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# Validation of the OAKS prognostic model for acute kidney injury after gastrointestinal surgery

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## Abstract

**Background:** Postoperative acute kidney injury (AKI) is a common complication of major gastrointestinal surgery with an impact on short- and long-term survival. No validated system for risk stratification exists for this patient group. This study aimed to validate externally a prognostic model for AKI after major gastrointestinal surgery in two multicentre cohort studies.

**Methods:** The Outcomes After Kidney injury in Surgery (OAKS) prognostic model was developed to predict risk of AKI in the 7 days after surgery using six routine datapoints (age, sex, ASA grade, preoperative estimated glomerular filtration rate, planned open surgery and preoperative use of either an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker). Validation was performed within two independent cohorts: a prospective multicentre, international study ('IMAGINE') of patients undergoing elective colorectal surgery (2018); and a retrospective regional cohort study ('Tayside') in major abdominal surgery (2011–2015). Multivariable logistic regression was used to predict risk of AKI, with multiple imputation used to account for data missing at random. Prognostic accuracy was assessed for patients at high risk (greater than 20 per cent) of postoperative AKI.

**Results:** In the validation cohorts, 12.9 per cent of patients (661 of 5106) in IMAGINE and 14.7 per cent (106 of 719 patients) in Tayside developed 7-day postoperative AKI. Using the OAKS model, 558 patients (9.6 per cent) were classified as high risk. Less than 10 per cent of patients classified as low-risk developed AKI in either cohort (negative predictive value greater than 0.9). Upon external validation, the OAKS model retained an area under the receiver operating characteristic (AUC) curve of range 0.655–0.681 (Tayside 95 per cent c.i. 0.596 to 0.714; IMAGINE 95 per cent c.i. 0.659 to 0.703), sensitivity values range 0.323–0.352 (IMAGINE 95 per cent c.i. 0.281 to 0.368; Tayside 95 per cent c.i. 0.253 to 0.461), and specificity range 0.881–0.890 (Tayside 95 per cent c.i. 0.853 to 0.905; IMAGINE 95 per cent c.i. 0.881 to 0.899).

**Conclusion:** The OAKS prognostic model can identify patients who are not at high risk of postoperative AKI after gastrointestinal surgery with high specificity.

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## Introduction

Postoperative acute kidney injury (AKI) is a common surgical complication, affecting one in seven patients after major gastrointestinal surgery<sup>1,2</sup>. It is an important contributor to perioperative morbidity and death<sup>2</sup>, as well as long-term poorer renal and cardiovascular outcomes<sup>3,4</sup>. AKI has high resource-usage implications, including critical care beds and kidney replacement therapy<sup>5–7</sup>. Reducing the burden of postoperative AKI is therefore a research priority to patients, anaesthetists, surgeons and health providers.

Given the lack of treatment options available for AKI<sup>8</sup>, targeted methods to prevent AKI and initiation of early supportive treatment are likely have the greatest patient benefit. UK national guidelines<sup>9</sup> recommend all patients undergoing major surgery should have preoperative assessment of their postoperative AKI risk. Although 18 prognostic models have now been developed to predict risk of postoperative AKI<sup>1</sup>, none are widely used in

routine practice for general surgery patients. Published tools are limited by the use of retrospective and single-centre data, high risk of bias and heterogeneity in the AKI definitions. Furthermore, no AKI prognostic scores have been externally validated for patients undergoing abdominal surgery.

In order to meet this research need, an Outcomes After Kidney injury in Surgery (OAKS) risk-prediction model has been derived in a large prospective series from the UK and Ireland<sup>1</sup>. This was the first prognostic model with direct relevance to major gastrointestinal surgery, and used six variables routinely available before surgery. Patients were stratified into three clinically relevant groups based on risk of AKI within 7 days of surgery, as defined by the Kidney Disease Improving Global Outcomes (KDIGO) criteria: low risk (less than 10 per cent), medium risk (10 to 20 per cent) and high risk (greater than 20 per cent)<sup>10</sup>. While this prognostic model demonstrated good discrimination in the development cohort, it has not yet undergone further external validation.

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This study aimed to validate externally the OAKS risk-prediction model in two independent data sets (one international, and one regional cohort study), and explore the prognostic accuracy of the tool in stratifying patients undergoing major gastrointestinal surgery by their risk of postoperative AKI.

## Methods

### Study design

This study reports an external validation of the OAKS risk prediction model to stratify patients by their postoperative acute kidney injury (AKI) risk within 7-days of major gastrointestinal surgery<sup>11</sup>. This study was designed and reported according to the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) statement<sup>12</sup>.

### Data sources

External validation was conducted within two independent data sets. The first data set was a prospective multicentre, international, snapshot study on postoperative ileus after elective colorectal surgery (Ileus Management International: 'IMAGINE cohort'). This was conducted according to a prespecified protocol<sup>13</sup>, and included consecutive adult patients undergoing elective colorectal resection or stoma reversal in Europe, Australasia and South Africa between January and April 2018 (end of study follow-up May 2018). The primary results of this study have been published separately<sup>14</sup>. This study had narrower inclusion criteria (elective colorectal surgery) compared with the OAKS development data (elective and emergency gastrointestinal and liver surgery).

The second data set was a retrospective cohort study performed across a single National Health Service (NHS) health board encompassing one tertiary care hospital and two secondary care hospitals ('Tayside cohort'). NHS Tayside serves a population of 400 000 people with a wide range of deprivation and a mix of urban and rural environments. The population for Tayside is greater than 99 per cent white ethnicity. Data were collated on all consecutive adults who met the OAKS inclusion criteria during a period from 5 January 2011 to 22 December 2015.

There were no additional exclusion criteria applied in this external validation study. Both studies were registered locally according to the appropriate approval pathways (audit approval, ethical or institutional review board) prior to study commencement, with the analysis described encompassed within the respective approvals.

### Outcome definitions

The IMAGINE and Tayside validation studies both used the same creatinine-based definition of postoperative AKI within 7 days after surgery as the development cohort. This matched the definition used in the development study<sup>1</sup>, based on Kidney Disease: Improving Global Outcomes (KDIGO) criteria<sup>10</sup> (serum creatinine concentration increase of 26.5 µmol/l within 48 h or greater than or equal to 1.5-fold from baseline within 7 days, or if undergoing unplanned kidney replacement therapy). The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to calculate the baseline estimated glomerular filtration rate (eGFR)<sup>15</sup>. This was calculated using the lowest preoperative serum creatinine recorded (preadmission or over the course of admission). Given the imprecision of measurement of eGFR above 120 ml/min/1.73 m<sup>2</sup>, eGFR values were bounded at this level. As diagnosis of AKI was assessed objectively using

biochemical data, no blinding of the outcome assessment was deemed to be required.

### Predictors

Predictor variables collected in both validation studies included the six prognostic factors required for the OAKS prediction model<sup>1</sup>. These were derived from a list of clinically plausible variables in the derivation cohort, with bootstrap stability used to guide selection<sup>1</sup>. The same definitions as the original study were used, including: age (continuous, whole years at time of surgery), sex (binary, male/female), ASA grade (ordinal, I/II/III/IV-V), preoperative estimated glomerular filtration rate (eGFR) (continuous, ml/min/1.73 m<sup>2</sup>), planned operative approach (binary, open/minimally invasive), and preoperative use of angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) (binary, yes/no). Data on ethnicity was not collected, and so no corresponding correction was applied within the CKD-EPI equation<sup>1</sup>. Data-collection teams were unaware of the predictors that would be included in this independent validation, therefore no blinding to outcomes or other predictors was deemed necessary.

### Statistical analysis

Differences in patient characteristics and outcomes were compared between cohorts. Continuous data were plotted to assess for normality, with data formally tested for normality using a Shapiro-Wilk test as required. Normally distributed data were summarized using the mean and range, and analysed using the appropriate parametric tests. Non-normally distributed data were summarized using median and interquartile range, and analysed using equivalent non-parametric tests. Categorical data were cross-tabulated, and differences in proportions were tested using chi-squared test with Fisher's exact modification where required.

Missing data in the validation data sets were handled using multiple imputation with chained equations, under the missing at random (MAR) assumption. Five imputed datasets, each with 10 iterations, were imputed using the specified predictor variables and combined using Rubin's rules<sup>16</sup>. A further sensitivity analysis based on complete cases was performed. No formal sample size calculation was calculated *a priori* for the purpose of prognostic model validation. All available data from both data sets were used for the purpose of validation.

The original OAKS prognostic model was applied to both validation datasets in turn (including coefficients and intercepts)<sup>17</sup> (Table S1). This allowed prediction of individual risk within these data sets based on the prespecified prognostication variables of postoperative AKI within 7 days as defined by KDIGO criteria (above). Three risk groups were predefined: low risk (less than 10 per cent), medium risk (10–20 per cent) or high risk (greater than 20 per cent) of postoperative AKI. The proportion of patients within each risk group were presented using descriptive statistics.

Model performance in prediction of risk across both data sets was assessed by comparing the area under the receiver operating characteristic (AUC) curve. In accordance with the development study calibration procedures<sup>1</sup>, prognostic accuracy was estimated based upon the ability of the model to predict patients who were at high risk (greater than 20 per cent) of postoperative AKI; this was deemed to be the most clinically important group for whom the most benefit could be realized from targeted quality-improvement interventions in the future. Prognostic accuracy was presented using sensitivity, specificity, positive

predictive value (PPV) and negative predictive value (NPV). Calibration was assessed through visual inspection, and the calibration intercept (calibration-in-the-large) and slope<sup>18</sup> (an intercept of 0 and slope of 1 indicates 'perfect' calibration). No model updating or recalibration was planned or performed. All statistical analyses performed in R, version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

## Results

### Validation study overview

The international, prospective validation cohort (IMAGINE) included data for 5758 patients across 338 centres in 26 countries (Fig. 1), with 652 patients excluded from this analysis due to insufficient serum creatinines recorded to determine the occurrence of postoperative AKI. Of the 5106 patients with an AKI status, data on predictor variables were complete for 4064 (79.6 per cent). The largest proportion of missing data was for preoperative baseline serum creatinine measurement (655 patients, 12.8 per cent) and preoperative use of ACEi/ARB (464 patients, 9.1 per cent); approval was not provided to collect data on drug administration in one contributing country accounting for 99.1 per cent (460 of 464 patients) of this missing data. In comparison, the retrospective, single-country cohort (Tayside) included data for 719 patients (Fig. 1). Data on predictors and outcomes were complete for all patients in this data set.

### Comparison with model development data

Both external validation data sets represented distinct cohorts from the development cohort, with a resultant difference in the distribution of predictors (Table 1). These had more minimally invasive operations planned, and the Tayside cohort had a higher baseline eGFR and higher ASA grade in comparison with the other cohorts. However, there was a similar postoperative AKI rate observed (Table 2) across the development (14.2 per cent, 646 of 4544 patients) and validation cohorts (IMAGINE: 12.9 per cent (661 of 5106); Tayside: 14.7 per cent (106 of 719 patients)).

### Prognostic model performance

Overall, 9.2 per cent of patients (470 of 5106) in the IMAGINE cohort and 12.2 per cent of patients (88 of 719) in the Tayside cohort were identified as being at high risk of AKI (Table 2). The AUC of the prognostic model was 0.655 (95 per cent c.i. 0.596 to 0.714) in the Tayside cohort, and the pooled AUC from the multiple imputed IMAGINE cohort was 0.681 (95 per cent c.i. 0.659 to 0.703).

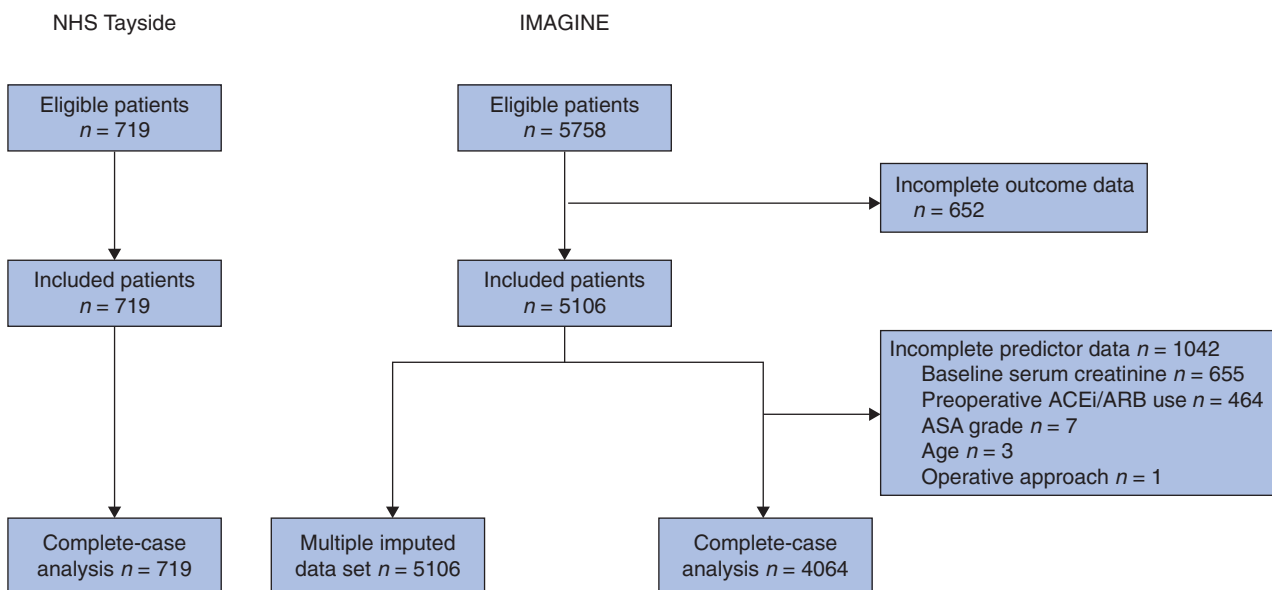
On visual assessment, the OAKS model appeared to remain well calibrated across a wide spectrum of risk (Fig. 2). However, in both external validation cohorts there was a consistent underestimation of the likelihood of postoperative AKI in patients at the highest predicted risk (positive intercept and slope greater than 1 in each model).

Consistent with the development data, almost a third of 'high-risk' patients developed a postoperative AKI in the validation cohorts, which was over four-fold higher than that observed in patients classified as low risk. Furthermore, the three prespecified risk subgroups remained clinically meaningful within the validation cohorts (Fig. 3).

### Prognostic accuracy summary statistics

The prognostic accuracy statistics of the OAKS model when calibrated to identify high-risk patients was similar in the internal validation and development cohorts (Table 3), with no statistically significant differences in the sensitivity and specificity observed. The model continues to have low sensitivity in identification of high-risk patients, with one-third of patients who were classed as high risk developing postoperative AKI. However, the specificity remained high with over 88 per cent of patients who did not develop postoperative AKI being stratified as lower risk. Notably, the negative predictive value (NPV) demonstrates that less than 10 per cent of patients who were stratified as lower risk experienced a postoperative AKI.

A complete-case analysis of the IMAGINE data set was also performed. This demonstrated calibration (Fig. S1) and prognostic accuracy (Table S2) which were consistent when compared with the results based on the multiple imputation data.



**Fig. 1** Flow chart of patient inclusion in the external validation data sets

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Table 1 Demographics of development and external validation cohorts

	Development cohort (OAKS)	Validation cohort (IMAGINE)	Validation cohort (Tayside)
<b>Country</b>			
UK/Republic of Ireland	5640 (100.0)	1972 (38.6)	719 (100.0)
Other	0 (0.0)	3134 (61.4)	0 (0.0)
<b>Subspecialty</b>			
Colorectal	4025 (71.4)	5106 (100.0)	—
Upper gastrointestinal	1121 (19.9)	0 (0.0)	—
Hepatopancreatobiliary	493 (8.7)	0 (0.0)	—
<b>Setting of surgery</b>			
Elective	4394 (77.9)	5106 (100.0)	283 (39.3)
Emergency	1246 (22.1)	0 (0.0)	436 (60.6)
<b>Age (years)</b>			
<55	1586 (28.1)	1197 (23.4)	168 (23.4)
55–64	1128 (20.0)	1115 (21.8)	166 (23.1)
65–74	1588 (28.2)	1624 (31.8)	205 (28.5)
≥75	1337 (23.7)	1167 (22.9)	180 (25.0)
Missing	—	3 (0.1)	0 (0.0)
<b>Sex</b>			
Female	2536 (45.0)	2209 (43.3)	327 (45.5)
Male	3104 (55.0)	2897 (56.7)	392 (54.5)
<b>eGFR (ml/min/1.73 m<sup>2</sup>)</b>			
≥90	2417 (42.9)	1910 (37.4)	383 (53.3)
60–90	2367 (42.0)	1996 (39.1)	278 (38.7)
30–59	740 (13.1)	493 (9.7)	54 (7.5)
<30	75 (1.3)	52 (1.0)	4 (0.6)
Missing	—	655 (12.8)	0 (0.0)
<b>Planned operative approach</b>			
Minimally invasive	2749 (48.7)	2949 (57.8)	436 (60.6)
Open	2878 (51.0)	2156 (42.2)	283 (39.4)
Missing	13 (0.2)	1 (0.0)	0 (0.0)
<b>ASA grade</b>			
I	646 (11.5)	547 (10.7)	37 (5.1)
II	2802 (49.7)	2916 (57.1)	242 (33.7)
III	1476 (26.2)	1515 (29.7)	330 (45.9)
IV–V	289 (5.1)	121 (2.4)	110 (15.3)
Missing	—	7 (0.1)	0 (0.0)
<b>Preoperative ACEi/ARB</b>			
No	4415 (78.3)	3468 (67.9)	559 (77.7)
Yes	1219 (21.6)	1174 (23.0)	160 (22.3)
Missing	—	464 (9.1)	0 (0.0)

Values in parentheses are percentages. eGFR, estimated glomerular filtration rate; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Table 2 Proportion of patients in each of the three risk groups for postoperative acute kidney injury in external validation cohort

	Development cohort (OAKS)		Validation cohort (IMAGINE)		Validation cohort (Tayside)	
	Patients	AKI	Patients	AKI	Patients	AKI
<b>Overall cohort</b>	All (n = 4544)	14.2 (n = 646)	All (n = 5106)	12.9 (n = 661)	All (n = 719)	14.7 (n = 106)
<b>High risk (&gt;20%)</b>	14.6 (n = 662)	28.5 (n = 189)	9.2 (n = 470)	32.3 (n = 152)	12 (n = 88)	35 (n = 31)
<b>Medium risk (10–20%)</b>	54.9 (n = 2494)	14.4 (n = 359)	57.0 (n = 2908)	13.8 (n = 402)	58.0 (n = 417)	14 (n = 57)
<b>Low risk (&lt;10%)</b>	30.6 (n = 1388)	7 (n = 99)	33.8 (n = 1728)	6.2 (n = 107)	29.8 (n = 214)	8 (n = 18)

Values are percentages. AKI, acute kidney injury.

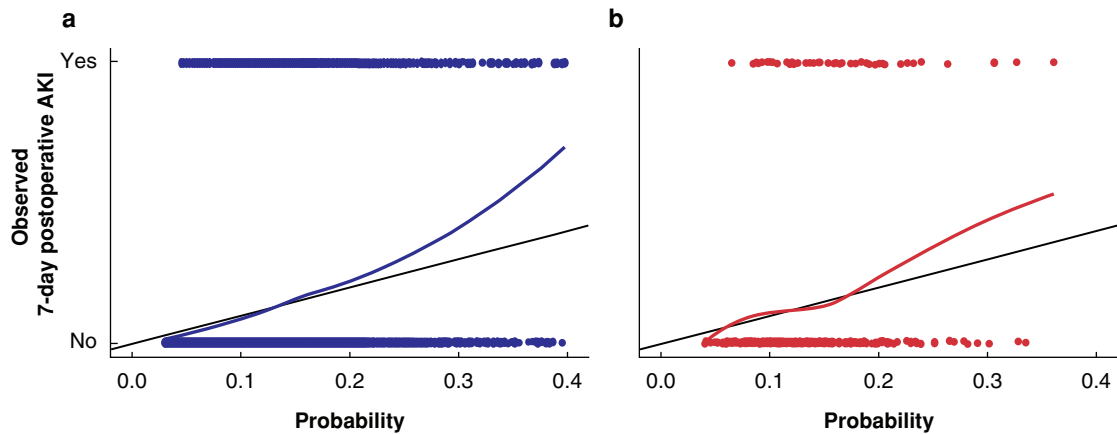
## Discussion

This study presents an external validation of a prognostic model for AKI after surgery across two large data sets: one international prospective study and one retrospective single-region study. The study is designed and reported in accordance with best practice guidelines for predictive model validation<sup>12</sup>. Whilst the model discrimination in validation data was affected by the ability to predict accurately who would develop AKI (low sensitivity), it continued to identify with high specificity groups of patients that were unlikely to be at high risk of AKI after surgery. This

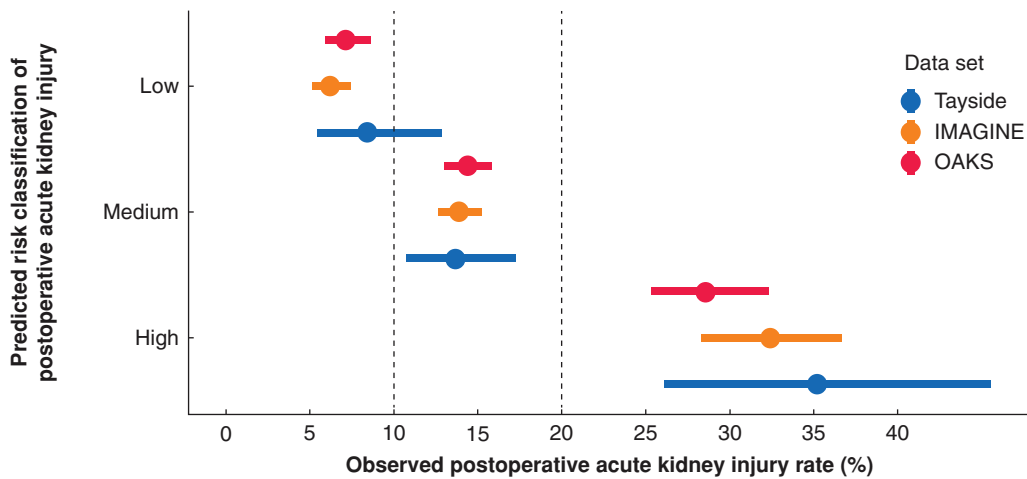
has direct relevance to clinical practice. The results of this validation study can be used to target perioperative interventions to prevent AKI towards patients at highest risk, including enhanced postoperative monitoring and specialist review<sup>8</sup>.

Previous postoperative AKI risk-prediction models have largely focused on cardiac surgery, owing to the high risk of AKI attributed to ischaemic injury following bypass procedures. However, few models have been described in non-cardiac surgery<sup>1</sup>, in particular the general surgical population where postoperative AKI continues to remain common<sup>2</sup>. This study represents the first external validation of a prognostic model for postoperative AKI in





**Fig. 2** Calibration Loess curve of observed 7-day postoperative acute kidney injury events versus predicted probability of these events  
**a** IMAGINE cohort (imputed); intercept 0.007, slope 1.40. **b** Tayside cohort; intercept 0.111, slope 1.20. AKI, acute kidney injury.



**Fig. 3** Predictive performance of the three prespecified risk subgroups in the external validation cohorts

**Table 3** Diagnostic accuracy of the OAKS prognostic model in identification of patients at high risk of acute kidney injury in the development and external validation cohorts

	Derivation cohort (OAKS)	Validation cohort (IMAGINE)	Validation cohort (Tayside)
<b>Sensitivity</b>	0.293 (0.258, 0.329)	0.323 (0.281, 0.368)	0.352 (0.253, 0.461)
<b>Specificity</b>	0.879 (0.868, 0.889)	0.890 (0.881, 0.899)	0.881 (0.853, 0.905)
<b>Positive predictive value</b>	0.285 (0.251, 0.322)	0.230 (0.198, 0.264)	0.292 (0.208, 0.389)
<b>Negative predictive value</b>	0.882 (0.872, 0.892)	0.928 (0.920, 0.936)	0.907 (0.881, 0.929)

Values in parentheses are 95 per cent confidence intervals.

this context. As a result, this is also the first to validate externally in large prospective cohorts and on an international basis, confirming the OAKS prognostic model remains robust across a range of different types of health systems and patient groups. Furthermore, the international validation has demonstrated that the six risk variables included are readily available in non-UK health settings, so risk calculation would be deliverable in practice. However, these predominantly represented high- and upper-middle-income countries. Further work is required to explore whether the OAKS model would be feasible, applicable or valid for use in low-resources settings.

AKI is a multifactorial and complex process dependent on baseline risk factors, perioperative care practices, physiological insults during the perioperative period (for example, invasive

major surgery) and postoperative complications. This may reduce the ability of prediction models to predict renal injury based on readily available variables. There were some differences in the demographics of patients included in the development and validation studies. However, the validation cohorts represented a subgroup of patients included within the development cohort, ensuring that application of the model was still valid. The OAKS model demonstrated good calibration in both validation data sets across a broad spectrum of risk, however there was evidence of underestimation of patients at the highest risk of postoperative AKI. Nevertheless, it should be noted that there would be no change to the stratification of these patients to the high-risk group (greater than 20 per cent) which had been defined *a priori*. These risk groups provide a useful way to improve relevance to

clinical practice, and this analysis has confirmed these remain meaningful cut-offs to delineate distinct subgroups. While the overall discriminative performance was affected by the ability to predict accurately who would develop AKI (low sensitivity), the OAKS prediction model was able to identify groups of patients that were unlikely to be at high risk of AKI after surgery with high specificity. This allows anaesthetists and surgeons to prioritize monitoring and resource-intensive perioperative optimization for a subset of patients who may be subject to increased risk. While there may be avenues to improve diagnostic accuracy further (whether through machine learning<sup>17</sup> and/or incorporation of novel prognostic factors<sup>19</sup>), these should be balanced with ensuring these remain feasible to implement within routine clinical practice.

This study had several limitations. First, no blinding to outcomes or predictors was performed to study investigators, however the outcome assessment was performed using biochemical data at low risk of measurement or observer bias. Second, as external validation was performed on observational cohorts, data completeness was limited by what was routinely recorded in clinical practice. In particular in the IMAGINE cohort, probably due to the lower risk nature of elective surgery and potential heterogeneity in international care protocols, an important minority of patients (12.8 per cent) did not have preoperative baseline creatinine measurement. Nevertheless, missing data were robustly handled via multiple imputation to minimize patient exclusion, with no evidence of significant bias on complete-case analysis. Third, each validation data set used here represents a subgroup of who were included in the original OAKS study (the Tayside study is limited to a specific region, and the IMAGINE study is limited to elective colorectal surgery). Therefore, this does not represent validation in a 'like-for-like' cohort, although consistency of the results on validation (in spite of these differences from the derivation cohort) would raise confidence in the robustness of the model. Finally, it must be recognized that the OAKS model has been derived and validated within predominantly high-income countries and as such may not have equal representation of all ethnicity groups, however it is likely to have diversity that represents the normal surgical population in included countries and regions. Furthermore, there was no racial adjustment made to the CKD-EPI equation in this study, and the ongoing inclusion of this component in calculating eGFR is under intense scrutiny<sup>20</sup>. As such, future external validation may be appropriate before these results can be applied confidently to other populations.

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## Data accessibility

Data-sharing requests will be considered by the respective management groups upon written request to the corresponding author. If agreed, deidentified participant data will be available, subject to a data-sharing agreement.

## Supplementary material

**Supplementary material** is available at *BJS Open* online.

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