

Title: Cost-effectiveness of point-of-care creatinine testing to assess kidney function prior to contrast-enhanced computed tomography imaging

Authors:

Ana Duarte¹, Simon Walker¹, James Altunkaya², Sofia Dias³, Mark Corbett³, Alexis Llewellyn³, Martine A. Harris⁴, Stephen Palmer¹, Marta Soares¹

Affiliations:

¹Centre for Health Economics, University of York, Heslington, UK

²Nuffield Department of Population Health, University of Oxford, Oxford, UK

³Centre for Reviews and Dissemination, University of York, Heslington, UK

⁴Mid Yorkshire NHS Hospitals Trust, Wakefield, UK

Corresponding author:

Ana Duarte

Centre for Health Economics, University of York, Heslington, YO10 5DD, UK

e-mail: ana.duarte@york.ac.co.uk

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Abstract

Background

Patients undergoing contrast-enhanced computed tomography (CECT) imaging in a non-emergency outpatient setting often lack a recent estimated Glomerular Filtration Rate measurement. This may lead to inefficiencies in the CECT pathway. The use of point-of-care (POC) creatinine tests to evaluate kidney function in these patients may provide a safe and cost-effective alternative to current practice, as these can provide results within the same CECT appointment.

Methods

A decision tree model was developed to characterise the diagnostic pathway and patient management (e.g., intravenous hydration) and link these to adverse renal events associated with intravenous contrast media. Twelve diagnostic strategies including three POC devices (i-STAT, ABL800 Flex and StatSensor), risk factor screening and laboratory testing were compared with current practice. The diagnostic accuracy of POC devices was derived from a systematic review and meta-analysis; relevant literature sources and databases informed other parameters. The cost-effective strategy from a health care perspective was identified based on highest net health benefit (NHB) which were expressed in quality-adjusted life years (QALYs) at £20,000/QALY.

Results

The cost-effective strategy, with a NHB of 9.98 QALYs and a probability of being cost-effective of 79.3% , was identified in our analysis to be a testing sequence involving screening all individuals for risk factors, POC testing (with i-STAT) on those screening positive, and performing a confirmatory laboratory test for individuals with a positive POC result. The incremental NHB of this strategy compared to current practice, confirmatory laboratory test, is 0.004 QALYs. Results were generally robust to scenario analysis.

Conclusions

A testing sequence combining a risk factor questionnaire, POC test and confirmatory laboratory testing appears to be cost-effective compared to current practice. The cost-effectiveness of POC

testing appears to be driven by reduced delays within the CECT pathway. The contribution of intravenous contrast media to acute kidney injury, and the benefits and harms of intravenous hydration remain uncertain.

Keywords: Point-of-care; Creatinine; post-contrast acute kidney injury; Computed tomography; Contrast media; Cost-effectiveness.

Abbreviations: CECT, contrast-enhanced computed tomography; CT, computed tomography; eGFR, estimated glomerular filtration rate; HRQoL, health related quality of life; IV, intravenous; MRI, magnetic resonance imaging; NHB, net health benefit; NHS, national health system; NICE, National Institute for Health and Care Excellence; PC-AKI, post-contrast acute kidney injury; POC, point-of-care; RF, risk factor; RRT, renal replacement therapy; QALY, quality-adjusted life year.

Introduction

Computed tomography (CT) is often enhanced with iodinated intravascular contrast media to improve soft-tissue contrast. Contrast media use, especially high-osmolality agents, has been found to be associated with increased risk of post-contrast acute kidney injury (PC-AKI)[1]. PC-AKI is defined as an increase in serum creatinine of 1.5 times the baseline within 48-72 hours of intravascular contrast media administration [2], and may impact on patient morbidity and mortality[3].

Current guidelines recommend the use of low and iso-osmolality contrast media, assessment of PC-AKI risk, and delivery of risk mediating actions prior to contrast administration to patients at higher PC-AKI risk [2, 4, 5]. The key patient-related predictor of PC-AKI risk is current renal function[6], which can be assessed by determining the estimated glomerular filtration rate (eGFR) based on a serum creatinine test. Although guidelines differ on how PC-AKI risk should be assessed and managed, patients are considered to be at high PC-AKI risk at $eGFR < 30 \text{ mL/min/1.73 m}^2$ [2, 4, 5]. For these patients, clinicians have the options to use prophylactic IV hydration, an alternative imaging method (including unenhanced CT) [2, 4, 5], or proceed with contrast-enhanced CT (CECT) when the expected benefits outweigh the renal risk[4, 5].

Whilst a recent eGFR measurement is typically requested prior to a CECT scan as part of PC-AKI prevention protocols, patients may still attend for a scan without one. An audit of NHS trusts found only 21% of institutions complied with the recommendation to test kidney function within 3 months of a scheduled outpatient CT scan[7]. When a patient attends without a recent eGFR measurement, clinicians may decide to proceed with the planned CT scan, delay the scan until a measurement can be obtained, or change the imaging modality.

Point-of-care (POC) creatinine testing can be used to calculate eGFR for patients without a recent measurement to avoid delaying the CT procedure because of the need for laboratory testing or the potential suboptimal management of patients in the absence of eGFR measurements (e.g., scanning without contrast or proceeding without knowledge of 'true' PC-AKI risk). However, the diagnostic accuracy of POC creatinine devices may be lower than laboratory testing, introducing a potential risk of misclassification and mismanagement of patients.

The cost-effectiveness of POC creatinine testing to evaluate kidney function of patients without a recent eGFR measurement who need CECT imaging is currently unknown. While previous studies have estimated the POC creatinine testing costs[8, 9] and the impact on resource use and costs of introducing POC creatinine testing in the workflow of UK diagnostic imaging departments[10], the joint impact of POC testing on total costs and health outcomes has not been assessed.

Our study aims to determine the cost-effectiveness of POC creatinine testing to evaluate kidney function in outpatients without a recent eGFR measurement who need non-emergency CECT imaging in England and Wales. A full technical report of this research is published elsewhere[11]. Here we summarise the cost-effectiveness of POC creatinine testing.

Methods

Costs were estimated from a health care perspective expressed as pound sterling (2018 price year) and health outcomes as quality-adjusted life-years (QALYs) using a decision analytic model. Outcomes and costs were discounted at 3.5% per annum[12].

Patient population

The patient population comprises individuals who need CECT imaging in a non-emergency situation (outpatient setting), without a recent eGFR measurement. This includes patients with and without compromised kidney function (i.e., eGFR lower or greater than 30mL/min/1.73m²).

The distribution of eGFR in the population of interest was estimated by fitting a probability distribution to a month of routine outpatient audit data from one UK Trust (n=816)[10]. These data, and a recent POC creatinine diagnostic accuracy study in outpatients undergoing CECT[13], jointly inform the population characteristics in the model (**Error! Reference source not found.****Error! Reference source not found.**).

Strategies

The model compares testing strategies combining risk factor (RF) screening, POC creatinine testing and laboratory testing. Whilst a generic laboratory creatinine test and a generic RF screening questionnaire were considered to assess renal function, the strategies including POC creatinine testing were evaluated separately for each of three POC creatinine devices commercially available in the UK: i-STAT (Alinity, Abbott Laboratories), StatSensor (Nova Biomedical), and ABL800 Flex (Radiometer). Fourteen screening/testing strategies were evaluated in this assessment with each classifying patients as positive or negative for high PC-AKI risk (eGFR<30mL/min/1.73m²). The strategies are described by strategy type in Table 1. Strategy types with a POC element include three separate strategies each (i.e., one for each POC device considered).

Table 1 Strategies evaluated in the base-case analysis

Strategy		Testing sequence
Number	Label	
1	Lab	Test all with a laboratory test.
2	RF+POC	Screen with RF questionnaire. Patients who screen positive are tested with POC device*.
3	RF + Lab	Screen with RF questionnaire. Patients who screen positive are also laboratory tested.
4	RF+POC+Lab	Screen with RF questionnaire. Patients who screen positive are tested with POC device*. Patients who test positive with POC device* are tested with a laboratory test.
5	POC	Test all with POC device*.
6	POC+Lab	Test with POC device*. Patients who test positive with POC device* are tested with a laboratory test.
* Strategies including a POC creatinine test were modelled separately for the three POC devices (i-STAT, StatSensor and ABL800 Flex). For simplicity, results are only shown for the device identified with the highest NHB."		

Decision model and parameterisation

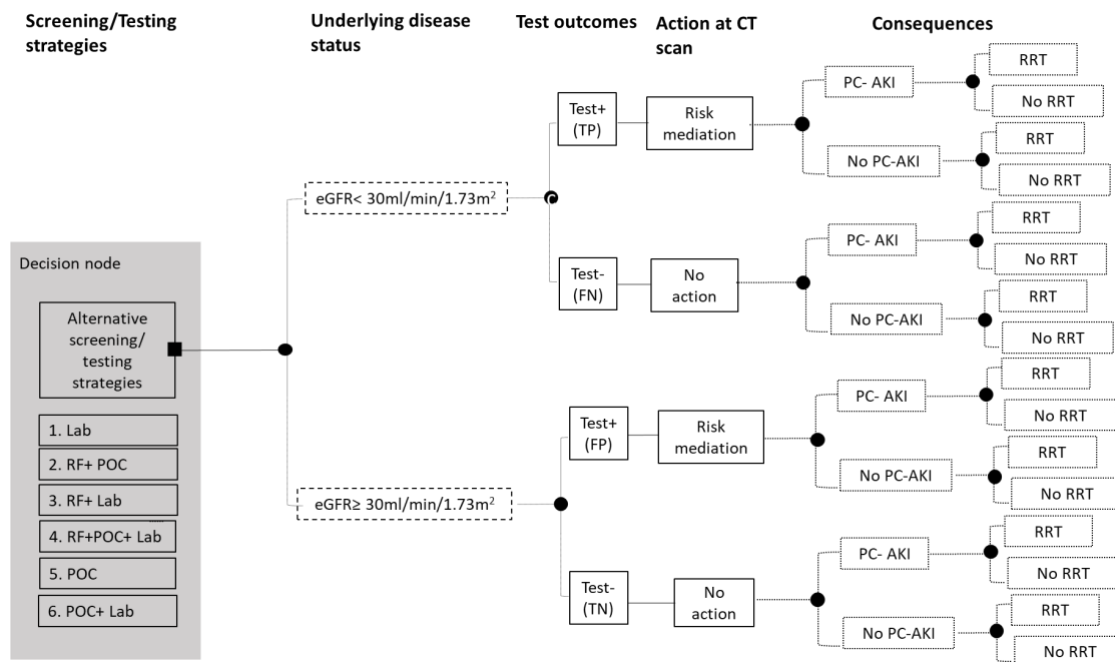
A decision tree model was developed in Microsoft Excel. The model established a link between the diagnostic accuracy of testing strategies to determine eGFR status, subsequent decisions to mediate PC-AKI risk and their impact on PC-AKI risk, quantifying consequences of PC-AKI with impact on health outcomes and costs. Key model parameters and data sources are presented in Table 2. Further details are presented in supplementary material (Table S1).

Table 2 Summary of model parameters

Model parameters					Source
Population characteristics					
Probability of eGFR being in each category	<30 mL/min/1.73m ²	30-44 mL/min/1.73m ²	45-59 mL/min/1.73m ²	≥60 mL/min/1.73m ²	Shinkins et al., 2021 [10]
	0.6%	6.3%	15.4%	77.7%	
Age and proportion of males	65 years, 51.7%				Snaith et al (2019) [13]
% missing eGFR measurement	34%				Cope et al. (2017) [7]
Patients per site	272 per month				Shinkins et al., 2021 [10]
Clinical effectiveness and HRQoL					
Probability of PC-AKI with contrast conditional on eGFR	eGFR<30 mL/min/1.73m ²		eGFR≥30 mL/min/1.73m ²		Park et al. (2016)[14], Ahmed et al. (2018) [15]: OR for IV hydration vs. placebo (eGFR<30 mL/min/1.73m ²): 0.97 (95% CrI: 0.52-1.9) **
	Without IV hydration	With IV hydration	Without IV hydration	With IV hydration	
	11.1%	10.8%	2.4%	2.4%	
Probability of RRT	If no PC-AKI		If PC-AKI		Park et al. (2016)[14]
	1.4%		11.1%		
Proportion of patients alive*	94.5%				Park et al. (2016)[14]
HRQoL	Adjusted life expectancy		Loss due to RRT		ONS mortality[16], Ara and Brazier, 2010[17], Wyld et al 2012[18]
	9.80 QALYs		0.0275 QALYs		
Costs					
Contrast-enhanced CT scan	Procedure	Cancellation	Rebooking		NHS reference costs[19]
	£111.65	£87.92	£1.83		
IV hydration	Procedure		Adverse events		AMACING trial [20], NHS reference costs[19]
	£340.89		£32.76		
Follow-up for patients with eGFR <30mL/min/1.73m ²	£186.49				NHS reference costs[19]
RRT	£9,758				NHS reference costs[19]
*at 6 months post-imaging; ** Probability of PC-AKI with IV hydration (for both eGFR groups) was sourced from Park et al. (2016) [14]; the probability of PC-AKI without IV hydration in patients with eGFR<30 mL/min/1.73m ² was derived by applying the OR from Ahmed et al. (2018) [15] to the probability of PC-AKI with IV hydration. CrI, credibility interval; ONS, Office for National Statistics; OR, odds ratio; RRT, renal replacement therapy					

Error! Reference source not found. Figure 1 illustrates the model structure. Patients move within the model using chance nodes (black circles) to denote events that occur with a given probability or to a certain proportion of patients. The decision node (black square) at the start of the model identifies the alternative strategies under comparison. Initially, the model dichotomises individuals according to their 'true' eGFR status (as per laboratory test result) at a 30mL/min/1.73m² cut-off value. This is the diagnostic threshold where existing evidence suggests an increased PC-AKI risk and a risk reduction associated with mediating actions [14, 15, 20].

Figure 1 Model structure diagram



● - Chance node; ■ - Decision node; FN, false negative; FP, false positive; Lab, laboratory testing; PC-AKI, post-contrast acute kidney failure; POC, Point-of-care creatinine testing; RF, risk factor screening questionnaire; RRT, renal replacement therapy; TN, true negative; TP, true positive.

Clinical management is assumed the same across strategies, depending only on the individual's level of PC-AKI risk as identified by the diagnostic strategy (positive or negative for high PC-AKI risk). Individuals who test negative receive no risk mediating action and proceed immediately to CECT. Those identified as positive at the end of the full testing sequence receive a risk mediating action, which consists of IV hydration prophylaxis or an alternative imaging approach (magnetic resonance imaging [MRI] or CT without contrast). The model allows specifying the proportion of patients (of those identified as requiring action) who undergo each type of mediating action. In the base-case analysis, all patients identified as having an eGFR < 30 mL/min/1.73m² are managed with IV hydration

and, subsequently, receive CECT. Strategies requiring a laboratory test or mediating action assume that the planned CECT is cancelled and rebooked, thus imposing the cost of a missed appointment and of rebooking. POC testing and RF screening components of the strategies are assumed to not impose delays resulting in CECT cancellation, unless a positive result leads to a subsequent laboratory test or requires the patient to receive mediating action.

In the short-term, individuals can either have a PC-AKI event or not. This probability of experiencing a PC-AKI depends on the individuals' 'true' eGFR and any mediating actions received. The PC-AKI risk was sourced from a large observational study in an outpatient setting (n=1,666) [14] identifying patients with $\text{eGFR} < 30 \text{ mL/min/1.73m}^2$ managed with IV hydration with a 10.8% risk, and those with $\text{eGFR} \geq 30 \text{ mL/min/1.73m}^2$ with a 2.4% risk. Based on a meta-analysis[15], IV hydration is assumed to have a small (non-statistically significant [Table 2]) effect on the PC-AKI risk only in patients with $\text{eGFR} < 30 \text{ mL/min/1.73m}^2$ [20].

Individuals who are misclassified as positive (FP), incur the costs of the PC-AKI risk mediating actions but do not have any reduction in PC-AKI risk and subsequent clinical events. Individuals who are misclassified as negative (FN) will not incur the cost of mediating actions, but will not benefit from PC-AKI risk reducing action.

PC-AKI events are assumed to be largely asymptomatic in this patient population and not consume health care resources or loss of health-related quality of life (HRQoL). However, the occurrence of a PC-AKI event increases the probability of individuals requiring renal replacement therapy [RRT]. In the model, individuals with a PC-AKI event have an increased risk of requiring temporary RRT within six months of imaging, but no impact on mortality [14]. It was assumed that RRT risk depends only on PC-AKI status, and not on underlying eGFR values, as the study did not report the risks of RRT jointly by 'true' eGFR and PC-AKI status.

The model attaches a cost and a HRQoL loss to RRT events. The QALYs accrued over the expected lifetime of individuals are also estimated by the model, which assumes no difference in mortality associated with RRT (see *Health-related quality of life and life expectancy*).

Diagnostic accuracy

The diagnostic laboratory test is assumed to perfectly identify disease status (100% sensitivity and specificity) at the $30 \text{ mL/min/1.73m}^2$ eGFR cut-off. The RF questionnaire diagnostic accuracy (100% sensitivity and 65.2% specificity) at the same threshold is based on the Choyke questionnaire[21] in

an outpatient setting[22]. The questionnaire identifies patients who report the presence of renal problems, renal surgery, hypertension, gout, diabetes mellitus, and/or proteinuria.

A review and meta-analysis of diagnostic accuracy of POC creatinine tests was conducted; full details are published elsewhere[11]. We identified 10 studies[13, 23-31] of adult patients receiving POC creatinine testing compared with laboratory testing. These studies reported diagnostic accuracy data for correctly identifying patients in different PC-AKI risk categories determined by different levels of eGFR (<30, 30-44, 45-59 and ≥ 60 mL/min/1.73m²), reflecting changes in the definition of thresholds for PC-AKI risk over time. The meta-analysis estimated the probability of being in a given eGFR category when tested with a POC device conditional on individual's 'true' eGFR category, using a Bayesian framework (with parameters estimated by Markov chain Monte Carlo)[32, 33], which provided a direct estimate of sensitivity (probability that each POC device correctly classifies individuals in the eGFR<30mL/min/1.73m² category) and allowed for calculation of specificity (by combining the remaining probabilities with the underlying distribution of eGFR). This approach was preferred to pooling study reported sensitivity and specificity at a single eGFR cut-off. Given that different eGFR cut-offs were used across studies, this maximised the available evidence informing the diagnostic accuracy of POC devices.

Diagnostic accuracy estimates are summarised in Table 3.

Table 3 Diagnostic accuracy and test costs in the base-case analysis

Test	Sensitivity	Specificity	Source	Cost per test*		Source
				No prior RF screening	Prior RF screening	
i-STAT	84.1%	98.9%	Systematic review and meta-analysis of diagnostic accuracy data combined with eGFR distribution[11]	£ 8.85	£11.96	Calculated: Includes annuitized capital cost of devices, test consumables, quality control and staff costs
ABL800 Flex	86.1%	99.2%		£15.73	£36.36	
StatSensor	73.9%	99.1%		£8.52	£14.25	
Laboratory	100.0%	100.0%	Assumption	£3.31		NHS reference costs [19]
RF screening	100.0%	65.2%	Too et al, 2015[22]	£1.11		NHS reference costs[19] Lederman et al, 2010[34]
*Patient throughput will vary depending on whether patients are risk factor screened prior to receiving the POC creatinine test or not; RF, risk factor						

Health-related quality of life and life expectancy

Health is expressed in QALYs, based on expected mortality and HRQoL weights. HRQoL was based on the general population with utility decrements applied to individuals undergoing RRT. Age and sex-specific HRQoL were estimated[17]. These estimates were applied to the proportion of patients expected to be alive each year, as derived from UK lifetables [16] and assuming that 94.5% of patients were alive at 6 months post-imaging [14]. RRT is assumed to consist of three months of haemodialysis, during which patients incur a QALY loss (Table 2). No HRQoL loss is included to account for IV hydration adverse events given their short duration[20].

Resource use and costs

POC creatinine test costs include the device capital costs, consumables, annual maintenance costs and staff time costs to conduct testing, interpret results and perform quality control. Unit costs for device related costs were obtained from the manufacturers, and for staff time from published sources [35]. A lifespan of seven years is assumed for all devices to estimate the expected annual capital cost of the device. Device capital, maintenance and quality control costs per test depend on patient throughput. The estimated patient throughput for POC devices (93 patients/month) was based on the number of patients presenting for a CT scan at each NHS Trust site in a previous study[10], combined with the percentage of patients who do not have a recent eGFR measurement at their scan appointment (Table 2)[7]. In strategies where POC is preceded by screening with a RF questionnaire, the throughput for the POC device will depend on the accuracy of the RF screening and the distribution of eGFR in the population (33 patients/month under base-case assumptions). Patient throughput informs the per patient cost of POC testing, and does not impact on patient flow within the model. The cost per patient tested for each POC device, laboratory testing and RF screening are shown in Table 3.

RF screening and POC testing are assumed to be conducted within the planned CT appointment. The blood collection for the POC test is assumed to be done while cannulating the patient[10], and is reflected on the cost of the tests (details on test costing are reported elsewhere [11]).

The costs of patient management and imaging include the costs of: imaging, cancelling and rebooking CT appointments, IV hydration and associated adverse events (based on the AMACING trial[20]) and nephrologist follow-up appointments for patients categorised as eGFR<30 mL/min/1.73m² (Table 2). Imaging modalities costed in the model are: CECT, unenhanced CT and MRI (Table S1, supplementary material).

The cost of three weekly haemodialysis sessions over three months (Table 2) is applied to patients who underwent RRT[36].

Cost-effectiveness analysis

Cost-effectiveness results for the alternative strategies are assessed in terms of net health benefits (NHB), that is the QALYs generated by the strategy less the QALYs that could have been generated elsewhere by alternative use of NHS resources (one QALY per £20,000 of NHS and PSS resources [12]). The intervention with the highest NHB is the cost-effective intervention. We also present the incremental NHB (i.e., the difference in NHB) for each strategy compared to strategy 1 ('Lab'), where all patients receive a laboratory test. To simplify presentation and interpretation, results for strategies including POC testing are only presented for the POC device with the highest NHB within each strategy type.

Scenario and Probabilistic sensitivity analyses

The robustness of results to alternative assumptions was explored extensively in scenario analyses[11]. Here we report the results of key analyses with alternative assumptions regarding the: 1. diagnostic accuracy of the RF screening questionnaire; 2. Decreased (2.1) or increased (2.2) patient throughput; 3. Increased PC-AKI risk for patients with $\text{eGFR} < 30 \text{ mL/min/1.73m}^2$ and without IV hydration; 4. Increased (4.1) and decreased (4.2) proportion of cancelled scans; and 5. an alternative distribution of eGFR values in the study population. Detailed description of these scenario analyses is presented in the results section below (Figure 2) and in supplementary material (Table S2).

The decision tree is evaluated probabilistically for the base-case analysis over 1,000 Monte Carlo simulations to reflect the joint uncertainty across all of the inputs according to their assigned probability distributions (Table S1, supplementary material), and estimate the probability of a strategy being cost-effective.

Results

Base-case results are presented in Table 4. Results are only presented for the POC creatinine device with the highest NHB within each strategy type (full results in the supplementary material, Table S3).

The results show that strategies combining risk factor screening with POC creatinine testing and laboratory testing ('RF+POC+Lab') result in higher NHB than other strategies (Table 4). The cost-effectiveness of this strategy type appears to be driven by its lower total costs, with total QALYs similar across strategies. 'RF+POC+Lab' has the lowest total costs compared to 'Lab' and 'RF+Lab', as it results in lower CECT cancellation rates due to fewer patients undergoing 'Lab' testing. The NHB of 'RF+POC+Lab' compared to 'RF+POC' is very similar; both strategies lead to similar CECT cancellation rates as patients who test positive with POC in 'RF+POC' receive IV hydration. The difference in costs between these strategy types is mostly due to the costs of managing FP results to 'RF+POC', as 'RF+POC+Lab' does not misclassify patients as FP. Strategies with POC at the start of the diagnostic pathway have higher total costs due to the POC tests being more costly than RF screening and laboratory testing.

Strategy 1, 'Lab', has higher total QALY across all strategies, as all patients with 'true' $\text{eGFR} < 30 \text{ mL/min/1.73m}^2$ receive appropriate management. The QALY gains associated with this are modest given the low prevalence and small reduction in PC-AKI risk from IV hydration for these patients (-0.3%). This strategy has the lowest NHB, because the small QALY gains from the appropriate management of patients are offset by the highest costs of cancellation and managing patients with $\text{eGFR} \geq 30 \text{ mL/min/1.73m}^2$. The mismanagement of patients with 'true' $\text{eGFR} \geq 30 \text{ mL/min/1.73m}^2$ has no impact on the QALY gains of any strategy, as it was assumed that IV hydration has no effect on the PC-AKI risk of these patients and its adverse events do not impose a QALY loss.

Within the cost-effective strategy of 'RF+POC+Lab', the POC device that results in the highest incremental NHB is the i-STAT (0.00437 QALYs compared to 'Lab'). The greater diagnostic accuracy of the table-top device, ABL800 Flex, does not offset the higher costs of testing with this device in this strategy, or in any of the strategies considered.

The device with the highest NHB within the 'RF+POC+Lab' strategy is i-STAT, but StatSensor takes its place for all other strategy types including POC testing. Within every strategy, the net benefits for i-STAT and StatSensor are similar, as the tests diagnostic accuracy costs are similar (), with any differences due to small differences in the level of throughput and accuracy.

There is little decision uncertainty, with a near 100% pooled probability of 'RF+POC+Lab' being cost-effective at £20,000 per additional QALY (results in Supplementary material, Table S3). Given the similarity in results for i-STAT and StatSensor, there is some uncertainty regarding which device is cost-effective within this strategy: the probability of i-STAT and StatSensor in the 'RF+POC+Lab' strategy being cost-effective is, respectively, 79.3% and 21.7%.

Table 4 Base-case cost effectiveness results, per patient, for each strategy type.

Strategy number	Strategy label	POC device with highest NHB*	Total costs	Total QALYs	NHB** (QALYs)	INHB in relation to 'Lab' (QALYs)
4	RF + POC + Lab	i-STAT	£279.70	9.993255167	9.97927	0.00437
2	RF + POC	StatSensor	£281.70	9.993255154	9.97917	0.00427
6	POC + Lab	StatSensor	£282.95	9.993255154	9.97911	0.00421
5	POC	StatSensor	£287.82	9.993255154	9.97886	0.00396
3	RF + Lab	NA	£307.94	9.993255191	9.97786	0.00296
1	Lab	NA	£367.12	9.993255191	9.97490	-

*POC device with the maximum NHB within the strategy; **At £20,000 per QALY

INHB, incremental net health benefit; NHB, net health benefit.

Sensitivity analysis

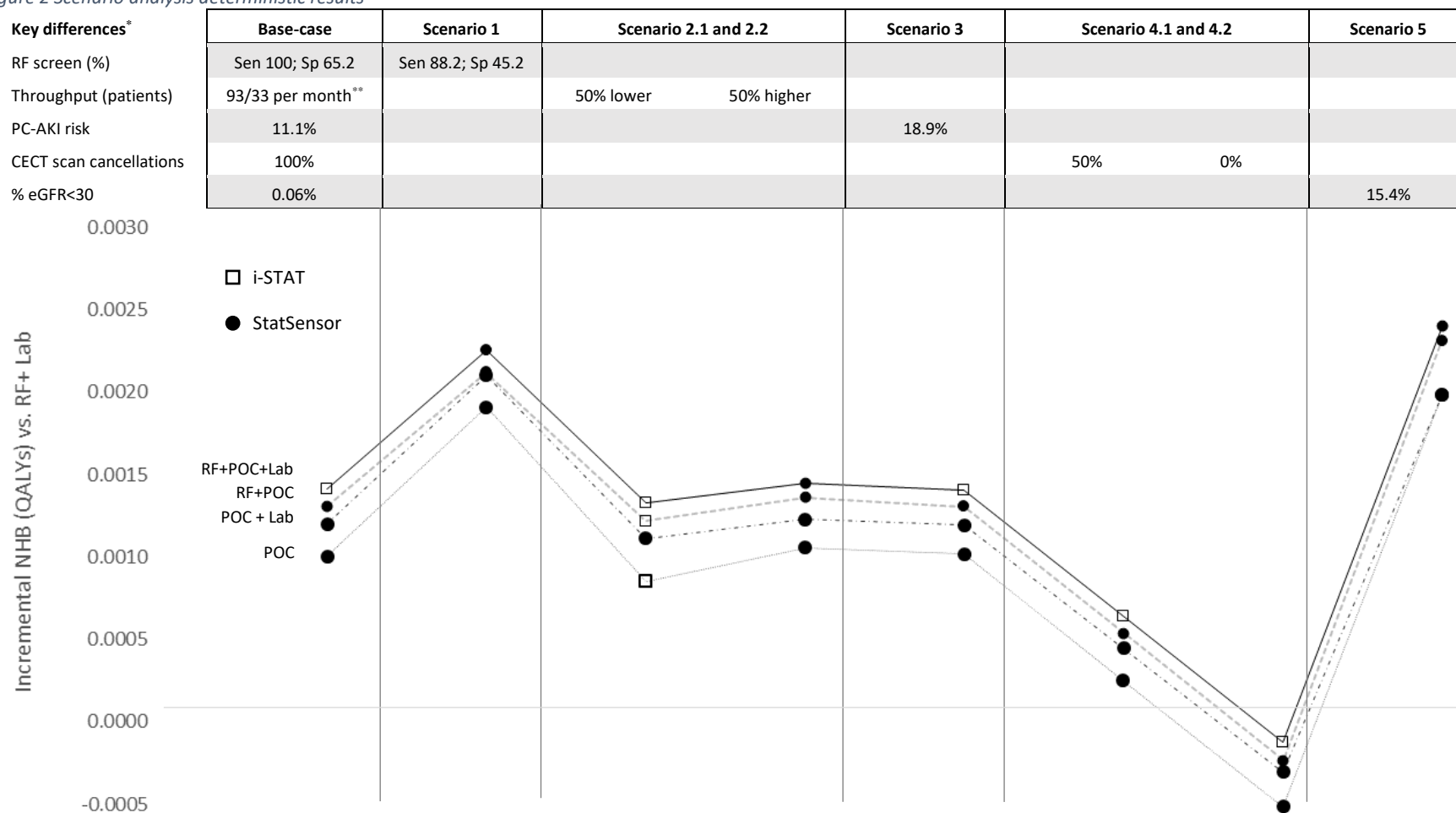
Scenario analysis results presented in Figure 2 show the incremental NHB for each of the strategies including a POC creatinine testing element (lines in the graph) in relation to the highest-ranking strategy without POC. The different scenarios implemented are reported along the x-axis with key differences between each and the base-case detailed above the graph and a fuller description in the legend. Across all analyses, the highest ranking strategy without POC is 'RF+Lab'; therefore, the 'Lab' strategy is omitted from the graph. The marker identifies, for each scenario, the POC device with highest NHB within each of the POC strategies.

Consistent with base-case results, the 'RF+POC+Lab' strategies yield the highest incremental NHB in all but one scenario (Scenario 4.2). The ranking of incremental NHB by type of strategy is also generally consistent ('RF+POC+Lab' > 'RF+POC' > 'POC+Lab' > 'POC'). The POC creatinine device that results in higher incremental NHB within each strategy type switches between i-STAT and StatSensor, depending on the position of POC in the testing sequence and on the scenario. However, differences in NHB between these two strategies remain small across scenarios (see Table S4 to S10 for full scenario analysis results).

It is only when patients are assumed not to incur the opportunity costs of a delayed CT scan (scenario 4.2), that the type of testing strategy with highest NHB changes. Under this scenario, 'RF+Lab' has the highest NHB, being considered cost-effective (Figure 2), followed by 'Lab' (Table S9, supplementary material). These two strategies become the least costly, since costs of managing test

positive patients are only incurred by true positives and the costs of testing are lower than for the other strategies (especially for 'RF+Lab') where screening reduces the proportion of patients for which laboratory tests are performed.

Figure 2 Scenario analysis deterministic results



Abbreviations: BL, baseline; RF screen, diagnostic accuracy of risk factor questionnaire; Sen, sensitivity; Sp, specificity.

***Description of scenarios:** Scenario 1 -- diagnostic accuracy of RF screening questionnaires informed by data on an alternative questionnaire[23](Sensitivity = 88.2% and specificity = 45.2%); Scenario 2.1 -- Throughput estimates 50% lower than base-case; Scenario 2.2 -- Throughput estimates 50% higher than base-case; Scenario 3 -- The effect of IV hydration on the risk of PC-AKI for patients with eGFR<30 mL/min/1.73m² is set to 0.52 (i.e. lower bound of the 95% confidence interval for the base-case estimate[15]), resulting in a higher risk of PC-AKI of 18.9%; Scenario 4.1, 50% of CT scans cancelled as a result of requiring a laboratory test or needing IV hydration; Scenario 4.2 -- 0% of CT scans cancelled; Scenario 5 -- distribution of eGFR based on audit data of outpatients referred to a CT scan at the Guy's and St Thomas' NHS trust, identifying a probability of eGFR being <30 mL/min/1.73m² of 15.9%. Further detail is presented in Table S2 in the supplementary material.

**93 patient per month if strategy does not include RF screening and 33 patients per month if the POC test is preceded by RF screening

Discussion

This paper evaluated the cost-effectiveness of POC creatinine testing compared to current practice in patients without a recent eGFR. It did so by reflecting the potential resource savings and improved management of PC-AKI risk in patients for whom a decision to proceed to CECT scan would have been made based on clinical judgement alone in the absence of POC testing. The model considered the potential for misclassification with POC devices given their lower diagnostic accuracy compared to laboratory testing: evidence on the ability of POC devices to discriminate eGFR values below and above the cut-off of 30mL/min/1.73m² indicates a low sensitivity (between 74 and 86%) and a high specificity (of around 99%).

The results showed that a strategy combining RF screening, POC testing and laboratory testing appears to be a cost-effective use of NHS resources for outpatients undergoing non-emergency CECT without a recent eGFR measurement. This is because POC creatinine tests (which have demonstrated reasonable accuracy) can avoid unnecessary CT scan cancellations and these savings appear to exceed the reduction in health benefits arising from any misclassification. Regarding the POC devices, our analyses showed that i-STAT and StatSensor generate similar NHB (i-STAT presented slightly higher NHB for the 'RF+POC+Lab' strategy, but the opposite was true for all other strategies including a POC testing). The additional costs associated with the table-top device (ABL800 Flex) were too large to justify its increased accuracy.

Our analyses were potentially restricted by the available evidence. First, all individuals were assumed to eventually proceed to a contrast-enhanced CT scan. This was a necessary simplification given data scarcity and the challenges of characterising the heterogeneity in the overall population and the underlying reason for imaging, and linking this to individualised clinical decision-making and associated outcomes. However, the results were robust to extensive scenario analyses exploring the potential impact of alternative assumptions. Second, the assumption that all cancelled CECT scans will result in the loss of the imaging slot, may not represent all NHS trusts, as some trusts may be able to avoid this to some extent (e.g., if they can quickly turnaround laboratory testing onsite and reorganise the daily CT schedule to minimise cancellations). However, our results are robust to variation in the proportion of lost CT scans, unless loss of imaging slots can be totally avoided. Third, diagnostic accuracy data was sourced from small studies, and comparative evidence was only available for three devices. Few patients in these studies were below the 30mL/min/1.73m² cut-off, which is reflective of the population, but also contributes to uncertainty in the diagnostic accuracy estimates. Fourth, data used to inform the distribution of eGFR values and health outcomes rates in the model were sparse. A single study[14] informed health outcomes rates and additional

assumptions were required to link PC-AKI with subsequent patient outcomes. Finally, the costs of implementing POC creatinine testing in radiology services were not included, due to lack of data and expected local level variation. However, these costs would have to be in excess of £80,000 per year to change our findings.

International guidelines are consensual on the need to assess PC-AKI risk, and deliver risk mediating actions prior to contrast administration to patients at higher PC-AKI risk [2, 4, 5]. Therefore, our findings will be relevant to other health systems, as long as delays leading to cancellation of planned CECT arise from patients presenting to imaging without a recent eGFR measurement.

Recently updated guidance by the National Institute for Health and Care Excellence (NICE) on AKI prevention recommends oral hydration for adults at increased AKI risk, with IV hydration only considered for inpatients at particularly high risk [37, 38]. NICE considered oral and IV hydration equivalent in preventing PC-AKI, and therefore, recommended oral hydration should be offered in outpatient settings. The guideline recommends PC-AKI risk assessment and delays to CT scans may still result from the need to orally hydrate patients with $\text{eGFR} < 30 \text{ mL/min/1.73m}^2$. As such, POC testing may be of value for the health system. It is only when hydration is assumed to result in no NHS costs, with fewer than 10% of CT scans rescheduled to rehydrate patients, that the cost-effective strategy appears to switch from 'RF+POC+Lab' to 'RF+Lab' (analysis not shown).

Uncertainties remain in the effect of IV hydration to prevent PC-AKI[15], as well as whether contrast modifies PC-AKI risk[39]. However, the findings were robust to variation on PC-AKI risk and the effect of IV hydration.

Our finding needs to be considered in light of the remaining uncertainties on PC-AKI risk and the effect of IV hydration. Exploratory analyses considering a 'no testing and manage all with CECT' strategy identified this as the strategy with the highest incremental NHB of 0.00482 QALYs (analysis reported elsewhere[11]). This suggests that the costs associated with routine testing to obtain an eGFR measurement (regardless of test used) may not be justified, in the context of the low level improvement in patient outcomes. However, decisions about forgoing eGFR testing should also consider the context of the underlying disease requiring CECT (which is variable) and the clinical efficacy of alternative mitigating strategies (such as changing imaging modality), which we have not modelled here. Further evidence and further analyses are therefore required to identify the value of foregoing eGFR testing, identifying the optimal patient management across a range of imaging referral reasons and underlying diseases. This would need to capture heterogeneity in reason for imaging, the diagnostic accuracy of alternative imaging (e.g., MRI or unenhanced CT), subsequent patient management for the underlying disease and their impact on outcomes.

Conclusion

A three-step testing sequence of screening all individuals for PC-AKI risk factors, testing individuals with at least one risk factor with a POC device, and a confirmatory laboratory test for individuals with a positive POC creatinine test, is potentially cost-effective. Using i-STAT as the POC device in this strategy type yields the highest NHB, but with minor differences compared to StatSensor. The key cost-effectiveness driver was the proportion of cancelled CECT scans. Findings were insensitive to the reduction of PC-AKI risk and associated consequences. This was due to the low PC-AKI risk estimated for this population, the lack of evidence suggesting an increased PC-AKI risk associated with the use of contrast, and the lack of evidence of impact of IV hydration in reducing the PC-AKI risk.

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