, 1 included StatSensor, iSTAT and ABL800 FLEX devices (Snaith et al. 2018) and the other only included the iSTAT device (Snaith et al. 2019). An additional analysis using only the data in these 2 studies was done. Results are presented in table 6.

Table 5 Estimated probabilities of being classified in each eGFR category by POC device (including adjusted data from Korpi-Steiner 2009 and Shephard 2010)

p[j,k]	StatSensor	
	Median	**95%CrI**
p[1,1]	0.84	(0.73, 0.93)
p[1,2]	0.11	(0.04, 0.22)
p[1,3]	0.02	(0.00, 0.08)
p[1,4]	0.01	(0.00, 0.08)
p[2,1]	0.11	(0.04, 0.22)
p[2,2]	0.51	(0.35, 0.67)
p[2,3]	0.28	(0.15, 0.44)
p[2,4]	0.09	(0.02, 0.22)
p[3,1]	0.01	(0.00, 0.04)
p[3,2]	0.12	(0.06, 0.20)
p[3,3]	0.49	(0.37, 0.60)
p[3,4]	0.38	(0.28, 0.49)
p[4,1]	0.00	(0.00, 0.01)
p[4,2]	0.00	(0.00, 0.01)
p[4,3]	0.12	(0.09, 0.14)
p[4,4]	0.88	(0.85, 0.90)

eGFR categories (ml/min/1.73 m^2): 1 = 0 to 29;
2 = 30 to 44, 3 = 45 to 59; 4 = 60 or higher.
Abbreviations: CrI, credible interval.

For StatSensor, there is good overlap in the first 2 categories, but the adjusted analysis gives a higher probability of correct classification as being at risk of post-contrast acute kidney injury (PC-AKI; sensitivity) than in the main analysis. However, the results from the main analysis and the adjusted data

analysis for categories 3 and 4 are conflicting. The main analysis suggests a lower probability of correctly classifying category 3 than the adjusted data analysis, but a higher probability of correctly classifying category 4.

Table 6 Estimated probabilities of being classified in each eGFR category by POC device (only including data from studies using the CKD-EPI equation)

p[j,k]	StatSensor		iSTAT		ABL800 FLEX (Radiometer)	
	median	95%CrI	median	95%CrI	median	95%CrI
p[1,1]	0.56	(0.32, 0.79)	0.83	(0.60, 0.96)	0.83	(0.60, 0.96)
p[1,2]	0.31	(0.12, 0.55)	0.05	(0.00, 0.22)	0.05	(0.00, 0.22)
p[1,3]	0.05	(0.00, 0.22)	0.05	(0.00, 0.22)	0.04	(0.00, 0.22)
p[1,4]	0.05	(0.00, 0.22)	0.05	(0.00, 0.22)	0.05	(0.00, 0.22)
p[2,1]	0.12	(0.04, 0.26)	0.10	(0.04, 0.21)	0.02	(0.00, 0.11)
p[2,2]	0.56	(0.39, 0.73)	0.76	(0.63, 0.87)	0.79	(0.63, 0.90)
p[2,3]	0.28	(0.14, 0.45)	0.10	(0.04, 0.21)	0.15	(0.05, 0.30)
p[2,4]	0.02	(0.00, 0.11)	0.02	(0.00, 0.08)	0.02	(0.00, 0.11)
p[3,1]	0.02	(0.00, 0.09)	0.01	(0.00, 0.04)	0.02	(0.00, 0.09)
p[3,2]	0.28	(0.15, 0.43)	0.09	(0.04, 0.17)	0.07	(0.02, 0.18)
p[3,3]	0.46	(0.31, 0.62)	0.79	(0.69, 0.86)	0.83	(0.69, 0.92)
p[3,4]	0.23	(0.11, 0.37)	0.11	(0.05, 0.18)	0.07	(0.02, 0.18)
p[4,1]	0.00	(0.00, 0.02)	0.00	(0.00, 0.01)	0.00	(0.00, 0.02)
p[4,2]	0.01	(0.00, 0.02)	0.01	(0.00, 0.02)	0.00	(0.00, 0.02)
p[4,3]	0.15	(0.11, 0.20)	0.05	(0.03, 0.07)	0.01	(0.00, 0.02)
p[4,4]	0.84	(0.79, 0.88)	0.95	(0.92, 0.96)	0.98	(0.96, 1.00)

eGFR categories (ml/min/1.73 m^2): 1 = 0 to 29; 2 = 30 to 44, 3 = 45 to 59; 4 = 60 or higher.
Abbreviations: CrI, credible interval.

Density strip figures showing the results are on pages 77 to 78 of the diagnostics assessment report. For StatSensor devices, the CKD-EPI analysis results broadly agree with the adjusted data analysis. However, the uncertainty in the probabilities for category 1 (eGFR less than 30 ml/min/1.73 m^2) is larger in the CKD-EPI analysis because only 1 study with a few people is included in this category. For both iSTAT and ABL devices, there is good overlap between the main analyses and the analyses of

CKD-EPI studies in all eGFR categories, with the main analysis producing slightly more precise results.

Studies reporting clinical, workflow or implementation outcomes

Details of studies reporting clinical, workflow or implementation outcomes start on page 80 of the diagnostics assessment report. There were 6 studies that reported a relevant outcome after the use of a POC device; patient sample sizes ranged from 113 to 3,087. Of these, 1 study was a survey of staff at 68 NHS trust sites. The results showed variation in practice in terms of both the proportions of patients who do not have a recent eGFR result and in the management decisions taken when a POC device shows an abnormal eGFR. For example, the proportion of people given scans with or without contrast, or given a reduced dose of contrast. In addition, many of the studies were done several years ago so the value of their results is limited because eGFR thresholds for defining an abnormal result have decreased over time. No data were available on clinical outcomes such as need for renal replacement therapy or hospital admissions.

2.2 Costs and cost effectiveness

The EAG identified existing studies investigating the cost effectiveness of POC creatinine tests in an outpatient non-emergency secondary care setting, to assess kidney function before contrast-enhanced CT imaging. Because only a single cost-consequence analysis was found, the EAG also constructed a de novo economic model to assess the cost effectiveness of POC creatinine tests.

Systematic review of cost-effectiveness evidence

The EAG did a systematic review to find published economic evaluations of POC creatinine tests in an outpatient non-emergency secondary care setting to assess kidney function before contrast-enhanced CT imaging. Full details of the review start on page 103 of the diagnostics assessment report. No studies were identified that met the inclusion criteria. However, a relevant

unpublished economic study was identified by a clinical expert and the EAG was given an academic-in-confidence draft version of the manuscript (Shinkins et al.).

The aim of the study was to assess [redacted]. Although the focus of the study was on the [redacted] other outcomes related to [redacted] were also reported. The study used an [redacted] and costs were reported [redacted]. The study [redacted]

[redacted]

[redacted]

The EAG noted that the findings from Shinkins [redacted]. However, the EAG also noted that:

- [redacted]

Economic analysis

The EAG developed a de novo economic model designed to assess the cost effectiveness of POC testing used to check kidney function before contrast-enhanced imaging. The model assesses a cohort of outpatients presenting for a non-emergency contrast-enhanced CT scan without a recent eGFR measurement.

Costs are presented from the perspective of the NHS and personal social services (NHS and PSS) and are reported in UK pounds at a 2018 price base. Outcomes past the first year are discounted at a rate of 3.5% per year. Most costs happen in the first year and are therefore not discounted. However, a discount rate of 3.5% is applied when calculating annual costs relating to the capital costs of the POC devices over the lifetime of the device.

Model structure

The model uses a decision tree cohort approach to estimate the costs and health outcomes of the different testing and treatment strategies. The model captures:

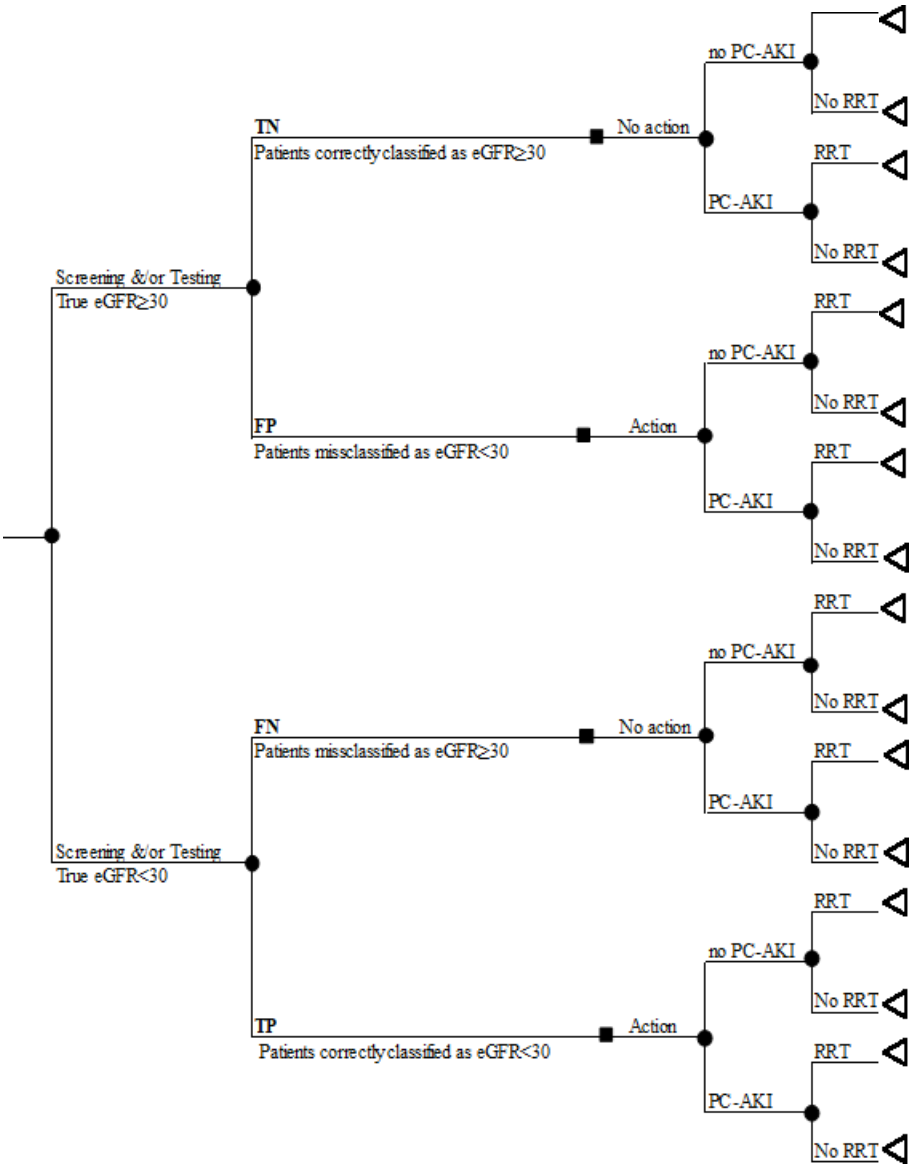
- true eGFR status (less than 30 ml/min/1.73 m^2 or 30 ml/min/1.73 m^2 and higher)
- how eGFR status is then classified by different testing strategies, using the same eGFR cut-off value of 30 ml/min/1.73 m^2 and probabilities conditional on true eGFR status (see section on the probability of being in each eGFR category)
- any actions taken to reduce PC-AKI risk in patients identified (correctly or incorrectly) as below the eGFR cut-off value
- the subsequent risk of PC-AKI (depends on eGFR status and any actions taken to reduce PC-AKI risk)
- the risk of renal replacement therapy (depends on whether a patient had a PC-AKI).

A simplified model diagram is shown in figure 1. The model assesses 6 types of strategy to identify and manage treatment of patients with an eGFR less than 30 ml/min/1.73 m^2:

- laboratory testing only
- risk factor screening with POC testing
- risk factor screening with laboratory testing
- risk factor screening with POC testing and laboratory testing
- POC testing only
- POC testing with laboratory testing.

The strategies are described on pages 123 to 128 of the diagnostics assessment report. For each type of strategy that includes POC testing, the model considers separate strategies for each of the POC devices, to give 14 alternative testing strategies. The 3 devices considered in the model are i-STAT Alinity, ABL 800 Flex and StatSensor.

Figure 1 Decision tree diagram



Abbreviations: FN, false negative; FP, false positive TN, true negative; TP, true positive.

The model considers 3 alternative management options if patients have an eGFR less than 30 ml/min/1.73 m^2 by any of the testing approaches described above. These approaches are:

- IV hydration followed by contrast-enhanced CT scan
- unenhanced CT scan

- unenhanced MRI scan.

Model inputs

Distribution of eGFR

The underlying distribution of eGFR in adult outpatients presenting as non-emergency for IV contrast-enhanced CT scanning without an eGFR measurement could not be determined from the published literature. A clinical adviser to the EAG (Dr Martine Harris) provided 1 month's routine outpatient audit data across 3 sites from the Mid Yorkshire NHS trust. Data were available for 816 outpatients, with 104 attending radiology without a recent eGFR measurement. The overall sample and the subgroup without a previous eGFR measurement appeared broadly comparable. Parametric distributions were fitted to estimate the probability of a patient being in one of 4 eGFR categories: less than 30, 30 to 45, 45 to 60 and 60 ml/min/1.73 m^2 or higher (table 7).

Table 7 Probability of each eGFR category

eGFR category (ml/min/1.73m^2)	Probability of eGFR in category		
	All patients (base-case analysis)	Patients with missing eGFR (scenario analysis)	KiTEC 2019 (scenario analysis)
	N=816	N=104	
Less than 30	0.62%	0.27%	15.86%
30 to 45	6.28%	5.1%	25.17%
45 to 60	15.45%	16.44%	58.97%
60 or higher	77.67%	78.18%	15.86%
Abbreviation: eGFR, estimated glomerular filtration rate			

Number of patients without a recent eGFR measurement

In the base case it was assumed that 34% of patients have missing eGFR values at the point of CT scan. This value was taken from Cope et al. 2017, an audit of compliance with UK guidelines for the prevention and detection of

AKI in adult patients having iodinated contrast agent injections for CT. Scenario analyses (12.7%; 50% higher than base case; and 50% lower than base case) were done to see the effect of heterogeneity and implications for the assumptions used to inform the costs of POC testing.

Diagnostic accuracy of POC creatinine devices

In the clinical effectiveness section (section 2.1), diagnostic accuracy was shown in terms of the probability of being classified in a given eGFR category by a POC device conditional on the person's true eGFR category. However, the economic model only considered a single cut-off of eGFR less than 30 ml/min/1.73 m^2 for alternative management decisions. The sensitivity of the tests was taken directly from the results of the quantitative synthesis, because it is equivalent to the probability that a person with eGFR less than 30 ml/min/1.73 m^2 is correctly categorised as eGFR less than 30 ml/min/1.73 m^2. The specificity of the POC devices was calculated by combining information on the distribution of population eGFR with the probability of having a classification of eGFR less than 30 ml/min/1.73 m^2 for a given true eGFR category (30 to 45, 45 to 60 and 60 or higher ml/min/1.73 m^2; a weighted average). Therefore, when the distribution of people in the different true eGFR categories changes, the specificity of the device would change.

The base-case analysis estimates were informed by the main analysis from the quantitative synthesis. Scenario analyses used results based on the sensitivity analyses from the quantitative synthesis (StatSensor adjusted data analysis; analysis with studies using CKD-EPI).

Table 8 POC creatinine diagnostic accuracy estimates in the model

	i-STAT		ABL800 FLEX		StatSensor	
	Sensitivity	**Specificity**	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
Base case						
Main analysis	84.1%	98.9%	86.1	99.2%	73.9%	99.1%

Scenario analyses						
StatSensor adjusted data	84.1%	98.9%	86.1	99.2%	84.1%	99.0%
CKD-EPI equation	81.7%	98.9%	81.4%	99.1%	56.4%	98.4%
Abbreviation: CKD-EPI, chronic kidney disease epidemiology						

Diagnostic accuracy of risk screening questionnaires

A pragmatic review was done to identify diagnostic accuracy evidence for risk factor questionnaires. Data reported suggest that sensitivity of the questionnaires is high, and tends to 100% at lower eGFR cut-offs. Specificity at eGFR less than 30 ml/min/1.73 m^2 varied between 45.2% and 82.9%. In the base-case analysis, the diagnostic accuracy estimates for risk factor screening were taken from Too et al. (2015). A scenario analysis was done with data from Azzouz et al. (2014).

Table 9 Risk factor screening diagnostic accuracy estimates in the model

	Sensitivity	Specificity	Source
Base case	100.0%	65.2%	Too et al. 2015
Scenario analysis	88.2%	45.2%	Azzouz et al. 2014

Risks of PC-AKI

Pragmatic reviews were done to find evidence of PC-AKI in outpatients. Estimates from Park et al. (2016) informed the model. This study reported the PC-AKI rate for different eGFR categories estimated from 1,666 patients with eGFR less than 60 ml/min/1.73 m^2 having contrast-enhanced CT after preventative IV hydration.

Table 10 PC-AKI events in patients having contrast-enhanced CT after IV hydration (Park et al. 2016)

eGFR (ml/min/1.73 m^2)	Number of patients	Number of PC-AKI events	PC-AKI rate
<30	250	27	10.80%
30-60	1,416	34	2.40%
Abbreviations: eGFR, estimated glomerular filtration rate; PC-AKI, post-contrast acute kidney injury			

In the base-case analysis, an odds ratio of 0.97 (95% confidence interval [CI] 0.52 to 1.9) for the impact of preventative IV hydration was used for patients with an eGFR below 30 ml/min/1.73 m^2 (Ahmed et al. 2018). It was assumed there would be no effect of IV hydration on risk in patients with an eGFR above 30 ml/min/1.73 m^2 (AMACING trial). A scenario analysis was done using the lower bound of the odds ratio (0.52), implying a greater protective effect of IV hydration compared with the base-case analysis.

A fixed effects meta-analysis of 3 studies (Hinson et al. 2017; Davenport et al. 2013; McDonald et al. 2014) suggested no effect of contrast on PC-AKI risk (odds ratio [OR] 0.98; 95% CI 0.88 to 1.08). It was therefore assumed in the base case that there was no effect of contrast on the risk of PC-AKI. Table 11 summarises the PC-AKI risks used in the model.

Table 11 Risks of PC-AKI in the model

eGFR ml/min/1.73m^2	Contrast-enhanced CT scan with IV hydration	Contrast-enhanced CT scan without IV hydration	Unenhanced CT scan
<30	10.80%	11.1%	11.1%
>30	2.40%	2.40%	2.40%
Abbreviations: eGFR, estimated glomerular filtration rate; IV, intravenous			

AKI consequences

Data from Park et al. 2016 suggest that any effect of PC-AKI on the rates of starting renal replacement therapy (RRT) happen within 6 months of the contrast-enhanced CT scan. The baseline probability of starting RRT in the model was estimated to be 0.014. A hazard ratio of 8.61 was applied to the baseline risk of starting RRT to estimate the probability of starting RRT for people who experience a PC-AKI event (0.111).

The proportion of people expected to be alive 6 months after the CT scan (94.5%) was derived from Park et al. 2016. UK life tables from the Office of National Statistics (2017) were used for mortality for more than 6 months after CT scan.

The model did not consider the effect of a delay of the planned CT scan on patient outcomes as a result of any change in their underlying condition during the waiting period.

Costs

POC device costs

Table 12 shows the capital cost per POC device used in the model. The higher capital cost of the Radiometer ABL800 flex is because this device is a benchtop unit that allows the user to measure a panel of up to 18 parameters on the same blood sample. This contrasts with the handheld design provided by the i-STAT Alinity and StatSensor devices, which only measure creatinine or have creatinine only cartridges available.

Table 12 Costs for POC devices

Device	Capital cost (per device)	Testing material costed	Cost per test	Time to result (minutes)	Cost per QC check (including consumables)	Annual maintenance cost (per year)
Abbott i-STAT Alinity	£6,500	Creatinine cartridge	£4.75	2	£6.80 Every week or every 25 tests	£850
Nova Biomedical StatSensor	£4,995[a]	Creatinine test strip	£3.95	0.5	£4.15 every 24 hours	£850
Radiometer ABL800 flex	£37,495	Per test proportion of all testing materials	£2.88	1	£5.01 Every 24 hours	£4,685

[a] VAT status unclear. Abbreviations: QC, quality control.

It was estimated that 92.6 patients per month would have a POC test. Using a risk factor screening questionnaire means that fewer patients would have a POC test. In the base case, risk factor screening before a POC test resulted in an estimated 32.6 patients per month having a POC test.

Table 13 Total device cost per POC test

	Capital cost	Annual servicing	Consumables	Quality control materials (including consumables)	Total device cost per test
Abbot i-STAT alinity	£0.92	£0.77	£4.75	£0.27	£6.71
Nova Biomedical StatSensor	£0.71	£0.77	£3.95	£1.36	£6.79
Radiometer (ABL800 flex)	£5.33	£4.22	£2.88	£1.65	£14.07

Staff cost per test, including time for taking blood, time for using the device and time for quality control testing were estimated to be £2.14 for i-STAT alinity, £1.73 for StatSensor and £1.66 for ABL800 flex. No staff time was included for training.

Other costs

Other costs considered in the model in the testing stage include risk factor screening (£1.11) and laboratory testing (including laboratory work and phlebotomist time; £3.31). There is an additional £2.50 cost of setting up the cannula if the contrast-enhanced CT scan is cancelled as a result of the POC test result.

Management costs include cancellation and rebooking of appointments (£87.92 for cancelled scan and [redacted] for rebooking), follow-up appointments with nephrologists for patients with eGFR less than 30 ml/min/1.73 m^2 (£186.49), IV hydration for patients before having full contrast CT scans (£340.89) and costs associated with adverse events from IV hydration (£32.76). The costs of imaging were £87.92 for an unenhanced CT scan, £111.65 for a contrast-enhanced CT scan and £151.98 for an MRI. The cost of RRT applied in the model was £9,758, assuming 3-weekly haemodialysis sessions for 3 months.

Health-related quality of life and quality-adjusted life year (QALY) decrements

Disutility from RRT was estimated to be −0.11 (Wyld et al. 2012). The disutility was applied for 3 months in the model based on NICE's clinical guideline on acute kidney injury. In a scenario analysis, disutility from anxiety was calculated by assuming that people would experience disutility associated with an EQ-5D-3L score change from level 1 to level 3 (−0.236) in the depression/anxiety domain for 2 weeks (assumed to be the maximum time that people would have to wait for a rescheduled scan). No disutility from PC-AKI or IV hydration was included.

Base-case assumptions

The following assumptions were applied in the base-case analysis:

- The laboratory test was assumed to have perfect diagnostic accuracy (100% sensitivity and specificity).
- Risk factor screening in the model was assumed to be done with a generic risk factor questionnaire.
- All patients having a laboratory test would have their CT scan cancelled and rebooked.
- A positive test result at the last step of the testing sequence resulted in the scan being cancelled and rebooked with IV hydration and contrast-enhanced CT scan.
- Adverse events from IV hydration were associated with costs but not with any health-related quality of life loss.
- Mortality in the model was assumed to be the same for all patients regardless of PC-AKI status.
- Mortality was assumed to be independent of eGFR levels.
- RRT was assumed to consist of haemodialysis.

Base-case results

Deterministic and probabilistic results were presented as net monetary benefit and net health benefit using a maximum acceptable incremental cost-effectiveness ratio (ICER) of £20,000 per QALY gained. Incremental net benefit was calculated for each strategy compared with laboratory testing. A fully incremental analysis was also done, but because the incremental cost and QALY differences between the strategies are so small, the ICERs are of limited use. This is because they are very sensitive to tiny changes in the denominator. If pairwise ICERs had been calculated, all strategies that include POC devices would be less costly and less effective compared with the strategy of laboratory testing for all. In general:

- Strategies that combine risk factor screening with POC testing and laboratory testing result in higher net benefit than other types of strategies, because they have a high positive predictive value. This avoids unnecessary management of false positives with IV hydration, which is associated with costs including cancelling and rebooking CT scans, giving IV hydration, treatment of IV hydration adverse events and patient follow up.
- Strategies that combine risk factor screening with POC testing, without confirmatory laboratory testing, are the next highest ranking. These have lower overall specificity and give more false positives, which are associated with increased costs from unnecessary management for patients whose results were misclassified as eGFR less than 30 (cancelling and rebooking CT scans, giving IV hydration, treatment of IV hydration adverse events and patient follow up).
- Strategies with POC testing that do not use risk factor screening have lower average net benefit than POC test strategies that do include risk factor screening because of the higher costs of testing when all patients have POC testing.
- The strategies using POC in isolation are the lowest ranking strategies involving POC, because they misclassify more patients' results as false positives and all patients incur the cost of POC testing.
- Laboratory testing alone and risk factor screening followed by laboratory testing are the lowest ranking strategies. Although they have the highest QALY gains because they give no false positives or false negatives, they are associated with the highest costs, because of cancellation, rebooking and managing treatment for people who test positive.

Table 14 Base-case probabilistic cost-effectiveness results – net benefit

	Identification	Management	Total costs	Total QALYs	NHB [c] (QALYs)	NMB [c]	INHB [c] (QALYs)	INMB [c]	NB rank	Probability of being cost effective	
										£20,000/ QALY	£30,000/ QALY
1	Lab	Test negative[a] – contrast-enhanced CT scan Test positive[b] – IV hydration + contrast-enhanced CT scan	£367.12	9.993255191	9.97490	£199,497.99	0.00000	£0.00	14	0.0%	0.0%
2	RF + i-STAT		£281.87	9.993255167	9.97916	£199,583.23	0.00426	£85.24	4	0.0%	0.0%
3	RF + ABL800 FLEX		£289.72	9.993255171	9.97877	£199,575.39	0.00387	£77.40	9	0.0%	0.0%
4	RF + StatSensor		£281.70	9.993255154	9.97917	£199,583.40	0.00427	£85.42	3	0.0%	0.0%
5	RF + Lab		£307.94	9.993255191	9.97786	£199,557.17	0.00296	£59.18	13	0.0%	0.0%
6	RF + i-STAT + lab		£279.70	9.993255167	9.97927	£199,585.40	0.00437	£87.42	1	79.3%	79.3%
7	RF + ABL800 FLEX + lab		£288.24	9.993255171	9.97884	£199,576.87	0.00394	£78.88	8	0.0%	0.0%
8	RF + StatSensor + lab		£280.01	9.993255154	9.97925	£199,585.09	0.00436	£87.10	2	20.7%	20.7%
9	i-STAT		£290.20	9.993255167	9.97875	£199,574.90	0.00385	£76.91	10	0.0%	0.0%
10	ABL800 FLEX		£294.83	9.993255171	9.97851	£199,570.27	0.00361	£72.28	12	0.0%	0.0%
11	StatSensor		£287.82	9.993255154	9.97886	£199,577.29	0.00396	£79.30	7	0.0%	0.0%
12	i-STAT+ lab		£283.93	9.993255167	9.97906	£199,581.17	0.00416	£83.19	6	0.0%	0.0%
13	ABL800 FLEX+ lab		£290.55	9.993255171	9.97873	£199,574.55	0.00383	£76.57	11	0.0%	0.0%
14	StatSensor + lab		£282.95	9.993255154	9.97911	£199,582.15	0.00421	£84.17	5	0.1%	0.1%

[a] According to any test in the testing sequence; [b] According to last test in the testing sequence; [c] At £20,000 per QALY.

Abbreviations: INHB, incremental net health benefit; INMB, incremental net monetary benefit; NB, net benefit; NHB, net health benefit; INMB, net monetary benefit; RF, risk

factor screening; lab, laboratory testing; QALY, quality-adjusted life year.

Table 15 Base-case cost-effectiveness deterministic results – full incremental analysis

	Identification	Management	Total costs	Total QALYs	Incremental costs	Incremental QALYs	ICER (per QALY gained)
6	RF + i-STAT + lab	Test negative [a] – contrast-enhanced CT scan Test positive [b] – IV hydration + contrast-enhanced CT scan	£275.84	9.99137100231	-	-	-
8	RF + StatSensor + lab		£276.15	9.99137099733	£0.31	-0.000000005	Dominated
4	RF + StatSensor		£277.84	9.99137099733	£1.99	-0.000000005	Dominated
2	RF+ i-STAT		£278.02	9.99137100231	£2.17	0.00000000000	Dominated
14	StatSensor+ lab		£279.09	9.99137099733	£3.25	-0.000000005	Dominated
12	i-STAT+ lab		£280.08	9.99137100231	£4.23	0.00000000000	Dominated
11	StatSensor		£283.96	9.99137099733	£8.12	-0.00000000499	Dominated
7	RF+ABL800 FLEX+lab		£284.39	9.99137100330	£8.55	0.00000000099	Extendedly dominated
3	RF+ABL800 FLEX		£285.87	9.99137100330	£10.03	0.00000000099	Dominated
9	i-STAT		£286.35	9.99137100231	£10.51	0.00000000000	Dominated
13	ABL800 FLEX+ lab		£286.70	9.99137100330	£10.86	0.00000000099	Dominated
10	ABL800 FLEX		£290.99	9.99137100330	£15.14	0.00000000099	Dominated
5	RF + lab		£304.06	9.99137101011	£28.22	0.00000000779	£3,620,669,780
1	Lab		£363.26	9.99137101011	£87.42	0.00000000779	Dominated

[a] According to any test in the testing sequence; [b] According to last test in the testing sequence.

Abbreviations: RF, risk factor screening; lab, laboratory testing; QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio.

The strategy with the highest incremental net benefit was strategy 6 (risk factor screening plus i-STAT plus laboratory testing). This strategy had the highest probability of being the most cost effective (79.3% for maximum acceptable ICERs of £20,000 and £30,000 per QALY gained). It was also the least costly of all strategies under comparison, but gave fewer QALYs than most other strategies. The corresponding strategy with StatSensor, strategy 8, only had a marginally smaller average incremental net benefit (£87.11 compared with £87.42 for strategy 6). Although ABL800 FLEX has the best diagnostic accuracy, strategies including testing with ABL800 FLEX have consistently lower net benefit compared with corresponding strategies with i-STAT and StatSensor because of higher costs of testing with this device.

The fully incremental ICER analysis showed that most strategies were dominated or extendedly dominated by strategy 6, except strategy 5 (risk factor screening plus laboratory testing) which had an ICER of £3.61 billion per QALY gained compared with strategy 6.

Analysis of alternative scenarios

Several scenario analyses were explored and are in the diagnostics assessment report starting on page 174. Results from most of the analyses are robust to changes in the assumptions. Some analyses cause strategy 8 (risk factor screening plus StatSensor plus laboratory testing) to become more cost effective than strategy 6 (risk factor screening plus iSTAT plus laboratory testing). This is generally because of changes to the assumptions on the diagnostic accuracy and on the costs of the POC tests.

The base-case analysis was also replicated, adding 2 new strategies:

- a ‘no testing’ strategy when all patients had a contrast-enhanced CT scan without testing for risk of PC-AKI
- a ‘no testing’ strategy combined with a greater reduction in risk of PC-AKI from IV hydration.

Both these strategies were associated with higher net benefit than other strategies included in the base-case analysis.

Table 16 Summary of scenario analyses and results

	Scenario	Result
1.	StatSensor adjusted analysis.	Results generally robust to alternative assumption.
2.	CKD-EPI equation studies (decrease in sensitivity of POC tests).	The false negative rate increases and therefore lowers the total management costs associated with treatment for patients with a positive test result. Strategy 8 (RF + StatSensor + lab) becomes more cost effective than strategy 6 (RF + iSTAT + lab) because the decrease in sensitivity is greatest for StatSensor.
3.	Alternative risk factor questionnaire (Azzouz et al. 2014). Sensitivity reduced from 100% to 88.2%; specificity reduced from 65.2% to 45.2%.	Lower specificity of the questionnaire results in an increase in throughput for POC testing for strategies when POC testing is preceded by risk factor screening, with consequent reduction in the costs of POC testing. The cost per test of StatSensor reduces proportionately more compared with i-STAT, and therefore strategy 8 (RF + StatSensor + lab) becomes more cost effective than strategy 6 (RF + iSTAT + lab).
4.	eGFR distribution – Harris subgroup (people without a prior eGFR measurement at referral).	Results generally robust to alternative assumption.
5	eGFR distribution – GSST audit (outpatients referred to a CT scan at the Guy's and St Thomas' NHS trust over 2 weeks in January 2019).	This population has a higher proportion of patients with eGFR less than 30 ml/min/1.73 m^2 compared with base case (15.9% compared with 0.6%). Therefore, more patients test positive and have IV hydration and follow up. More patients can benefit from management to reduce PC-AKI risk, but the benefit remains small. The proportion of patients who test positive is higher for strategies with lower specificity and higher sensitivity. The strategy with highest net benefit is strategy 8 (RF + StatSensor + lab), followed by strategy 4 (RF + StatSensor), and strategy 14 (StatSensor + lab), because StatSensor is the device with lowest sensitivity.
6.1	Throughput - the proportion of people attending a scan appointment without a recent eGFR measurement is 12.7% (compared with 34% in the base case).	Higher levels of throughput reduce the cost per POC test for all devices. The cost of per test of StatSensor is more sensitive (because of the costs of quality control) to changes in throughput than i-STAT and reduces proportionately more than the cost per i-STAT test. Therefore, when throughput estimates are 50% higher than in the base case, strategy 6 (RF + StatSensor + lab) becomes less costly and more cost effective than strategy 8 (RF + i-STAT + lab).
6.2	Throughput estimates 50% lower than base case.	
6.3.	Throughput estimates 50% higher than base case.	
7.1	0% of CT scans cancelled as a result of doing a laboratory test (all lab testing assumed to be processed urgently).	Strategy 5 (RF + lab) has the highest net benefit followed by strategy 1 (lab test alone). The 2 strategies are equivalent in terms of QALY gains, but risk factor screening reduces the overall costs of testing because only patients who are risk factor positive have the lab test. These strategies have the highest QALYs compared with all other strategies, and when no scans need to be cancelled and rebooked they also become the least costly.

7.2	25% of CT scans cancelled as a result of doing a laboratory test (75% of lab testing assumed to be urgent and 25% non-urgent).	Results generally robust to alternative assumption.
7.3	50% of CT scans cancelled as a result of doing a laboratory test (50% of lab testing assumed to be urgent and 50% non-urgent).	Results generally robust to alternative assumption.
7.4	75% of CT scans cancelled as a result of doing a laboratory test (25% of lab testing assumed to be urgent and 75% non-urgent).	Results generally robust to alternative assumption.
8.	Disutility from anxiety is included for patients who have their CT scan delayed.	Results generally robust to alternative assumption.
9.	Effect of IV hydration in reducing the risk of PC-AKI increased (OR = 0.52 compared with 0.97 in the base case; eGFR less than 30 ml/min/1.73 m^2).	Results generally robust to alternative assumption.
10.1	Management approach for people who test positive: 50% have IV hydration followed by contrast-enhanced CT scan; 50% have unenhanced CT scan.	Results generally robust to alternative assumption.
10.2.	Management approach for people who test positive: a third have IV hydration followed by contrast-enhanced CT scan; unenhanced CT scan; the other third have MRI.	Results generally robust to alternative assumption.
11.1	No testing – IV contrast media for all (without IV hydration).	This strategy was associated with the highest net benefit compared with other strategies.
11.2	No testing – IV contrast media for all (combination of scenario 9 and 11.1).	This strategy was associated with the highest net benefit compared with other strategies.

3 Summary

Clinical effectiveness

- There were 54 studies eligible for inclusion in the clinical systematic review. Most reported only measurement bias or correlation outcomes and so had limited relevance to the economic modelling part of the assessment.
- Results from the StatSensor studies showed wide variation in both the size and direction of measurement bias. Although potentially important measurement bias was found in some studies of the i-STAT and ABL devices, in most of these studies the concordance of results was generally better than in most of the StatSensor studies. No eligible studies were available on the Dri-chem NX500 device and only a few studies were available on the epoc and Piccolo Xpress devices.
- There were 7 studies (all of StatSensor) that reported diagnostic accuracy results based on creatinine thresholds. However, these results are not as clinically relevant as results based on eGFR thresholds.
- The 12 studies that reported diagnostic accuracy results based on eGFR thresholds covered 3 types of device: StatSensor, i-STAT and ABL devices. Although half of these studies were assessed as having a low risk of bias, there were concerns about the applicability of results to the outpatient CT scan setting in all but 2 studies.
- Results of the data synthesis showed that i-STAT and ABL devices have better sensitivity to detect low eGFR than StatSensor devices. In addition, i-STAT and ABL devices also have higher probabilities of correct classification for patients in the same eGFR categories as the reference laboratory test, than StatSensor devices. This is particularly clear for the lower categories (eGFR less than 45 ml/min/1.73 m^2), which are of greatest clinical importance.

Cost effectiveness

- In the review of cost-effectiveness evidence, no published studies were found that met the inclusion criteria. There was 1 unpublished economic study identified by clinical experts and this was given as an academic-in-confidence manuscript.

[redacted] In the EAG's model, the base-case results showed that the testing strategy with highest net benefit was a 3-step testing sequence that involves initially screening everyone for risk factors, a POC creatinine test for all people identified as having at least 1 risk factor, and a final confirmatory laboratory test for people who also test positive with a POC device. In this testing strategy, the POC device with the highest net benefit was i-STAT. However, differences in the net benefit between the i-STAT and StatSensor devices were very small.

- Although ABL800 FLEX had the best diagnostic accuracy, strategies including this device have consistently lower net benefit compared with corresponding strategies with i-STAT and StatSensor, because of the higher costs of testing with this device.
- Laboratory testing alone and risk factor screening followed by laboratory testing give the highest QALY gains because they result in no false positives or false negatives. But they are associated with the highest costs because of cancelling and rebooking scans, and managing treatment for people who test positive.
- The cost of testing and the diagnostic specificity were the factors that had the biggest influence on model results. Reducing PC-AKI risk was not an influential factor in the model because of: the low risk of PC-AKI estimated for this population; the evidence suggesting no increased risk of PC-AKI after the use of contrast agent; and the evidence suggesting IV hydration only reduces the risk of PC-AKI slightly.

- The scenario analysis of a 'no testing and manage all with contrast-enhanced CT (without IV hydration)' strategy had the highest net benefit of all the strategies.

4 Issues for consideration

Clinical effectiveness

- Few studies directly compared different POC creatinine devices and eGFR diagnostic accuracy data were not available for the ABL90 FLEX PLUS, Dri-chem NX500, epoc Blood Analysis System and Piccolo Xpress POC devices.
- There is considerable uncertainty in the probabilities of the POC creatinine devices correctly classifying eGFR when the true eGFR is less than 60 ml/min/1.73 m^2, particularly for StatSensor devices.
- No data were available on clinical outcomes such as need for renal replacement therapy or hospital admissions. The impact of POC devices on these outcomes is therefore uncertain.

Cost effectiveness

- The EAG model assumed that there was no effect of contrast on the risk of PC-AKI for any patient, regardless of eGFR. This was based on a fixed effects meta-analysis of 3 studies that used low- or iso-osmolar contrast agents (Hinson et al. 2017 [iohexol or iodixanol], Davenport et al. 2013 [iopamidol, iodixanol, iopromide or iohexol], and McDonald et al. 2014 [iohexol or iodixanol]; OR 0.98; 95% CI 0.88 to 1.08). However, many guidelines, including NICE's clinical guideline on acute kidney injury, highlight IV contrast agent as a risk factor for developing AKI and make recommendations to calculate eGFR to assess the risk of developing PC-AKI.
- Because of the low prevalence of patients who have a true eGFR less than 30 ml/min/1.73 m^2, the low risk of PC-AKI in the model population and the

limited effect of IV hydration in reducing this risk, the expected risk of PC-AKI is similar across strategies. Therefore, the QALY gains and the costs resulting from renal replacement therapy are also similar across all strategies.

- The QALY gains of appropriately managing treatment for patients who have a true eGFR less than 30 ml/min/1.73 m^2 are small (QALY difference between true positive and false negative is only 0.0000079237), while costs of managing treatment for patients who test positive are high. The low prevalence of patients who have a true eGFR less than 30 ml/min/1.73 m^2 combined with other factors, means that specificity appears a more important cost-effectiveness driver than sensitivity, because avoiding false positives gives considerably higher net benefit gains than mismanaging false negatives.
- The additional testing costs needed for a laboratory assessment or a POC test may not give enough improvements in patient outcomes to warrant routine testing.

5 Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Kidney disease occurs more frequently in men, people over the age of 60, and those of African-Caribbean, African or South-Asian family origin. The eGFR equation can be adjusted to reflect the race, age and sex of the patient. eGFR should be interpreted with caution in people with extremes of muscle mass, for example, in bodybuilders, people who have had an amputation or people with muscle wasting disorders.

In addition, people who have an ileostomy are at an increased risk of becoming dehydrated and may need special consideration when pre- and post-scan hydration is recommended.

6 Implementation

If POC creatinine testing were used in the NHS, the following implementation issues would need to be considered:

- Quality assurance processes are needed to give confidence in the results' reliability.
- POC creatinine in radiology will move the cost of creatinine measurement from the referring clinician's department budget to the radiology budget.
- For clinicians to have confidence in POC creatinine tests, the results from the POC device would have to be shown to be repeatable and reproducible, and correlate with laboratory results.
- Different eGFR algorithms are available and clinicians would need to ensure that the one used on the POC device was the same one used in the laboratory to compare results if necessary.

POC creatinine devices would ideally connect with laboratory IT systems to allow results to be uploaded. This would enable POC teams to remotely monitor performance and activity.

7 Authors

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Appendix A: Sources of evidence considered in the preparation of the overview

A. The diagnostics assessment report for this assessment was prepared by Centre for Reviews and Dissemination and Centre for Health Economics, University of York:

Corbett M, Duarte A, Llewellyn A, et al. Point-of-care creatinine tests to assess kidney function before administering intravenous contrast for CT imaging: systematic review, meta-analysis and economic evaluation. A diagnostics assessment report. York EAG, 2019

B. The following organisations accepted the invitation to participate in this assessment as stakeholders. They were invited to attend the scoping workshop and to comment on the diagnostics assessment report.

Manufacturer(s) of technologies included in the final scope:

- Abaxis
- Abbott Diagnostics
- Fujifilm UK Limited
- Nova Biomedical
- Radiometer Ltd
- Siemens Healthcare Limited

Other commercial organisations:

- None

Professional groups and patient/carer groups:

- Association for Clinical Biochemistry and Laboratory Medicine
- British Renal Society
- British Society of Interventional Radiology
- Institute of Biomedical Science
- Kidney Care UK

- Polycystic Kidney Disease Charity
- Renal Association
- Royal College of Physicians
- Royal College of Radiologists
- The Society and College of Radiographers

Research groups:

- Kidney Research UK

Associated guideline groups:

- None

Others:

- Department of Health and Social Care
- Healthcare Improvement Scotland
- NHS England
- Welsh Government

Appendix B: Glossary of terms

Acute kidney injury

Acute kidney injury is a condition that affects the structure and function of the kidneys. It can be caused by many different conditions and is defined based on serum creatinine levels and urine output.

Chronic kidney disease

A long-term condition characterised by a loss of kidney function over time. It is normally asymptomatic.

Contrast agents

Chemical substances which are used to improve the quality of medical images by increasing the visibility of specific organs, blood vessels or tissues.

Creatinine

Creatinine is the waste product of creatine, which the muscles use to make energy. Creatinine is excreted in the urine through the kidneys. High levels in the blood might indicate that the kidneys are not working correctly.

End-stage renal disease

End-stage renal disease occurs when chronic kidney disease reaches an advanced state. The kidneys do not work well enough to support the body, therefore dialysis or a kidney transplant is needed.

Glomerular filtration rate

A measure of the flow rate of blood passing through the kidneys.

Nephrotoxic drugs

Drugs that can cause damage to the kidneys.