




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

STARSurG Collaborative and EuroSurg Collaborative\* 

\*Correspondence to: James Glasbey, Academic Department of Surgery, Room 29, 4th Floor, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Edgbaston, Birmingham B15 2TH, UK (e-mail: [j.glasbey@bham.ac.uk](mailto:j.glasbey@bham.ac.uk); [collaborate@starsurg.org](mailto:collaborate@starsurg.org), [@STARSurgUK](https://twitter.com/STARSurgUK))

Members of the STARSurG Collaborative and EuroSurg Collaborative are co-authors of this study and are listed under the heading Collaborators.

## 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).

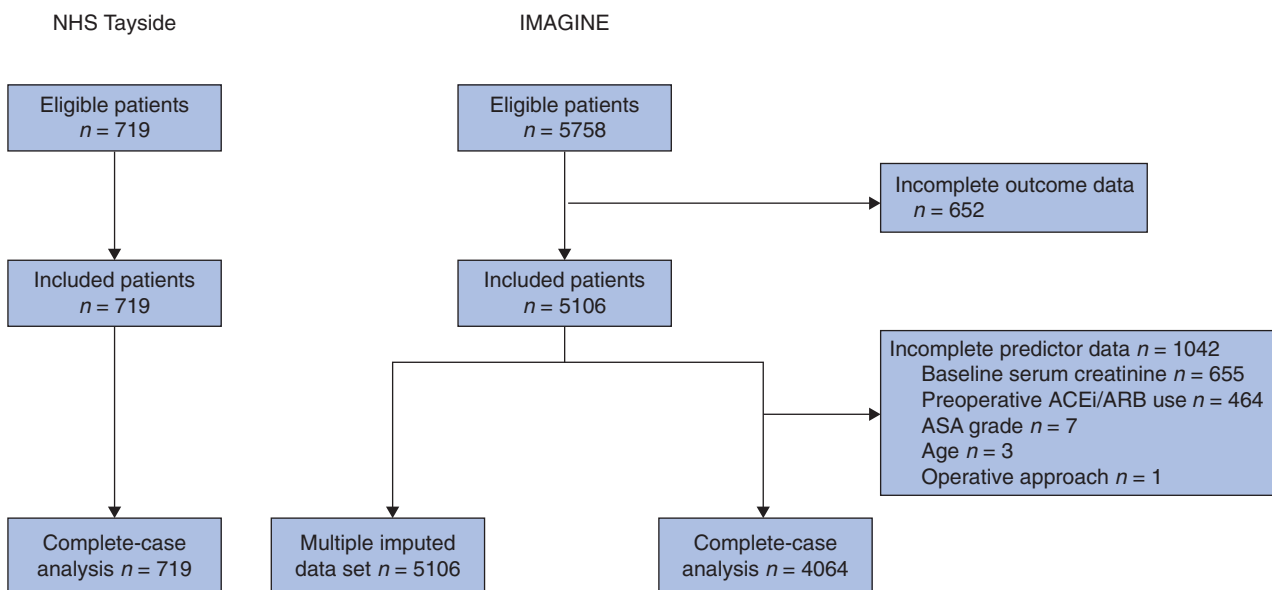
On visual assessment, the OAKS model appeared to remain well calibrated across a wide spectrum of risk (Fig. 2). However, in both external validation cohorts there was a consistent underestimation of the likelihood of postoperative AKI in patients at the highest predicted risk (positive intercept and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

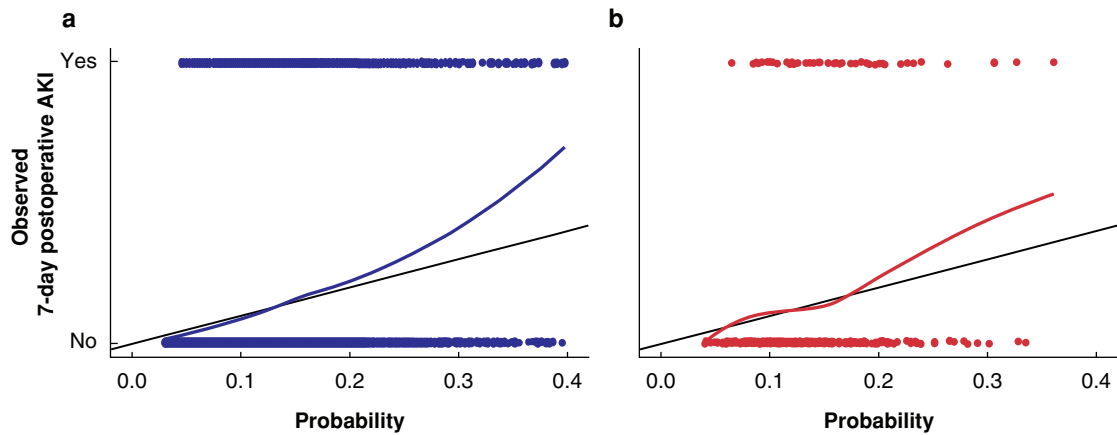
Values are percentages. AKI, acute kidney injury.

## Discussion

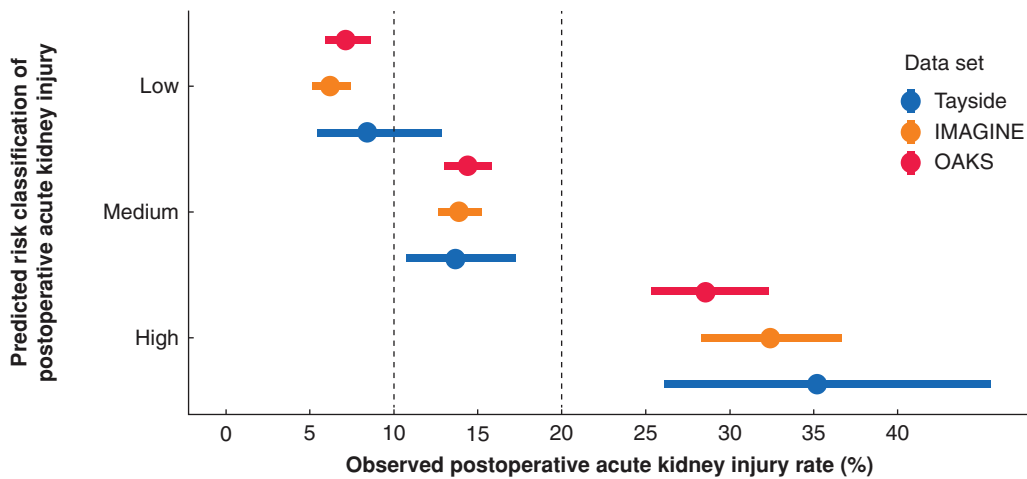
This study presents an external validation of a prognostic model for AKI after surgery across two large data sets: one international prospective study and one retrospective single-region study. The study is designed and reported in accordance with best practice guidelines for predictive model validation<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.

## Collaborators

W. U. R. Ahmed (University of Oxford, Oxford, UK), S. Bhatia (University of Cardiff, Cardiff, UK), K. A. McLean (University of Edinburgh, Edinburgh, UK), R. Khaw (University of Newcastle, Newcastle, UK), D. Baker (University of Sheffield, Sheffield, UK), S. K. Kamarajah (University of Birmingham, Birmingham, UK), S. Bell (University of Dundee, Dundee, UK), D. Nepogodiev (University of Birmingham, Birmingham, UK), E. M. Harrison (University of Edinburgh, Edinburgh, UK), J. C. Glasbey (University of Birmingham, Birmingham, UK), A. Borakati (Royal Free Hospital, London, UK), J. Burke (University of Leeds, Leeds, UK), T. M. Drake (University of Edinburgh, Edinburgh, UK), M. F. Bath (Whipps Cross University Hospital, London, UK), H. A. Claireaux (University of Oxford, Oxford, UK), B. Gundogan (University College London Hospital, London, UK), M. Mohan (University of Cambridge, Cambridge, UK), P. Deekonda (University of Exeter, Exeter, UK), C. Kong (University of

Glasgow, Glasgow, UK), H. Joyce (King's College London, London, UK), L. McNamee (Royal College of Surgeons in Ireland, Dublin, Ireland), E. Woin (University College London, London, UK), C. Khatri (University of Warwick, Warwick, UK), J. E. Fitzgerald (University College London, London, UK), A. Bhangu (University of Birmingham, Birmingham, UK), N. Arulkumaran (University College London, London, UK), S. Bell (University of Dundee, Dundee, UK), F. Duthie (University of Edinburgh, Edinburgh, UK), J. Hughes (University of Edinburgh, Edinburgh, UK), T. D. Pinkney (University of Birmingham, Birmingham, UK), J. Prowle (Queen Mary University of London, London, UK), T. Richards (University of Western Australia, Perth, Australia), M. Thomas (Heart of England NHS Foundation Trust, Birmingham, UK), R. Blanco-Colino (Vall d'Hebron, Barcelona, Spain), S. J. Chapman (University of Leeds, Leeds, UK), J. C. Glasbey (University of Birmingham, Birmingham, UK), F. Pata (Azienda Sanitaria Provinciale Cosenza, Giannettasio Hospital, Cosenza, Italy), G. Pellino (Università degli Studi della Campania "Luigi Vanvitelli, Caserta, Italy), A. Sgrò (University of Edinburgh, Edinburgh, UK), A. Soares (University College London, London, UK), T. van Elst (Amsterdam UMC, Amsterdam, Netherlands), S. Van Straten (Amsterdam UMC, Amsterdam, Netherlands), C. H. Knowles (University College London, London, UK), D. Nepogodiev (University of Birmingham, Birmingham, UK); K. Dynes (University of Aberdeen, Aberdeen, UK); M. Patel, P. Patel (Queen Mary University, London, UK); C. Wigley, R. Suresh (University of Birmingham, Birmingham, UK); A. Shaw (University of Bristol, Bristol, UK); S. Klimach (Brighton and Sussex Medical School, Brighton, UK); P. Jull (University of Cambridge, Cambridge, UK); D. Evans, R. Preece (Cardiff University, Cardiff, UK); I. Ibrahim (University of Dundee, Dundee, UK); V. Manikavasagar (Durham University, Durham, UK); R. Smith (University of East Anglia, UK); F. S. Brown (University of Edinburgh, Edinburgh, UK); P. Deekonda (Peninsula, Exeter and Plymouth, UK); R. Teo, D. P. Y. Sim (University of Glasgow, Glasgow, UK); A. Borakati (Hull and York Medical School, Hull and York, UK); A. E. Logan, I. Barai (Imperial College, London, UK); H. Amin (Keele University, Keele, UK); S. Suresh, R. Sethi (King's College, London, UK); W. Gul (University of Lancaster, UK); W. Bolton (University of Leeds, Leeds, UK); O. Corbridge (Leicester Medical School, Leicester, UK); L. Home, M. Attalla (University of Liverpool, Liverpool, UK); R. Morley, C. Robinson (University of Manchester, Manchester, UK); T. Hoskins (Newcastle University Medical School, Newcastle upon Tyne, UK); R. McAllister (University of Nottingham, Nottingham, UK); S. Lee (National University of Ireland, Galway, UK); Y. Dennis (University of Oxford, Oxford, UK); G. Nixon (Queen's University Belfast, Belfast, UK); E. Heywood (University of Sheffield, Sheffield, UK); H. Wilson (Southampton Medical School, Southampton, UK); L. Ng, S. Samaraweera (St George's University of London, London, UK); A. Mills (Swansea University, Swansea, UK); C. Doherty (Trinity College, Dublin, UK); E. Woin (University College London, London, UK); J. Belchos (University College Dublin, Dublin, UK); V. Phan (University of Warwick, Coventry, UK); M. Lim, F. A. Miller, T. Chouari, T. Gardner, N. Goergen, J. D. B. Hayes, C. S. MacLeod, R. McCormack, A. McKinley, S. McKinstry, W. Milligan, L. Ooi, N. M. Rafiq, T. Sammut, E. Sinclair, M. Smith, J. Wong, A. D. Ablett, T. Tie-Gill, G. Ramsay, L. De Paola, S. McGuckin, A. Alshakhs, A. Ahmeidat, J. Wong, N. Goergen, A. A. Francis (Aberdeen Royal Infirmary, UK); C. Baker, A. P. R. Boulton, J. Collins, H. C. Copley, N. Fearnhead, H. Fox, T. Mah, J. McKenna, V. Naruka, N. Nigam, B. Nourallah, S. Perera, A.

Qureshi, S. Saggarr, L. Sun, X. Wang, D. D. Yang, Z. Ali, L. Mullarkey, M. F. Bath, R. Walshe, E. Lewis, B. Berry, J. Moneim, S. Mookerjee, A. Al-hadithi (Addenbrooke's Hospital, UK); P. Carroll, C. Doyle, S. Elangovan, A. Falamarzi, K. Gascon Perai, E. Greenan, D. Jain, M. Lang-Orsini, S. Lim, L. O'Byrne, P. Ridgway, S. Van der Laan, J. Wong (Adelaide and Meath Hospital, Tallaght, UK); J. Arthur, J. Barclay, P. Bradley, C. Edwin, E. Finch, E. Hayashi, M. Hopkins, D. Kelly, M. Kelly, N. McCartan, A. Ormrod, A. Pakenham, S. Christy (Aintree University Hospital, UK); J. Hayward, C. Hitchen, A. Kishore, T. Martins, J. Philomen, R. Rao, C. Rickards (Airedale General Hospital, UK); N. Burns, M. Copeland, C. Durand, A. Dyal, A. Ghaffar, A. Gidwani, M. Grant, C. Gribbon, A. Gruhn, M. Leer, O. Ojofeitimi, L. Carroll, A. Hylands, L. P. Delaugere, D. Reveendran (Altnagelvin Area Hospital, UK); K. Ahmad, G. Beattie, M. Beatty, G. Campbell, G. Donaldson, S. Graham, D. Holmes, S. Kanabar, H. Liu, C. McCann, R. Stewart, S. Vara, C. Coulter, C. Ralston, L. Lavery, P. Gallagher (Antrim Area Hospital, UK); O. Ajibola-Taylor, E. J. E. Andah, C. Ani, N. M. O. Cabdi, G. Ito, M. Jones, A. Komoriyama, P. Patel, L. Titu, A. Ahmed, Y. Q. Yeo, D. Elliott, J. Bennett, M. Mcnamara, S. Sivarajah, C. Dunmore (Arrowe Park Hospital, UK); M. Basra, P. Gallogly, G. Harinath, S. H. Leong, A. Pradhan, I. Siddiqui, S. Zaat (Ashford William Harvey Hospital, UK); A. Ali, M. Galea, W. L. Looi, J. C. K. Ng, M. M. H. Farhan-Alanie, G. Aitken, M. Nair, M. H. Aly, M. Buari, M. M. H. Farhan-Alanie (Ayr Hospital, UK); G. Atkin, A. Azizi, Z. Cargill, Z. China, J. Elliot, R. Jebakumar, J. Lam, G. Mudalige, C. Onyerindu, M. Renju, V. Shankar Babu, K. Ahmed, Z. Sheikh, M. Monks, J. Lehmann, O. Rotimi (Barnet General Hospital, UK); M. Hussain, N. Joji, B. Lovett, H. Mownah, L. Dwyer-Hemmings, A. Busuttill, J. Powell, C. Hensher, F. Vivian (Basildon University Hospital, UK); B. Ali, B. Cresswell, A. K. Dhillon, Y. S. Dupaguntla, C. Hungwe, J. D. Lowe-Zinola, J. C. H. Tsang, K. Wcislo (Basingstoke and North Hampshire Hospital, UK); K. Bevan, C. Cardus, A. Duggal, S. Hossain, M. McHugh, M. Scott, Z. Millar, S. Hirose, I. Ogunmwonyi, D. Nakakande (Bedford Hospital, UK); F. Chan, R. Evans, E. Gurung, B. Haughey, B. Jacob-Ramsdale, M. Kerr, J. Lee, E. McCann, K. O'Boyle, N. Reid, I. Kwek, H. Gaze, A. Nirmalanantha, M. A. Bin Amran, A. Foulkes, N. Jones, I. S. F. Lau (Belfast City Hospital, UK); F. Hayat, S. Hodgson, R. Johnston, W. Jones, M. Khan, T. Linn, S. Long, P. Seetharam, S. Shaman, B. Smart, S. Pillai, G. Khoury, T. Powell, I. Maleyko, A. Sangheli, M. Ransome, M. Isse, O. Aromolaran, H. Bholah (Blackpool Victoria Hospital, UK); A. Anilkumar, J. Davies, J. Griffith, B. Hughes, Y. Islam, D. Kidanu, N. Mushaini, I. Qamar, H. Robinson, M. Schramm, C. Yan Tan, V. Murray, L. Theocharidou, T. Malik, I. Janmohamed, B. Carhart, A. Khan (Bradford Royal Infirmary, UK); H. Apperley, C. Billyard, J. M. Blazeby, S. P. Cannon, S. Carse, A. Göpfert, A. Loizidou, J. Parkin, E. Sanders, S. Sharma, G. Slade, R. Telfer, I. Whybrow Huppertz, E. Worley, A. Asif, A. Asif, R. Hullait, P. Quinn, A. Rylance, S. Butt, J. Leathes (Bristol Royal Infirmary, UK); L. Chandramoorthy, C. Friend, L. Harris, P. Jain, M. J. Karim, K. Killington, J. McGillicuddy, C. Rafferty, N. Rahunathan, T. Rayne, Y. Varathan, N. Verma, D. Zanichelli (Castle Hill Hospital, UK); M. Arneill, F. Brown, B. Campbell, L. Crozier, J. Henry, C. McCusker, P. Prabhakaran, R. Wilson, S. Karelia, J. M. Clements, M. Rainey (Causeway Hospital, UK); U. Asif, M. Connor, S. Dindyal, N. Math, A. Pagarkar, H. Saleem, I. Seth, S. Sharma, N. Standfield, T. Swartbol (Charing Cross Hospital, UK); R. Adamson, J. E. Choi, O. El Tokhy, W. Ho, N. R. Javaid, M. Kelly, A. S. Mehdi, D. Menon, I. Plumpre, S. Sturrock, J. Turner, O. Warren, N. Joshi, A. Rahman, M. Gallagher (Chelsea and Westminster Hospital, UK); E. Crane, B. Ferris, C. Gadsby, J. Smallwood, M. Vipond, V. Wilson (Cheltenham General Hospital, UK); T. Amarnath, A. Doshi, C. Gregory, K. Kandiah, B. Powell, H. Spoor, C. Toh, R. Vizor, N. Rebuffa, R. Abdelgalil, R. Siaw Yen Lai, E. Smith (Chesterfield Royal Hospital, UK); M. Common, K. Dunleavy, S. Harris, C. Luo, Z. Mesbah, A. Prem Kumar, A. Redmond, S. Skulsky, T. Walsh (Connolly Hospital, Blanchardstown, UK); D. Daly, L. Deery, E. Epanomeritakis, M. Harty, D. Kane, K. Khan, R. Mackey, J. McConville, K. McGinnity, G. Nixon, H. L. Wong, C. McCusker (Craigavon Area Hospital, UK); A. Ang, J. Y. Kee, E. Leung, S. Norman, S. V. Palaniappan, P. Partha Sarathy, T. Yeoh (Crosshouse Hospital, UK); J. Frost, P. Hazeldine, L. Jones, M. Karbowski, C. Macdonald, A. Mutarambirwa, A. Omotade, M. Runkel, G. Ryan, N. Sawers, C. Searle, S. Suresh, S. Vig, L. Hlukha, G. Pike, F. Kamel, R. Thakkar, O. McAuliffe (Croydon Hospital, UK); A. Ahmad, R. McGartland, R. Sim, A. Song, J. Wayman (Cumberland Infirmary, UK); R. Brown, L. H. Chang, K. Concannon, C. Crilly (Daisy Hill Hospital, UK); T. J. Arnold, A. Burgin, F. Cadden, C. H. Choy, M. Coleman, D. Lim, J. Luk, P. Mahankali-Rao, A. J. Prudence-Taylor, D. Ramakrishnan, J. Russell (Derriford Hospital, UK); A. Fawole, J. Gohil, B. Green, A. Hussain, L. McMenamin, L. McMenamin, M. Tang (Dewsbury Hospital, UK); F. Azmi, S. Benchetrit, T. Cope, A. Haque, A. Harlinska, R. Holdsworth, T. Ivo, J. Martin, T. Nisar, A. Patel, K. Sasapu, J. Trevett, G. Vernet (Diana, Princess of Wales Hospital, UK); A. Aamir, C. Bird, A. Durham-Hall, W. Gibson, J. Hartley, N. May, V. Maynard, M. Goble, E. Downs, L. Wheldon, E. Baggus, A. Mandal, A. Nayeem, S. Ahmed, W. Fradley (Doncaster Royal Infirmary, UK); S. Johnson, C. McDonald Wood, M. O'Brien, J. Orbell, T. D. Stringfellow, F. Tenters, S. Tresidder, C. Wilson, S. Gallagher, T. Criswell, J. Ward, A. Mukkavilli, B. Stubbs, W. Fordyce (Dorset County Hospital, Dorchester, UK); W. Cheung, A. Grant, N. Tod, Z. Yi Tew, N. Suchdev, S. Wei Lim, Z. Yi Tew, A. A. Francis (Dr Gray's, Elgin, UK); M. Bews-Hair, Z. H. Lim, S. W. Lim, M. Vella-Baldacchino (Dumfries and Galloway Infirmary, UK); S. Auckburally, A. Chopada, S. Easdon, R. Goodson, F. McCurdie, M. Narouz, A. Radford, E. Rea, O. Taylor, T. Yu, S. R. Sookramanien, A. Chan, G. Bointas (Ealing Hospital, UK); M. Alfa-Wali, L. Amani, I. Auluck, P. Bruce, J. Emberton, R. Kumar, N. Lagzouli, A. Mehta, A. Murtaza, M. Raja (Epsom Hospital, UK); I. S. Dennahy, K. Frew, A. Given, Y. Y. He, M. A. Karim, E. P. MacDonald, E. McDonald, D. McVinnie, S. K. Ng, A. Pettit, D. P. Y. Sim (Forth Valley Royal Hospital, UK); S. D. Berthaume-Hawkins, R. Charnley, K. Fenton, D. Jones, C. Murphy, J. Q. Ng, R. Reehal, H. Robinson, S. S. Seraj, E. Shang, A. Tonks, P. White, A. Yeo, M. Paul, K. L. Ward, M. Bagnall (Freeman Hospital, UK); P. Chong, R. Gabriel, N. Patel, E. Richardson, L. Symons (Frimley Park Hospital, UK); D. Aubrey-Jones, S. Dawood, M. Dobrzynska, S. Faulkner, H. Griffiths, F. Mahmood, P. Patel, M. Perry, A. Power, R. Simpson, S. A. Pherwani, K. Wang, L. Mitchell, J. Heyworth, S. Ayyar (Furness general hospital, UK); A. Ali, P. Brobbey, A. Burrows, P. Elder, R. Ganyani, C. Horseman, P. Hurst, H. Mann, K. Marimuthu, S. McBride, E. Pilsworth, N. Powers, P. Stanier, R. Obukofe, R. Obukofe, R. Polson, D. Mason, E. Mackenzie (George Eliot Hospital, UK); R. Innes, T. Kersey (Gilbert Bain Hospital, Shetland, UK); M. Kopczynska, N. Langasco, N. Patel, R. Rajagopal, C. Russell, C. Russell, N. Doyle, Z. Habib, M. Zardab, F. Sartaj, H. Farooq, M. Tabibi, L. Imam (Glan Clwyd Hospital, Rhyl, UK); B. Atkins, W. Beasley, Z. Cheng Lim, A. Gill, H. Li Ang, H. Williams, T. Yogeswara, D. J. Drury, S. J. James, R. Barnett, A. B. Teasdale, E. T. J. Richardson, D. A. Thomas, S. Ahmed, R. L. Williams, H. F. Najabat-Lattif, B.

Akram (Glangwili General Hospital, Carmarthen, UK); R. Carter, M. Fam, J. Fong, J. Latter, M. Long, S. Mackinnon, C. McKenzie, J. Osmanska, V. Raghuvir, A. Shafi, K. Tsang, L. Walker, E. Cahya, G. Lou, M. Coyle, K. Homyer, L. Y. Zhu, M. Woods (Glasgow Royal Infirmary, UK); K. Bountra, O. Coldicutt, D. Fletcher, S. Hudson, S. Iqbal, T. Lopez Bernal, J. W. B. Martin, F. Moss-Lawton, J. Smallwood, M. Vipond, I. Suchett-Kay, J. Chang, H. O'Callaghan, I. Suchett-Kaye, T. H. Mihailidis (Gloucestershire Royal Hospital, UK); A. Cardwell, K. Edgerton, J. Laws, A. Rai, K. Robinson, K. Waite, J. Ward, H. Youssef, H. Alawattegama, E. Seite, A. Barrett, E. Riordan, W. Lam, M. Dowdeswell, C. Mulvenna (Good Hope Hospital, UK); C. Knight, P. Y. Koo, A. Lazarou, S. Stanger, C. Thorn, M. C. Triniman, T. Netke, T. Netke, O. Awokoya, L. Gurowich, K. Dhera, S. Hossaini (Great Western Hospital, Swindon, UK); A. Botha, L. Boyles, S. Cumming, S. Deepak, A. Ezzat, A. J. Fowler, A. M. Gwozdz, S. F. Hussain, S. Khan, H. Li, B. Lu, Morrell, J. Neville, R. Nitiahpapand, O. Pickering, H. Sagoo, E. Sharma, K. Welsh, L. Williams, S. Hayat, L. Williams, L. Tincknell, M. Spazzapan, F. Teeling, K. Sysum (Guys and St. Thomas' Hospital, UK); S. Denley, S. Khan, J. Latter, M. Latter, S. Khan (Hairmyres Hospital, UK); M. Agarwal, N. Al-Saadi, R. Bhabra, A. Gupta, Z. A. R. Jawad, L. R. Jiao, K. Khan, G. Mahir, S. Singagireson, B. L. Thoms, B. Tseu, R. Wei, N. Yang (Hammersmith Hospital, UK); N. Britton, D. Leinhardt, M. Mahfooz, A. Palkhi, M. Price, S. Sheikh (Harrogate District Hospital, UK); M. Barker, D. Bowley, M. Cant, U. Datta, M. Farooqi, A. Lee, G. Morley, M. Naushad Amin, A. Parry, S. Patel, S. Strang, N. Yoganayagam, M. Guruswamy, W. Beedham, E. Brazier, M. Elghobashy, M. Bajaj, H. Mann, E. Etel (Heartlands Hospital, Birmingham, UK); A. Adlan, S. Chandramoorthy, Y. Choudhary, K. Das, M. Feldman, B. France, R. Grace, H. Puddy, P. Soor, A. Kisiel, M. Woodmass, H. Hayden, A. Kisiel, Y. Ali, S. Husain (Hereford County Hospital, UK); M. Ali, P. Dhillon, A. Faraj, L. Gerard, M. Glover, H. Imran, S. Kim, Y. Patrick, J. Peto, A. Prabhudesai, R. Smith, A. Tang, N. Vadgama (Hillingdon Hospital, UK); R. Dhaliwal, T. Ecclestone, A. Harris, D. Ong, D. Patel, C. Philp, E. Stewart, L. Wang, E. Wong, Y. Xu (Hinchingbrooke Hospital, UK); T. Ashaye, T. Fozard, F. Galloway, S. Kaptanis, P. Mistry, T. Nguyen, F. Olagbaiye, M. Osman, Z. Philip, R. Rembacken, S. Tayeh, K. Theodoropoulou, F. Y. Liu, A. Arnold, A. C. Pedersen, P. Cunha, M. Ahmed, S. Al Zawawi, V. Kudva, F. Y. Liu, K. Theodoropoulou (Homerton Hospital, UK); A. Herman, J. Lau, A. Saha, M. Trotter, M. Miscampbell, A. V. Robinson, J. Johnston, A. Dharni, S. Lamb, T. Westerman (Huddersfield Royal Infirmary, UK); O. Adeleye, D. Cave, T. Gunwa, J. Magalhães, S. Makwana, R. Mason, M. Parish, H. Regan, P. Renwick, G. Roberts, D. Salekin, C. Sivakumar, A. Tariq (Hull Royal Infirmary, UK); I. Liew, A. McDade, D. Stewart, E. Evans, L. Campbell, M. Gillespie, C. M. Cheong (Inverclyde Royal Hospital, UK); M. Hague, N. Hudson-Peacock, C. E. S. Jackson, F. James, J. Pitt, E. Y. Walker, K. Kulathevanayagam, A. Varghese, S. I. Ike (Ipswich Hospital, UK); R. Aftab, J. J. Ang, S. Anwar, J. Battle, E. Budd, J. Chui, H. Crook, P. Davies, S. Easby, E. Hackney, B. Ho, S. Z. Imam, J. Rammell, T. S. M. Chu, B. Baljer, J. A. W. Mogg, P. Rai (James Cook University Hospital, UK); H. Andrews, C. Perry, P. Schinle (Jersey General Hospital, UK); P. Ahmed, T. Aquilina, E. Balai, M. Church, E. Cumber, A. Curtis, G. Davies, Y. Dennis, E. Dumann, S. Greenhalgh, P. Kim, S. King, K. H. M. Metcalfe, L. Passby, N. Redgrave, Z. Soonawalla, S. Waters, A. Zornoza, H. Claireaux, H. A. Claireaux, M. Williams, R. Smillie, J. Goetz, E. Appleby, T. Fadipe, S. Vaughan-Burleigh, R. Davies (John Radcliffe Hospital and Churchill Hospital, UK); I. Gulzar, J. Hole, K. Hull, H. Ishaq, J. Karaj, A. Kelkar, E. Love, S. Patel, D. Thakrar, M. Vine, A. Waterman, P. James, G. Puri, P. Hussain, P. James, R. Flather, A. Cutler, S. Pathak, J. Sheldon, T. Collicott, M. al-Ausi, M. Ko (Kettering General Hospital, UK); N. P. Dib, N. Francis, M. Hanson, R. Ingleton, K. S. Sadanand, N. Sukirthan, A. Mondal, A. Mondal, A. Jovaisaite, S. M. Shah, N. Khalid, D. Gutmann, S. Davison, Y. J. Alame, L. Syed, W. J. Owen (King Georges Hospital, London, UK); S. Arnell, M. Ball, N. Bassam, G. Beghal, A. Chang, V. Dawe, A. George, T. Huq, A. Hussain, B. Ikram, L. Kanapeckaite, M. Khan, D. Ramjas, A. Rushd, S. Sait, M. Serry, E. Yardimci, R. Kalderon, S. D. Ahsan, R. Kalderon, U. Anthony-Uzoeto, C. Macleod Hall, S. Zheng, K. Wynter (King's College Hospital, UK); S. Capella, L. Chenciner, C. Episkopos, E. Karam, C. McCarthy, W. Moore-Kelly, N. Watson, H. H. Nadama, C. James, D. Sapre, R. Ghosh, J. Baird, L. Cockburn, O. Blackwood, H. H. Nadama, W. Simpson (King's Mill Hospital, UK); V. Ahluwalia, J. Barnfield, O. Ben-Gal, I. Bloom, A. Gharatya, K. Khodatars, N. Merchant, A. Moonan, M. Moore, K. Patel, H. Spiers, K. Sundaram, J. Turner, S. Jeong, S. Bishop, J. Collins (Kingston Hospital, UK); M. F. Bath, J. Black, H. Chadwick, L. Huisman, H. Ingram, S. Khan, L. Martin, M. Metcalfe, P. Sangal, J. Seehra, A. Thatcher, S. Venturini, I. Whitcroft, R. Bate, C. Hobson, A. H. Adam, C. Redclift, J. Do, O. Adeleye, F. Poli, A. Batterham, S. Brown, A. Pandya (Leicester General Hospital, UK); Z. Afzal, S. Brown, A. Gani, A. Gooma, N. Hussein, S. Y. Oh, N. Pazhaniappan, E. Sharkey, T. Sivagnanasithiyar, C. Williams, J. Yeung, J. N. Parekh, W. Clay, K. Pieri, A. Jackson, S. Brown, A. Saxena, B. Gurung, T. Oyebola, F. O'Brien, S. Reilly (Leicester Royal Infirmary, UK); L. Cruddas, S. Gurjar, A. Pau, R. Prakash, R. Randhawa, B. Djeugam, S. Gardezi, S. Ul-Hasan, M. P. Martin-Hernandez, M. Sisley, S. Modi, R. Antakia, J. Archer (Luton and Dunstable University Hospital, UK); L. Chen, I. Eiben, M. Naylor, D. Osei-Bordom, R. Trenear (Maidstone Hospital, UK); J. Bannard-Smith, N. Griffiths, B. Y. Patel, F. Saeed, Z. Al-Saraff, A. Elbayouk, Y. J. Soh, J. Mather, Z. Yusuf, Z. Al-Sarraf, M. Naja, S. B. Rassool, J. Convill, C. Auty (Manchester Royal Infirmary, UK); H. Abdikadir, M. Bennett, R. Church, S. E. Clements, J. Court, A. Delvi, J. Hubert, B. Macdonald, F. Mansour, R. R. Patel, R. Perris, S. Small, J. P. H. Tam, Y. Nikookam, A. Warsame, J. P. H. Tam, C. Pace, M. Kiandee, R. Ridwan, C. Carey, F. Hirri (Manor Hospital, Walsall, UK); A. Betts, N. Brown, A. Chong, C. Croitoru, A. Grey, P. Hickland, C. Ho, D. Hollington, L. McKie, A. R. Nelson, H. Stewart (Mater Hospital, Belfast, UK); P. Eiben, M. Nedham (Medway NHS Trust, UK); I. Ali, T. Brown, S. Cumming, C. Hunt, C. Joyner, C. McAlinden, J. Roberts, D. Rogers, A. Thachettu, N. Tyson, R. Vaughan, N. Verma, T. Yasin, A. Powell-Chandler, M. J. A. McMillan, J. J. Ling, A. Powell-Chandler, L. Pendelbury, K. Kerimzade, A. Tang, E. O. Howard, S. Humayun, O. J. Wadsworth, C. D. Roche (Morrison Hospital, UK); K. Andrew, N. Bhamra, S. Leong, R. Mistry, H. Noble, F. Rashed, N. R. Walker, L. Watson, M. Worsfold, E. Yarham, F. Wood (Musgrove Park Hospital, Taunton, UK); H. Abdikadir, A. Arshad, B. Barmayehvar, L. Cato, N. Chan-lam, V. Do, A. Leong, Z. Sheikh, T. Zheleniakova, K. Tan, F. Abdelhameed, C. Haglund, I. Radnaeva, N. Hu, S. Rambhatla, D. Waldron, P. Madahar, S. Malik (New Cross Hospital, Wolverhampton, UK); J. Coppel, S. T. Hussain, R. Mahmood, R. Nourzaie, J. Prowle, S. Sheikh-Ali, A. Thomas (Newham Hospital, UK); A. Alagappan, R. Ashour, H. Bains, J. Diamond, J. Gordon, B. Ibrahim, M. Khalil, D. Mittapalli, Y. N. Neo, P. Patil, F. S. Peck, N. Reza, I. Swan, M. Whyte, A. Campbell, A. Campbell, L. C. Meney, I. Ibrahim, C. K. Kang, J. Z. J. Chiu, V. Livie, B. Ibrahim, M. Khalil, J. Livie (Ninewells Hospital, UK); S. Chaudhry, J. Hemon, H. Khawar, J. O'Brien, M.



Pullinger, K. Rothnie, S. Ujjal, R. e. b. e. c. c. a. Gorgievska, G. Pooley, B. Shishkin, R. Gorgievska, J. Docherty, A. Southgate, A. Coomes, F. A. Chaudhry (Norfolk and Norwich University Hospital, UK); S. Bhatte, J. Curtis, S. Green, A. Mayer, G. Watkinson, A. Ragavoodoo, A. Ragavoodoo, L. Mercer, C. Mercer (North Durham University Hospital, UK); K. Chapple, T. Hawthorne, M. Khaliq, L. Majkowski, T. A. M. Malik, K. Mclauchlan, B. Ng Wei En, T. O'Connor, S. Parton, S. D. Robinson, M. I. Saat, B. N. Shurovi, K. Varatharasasingam, A. E. Ward (Northern General Hospital, UK); K. Behranwala, M. Bertelli, J. Cohen, F. Duff, O. Fafemi, R. Gupta, M. Manimaran, J. Mayhew, D. Peprah, M. H. Y. Wong, S. Patel, O. Morice, A. Burzic, J. Cheung, A. Shashidhara, G. Theodoraki, J. Birk, A. Ong (North Middlesex Hospital, UK); N. Farmer, C. Houghton, N. Kandhari, K. Khan, D. Ladha, J. Mayes, F. McLennan, P. Panahi, H. Sehra (Northumbria Specialist Emergency Care Hospital, UK); R. Agrawal, I. Ahmed, S. Ali, F. Birkinshaw, M. Choudhry, S. Gokani, S. Harrogate, S. Jamal, F. Nawrozzadeh, A. Swaray, A. Szczap, J. Warusavitarne (Northwick Park / St. Mark's Hospitals, UK); M. Abdalla, N. Asemota, R. Cullum, M. Hartley, C. Maxwell-Armstrong, C. Mulvenna, J. Phillips, A. Yule (Nottingham City Hospital, UK); L. Ahmed, K. D. Clement, N. Craig, E. Elseedawy, D. Gorman, L. Kane, J. Livie, V. Livie, E. Moss, A. Naasan, F. Ravi, P. Shields, Y. Zhu, C. Palmer, T. Melaugh, J. D. Hall, C. Palmer, O. Kouli, A. S. I. Hassane, A. W. Azhar, T. K. Tan (Perth Royal Infirmary, UK); M. Archer, H. Cobley, R. Dennis, C. Downes, B. Guevel, E. Lamptey, H. Murray, A. Radhakrishnan, S. Saravanabavan, M. Sardar, C. Shaw, V. Tilliridou, R. Wright, W. Ye, K. Davidson, W. Perchar, T. Scurr, K. Davidson, E. Campbell, L. Kelk, A. Ghosh, A. Gibbins, D. Mala, A. Loizidou (Peterborough City Hospital, UK); N. Alturki, R. Helliwell, E. Jones, D. Kelly, S. Lambrotharan, K. Scott, R. Sivakumar, L. Victor, O. Hall, L. Mecia, C. Hew, K. Varathan, L. Tong, B. Chandrasekar (Pinderfields Hospital, UK); H. Boraluwe-Rallage, P. Froggatt, S. Haynes, Y. M. A. Hung, A. Keyte, L. Matthews (Poole Hospital, UK); E. Evans, P. Haray, I. John, A. Mathivanan, L. Morgan, O. Oji, C. Okorochoa, A. Rutherford, H. Spiers, N. Stageman, A. Tsui, R. Whitham, L. Giacci, L. Giacci, E. Buchanan, M. O'Connell, S. Y. Kwak, E. H. Ong, S. Gardner, J. Lim, C. Maden, M. Illahi (Prince Charles Hospital, Merthyr, UK); A. Amoah-Arko, E. Cecil, A. Dietrich, H. Fitzpatrick, C. Guy, J. Hair, J. Hilton, L. Jawad, E. McAleer, Z. Taylor, J. Yap, J. Hale, J. Hale, Z. Xuan Tan, S. Edwards (Princess of Wales, Bridgend, UK); M. Akhbari, D. Debnath, T. Dhir, M. Elbuzidi, M. Elsaddig, S. Glace, H. Khawaja, R. Koshy, K. Lal, L. Lobo, A. McDermott, J. Meredith, M. A. Qamar, A. Vaidya (Princess Royal University Hospital, Orpington, UK); F. Acquaaah, L. Barfi, N. Carter, D. Gnanappiragasam, C. Ji, F. Kaminski, S. Lawday, K. Mackay, S. K. Sulaiman, R. Webb (Queen Alexandra Hospital, Portsmouth, UK); P. Ananthavarathan, F. Dalal, E. Farrar, R. Hashemi, M. Hossain, J. Jiang, M. Kiandee, J. Lex, L. Mason, J. H. Matthews, E. McGeorge, S. Modhwadia, T. Pinkney, A. Radotra, L. Rickard, L. Rodman, A. Sales, K. L. Tan, R. Stahl, J. Stahl, A. Hickman, D. Collett, Z. Goolam-Mahomed, B. Allen, A. Atiyah, H. Ahmad, J. Jones (Queen Elizabeth Hospital, Birmingham, UK); A. Bachi, D. S. Bajwa, J. Battle, L. R. Brown, A. Butler, A. Calciu, E. Davies, I. Gardner, T. Girdlestone, O. Ikogho, G. Keelan, P. O'Loughlin, J. Tam (Queen Elizabeth Hospital, Gateshead, UK); J. Elias, M. Ngaage, J. Thompson (Queen Elizabeth Hospital, Kings Lynn, UK); S. Bristow, E. Brock, H. Davis, M. Pantelidou, A. Sathiyakeerthy, K. Singh, F. W. Gan, O. McGregor, E. Ogundiya, F. W. Gan, A. Boulbadaoui, O. Kirnon-Jackman, E. Ntakomyti (Queen Elizabeth Hospital, Woolwich, UK); A. Chaudhry, G. Dickson, P. Glen, K. Gregoriou, H. Hamid, A. Mclean, P. Mehtaji, G. Neophytou, S. Potts, Q. X. Lim, H. Peckham, T. Yeoh, S. Q. Yong, J. Y. Chen, S. Siva, Z. H. Sam, M. Gilani (Queen Elizabeth University Hospital, Glasgow, UK); D. R. Belgaid, J. Burke, J. Durno, N. Ghailan, M. Hanson, V. Henshaw, U. R. Nazir, I. Omar, B. J. Riley, J. Roberts, G. Smart, K. Van Winsen, R. Makin-Taylor, Y. N. Goh, M. G. Muthukumar, S. Phillips, R. Makin-Taylor, J. Tjoakarfa, A. Giri, S. Suresan (Queens Hospital, London, UK); A. Bhatti, M. Chan, M. D'Auria, S. Green, C. Keshvala, H. Li, C. Maxwell-Armstrong, M. Michaelidou, L. Simmonds, C. Smith, A. Wimalathasan, C. Y. Hey, R. Thavayogan, C. Y. Hey, P. Thomas, T. A. Johnson, R. I. Williams, A. Rashid, A. Kushairi, A. Rais, R. Diallo (Queens Medical Centre, Nottingham, UK); J. Abbas, C. Cairns, Y. R. Chin, A. Connelly, S. Moug, A. Nair, D. Svolkinas, E. Bradley, M. McTiernan, S. Macdonald, S. Sharkey, N. McLaughlin, C. Amey, L. Kraria (Royal Alexandra Hospital, Paisley, UK); P. Coe, D. Subar, H. Wang, V. Zaver (Royal Blackburn Hospital, UK); J. Brayley, P. Cookson, L. Cunningham, A. Gaukroger, M. Ho, A. Hough, J. King, D. O'Hagan, A. Widdison (Royal Cornwall Hospital, UK); R. Brown, B. Brown, A. Chavan, S. Francis, L. Hare, J. Lund, N. Malone, B. Mavi, A. McIlwaine, S. Rangarajan, N. Griffiths, M. Ahmed, L. Jegatheeswaran, N. Griffiths, A. Madhavan, M. Warne, F. L. Malcolm, T. Lessware, H. T. Wilkerson, S. Chatterjee-Woolman, J. Wright (Royal Derby Hospital, UK); N. Abuhusseini, H. S. Campbell, J. Daniels, I. Fitzgerald, S. Mansfield, A. Pendrill, D. Robertson, Y. W. Smart, T. Teng, J. Yates, A. Yoong, W. U. R. Ahmed, A. Longshaw, O. Flannery, R. Green, M. Leaning, J. Cragg, H. Sharriff, C. Doherty, S. Lawday (Royal Devon and Exeter Hospital, UK); A. Belgaumkar, A. Katira, J. Kossoff, S. Kukran, C. Laing, B. Mathew, T. Mohamed, S. Myers, R. Novell, B. L. Phillips, M. Thomas, T. Turlejski, S. Turner, M. Varcada, L. Warren, W. Wynell-Mayow (Royal Free Hospital, UK); R. Church, L. Linley-Adams, G. Osborn, M. Saunders, R. Spencer, M. Srikanthan, S. Tailor, A. Tullett, S. Ganesananthan, S. Ganesananthan, K. W. L. Kwan, L. Sanders-Crook, S. Bhatia (Royal Glamorgan Hospital, UK); M. Ali, S. Al-Masri, G. Carr, O. Ebhogiaye, S. Heng, S. Manivannan, J. Manley, L. E. McMillan, C. Peat, B. Phillips, S. Thomas, H. Whewell, G. Williams (Royal Gwent Hospital, Newport, UK); A. Bienias, E. A. Cope, G. R. Courquin, L. Day, C. Garner, A. Gimson, C. Harris, K. Markham, T. Moore, T. Nadin, C. Phillips, S. M. Subratty, S. Eames, F. Lewis (Royal Hampshire Hospital, Winchester, UK); K. Brown, J. Dada, M. Durbacz, T. Filipescu, E. Harrison, E. D. Kennedy, E. Khoo, D. Kremel, I. Lyell, S. Pronin, R. Tummson, C. Ventre, L. Walls, E. Wootton (Royal Infirmary of Edinburgh, UK); A. Akhtar, E. Davies, D. El-Sawy, M. Farooq, M. Gaddah, H. Griffiths, I. Katsaiti, N. Khadem, K. Leong, I. Williams, E. Masiha (Royal Lancaster Hospital, UK); C. S. Chean, D. Chudek, H. Desai, N. Ellerby, A. Hammad, S. Malla, B. Murphy, O. Oshin, P. Popova, S. Rana, T. Ward (Royal Liverpool University Hospital, UK); T. E. F. Abbott, O. Akpenyi, F. Edozie, R. El Matary, W. English, S. Jeyabaladevan, C. Morgan, V. Naidu, K. Nicholls, S. Peroos, J. Prowle, S. Sansome, H. D. Torrance, D. Townsend, S. Jasionowska, L. Boyce, S. Jasionowska, W. J. English, S. Lam, C. Chipeta, D. Yilmaz, C. Jain, T. Garofalidou, S. A. Novotny (Royal London Hospital, UK); J. Brecher, H. Fung, Z. Kazmi, P. Outlaw, K. Pursnani, N. Ramanujam, A. Razaq, M. Sattar, S. Sukumar, T. S. E. Tan, M. Poustie, S. Locke, C. Bowman, A. Begaj, C. Murphy, K. Radcliffe, J. T. Chong, M. Poustie, E. Jeffrey (Royal Preston Hospital, UK); K. Chohan, S. Dhuna, T. Haq, S. Kirby, J. Lacy-Colson, P. Logan, Q. Malik, J. McCann, Z. Mughal, S. Sadiq, I. Sharif, C. Shingles, A. Simon, N. Chaudhury, K. Rajendran, Z. Akbar (Royal Shrewsbury Hospital,

UK); S. Burnage, S. S. N. Chan, A. R. J. Craig, J. Duffield, A. Dutta, M. Eastwood, F. Iqbal, F. Mahmood, W. Mahmood, C. Patel, A. Qadeer, A. Robinson, A. Rotundo, A. Schade, R. D. Slade, B. Walters, B. Kulendrarajah, N. Tran, S. Shrestha, S. Parmar, C. Gallagher (Royal Stoke University Hospital, UK); M. De Freitas, H. Kinnersley, E. McDowell, S. Moens-Lecumberri, J. Ramsden, T. Rockall, L. Wiffen, S. Wright (Royal Surrey Hospital, Guildford, UK); C. Bruce, V. Francois, K. Hamdan, C. Limb, A. J. Lunt, L. Manley, M. Marks, C. F. E. Phillips, L. Hennessy, E. Pentti, S. Badhrinarayanan, A. Fung, M. Mansoor, R. Kenny, P. Kan, D. E. Lee, S. Khosla, J. Tung (Royal Sussex County Hospital, UK); C. J. F. Agnew, C. J. Barr, N. Benons, S. J. Hart, D. Kandage, R. Krysztolik, P. Mahalingam, J. Mock, S. Rajendran, M. T. Stoddart (Royal United Hospital, Bath, UK); B. Clements, H. Gillespie, S. Lee, R. McDougall, C. Murray, R. O'Loane, S. Periketi, S. Tan (Royal Victoria Hospital, Belfast, UK); R. Amoah, R. Bhudia, B. Dudley, A. Gilbert, B. Griffiths, H. Khan, N. McKigney, B. Roberts, R. Samuel, A. Seelarbokus, A. Stubbing-Moore, G. Thompson, P. Williams, M. Samake, F. Shaban, R. Aftab, M. Gough, B. Woodburn (Royal Victoria Infirmary, Newcastle, UK); N. Ahmed, R. Akhtar, E. Chandler, I. Chappelow, H. Gil, T. Gower, A. Kale, G. Lingam, L. Rutler, C. Sellahewa, A. Sheikh, H. Stringer, R. Taylor, C. Wong, S. Vayalapa, K. McMurrugh, C. Wong, D. Jimulia, S. Deol, S. Pike, Y. Embury-Young (Russell's Hall Hospital, UK); H. Aglan, M. R. Ashraf, S. Choo, E. Das, J. Epstein, R. Gentry, D. Mills, Y. Poolovadoo, N. Ward, T. Turner, T. Turner, M. Patel, E. Kilgallon, R. Keating, A. Walsh, H. Khan, G. Logue, M. Orekoya, M. Alasmar, B. Shirazi (Salford Royal Hospital, UK); K. Bull, A. Cole, J. Hack, S. Khawari, C. Lake, T. Mandishona, R. Perry, S. Sleight, S. Sultan, T. Thornton, S. Williams (Salisbury District Hospital, UK); T. Arif, A. Castle, P. Chauhan, R. Chesner, T. Eilon, S. Kamarajah, C. Kambasha, L. Lock, T. Loka, F. Mohammad, S. Motahariasl, L. Roper, S. S. Sathra, A. Sheikh, T. Toma, Q. Wadood, J. Yip, M. Charalambides, A. Clavé Llavall, E. Williamson, Y. Bharwada, S. Zeermal, H. Evans, M. Panikkar, G. de la Cruz, J. Caplan (Sandwell General Hospital, UK); E. Ainger, S. Busti, L. Cunliffe, T. Flamini, S. Gaffing, C. Moorcroft, M. Peter, L. Simpson, E. Stokes, G. Stott, J. Wilson, J. York, A. Yousaf, A. Ruparelia, T. Tanvir, C. Soare, Y. L. Pang, J. Trotter, A. Zaidi, V. Thakrar (Scarborough General Hospital, UK); A. Borakati, M. Brown, A. Goaman, B. Hodgson, A. Ijeomah, U. Iroegbu, G. Kaur, C. Lowe, S. Mahmood, Z. Sattar, P. Sen, A. Szuman (Scunthorpe General Hospital, UK); N. Abbas, M. Al-Ausi, N. Anto, R. Bhome, L. Eccles, J. Elliott, E. J. Hughes, A. Jones, A. S. Karunatileke, J. S. Knight, C. C. F. Manson, I. Mekhail, L. Michaels, T. M. Noton, E. Okenyi, T. Reeves, I. H. Yasin, P. Pulickal, H. Ahmed, J. Parnell, H. Khan, S. Lennox, V. Ford (Southampton General Hospital, UK); D. A. Banfield, R. Harris, D. Lim, C. Mason-Apps, T. Roe, J. Sandhu, N. Shafiq, E. Stickler, J. P. Tam, L. M. Williams, W. Pyc, W. Pyc, R. Brignall, D. O'Neill, R. Hanna (Southmead Hospital, Bristol, UK); P. Ainsworth, Y. Boualbanat, C. Doull, E. Egan, L. Evans, K. Hassanin, G. Ninkovic-Hall, W. Odunlami, M. Shergill, M. Traish, R. Kane, M. Nicola, K. Rajput, Y. Xiao (Southport and Formby Hospital, UK); D. Cummings (South Tyneside District Hospital, South Shields, UK); S. Kershaw, J. Ong, F. Reid, H. Toellner, C. Warner, C. Warner, S. Michael, E. Wright, S. Juniper, E. Thompson, L. Hoskyns, A. Kanitkar, C. Ross, A. Unsworth, A. Neilson (Stepping Hill Hospital, UK); A. Alwandi, M. Amer, D. George, K. Haynes, K. Hughes, L. Peakall, Y. Premakumar, N. Punjabi, A. Ramwell, H. Sawkins, H. Rshaidat, K. Demarre, A. Chiang, A. Bareh, J. van Dellen, S. Epton (St. Georges Hospital, UK); J. Ashwood, A. Baker, C. Baron, I. Bhide, E. Blake, C. De Cates, R. Esmail, H. Hosamuddin, J. Kapp, N. Nguru, M. Raja, F. Thomson, C. Faqihinejad, A. Gadhvi, R. Grant, J. Lewsey, A. Morris (St. Helier Hospital, UK); H. Ahmed, G. Aishwarya, R. Al-Huneidi, S. Ali, R. Aziz, D. Burke, B. Clarke, A. Kausar, D. Maskill, L. Mecia, L. Myers, A. C. D. Smith, G. Walker, N. Wroe (St. James Hospital, UK); C. Donohoe, D. Gibbons, P. Jordan, C. Keogh, A. Kiely, P. Lalor, M. McCrohan, C. Powell, M. Power Foley, J. Reynolds, E. Silke, O. Thorpe, J. Tseun Han Kong, C. White (St. James University Hospital, UK); Q. Ali, J. Dalrymple, Y. Ge, H. Khan, R. S. Luo, H. Paine, B. Paraskeva, L. Parker, K. Pillai, J. Saliccioli, S. Selvadurai, V. Sonagara, L. R. Springford, L. Tan, S. Vishnu K, A. Papanikolaou, A. Mitra, A. Nur, F. Ali (St. Mary's Hospital, London, UK); S. Appleton, N. Leadholm, Y. Zhang (Stoke Mandeville Hospital, UK); D. Ahern, M. Cotter, S. Cremen, T. Durrigan, V. Flack, N. Hrvacic, H. Jones, B. Jong, K. Keane, P. R. O'Connell, J. O'sullivan, G. Pek, S. Shirazi (St. Vincent's University Hospital, UK); C. Barker, A. Brown, W. Carr, Y. Chen, C. Guillotte, J. Harte, A. Kokayi, K. Lau, S. McFarlane, S. Morrison, E. Irwin, L. Matthews, W. S. Ngu, T. Hosfield (Sunderland Royal Hospital, UK); J. Broad, N. Kenefick, D. Makanji, V. Printz, R. Saito, O. Thomas, J. Brayley, A. Palmer, M. Charalambos, C. S. Jones (Torrey Hospital, UK); H. Breen, S. Kirk, C. H. Kong, A. O'Kane, S. Toner, R. Cowden, L. Lee, P. Nicol (Ulster Hospital, UK); M. Eddama, A. Engledow, S. K. Freeman, A. Frost, C. Goh, G. Lee, R. Poonawala, A. Suri, P. Taribagil, O. Holman, M. Imtiaz, V. Albert, S. P. Leung, M. Erotocritou, J. Wong (University College Hospital, UK); H. Brown, S. Christie, S. Dean, R. Gravell, E. Haywood, F. Holt, E. Pilsworth, R. Rabiou, H. W. Roscoe, S. Shergill, A. Sriram, A. Sureshkumar, L. C. Tan, A. Tanna, A. Vakharia, D. Mason, R. Stroud, D. Mason, R. Wilkin, W. Thomson, L. Mackee, A. Couldrey (University Hospital Coventry and Warwickshire, UK); S. Bhullar, S. Brannick, E. Dunne, M. Frere, M. Kerin, K. Muthu Kumar, T. Pratumswan, R. Quek, M. Salman, N. Van Den Berg, C. Wong (University Hospital Galway, UK); J. Ahluwalia, R. Bagga, C. M. Borg, C. Calabria, A. Draper, M. Farwana, H. Joyce, A. Khan, M. Mazza, G. Pankin, M. S. Sait, N. Sandhu, N. Virani, J. Wong, K. Woodhams, S. Sait, N. G. Y. Bei, S. Sait, S. McKenna Favier, A. Ibrahim (University Hospital Lewisham, UK); N. Croghan, S. Ghag, G. Hogg, O. Ismail, N. John, K. Nadeem, M. Naqi, S. M. Noe, A. Sharma, S. Tan, M. Kowal, A. Kler, L. Reynolds, S. H. Mohamed, Y. Majeed, B. Fakim, A. Jones, M. Kowal, C. Donnelly (University Hospital of South Manchester, UK); F. Begum, R. Best, A. Collishaw, J. Glasbey, D. Golding, B. Gwilym, P. Harrison, T. Jackman, N. Lewis, Y. L. Luk, T. Porter, S. Potluri, M. Stechman, S. Tate, D. Thomas, B. Walford (University Hospital of Wales, UK); F. Auld, A. Bleakley, S. Johnston, C. Jones, J. Khaw, S. Milne, S. O'Neill, K. K. R. Singh, R. Smith, A. Swan, N. Thorley, S. Yalamarthi, Z. D. Yin (Victoria Hospital, Kirkcaldy, UK); A. Ali, V. Balian, R. Bana, K. Clark, C. Livesey, G. McLachlan, M. Mohammad, N. Pranesh, C. Richards, F. Ross, M. Sajid, G. Liversedge, Z. Carrington, J. Windebank, A. Izzarina, U. Akbani, J. Craven, A. Aldarragi, S. Harding, A. Millward (Warrington Hospital, UK); M. Brooke, J. Francombe, J. Gresly, S. Hutchinson, K. Kerrigan, E. Matthews, S. Nur, L. Parsons, A. Sandhu, M. Vyas, F. White, A. Zulkifli, L. Zuzarte, T. C. Shortland, T. C. Shortland, M. Bedford, R. Stroud, R. Obukofe, E. Mackenzie (Warwick Hospital, UK); A. Al-Mousawi, J. Arya, S. Azam, A. Azri Yahaya, K. Gill, R. Hallan, C. Hathaway, I. Leptidis, L. McDonagh, S. Mitrasinovic, N. Mushtaq, N. Pang, G. B. Peiris, S. Rinkoff, V. Gopalan, A. Midgen, P. Khadka, O. Cheng, S. Taneja, N. Manobharath (Watford General Hospital, UK); L. Chan, E. Christopher, M. M. H. Farhan-Alanie, A. Gonzalez-Ciscar, C. J.

Graham, H. Lim, K. A. McLean, H. M. Paterson, A. Rogers, C. Roy, D. Rutherford, F. Smith, G. Zubikarai, J. Y. Kok, D. W. E. Lim, T. Buick, M. Boland, S. Piya, R. Devlin, C. J. Fairfield, R. J. George, M. Rahi (Western General Hospital, Edinburgh, UK); R. Al-Khudairi, M. Bamford, M. Chang, J. Cheng, C. Hedley, R. Joseph, B. Mitchell, S. Perera, L. Rothwell, A. Siddiqui, J. Smith, K. Taylor, O. Wroe Wright, S. Zaman, S. Hajiev, T. Ross (West Middlesex University Hospital, UK); H. K. Baryan, G. Boyd, H. Conchie, L. Cox, J. Davies, S. Gardner, N. Hill, K. Krishna, F. Lakin, S. Scotcher, M. Owen, M. Owen, E. Crisp, C. Thompson (Weston General Hospital, UK); J. Alberts, M. Asad, J. Barraclough, A. Campbell, D. Marshall, W. Wakeford (West Suffolk Hospital, Bury St Edmunds, UK); P. Cronbach, F. D'Souza, E. Gammeri, J. Houlton (Wexham Park Hospital, UK); M. Hall, A. Kethees, R. Patel, M. Perera, J. Prowle, M. Shaid, E. Webb, A. Saiyed, A. Charalambous, J. L. Hollywood, A. Saiyed, R. F. L. Hammond (Whipps Cross Hospital, UK); S. Beattie, M. Chadwick, O. El-Taji, S. Haddad, M. Mann, M. Patel, K. Popat, L. Rimmer, H. Riyat, H. Smith, J. Matthews, V. Mendonca, J. Spinty, K. Khan, J. Cheng, N. Glynn, U. Muhammad, M. Khan, L. Anderson (Whiston Hospital, UK); C. Anandarajah, M. Cipparrone, K. Desai, C. Gao, E. T. Goh, M. Howlader, N. Jeffreys, A. Karmarkar, G. Mathew, H. Mukhtar, E. Ozcan, A. Renukathan, N. Sarens, C. Sinha, A. Woolley (Whittington Hospital, UK); R. Bogle, O. Komolafe, F. Loo, D. Waugh, R. Zeng, K. McCormack (Wishaw General Hospital, UK); A. Crewe, J. Mathias, A. Mills, A. Owen, A. Prior, I. Saunders (Withybush Hospital, UK); A. Baker, L. Crilly, J. McKeon, H. K. Ubhi, I. Ashworth, I. Ashworth, L. Nelson, D. Ratnasingham (Wrexham Maelor Hospital, UK); A. Adeogun, R. Carr, C. Davison, S. Devalia, A. Hayat, R. B. Karsan, C. Osborne, K. Scott, C. Weegenaar, M. Wijeyaratne, M. Curran, C. Horner (Yeovil District Hospital, UK); F. Babatunde, E. Barnor-Ahiaku, G. Beattie, P. Chitsabesan, O. Dixon, N. Hall, N. Ilenkovan, T. Mackrell, N. Nithianandasivam, J. Orr, F. Palazzo, M. Saad, L. Sandland-Taylor, J. Sherlock (York Hospital, UK); T. Ashdown, S. Chandler, T. Garsaa, J. Lloyd, S. Y. Loh, S. Ng, C. Perkins, A. Powell-Chandler, F. Smith, R. Underhill (Ysbyty Gwynedd, Bangor, UK); T. Arthur, T. Arthur, J. Ng (Gold Coast University Hospital, Australia); M. Kovacevic, S. Delibegovic, S. Delibegovic (University Clinical Center Tuzla, Bosnia and Herzegovina); M. Karamanliev, T. Ivanov, T. Yotsov, I. Ilieva, M. Karamanliev, A. Akisheva, M. Shoshkova, E. Nawaz (Medical University - Plevna, UMHAT 'Georgi Stranski', Clinic of Oncosurgery, Bulgaria); M. Swamad, V. Neykov (Medical University - Plevna, Bulgaria); R. Žebrák, R. Žebrák (Fakultní nemocnice Hradec Králové, Czech Republic); R. Paramasivam (Aarhus University Hospital, Denmark); A. Martensen HM Larsen (Aarhus University Hospital) HM Larsen (Aarhus University Hospital, Denmark); L. Rådecker, P. E. Frey (University of Heidelberg, Germany); A. Kechagias, A. Kechagias, A. Kechagias, A. Turunen, J. Katunin, M. Niskakangas, A. Ojakäär (Kanta-Häme Central Hospital, Finland); A. Venara, P. LeNaoures (CHU Angers, France); E. Duchalais, E. Duchalais, T. Vignaud, S. Frey, C. Ricolleau, E. Duchalais (CHU de Nantes, France); A. Ioannidis, M. Konstantinidis, A. Ioannidis, F. Antonakopoulos, M. Konstantinidis, A. Mathioulaki, P. Chrysoheris, P. G. Athanasopoulos, C. Koutserimpas (Athens Medical Center, Greece); F. Pata, F. Pata, S. M. Tenconi, S. Rausei, D. Maioli, V. Marchionini, F. Pata (Ospedale Sant'Antonio Abate di Gallarate, Italy); G. Pellino, G. Pellino (Università degli Studi della Campania "Luigi Vanvitelli", Italy); S. Pasquali (Fondazione IRCCS Istituto Nazionale Dei Tumori di Milano, Milano, Italy); A. Sgrò (Università di Pavia, Italy); A. Simioni, A. Simioni (Università di Padova, Italy); V. Farina (Department of Surgical Sciences, University of Turin, Turin, Italy); M. Podda, M. Podda (Ospedale San Francesco, Nuoro, Italy); L. Lorenzon, F. Tirelli, F. Tirelli, V. Fico, F. Santullo, F. Belia (Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Italy); V. Schaeff, V. Schaeff (Riga Eastern University Hospital, Latvia); A. Otto, A. Otto (Riga Stradins University, Latvia); M. Jakubauskas, M. Jakubauskas, E. Poškus, D. Danys, M. Kryžauskas, S. Mikalauskas, R. Rackauskas, M. Drungilas, T. Poškus, V. Jotautas, K. Strupas, M. Petrulionis (Vilnius University, Faculty of Medicine, Lithuania); T. R. van Elst, Z. Abdulrahman (Leiden University Medical Center, Netherlands); M. Chu, M. Chu (Christchurch Hospital, New Zealand); P. V. B. Fagan, P. V. B. Fagan (Taranaki Base Hospital, New Zealand); C. I. Wells (Department of Surgery, University of Auckland, Auckland, New Zealand); A. Alagoa João, A. Soares, D. J. Aparício, M. Fragoso, J. Guimarães, G. Cruz, D. J. Aparício, J. Ribeiro, I. Borges da Ponte, S. Almeida, A. R. Martins, A. Alagoa João (Hospital Professor Doutor Fernando da Fonseca, Portugal); J. Juloski, V. V. Cuk, R. Radulovic, K. Milošević, V. V. Cuk, J. Bojicic, J. Juloski, M. Gencic, U. Jankovic, M. Jovanovic (Zvezdara University Medical Center, Belgrade, Serbia); R. Blanco-Colino, Y. El Kasmy El Kasmi, Y. El Kasmy El Kasmi, M. J. Gómez Jurado, P. Alberti Delgado, A. Bordanova Reverter, A. Gómez del Pulgar, Y. El Kasmy El Kasmi, J. F. Belzunce-Capó, M. Verdaguer Tremolosa, Q. Lin (Hospital Universitario Vall d'Hebron, Spain); S. Pérez-Ajates, S. Pérez-Ajates, N. Ramayo Díaz, I. González Caraballo, T. Pascual Vicente, M. I. Orue-Echebarria, L. Sánchez-Calvo, D. Wang, C. Trueba-Collado, J. T. Morales Bernaldo de Quirós (Hospital General Universitario Gregorio Marañón, Spain); O. Anabitarte Bautista, O. Anabitarte Bautista, A. Yebes, O. Anabitarte Bautista (Clinico San Carlos, Spain); E. Espin-Basany (Hospital Universitario Vall d'Hebron, Spain); D. Clerc, D. Clerc, G. Mignon, A. Vanoni, A. Henkens, G. Jarrar, M. Odovic, M. Willemin, O. Milliet, D. Hahnloser, D. Clerc, N. Demartines, P. Curchod (Centre Hospitalier Universitaire Vaudois, Switzerland); C. Ciubotaru, S. Popescu, S. Popescu, S. S. Popescu, K. Piras, C. I. Ciubotaru (Emergency Hospital of Bucharest, Romania); A. Yanishev, A. Yanishev, A. Yanishev, R. Luzan, E. Lutovinova, A. Gavrilina, A. Barkovskaya, N. Kudelkina, D. Topchubaev (Nizhny Novgorod regional clinical hospital, Privolzhsky Research Medical University, Russia); S. Lee (National University of Ireland Galway, Republic of Ireland); B. B. Ozkan (Ondokuz Mayıs University Faculty of Medicine, Samsun, Turkey); A. Yagiz Sen, A. Yagiz Sen (Dokuz Eylül Üniversitesi Tıp Fakültesi Hastanesi, Turkey); M. K. Aktas, M. K. Aktas, M. K. Aktas, N. Aykun, M. H. Agca, C. Bilen, I. Kilinc, C. Atar, V. Kilic, C. Aktuna, M. Aba, I. C. Eray (Çukurova Üniversitesi Tıp Fakültesi Balçalı Hastanesi, Turkey); B. E. Baki, E. Arslan, B. E. Baki, G. Alemdag, M. Ulusahin, E. Arslan, E. B. Gul, R. Yildirim, A. Semiz, G. Bektur, K. Tomas, S. Bodur (Karadeniz Teknik Üniversitesi Tıp Fakültesi Hastanesi, Turkey); B. Yüsek, H. Serin, B. Yüsek, H. Erdönmez, F. Gürsoy, H. Serin, H. Kara, U. Önsal, M. Özbek, P. A. Kasar, A. Ipor, M. F. Çetin (Düzce Üniversitesi Araştırma Hastanesi, Turkey); I. H. Yasin (University of Southampton, Turkey); R. A. Khaw (University of Manchester Medical School, Turkey); E. Mills, L. R. Manley (Brighton and Sussex Medical School, Turkey); R. Goodson, K. Vutipongsatorn (Imperial College School of Medicine, Turkey); N. Thakral (University of Exeter Medical School, Turkey); A. D. Ablett (Aberdeen Medical School, Turkey); M. Adra (Barts and the London School of Medicine, Turkey); I. Kwek (Queen's University of Belfast, Turkey); S. M. Khan

(University of Birmingham Medical School, Turkey); P. Quinn (Bristol Medical School, Turkey); A. Badran (University of Cambridge School of Clinical Medicine, Turkey); A. Ramjeeawon (Cardiff University School of Medicine, Turkey); A. Campbell (Ninewells Hospital, Turkey); H. L. Tan (University of Edinburgh Medical School, Turkey); D. S. Rye (Royal Devon and Exeter Hospital, Turkey); N. Rajaraman (University of Glasgow Medical School, Turkey); J. G. Norman (Hull York Medical School, Turkey); G. Solomou (Keele University, Turkey); M. Akhbari (The GKT School of Medical Education, King's College London, Turkey); A. Ali (Ayr Hospital, Turkey); V. Murray (Leeds Medical School, Turkey); D. M. Baker (Leicester Medical School, Turkey); B. D. Brandao (Manchester Medical School, Turkey); B. Stainer (Newcastle Medical School, Turkey); R. Thavayogan (Nottingham Medical School, Turkey); D. Jones (Oxford University Medical School, Turkey); O. O. Onafowokan (Peninsula College of Medicine & Dentistry, Turkey); A. Gharooni (Sheffield Medical School, Turkey); N. Dabab (Southampton Medical School, Turkey); S. Carlton-Carew (St George's, University of London Medical School, Turkey); G. Kungwengwe (Swansea University Medical School, Turkey); M. Gabriel (The James Paget Hospital, Norfolk, Turkey); E. Sewart (UCL Medical School, Turkey); T. C. Shortland, S. Lawday (Warwick Medical School), S. Lawday (Royal Devon and Exeter Hospital), Turkey); P. Pockney, A. Chrimes, A. Agarwal, J. Zhao, S. Williams, J. M. S. N. Jayalath, P. Liebenberg, S. Khor, T. Muddasani (John Hunter Hospital, Australia); A. Dawson, N. Taylor, C. Stevenson, A. Drane, U. Pahalawatta, L. T. Lai, A. Debiasio, M. Jung (Gosford Hospital, Australia); C. D. Brumfitt, C. D. Brumfitt, Y. Z. Beh, N. N. Dudi-Venkata, Y. D. Lee (Royal Adelaide Hospital, Australia); P. Stewart, A. Nair, V. Thirugnanasundralingam, K. Muir (Wyong Hospital, Australia); B. Ng, D. M. Mendis, P. M. Robb, H. J. Lee, A. A. B. Wyche, L. T. Davis, H. J. Lee (Hervey Bay Hospital, Australia); J. K. Luong, T. Jegathees, S. M. C. J. Coulter-Nile, M. P. Gosselink, J. K. Luong, Y. L. Wang, M. Maciaszek, P. S. Chrapko, S. White (Westmead Hospital, Australia); V. Ivanov, V. Ivanov (Medical University of Plovdiv, Medical Simulation and Training Center, Bulgaria); A. Borisova (Alexandrovska hospital, Bulgaria); K. Kuncarová, J. Riško, M. Ludvik, M. Stercz, R. Treskon, M. Pospíšil, L. Hlaváčová, K. Kuncarová, D. Tomanová, J. Riško (Fakultní nemocnice Olomouc, Czech Republic); B. Kološová, K. Sobotková, S. Cha, K. Šuta Kimle, K. Jirankova, M. Bujda, A. Pačlík, K. Chrz (Všeobecná fakultní nemocnice v Praze, Czech Republic); T. Antonova, S. Chodora, O. Houdek, R. Novický, T. Antonova, A. Skalický (Fakultní nemocnice Plzeň Lochoťín, Czech Republic); M. Farkašová, V. Jozaf, M. Farkašová, T. Klail, V. Prochazka (Fakultní nemocnice Brno Bohunice, Czech Republic); J. L. Harbjerg, M. Enevoldsen, J. L. Harbjerg, J. Højgaard Pedersen (Regionshospitalet Randers, Denmark); S. Brandsborg, S. Brandsborg, S. Amiri (Regionshospitalet Horsens, Denmark); S. Brinck, B. N. Jepsen, T. K. Hillgaard, S. B. Erichsen, C. V. Nielsen, C. P. Madsen, J. Bjerke, C. D. Skej, R. R. Aabling, (Regionshospitalet Viborg, Denmark); M. D. Kjaer, K. P. Unbehaun, K. P. Unbehaun, M. D. Kjaer (Odense Universitetshospital, Denmark); A. Mark-Christensen (Svendborg sygehus, Denmark); P. Dalsgaard, A. Trap, J. Jürgens-Lahnstein, M. Storm, P. Dalsgaard, I. Damgaard, F. Olawi, F. Ehler, M. Raos, S. Ravn (Aarhus Universitetshospital, Denmark); K. D. Lycke, F. P. Kristensen, K. D. Lycke, K. Bønnerup (Hospitalsenheden Vest, Denmark); C. Brigand, E. Dumange, M. Gout (CHU Francois mitterand, Dijon, France); C. Moehwald, M. Prem, J. Krupp (Charité Berlin, Germany); O. Alhalabi, S. Sliwinski, E. Gablenz, T. Seiboldt, L. Beck, L. J. Pohl, K. Zamzow, F. Betge, A. Poncelet, M. Truant, H. Hauschild, N. Neugebauer, C. Dörr-Harim (Universitätsklinikum Heidelberg, Germany); L. Schmitzer, A. Kopp (LMU Munich, Germany); J. Steinle (Münster, Germany); J. Gsenger, L. J. Pohl (Universitätsklinikum Mannheim, Germany); M. Riccardi (St. Josefs Clinic, Potsdam, Germany); I. M. Christodoulou, A. Zoikas, A. Zoikas, I. M. Christodoulou (Sismanoglio General Hospital of Athens, Greece); N. Machairas, A. Paspala, N. Machairas, D. Papaconstantinou, E. Spartalis, N. Arkadopoulos, A. Prodromidou, Z. Garoufalia (Attikon University Hospital, Greece); D. Balalis, D. Balalis (Saint Savvas Anticancer Hospital, Greece); D. K. Manatakis, V. Kalles, I. Spyrou, C. Barkolias (Athens Naval and Veterans Hospital, Greece); M. L. Aguilera, D. Mendez, J. Rosales, M. Flores, M. Garcia, A. Garcia, M. Garcia, Z. Noriega, D. Torselli, M. L. Aguilera, J. Rodriguez (Hospital General San Juan de Dios, Guatemala); A. Sgrò, A. Sgrò, F. Argenti, M. S. Milani, S. Malabarba, G. Giambartolomei, I. Vella, F. Gronchi, A. Ruggieri (Policlinico San Matteo, Pavia, Italy); L. Marano (Ospedale 'San Matteo degli Infermi' - AUSL Umbria 2 - Spoleto, Italy); F. Fleres (Department of Human Pathology of the Adult and Evolutive Age "Gaetano Barresi", Section of General Surgery, AOU, University of Messina, Italy); F. Lovisetto, A. Barberis, D. Serra (Ospedale Castelli, SOC Chirurgia Generale e Vascolare, Italy); D. Sasia, P. Geretto, L. Pellegrino, B. Borghi, D. Sasia, A. Marano, C. Corino, G. Cannata, M. C. Giuffrida, F. Landra, G. Girauo (Ospedale Santa Croce e Carle, Cuneo, Italy); E. Segalini, E. Segalini, M. Monti, M. Magnoli (Ospedale Maggiore di Crema, Italy); G. Pata (ASST Spedali Civili di Brescia - Chirurgia Generale 2, Italy); A. Lucchi, A. Lucchi, M. Grassia, M. E. Cufari (Ospedale Ceccarini, Italy); A. Sagnotta, A. Di Cintio, A. Gemini, S. Trastulli, M. De Luca, A. Sagnotta, J. Desiderio, F. Gubbiotti (Azienda Ospedaliera Santa Maria - Terni, Italy); T. Campagnaro, C. Pedrazzani, T. Campagnaro, G. Turri, E. Lazzarini, C. Conti, A. Ruzzenente (Azienda Ospedaliera Universitaria Integrata Verona, Italy); F. Petrelli, I. Marziali, S. Mazzocato, F. Petrelli, R. Vergari, F. Piazzai, I. Kubolli, A. Aggiusti, A. Paolucci, M. Ortenzi (Azienda Ospedaliera Universitaria 'Ospedale Riuniti - Umberto I - Lancisi - Salesi', Italy); G. Gallo, G. Gallo, G. Clerico, G. De Santi, M. F. Bitonti, M. Trompetto, A. Realis Luc (Dipartimento di Chirurgia Colorettale - Clinica S. Rita - Vercelli, Italia, Italy); M. Papandrea, C. Cerra, M. Pirillo, M. Papandrea, S. Cravano, I. Libri, N. Laquatra, A. Isabello, E. De Luca (U.O. di Chirurgia Generale, Policlinico Universitario di Catanzaro, Italy); V. Testa, M. Morino, M. Mistrangelo, V. Testa ('Città della Salute e della Scienza' di Torino, Italy); G. Sinibaldi, G. P. Angelucci, R. Scaramuzzo, A. Larcinese, C. Fioriti, E. Picone, M. Nardi (Ospedale San Giovanni Calibita Fatebenefralli, Isola Tiberina, Roma, Italy); F. Di Candido, A. Spinelli, M. Marco, F. Di Candido, M. Bevilacqua, A. Maroli (Istituto Clinico Humanitas, Italy); F. Colombo, M. Cigognini, G. Zaffaroni, A. Maffioli, S. Colombo, A. Bondurri, G. Sampietro, D. Foschi, F. Colombo (Azienda Ospedaliera Universitaria L.Sacco, Milano, Italy); G. Perrone, G. Perrone, E. Bonati (Ospedale Maggiore di Parma, Italy); S. Aresu, S. Aresu, A. Saba (Ospedale Nostra Signora della Mercedes, Italy); A. Biancafarina, A. Biancafarina, M. Angelini, E. Andolfi, E. Miranda, M. Scricciolo, G. Provenza, G. Cavallina, B. Frezza, A. Fontani, R. Malatesti, G. A. Pellicanò, G. Ceccarelli (Ospedale San Donato, Italy); G. Canonico, E. Falsetti (San Giuseppe, Italy); M. Pagnanelli, M. Pagnanelli, P. De Nardi, R. Rosati, G. Marcocci, A. Vignali, R. Quattromani (Ospedale San Raffaele, Milan, Italy); G. Curletti, G. Curletti, R. Galleano, A. Badran, M. Malerba, A.

Percivale, O. Ghazouani, L. Reggiani, C. Spirito (Ospedale Santa Corona, Pietra Ligure, Italy); R. Bini, A. de Manzoni Garberini, A. de Manzoni Garberini (Ospedale 'Spirito Santo' di Pescara, Italy); H. Impellizzeri, G. Moretto, M. Bacchion, H. Impellizzeri, A. Casaril, M. Inama, M. Creciun, M. Vitali (Ospedale Pederzoli, Italy); N. Cillara, L. Mosino, M. Peddis, S. Melis, G. De Donno, A. C. Aru, G. A. Loche (PO SS Trinità, Cagliari, Italy); R. Tutino, L. Licari, S. Campanella, G. Profita, N. Falco, G. Rotolo, P. Venturelli, R. Tutino, P. De Marco, M. Marciandò (Dept. of Surgical, Oncological and Stomatological Disciplines, University of Palermo, Italy); A. Picciariello, A. Picciariello, N. Chetta, F. Aquilino, V. Papagni (Policlinico di Bari, Italy); D. Coletta, S. Cerasari, G. Galiffa, P. Lapolla, D. Coletta, C. Del Basso, B. Cirillo, G. De Toma, K. Fazzi, S. Bini, C. De Padua (Azienda Ospedaliera Universitaria Policlinico Umberto I, Italy); G. Savino, G. Savino, E. Finotti (AULSS 5 'Santa Maria Regina degli Angeli', Italy); F. Ferrara, F. Ferrara, M. Stella, D. Gobatti (Ospedale San Carlo Borromeo, Italy); N. Tamini, R. Brenna, A. Giani, F. Tirota, S. Famularo, M. Angrisani, M. Ceresoli (Ospedale San Gerardo, Italy); G. Talamo, F. Sucameli, A. Gennai, E. Moggia, C. Bianchi, P. Bonfante, S. Macina, C. Feleppa, G. Talamo, M. Imperatore, S. Berti (Ospedale Sant'Andrea ASL 5, Italy); D. Parini, D. Parini, J. Lanari (Santa Maria della Misericordia, Italy); P. Giamundo (Ospedale Santo Spirito, Bra, Italy); A. Io Conte (Azienda Ospedaliera Sant'Andrea, Roma, Italy); G. Pagano, M. Manigrasso, M. Danzi, R. Amato, L. Anastasio, F. Mastella, R. Basile, R. Peltrini, E. Marra, G. Luglio, G. Pagano, M. Giglio, M. Manigrasso, P. Anoldo, S. Vertaldi, L. Grimaldi, N. Tammaro (Azienda Ospedaliera Universitaria Federico II, Italy); V. Ripetti, R. D'Alessio, D. Benvenuto (Policlinico Universitario Campus Bio-Medico, Italy); A. Pesce (Department of Medical, Surgical Sciences and Advanced Technologies 'G. F. Ingrassia' - University of Catania, Italy); N. Menduni (Università degli Studi G.D'Annunzio, Italy); R. Giudicissi, R. Giudicissi, T. Zalla, M. Baraghini, L. Romoli, M. Calussi, S. Vellei, C. Genzano, F. Feroci, M. Vita, I. Giani (Nuovo Ospedale di Prato, Santo Stefano, Italy); E. Goldin, E. Ciccio, A. Galgano, M. Zuin, A. Simioni, A. Bettella, A. Barina, E. Vendramin, G. Palano, D. Schiavone (Azienda Ospedaliera di Padova, Italy); D. Rega, V. La Manna, G. Migliore, A. Aversano, A. Fares Bucci (Colorectal Surgical Oncology, Abdominal Oncology Department, Istituto Nazionale per lo Studio e la Cura dei Tumori - 'Fondazione Giovanni Pascale' IRCCS, Naples, Italy); A. Belli (Department of Abdominal Oncology, Istituto Nazionale Tumori Fondazione 'G. Pascale' - IRCCS, Naples, Italy); V. Andriola, S. Lafranceschina (AOUC Policlinico di Bari, Italy); L. Gordini, L. Gordini, E. Erdas, F. Podda, F. Cappellacci, C. Salaris, S. Sanna, J. Marcialis, A. Longheu (Policlinico Universitario di Monserrato 'Duilio Casula', Italy); C. Foppa, F. Coratti, P. Montanelli, S. Grandi, T. Nelli, N. Ben Khaled, F. Cammelli, E. Ferrini, M. E. Billo (Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy); G. Piccolo, S. Romano, P. Gaetano, F. Pilotta, L. Baldassarre (Ospedale Maggiore di Lodi, Italy); A. Birindelli, U. D'Errico, S. Bianchini, A. Birindelli (S.Orsola-Malpighi, Italy); C. Ferrari, A. Franceschi, G. Caristo (Ospedale San Paolo, Savona, Italy); Z. Ballarini, M. Romelli, S. Ruggiero, A. Percassi (Ospedale di Esine, Italy); M. Milone (University of Naples 'Federico II' Department of Clinical Medicine and Surgery, Italy); M. De Rosa ('San Giovanni Battista' Hospital, Italy); N. S. Pipitone Federico (SC Chirurgia generale, Ospedale Edoardo Agnelli Pinerolo, Torino, Italy); B. Molteni, C. Ferrari, B. Molteni, A. Magri Piccinini (Ospedale di Gardone val Trompia, Italy); P. L. Tilocca, P. L. Tilocca, A. G. Marrosu, F. Scognamiglio, C. Pala, F. Attene, L. Carboni, M. W. Ruggiu, G. Gabbas (Azienda Ospedaliero Universitaria di Sassari, Italy); G. Sancini, G. Sancini, A. Roggiani, F. Balsamo, A. Gori, D. Cuicchi, L. Vittori (Policlinico Sant'Orsola-Malpighi, Italy); G. N. Piozzi, D. Tringali, E. Bevilacqua, V. Panizzo, G. N. Piozzi (Istituto Clinico Sant'Ambrogio, Italy); A. Lauretta (Chirurgia Oncologica Generale, C. e. n. t. r. o. di Riferimento Oncologico di Aviano, I. R. C. C. S. ). (Chirurgia Oncologica Generale, Centro di Riferimento Oncologico di Aviano (CRO), IRCCS, Italy); G. Poillucci (Chirurgia dell'Apparato Digerente - Policlinico Universitario Umberto I - Roma, Italy); S. Mulas (Chirurgia d'urgenza Ospedale Santissima Annunziata, Sassari, Italy); D. Simcikis, N. E. Samalavicius, D. Simcikis, V. Nutautiene, P. Zeromskas, J. Jurgaitis, O. Aliosin, A. Slepavicius, V. Eismontas, M. Kybranskiene (Klaipeda University Hospital, Klaipeda University, Lithuania); L. Portelli, C. Cachia, C. Cefai, L. Portelli, Y. Youssef, D. Degaetano, S. Debono, M. Sammut, J. Cassar, K. Sammut, P. Andrejevic (Sptar Mater Dei, Malta); J. W. M. van Wijnbergen, T. L. Dinger (Utrecht University, Netherlands); S. F. H. ten Doesschate (Erasmus University Medical center, Rotterdam, Netherlands); A. S. H. M. van Dalen, R. C. Looijen, A. S. H. M. van Dalen, M. A. J. Becker, D. Comert, M. E. Stellingwerf, N. Abdulrahman (Amsterdam UMC, University of Amsterdam, Netherlands); D. D. van den Bos, A. Grüter, Y. Vroom, D. M. Voeten, T. Feenstra, D. de Roy van Zuidewijn (Amsterdam UMC, Vrije Universiteit, Netherlands); M. Hansmann, B. Nasimi, M. Gerdson, R. C. H. Stijns, T. Y. S. Leow, G. Penningniewland, J. Davids (Radboudumc, Netherlands); J. Medina Feliz (Groningen University, Netherlands); S. Z. Kuiper, N. R. F. Sluijpers, K. G. H. van de Pas (Maastricht University Medical Centre, Netherlands); S. R. Pruijssers, S. R. Pruijssers, C. J. L. Molenaar, G. Thomas (Maxima Medisch Centrum, Netherlands); S. Farik, S. Farik, S. Y. Chen, K. Kilpatrick, D. H. Kim, H. I. Ong (North Shore Hospital, New Zealand); B. M. Elliott (Whangarei Hospital, New Zealand); V. P. Geneta, R. Alsadat, R. Cherry, D. A. Chapman, N. Singh, A. Clucas, G. Gatenby, B. Kelly, P. Ruppeltd, N. D. McIntosh, Y. Li (Waikato Hospital, New Zealand); S. Wilton, S. J. P. McLaughlin, J. Kearney, S. Wilton, H. Sprosen, P. Kerckhoffs (Tauranga Hospital, New Zealand); H. Kandelaki, D. Welman, J. Coulter, M. Morreau, E. Li, A. Rankin, J. Winders, C. Skipworth (Rotorua Hospital, New Zealand); S. L. Peng (Middlemore Hospital, New Zealand); Y. K. Lim (Hawkes Bay Hospital, New Zealand); S. S. Yassaie, S. Dixon, S. Yassaie (Palmerston North Hospital, New Zealand); M. Murray (Hutt Hospital, New Zealand); C. Haran, S. Koh, H. Wilms, F. Dalzell, J. Tewhaiti-Smith, T. Kader, S. T. Yam, D. Dahya, M. Hardie Boys, W. Fleischl, B. Desmond (Wellington Hospital, New Zealand); J. Tan, J. Tan, A. Skavys (Whanganui Hospital, New Zealand); J. Castro, L. Orelhas, J. Santos, A. Pacheco, A. F. Rocha, M. J. Jervis, V. Pedro, V. Paixão, A. Guerreiro, D. Melo (Hospital de Beja, Portugal); A. Laranjeira, A. Machado, V. Horta, M. Rocha-Melo, J. Patrício, M. Pereira, R. Lima, A. M. Cinza, J. Oliveira, C. Velez, R. Senhorinho (Hospital Espírito Santo Évora, E.P.E., Portugal); S. Catarino, S. Catarino, D. Aveiro, M. Couto, A. R. Loureiro (Centro Hospitalar Tondelaviseu, Portugal); C. Neves-Marques, T. Louro, M. Morgado, A. S. Ferreira, M. Alves, N. Oliveira, R. Lérias, C. Neves-Marques, I. Estalagem, C. Botelho, C. Alves-Vale (Hospital Vila Franca de Xira, Portugal); J. G. Correia, J. A. M. Jardim, S. P. Domingos, J. M. Baião, B. S. Rocha, N. M. R. O. Lopes, D. M. Jordão, J. G. Correia, M. D. Ângelo, T. Carço (Instituto Português de Oncologia Francisco Gentil de Coimbra, Portugal); B. N. Vieira, B. N. Vieira, A. G. Silva, D. Galvão, A. Mora, R. Bettencourt

(Hospital de Santo Espírito da ilha Terceira, Portugal); A. C. Quintela, D. Alves, B. Dias, C. Costa, J. P. Gonçalves, P. Valente, J. Oliveira, L. Freire, R. Saraiva, M. Moreira, R. Peixoto (Hospital Pedro Hispano, Portugal); M. L. Serra, M. L. Serra, T. C. Santos, R. R. Lages, A. Pimentel, M. Martins (Centro Hospitalar do Baixo Vouga, Portugal); J. Maciel, J. Bártolo, C. Fidalgo Antunes, F. Cabral, F. Brito Silva, A. Dias Matos, M. Santos, R. Cunha, M. Duarte, M. Sousa (Instituto Português de Oncologia de Lisboa, Portugal); M. Cunha (Centro Hospitalar Universitário do Algarve, Portugal); J. Neves, J. Neves, I. Mónica, S. Oliveira, H. Ribeiro, M. Ferreira, N. Guimarães (Hospital Distrital da Figueira da Foz, Portugal); J. Azevedo, H. Louro, T. Queiros, B. Castro, S. Fonseca, L. Carvalho, A. P. Torre, A. Amado, M. Leite, M. Santos (Centro Hospitalar Vila Nova de Gaia/Espinho, Portugal); M. Romano, M. Romano, J. R. Gomes, R. G. Monteiro (Unidade Local de Saúde de Castelo Branco, Portugal); F. Eiró, M. Ferreira, F. Borges, J. Simões, F. Eiró, P. Botelho, B. Cismasiu (Hospital Garcia de Orta, Portugal); J. Romano (Centro Hospitalar de Lisboa Ocidental, Portugal); C. Monteiro, C. Monteiro, M. Silva (Hospital de Santa Luzia, Portugal); M. Claro, P. Almeida, A. Cruz, M. Claro, G. Vaz Pinto, D. Sousa, D. Costa Santos, A. Silva, F. Silva (Hospital do Litoral Alentejano, Portugal); M. R. Almeida, M. R. Almeida, R. Parreira, A. Faustino, N. Medeiros, R. Castro, B. Soares, M. Resendes (Hospital do Divino e Espírito Santo, Portugal); M. Peyroteo, R. Canotilho, M. Peyroteo, A. M. Correia, P. C. Martins (Instituto Português de Oncologia do Porto, Portugal); N. D. Machado, N. D. Machado, T. C. Sá, F. M. Bernardes, P. Saraiva, J. Almeida, M. Mendes, V. Fernandes, A. Ribeiro, D. Soares (Centro Hospitalar do Tâmega e Sousa, Portugal); H. Capote, G. Fialho, M. Reia, N. Pratas, H. Capote, C. Costa, J. Costa, S. Morais (Hospital Doutor José Maria Grande, Portugal); M. Ferreira, P. Miranda, C. Cunha, M. Ferreira (Hospital Beatriz Angelo, Portugal); X. Sousa, F. Amado, A. Batista, J. Seabra, V. Praxedes, N. Monteiro, I. Martins, M. Lamas (Centro Hospitalar de Setúbal, Portugal); H. Devesa, M. Duarte, J. Miranda, S. F. Martins (Hospital Distrital de Santarém, Portugal); D. Cavadas, D. Cavadas, R. Silva, S. Pina, I. Paixão, S. Frade (Hospital Curry Cabral, Portugal); I. Guerreiro, I. Guerreiro, M. Tomé, S. Patrocinio (Centro Hospitalar Barreiro Montijo, Portugal); M. Costa, M. Rosete, M. Costa, M. Rosete (Centro Hospitalar e Universitário de Coimbra - polo HUC, Portugal); M. Salman, R. Senaratne, P. Kakodkar, I. Balasubramanian, A. Hogan, A. Al-Salihi, V. Vyas, A. Vedadi (University Hospital Galway, Republic of Ireland); C. English (University College Dublin, Republic of Ireland); N. Mohammed, L. Dervan, S. J. Kang, O. Dixon, E. Morrissey, M. Compton (Mayo University Hospital, Republic of Ireland); A. Litvin, A. Litvin, E. Romanova, N. Ponomarev, A. Savchenko (Immanuel Kant Baltic Federal University, Kaliningrad Regional Clinical Hospital, Russia); K. Mészárosóvá, M. Zubowicz, P. K. Suchán, J. Gerstmeier, K. Mészárosóvá, E. Brazitikou, E. Fytrou, M. Celik, M. Dubovský, J. Schmalenbeck, S. C. Sautter, H. Ceyran, A. Panyko (Univerzita nemocnica Bratislava Ružinov, Slovakia); S. Van Straten (University of the Witwatersrand, South Africa); R. Jaich, R. Jaich, N. Fitchat (Chris Hani Baragwanath Academic Hospital, South Africa); H. De Lima, K. Withey, A. Piperidis, Y. Toyi, A. Nicolaidis, H. De Lima (Helen Joseph Hospital, South Africa); S. Brooks, T. Jaffer, A. Sparke, N. Van Staden, C. R. McDuling, L. Claassen, S. Van Vuuren (Kalafong Academic Hospital, South Africa); M. Marx, C. Kruger, J. Weyers, M. Marx, J. Lecler (Steve Biko Academic Hospital, South Africa); M. Nshalati Salvation, S. Mathebula, J. Chauke, W. Mculu, Z. Ngwenya (Dr George Mukhari Academic Hospital, South Africa); J. García Cardo (Hospital Universitario Marqués de Valdecilla, Spain); I. Mora-Guzmán (Hospital Universitario de La Princesa, Spain); J. Sancho Muriel (Hospital Universitario y Politécnico la Fe, Valencia, Spain); U. de Andres Olabarria, L. Casaval Cornejo, I. Vicente Rodríguez, F. Jiménez Escovar, U. de Andres Olabarria, M. Calvo Fernández, A. Portugal Martínez, I. Badiola Bergara, A. Landaluce Olavarria, E. del Pozo Andrés (Hospital Universitario Galdakao-Usansolo, Spain); P. Muriel, P. Muriel, N. Mestres, E. Cuello, M. Merichal, J. E. Sierra, J. Escoll, M. Rufas, A. I. Pinillos, J. Ortega, C. Cerdán (Hospital universitari Arnau de Vilanova, Spain); C. Jimenez Viñas (Hospital Comarcal Inca, Mallorca, Spain); F. Alconchel, J. M. Martínez Díaz, J. J. Ruiz Manzanera, Á. Navarro Barrios, L. Rodríguez Pedreño, F. Alconchel, P. García Moreno, M. García Gómez, K. Rodrigues, J. Abrisqueta (Hospital Clínico Universitario Virgen de la Arrixaca, Spain); O. Esteban Sinovas (Hospital Clínico Universitario de Valladolid, Spain); C. Fairén Oro (Hospital Clínico Universitario de Valencia, Spain); M. López Otero, M. López Otero, C. Samartín Toimil, J. C. Primo Álvarez, L. Rodriguez Fernandez, M. Paniagua Garcia Señorans (Hospital Álvaro Cunqueiro, Spain); S. Figueroa Jiménez, P. Livianos Arias-Camisón, S. Figueroa Jiménez, J. M. Nieto Arranz, M. J. Mateos Sexmero, E. Diego Alonso, L. González Amor (Hospital Clínico Universitario de Salamanca, Spain); O. Claramonte Bellmunt (Hospital Universitari Son Llàtzer, Spain); J. Martínez Caballero (Hospital Universitario 12 de Octubre, Spain); I. Rubio-Pérez, P. Ramos Martín, P. Mate Mate, C. Marcano Chavez, I. Rubio-Perez, H. Ayllon (Hospital Universitario La Paz, Spain); M. M. Aguilar-Martínez, A. Arroyo (Hospital General Universitario de Elche, Spain); J. J. Segura-Sampedro, S. Jerí-McFarlane, C. Soldevila-Verdeguer, C. Pineño-Flores, D. Ambrona-Zafra, L. Fernández-Vega, A. Gil-Catalán, A. Craus-Miguel, N. Pujol-Cano, F. Sena-Ruiz (Hospital Universitario Son Espases, Spain); C. Olmedo Moreno, C. Olmedo Moreno, C. Pastor Idoate (Hospital Universitario Fundación Jiménez Díaz, Spain); D. Negre Parra, M. M. Soriano Liébana, D. Negre Parra, C. F. Campo Betancourth, S. Sevilla Mico (Hospital General Universitario de Alicante, Spain); A. M. Estévez Diz (Hospital POVISA de Vigo, Spain); R. Martín-Balbuena, A. García-Vico, A. Roman-Rando, M. Á. Sánchez-Gálvez, I. M. Bersabe-Alonso, A. Vadillo-Bohorquez (Hospital Universitario de Valme, Spain); C. Bustamante Recuenco, M. G. Calzada, C. B. Recuenco, M. C. Martín (Hospital Universitario de Getafe, Spain); R. E. Licardie Bolaños, J. J. Garcia Orozco, D. A. Ferrusola Diaz, R. E. Licardie Bolaños, M. L. Garcia Jimenez, L. Castro Diez, C. Mosquera Fernandez (Hospital Universitario A Coruña, Spain); P. Fernández, J. Platero Diago, M. Veras Lista, S. 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C. García Hernández, S. Orozco Nuñez, M. Suarez-

Sanchez, J. Martin-Fernandez , M. Estaire Gomez (Hospital General de Ciudad Real, Spain); C. C. Lopes Moreira , R. D. Gutierrez Rios, M. Eizaguirre Ubegun, I. Novo Sukia, M. Uribe Isado, M. Ibañez Alda, C. C. Lopes Moreira, J. M. Enriquez-Navascues (Hospital Universitario Donostia, Spain); P. Uriol Peralta , P. Uriol Peralta, F. Lima Pinto, S. Núñez O’Sullivan (Hospital Infanta Sofía, Spain); M. Serrano Navidad , M. Serrano Navidad, P. Vivas Angeles, R. Vives Figueras, E. Baena Sanfeliu, B. Campillo Alonso, M. Alberich Prats, J. Duran Arrocha, N. Cornellà Garceso, C. Uribe Galeano, F. Collado-Roura (Hospital Universitari de Bellvitge, Spain); J. Ripollés-Melchor (Hospital Universitario Infanta Leonor, Madrid, Spain); A. Garcea (Hospital de Torre Vieja, Spain); H. Gómez Facundo (Consorci Sanitari Integral, Hospital Moises Broggi, Spain); P. Troncoso Pereira , P. Troncoso Pereira, J. M. Garcia, A. Gil, H. E. Giordano (Mateu Orfila, Spain); C. V Pérez Guarinos (H. Morales Meseguer, Spain); B. Blaser, L. Imadalou (Hôpital neuchâtelois, Switzerland); G. Piazza , G. Piazza, H. Teixeira, O. Pittet , S. Gaspar (Hôpital de Monthey, Switzerland); B. Gagliardi, M. L. Haller, B. Gagliardi, A. Huot (Hôpital de Morges, Switzerland); S. S. Yurdaor , Y. E. Alim, M. Binbuga, Ö. Kürklü, S. S. Yurdaor, C. Ceylan, S. Yilmaz, S. N. Çalar, N. Yildirim, G. Yavuz, O. Biyiklioglu (Cumhuriyet Üniversitesi Tıp Fakültesi, Turkey); O. Kopac , B. Baykan, H. Abbasgulyev, V. Mutlu, Y. Mahmoudi, S. A. A. Dossa, S. R. Mizan, B. Demirtas, T. Cavus, A. Yuksek , K. Karabulut (Ondokuz Mayıs Üniversitesi Tıp Fakültesi Hastanesi, Turkey); A. Uyanik , K. Kargici, T. Banaz, S. M. F. Abdulrahman, M. Yesilsancak, E. Yanikoglu, A. Karabulut, D. Yilmaz, O. F. Kuyumcu, F. Kutluk , E. Tunc (Istanbul Üniversitesi-Cerrahpaşa Tıp Fakültesi, Turkey); B. B. Ozmen, G. K. Kurtoglu, E. K. Sel, V. C. Isler, B. S. Yilmaz, C. Adiyaman, M. Kara, H. C. Demirkaya, H. K. Korkmaz, A. M. Pektas , D. Mutlu (Acibadem Mehmet Ali Aydınlar Üniversitesi Atakent Hastanesi, Turkey); E. Tiftik, E. Tiftik, A. B. Aksoy, E. Karagöz, R. Sabanci, S. S. Tümer, L. Sarigül (Istanbul Medipol Üniversitesi Hastanesi, Turkey); B. Aksoy, B. Emiroglu, B. Aksoy, B. Mollavelioglu, D. Gereklioglu, M. Guler, S. Toprak, H. B. Afsar, S. E. Guler, E. Alizade, T. Aydın (Istanbul Üniversitesi İstanbul Tıp Fakültesi, Turkey); A. Yalcinkaya, M. Erdem, S. Kayacan, C. Sahin, M. Uysal, K. Karakus, S. Altiner, Z. S. Demirci, E. Eren, M. Yavas, H. Dogan (Gazi Üniversitesi Hastanesi, Turkey); F. Ozoglu, S. S. Mazlum, C. Yelkenci, T. Baran, M. Satilmisoglu, A. Z. Sahin, A. Kiling, K. Isik (Recep Tayyip Erdogan Üniversitesi Egitim ve Arastirma Hastanesi, Turkey); M. D. Kocer , B. Güner, E. C. Islek, H. B. Tombul, C. Y. Boztug, A. Tinaz, M. Yilmaz, Y. Karaman, F. A. Akin, S. Dansuk, M. Başçavus, M. Kaya, B. Kutlu, C. Akyol (Ankara Üniversitesi Tıp Fakültesi, Turkey); G. Bilicen, G. Bilicen, E. Yarenci, Y. Demiroglu, A. Sunal (MCBÜ Tıp Fakültesi Hafsa Sultan Hastanesi, Turkey); E. N. Cinar, O. U. Tipi, G. E. Benli, I. Tasdelen, A. Tura, A. Ucar, B. Ekcı, A. C. Bilgili, I. N. Kiraz, H. Aksoy, E. N. Cinar, A. Basak , B. Karip (Fatih Sultan Mehmet Egitim Arastirma Hastanesi, Turkey); Ö. Uslu , M. C. Seker, V. Erten, U. Memis, Z. B. Koçak, Y. E. Karapinar, M. Fakirullahoglu, Ö. Uslu, E. Köseoglu, M. Yeni, F. A. Uygur (Atatürk Üniversitesi Arastirma Hastanesi, Turkey); Y. Kaya, D. Özen, M. Ölmez, E. Altintas, Y. Kaya, R. Toklu, T. Sariçiçek, A. E. Isik (Erzincan Üniversitesi Mengücek Gazi Egitim ve Arastirma Hastanesi, Turkey); K. Demirci (Trakya University, Edirne, Turkey); G. Suresh, J. Anbarasan, S. Rehman, E. Hu, S. Timms, W. Reynolds, A. Hotchkies, V. Misra, G. Suresh (Bolton Royal Hospital, UK); B. J. Finch , B. J. Finch, T. Philip Rajathan, H. Jeddy, H. A. Kyaw, N. Wong (Broomfield Hospital, UK); Y. Bhahirathan, C. Donaldson, M. Sequeira Campos, Y. Bhahirathan, M. N. Armitage, A. S. Hussain, B. Hardy, M. Y. Hassan Serry (Darent Valley Hospital, UK); J. Herron , J. Herron (Darlington Memorial Hospital, UK); C. Thakrar (Northampton General Hospital, UK); D. Rojoa , B. Yeap, Z. Iqbal, D. M. Rojoa, C. Cabaleiro Barciela, M. Hussain, C. M. Ruddy, S. Lindwe, Y. Qamar, S. Chuita (Oldham Royal Hospital, UK); C. Toh , A. James, M. Bugelli, Y. Chechelnskaya, N. Sandhu, C. Toh , T. Bylinski (Raigmore Hospital, Inverness, UK); J. M. Findlay , O. Skan, C. Kind, J. M. Findlay, P. Tupper, C. Van Rhee, S. I. Honeyman, G. Menon (Royal Berkshire Hospital, UK); W. Sloper , C. Burford, T. Huq, W. Sloper (St Richard’s Hospital, Chichester, UK); J. Coey (Tameside General Hospital, UK); K. Akbari , K. Akbari, T. Whitehead, S. Dimitriadis, K. Marshall, E. J. Flint (Wycombe General Hospital, UK); M. Curran . (Yeovil District Hospital, UK); A. Yagiz Sen, B. Can, E. Casmeli, D. Kus, R. C. Kavar, A. D. Cevlik, U. Cengiz, E. G. Turk, I. Yilmaz (Dokuz Eylül Üniversitesi Tıp Fakültesi, Turkey); Ö. Yumurtacı, A. Emin, Ç. a. g. r. i. Girit, M. K. Yildirak, E. Senyigit, A. Güldag, B. Söyleyici, Y. E. Aytin, F. E. Akay, N. G. Iskan, B. Mutlu, A. O. Sunay (Trakya Üniversitesi Hastanesi, Turkey); T. Bell, D. Limnatitou, S. Gormley, P. Taleongpong, V. Patel, L. Macgregor, S. Amini, C. Turner , N. To (Barnsley Hospital, UK); N. Laurence, S. Thomas, C. Green, R. Frostick, R. Khera, M. Povey , S. Mahapatra (Countess of Chester Hospital, UK); M. Bradbury, T. Osunronbi, L. Y. C. Tam, A. Khanan Kaabneh, J. Lawther, P. Fisher, T. Tribedi, A. Moosa, A. Ramdin (University Hospital Plymouth, UK); F. McGee, S. Flanagan, C. Thakrar, Q. J. Tan, H. Anwar, R. Clough, B. Chrisp, J. Cassels, G. W. V. Cross (Northampton District General Hospital, UK); A. Refalo, R. Hadley, A. McTighe, F. Farrow, A. Brodie, G. Davis, D. R. Shah, C. Bowers (Northern General Hospital, Sheffield, UK); M. P. E. Ng, R. T. W. Wong, S. Maese (Northwick Park/St. Mark’s Hospitals, UK); R. Tandon, M. Gray, A. Kumar, C. Ciurleo, I. Nyamali, S. Hiremath, S. Sinha, M. Chowdhary (Rotherham General Hospital, UK); P. Kirupananthan, Z. Y. Boh, S. Dass, A. Soma, A. Newton, M. Hill, Y. Shafiq, M. Brkljac (Royal Lancaster Infirmary, UK); H. Martin, C. McClarty, S. Sanyal, A. Alsaif, A. Palkhi, S. Bhopal , N. Patel (St James University Hospital, Leeds, UK); F. Muneeb, O. Page, E. Zeb, J. Coey, A. Al-Azzawi, J. McIntosh, A. Vucicevic, M. Hughes (Tameside Hospital, UK); L. Brooks, B. Fanibi, M. Dixon, P. Njoku, D. Morris, J. Jobson , S. Trussell (The James Paget Hospital, UK); H. Chowdhury, D. O. T. Alawode, W. Wynell-Mayow, V. Udayachandran, D. Alsoof, J. Ekert (The Royal Free Hospital, UK); N. Joseph, N. Zulkefley, G. Hunt, T. Christodoulou, O. Wright, S. Soman, M. Jamal (The Royal Liverpool University Hospital, UK); S. Beqiri, P. Borgas, S. Christie, F. Pereira, S. Browne, J. Yiu, A. Dworkin (The Whittington Hospital, UK); J. Mak, S. Patrawala, N. Milinkovic, R. Schofield, M. Chauhan, L. Hartley, J. Hind (Worcestershire Royal Hospital, UK); A. Heybourne, H. Morgan, C. Wickstone, D. Panagiotou, E. O’Connell, K. Dean, R. Iqbal, L. Walsh, N. Yu, N. Rana, E. Massie . (York Hospital), UK); J. Foong, Y. J. Lee, P. Liebenberg, D. Mijalkov, A. Wells, N. Bull, A. Ajmera, T. Warburton (Calvary Mater Hospital, Newcastle, Australia); S. Morgan, A. Mahmoud, M. Schachtel, B. Mikhail, I. Fomin, B. Mekaeil (Gold Coast University Hospital, Australia); J. Wong, H. J. S. Jun, R. Hengpoonthana (Gosford Private Hospital, Australia); S. Childs, S. Ridgway, N. D. A. Blefari, H. Tam, N. Puchalski, C. Ngai (Manning Hospital, Australia); J. Mackenzie, N. Johnson, M. Holmes, R. Zuzek, T. Saluja, T. Gould, Y. K. Goh, T. Selvaraj (Newcastle Private Hospital, Australia); D. Horne, J. L. Borrow, C. Campbell, G. Cousins, L. Jackson, K. Maheepala, S. Zhao, E. Holden, L. Tutt (Tamworth Hospital, Australia); B. Thompson,

- H. Collins, F. Louie, B. Buckland, D. Smith (The Armidale Hospital, Australia); C. Chong, T. H. Chua, C. Nayak, J. Redmond, R. R. Tan, M. Gramlick, J. S. Teh, S. Y. Ng (The Maitland Hospital, Australia); P. Britten-Jones, R. Mohd Rosli, H. D. V. Pham, M. Harris (The Queen Elizabeth Hospital, Australia); M. Salibasic (University Clinical Center Sarajevo, Bosnia & Herzegovina); V. Pavlov, T. Paycheva, A. Borisova (Alexandrovska hospital - Second surgery clinic, Bulgaria); E. Lyulenina, N. Kolev, B. Boev (Kaspela, Bulgaria); D. Nguen, Y. Mitkov, E. Mitkov, P. Vladova, V. Dimitrov, M. Hussain, A. Gabarski (Medical university - Pleven, UMHAT 'Georgi Stranski', Clinic of Coloproctology, Bulgaria); H. Feradova, T. Mladenov, V. Neykov (Medical University - Pleven, UMHAT 'Saint Marina', Bulgaria); M. Pös, A. Adel, O. Sotona, M. Bartoš, T. Amjad, O. Malý, S. Berec, M. Hanušová, M. Hurný, J. Ůrhalmi (Fakultní nemocnice Hradec Králové, Czech Republic); J. S. Sørensen, A. Mark-Christensen (Svendborg Sygehus, Denmark); F. Chanut, J. Magnin, M. Gout (CHU Francois mitterand, France); L. Schöning, S. CS Simon, C. Galata, I. Karampinis, T. Thäwel, A. M. Seckler, C. Kerem, S. Durdevic, F. Herrle (Universitätsmedizin Mannheim, Germany); E. Artioli, S. Giaccari, V. Neviso, A. Schimera, S. Marino, G. Resta (Arcispedale Sant'Anna, Università degli studi di Ferrara, Italy); G. Pata, D. Ongaro, G. Baronio, S. Raimondo, S. Casiraghi, R. Salvadori, A. Armellini (ASST Spedali Civili di Brescia, Italy); I. Vulcano, E. Bertilone, G. Pintabona, F. Viscosi, C. Mazzeo (Department of Human Pathology of the Adult and Evolutive Age "Gaetano Barresi", Section of General Surgery, AOU G. Martino, University of Messina, Italy); M. Olivieri, C. Belluco, A. D. Antona, S. Basso (Centro di Riferimento Oncologico di Aviano, I. R. C. C. S. ). (Centro di Riferimento Oncologico di Aviano (CRO), IRCCS, Italy); N. S. Pipitone Federico, M. Frattalone (Eduardo Agnelli, Italy); F. Marino (IRCCS S. de Bellis, Italy); F. Carbone, P. Incollingo, F. M. Romano (Istituto Nazionale Tumori - 'G. Pascale', Italy); M. Podda, M. Anania, F. Pulighe, A. Cruccu, M. L. Murru, C. Massaiu, F. Balestra, M. Pazzona, C. De Nisco, G. P. Gusai (Ospedale San Francesco, Italy); A. Giannella, M. Santangelo, M. Olivieri, F. Frangella, D. Magagnano, P. Liberatore (Chirurgia dell'Apparato Digerente, Policlinico Universitario Umberto I, Roma, Italy); M. De Rosa, F. Rondelli, G. Ceccarelli (Ospedale 'San Giovanni Battista', Italy); L. Marano, G. Castagnoli, A. Bartoli, R. Bellochi, A. Spaziani, D. Conti, V. Poponesi, M. Trippetti, S. Amicucci, G. Tazza, P. Procacci, F. Giovannini, E. Basile (Ospedale 'San Matteo degli Infermi' - AUSL Umbria 2, Italy); G. Moschetta, F. Cosmi, G. Romeo, M. Gasparrini, E. Virgilio (Azienda Ospedaliera Sant'Andrea, Roma, Italy); C. Sparta, F. A. Mura, M. Barmina, A. Loretto, C. Rettaroli, G. Mastino, G. V. Ruggiu, G. A. Mura, B. A. Perrone, S. Mulas (Ospedale Santissima Annunziata, Italy); M. De Angelis, A. Mereu, V. Adamo, C. Bianco (Ospedale 'Santo Spirito', Bra, Italy); M. Ricciardiello, C. Campanaro, P. Panaccio, L. M. Esposito, F. F. Di Mola (Ospedale SS Annunziata, Chieti, Italy); F. D'Ascanio, R. Pietroletti (Surgical Coloproctology Val Vibrata Hospital, Sant'Omero, Teramo, Italy); F. Di Marco, A. Amico, E. Schembari, S. Puglisi, F. Tuminello (Policlinico 'Gaspere Rodolico', Italy); F. Figà, A. Caiazzo, L. Selvaggi, A. Capozzolo, B. Braccio (Università degli Studi della Campania 'Luigi Vanvitelli', Italy); A. Truškovs, A. Bartnick, E. Malcevs, M. J. Machatschek, J. Alm, S. Lapsa, M. Delorme, F. Zeynalov, J. Larnovskis (Paula Stradina Kliniska universitates slimnica, Latvia); J. Sauka, D. Bodrov, R. Gailumsis, A. M. Wiemann, N. L. Müller, I. Jelovskis, D. Deksnis, O. Bauermeister Potts, T. Slimbajevs, G. Ancans (Rigas Austrumu kliniska universitates slimnica, Latvia); A. Dulskas, J. Kuliavas, P. Kavaliauskas, R. Kavaliauskaite (National Cancer Institute, Lithuania); L. te Molder, J. Tromp, E. Matthee, Y. M. Tissen (Canisius Wilhelmina Ziekenhuis, Netherlands); E. Brinkhuis, H. S. de Vries, E. 't Hart, K. Beckers, Y. Bekker (Elisabeth Tweesteden Ziekenhuis, Netherlands); S. Kakar, S. F. H. ten Doesschate, T. C. van Smaalen (Erasmus University Medical Center, Rotterdam, Netherlands); O. C. Veen, S. A. Dingemans, L. C. van den Brink (Flevoziekenhuis, Netherlands); G. H. E. J. Vijgen, E. M. F. van de Voort (Franciscus gasthuis & Vietland, Netherlands); A. van der Pool, K. L. C. van Rest, T. Haak (Haaglanden MC, Netherlands); M. C. Gordinou de Gouberville, S. Saleh, M. A. Mens, . (MC Slotervaart, Netherlands); E. M. Hoeks, S. Nieuwenhuizen, A. M. Brandsma (Medisch Centrum Leeuwarden, Netherlands); E. M. van Praag, E. Westerduin, M. P. C. M. Smit, S. J. van der Lely (Onze Lieve Vrouwe Gasthuis locatie oost) (Onze Lieve Vrouwe Gasthuis (OLVG) locatie oost, Netherlands); A. de Ruiter, T. Ribbers, C. A. M. Aarts (Rijnstate Ziekenhuis, Netherlands); M. S. Tulek, J. de Jonge, S. Kocak (Ter Gooi Ziekenhuis, Netherlands); H. J. Alqethami, R. Constansia (Treant Zorggroep, Netherlands); P. C. van Elst, M. W. Tissink (Universitair Medisch Centrum Groningen, Netherlands); J. Azzahhafi, S. Bofarid, M. Kip, W. Saleh (Ziekenhuis St Jansdal, Netherlands); S. Franssen, C. L. Boon, R. J. M. Franssen, I. Romaen, M. T. F. Jense (Zuyderland Medisch Centrum, Netherlands); J. D'Souza, R. Pascoe, A. Scott, E. Stark, K. Mulholland, W. K. Lau, B. Smith, S. I. B. Adams, N. Shah (Christchurch, New Zealand); E. Ling, J. Young, R. Hawkins (Hawkes Bay, New Zealand); S. L. Peng, A. Jacobson, H. Macfater (Middlemore, New Zealand); P. V. B. Fagan, B. Stanfield, N. Henderson, A. Chuang, L. Maskill, H. Ker (Taranaki base hospital, New Zealand); K. Mouldley, B. M. Elliott, R. Hu, S. Edwards, C. Matthews, E. Aitken, M. Walker, J. Winstanley (Whangarei Hospital, Northland District Health Board, New Zealand); T. Martins, I. Miguel, J. Martins, M. F. Cunha, J. Melo, D. N. Veiga, J. Rachadell, J. Rachadell, E. Amorim, R. Vareda, J. Roseira, M. Americano (Centro Hospitalar e Universitário do Algarve, Portugal); D. Correia, V. Capella, T. Moinhos (Hospital de Egas Moniz, Portugal); F. Costa, I. Gil, J. Morgado (Hospital de São Francisco Xavier, Portugal); S. Varghese, E. Boyle, L. Aljohmani, J. Alexander, V. Graziadei, C. McCaughey, A. Jain, J. Lee, D. B. O'Connor (Tallaght University Hospital, Trinity College Dublin, Republic of Ireland); H. Ramanayake, R. Sabnani, L. F. Colon, N. Bansal, I. Stephens, R. Tan, S. Sharma, M. Hoo (Beaumont Hospital, Dublin, Republic of Ireland); G. Doherty, S. Fenn, E. Mulhare, M. Walsh, C. Leavey, O. Costigan (Letterkenny University Hospital, Republic of Ireland); S. Griffin, É. Dockry, E. Khogali, A. K. Aly, R. McPhedran, D. O'Gorman, D. Vermeulen, A. Gopaul (Mater Misericordiae University Hospital, Republic of Ireland); A. R. Pentony, C. L. Piong, R. Nossier, J. Hanna, K. Sabir, S. Y. Eow (Sligo Regional Hospital, Republic of Ireland); N. Ladak, D. Boersma, P. J. Kamath, T. B. W. Soh, A. H. Dyer, S. Y. Chee, I. X. H. Tan, A. Kelliher, K. Scanlon (St James's Hospital, Dublin, Republic of Ireland); L. Adeusi, N. Howarth, N. McCawley, A. O'Neill, M. R. Jones, R. Saleh, A. Singh, N. O'Dwyer (St Vincent's University Hospital, Republic of Ireland); O. C. Mana, H. Gomez, L. Riba, J. Perez, A. Centeno (Consorti Sanitari Integral, Hospital Moisés Broggi, Spain); A. Yebes, C. Ortega, M. E. Ossola, E. Camarero, M. Martínez Illán, L. Aranda García, M. Lázaro Cardona, C. Montalvo Olmedo (Hospital Clínico San Carlos, Spain); C. Fairén Oro, A. Izquierdo Moreno, A. Cuenca Ramírez (Hospital Clínico Universitario de Valencia, Spain); A. Margarida, B. Pando, L. Liqueste Marín, M. Pérez Calle, M. J. Ramos Cordero, A. Sagredo Cuartango, E. Sánchez, A. Marcos Rodrigo (Hospital Clínico Universitario Valladolid,



Spain); A. Fernandez, C. Curtis, M. Bosch, D. Triguero, M. Bosch Ramírez (Hospital General Universitario de Elche, Spain); O. Claramonte Bellmunt, A. De La Llave Serralvo (Hospital Son Llàtzer, Spain); M. J. Sánchez, P. Martín-Borregón, A. Quevedo, J. Martínez, J. M. Marín, P. Rodríguez (Hospital Universitario 12 de Octubre, Spain); I. Esteban Avendaño, C. Jiménez Relimpio, P. Lancho Lavilla, I. Blanco Bartolomé, I. Gómez Cano, C. Blasco Andrés (Hospital Universitario de la Princesa, Spain); A. Abad-Motos, E. Marínez-Hurtado, R. Salvachua-Fernández (Hospital Universitario Infanta Leonor, Spain); C. Muniesa, L. Avelino, H. Cholewa, J. Sancho-Muriel, M. Navasquillo, A. Navío, D. Abelló, M. De Jesus, E. Alvarez (Hospital Universitario y Politécnico La Fe, Spain); B. Blaser, A. Kefleyesus, A. Bugmann, L. M. Piotet, L. Meijers . (Hôpital neuchâtelois, Switzerland); S. Delibegovic (Univerzitetско klinicki Centar Tuzla, Bosnia & Herzegovina); P. Tonchev (UMHAT 'Georgi Stranski', Clinic of Oncosurgery, Bulgaria); M. Magnoli (Policlinico San Matteo, Italy); A. Tamosiunas (Klaipedos universitetine ligonine, Lithuania); S. J. Rottier (Tergooi Ziekenhuis, Netherlands); I. Negoï (Carol Davila University of Medicine and Pharmacy Bucharest, Emergency Hospital of Bucharest, Romania); I. R. Bernado (Consorti Sanitari Integral, Spain); S. Eftychiou (Whipps Cross Hospital, UK).

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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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