Development and internal validation of a model for postoperative morbidity in adults undergoing major elective colorectal surgery: the peri-operative quality improvement programme (PQIP) colorectal risk model

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Summary
Over 1.5 million major surgical procedures take place in the UK NHS each year and approximately 25% of patients develop at least one complication. The most widely used risk-adjustment model for postoperative morbidity in the UK is the physiological and operative severity score for the enumeration of mortality and morbidity. However, this model was derived more than 30 years ago and now overestimates the risk of morbidity. In addition, contemporary definitions of some model predictors are markedly different compared with when the tool was developed. A second model used in clinical practice is the American College of Surgeons National Surgical Quality Improvement Programme risk model; this provides a risk estimate for a range of postoperative complications. This model, widely used in North America, is not open source and therefore cannot be applied to patient populations in other settings. Data from a prospective multicentre clinical dataset of 118 NHS hospitals (the peri-operative quality improvement programme) were used to develop a bespoke risk-adjustment model for postoperative morbidity. Patients aged ≥ 18 years who underwent colorectal surgery were eligible for inclusion. Postoperative morbidity was defined using the postoperative morbidity survey at postoperative day 7. Thirty-one candidate variables were considered for inclusion in the model. Death or morbidity occurred by postoperative day 7 in 3098 out of 11,646 patients (26.6%). Twelve variables were incorporated into the final model, including (among others): Rockwood clinical frailty scale; body mass index; and index of multiple deprivation quintile. The C-statistic was 0.672 (95% CI 0.660–0.684), with a bootstrap optimism corrected C-statistic of 0.666 at internal validation. The model demonstrated good calibration across the range of morbidity estimates with a mean slope gradient of predicted risk of 0.959 (95% CI 0.894–1.024) with an index-corrected intercept of −0.038.

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(95% CI –0.112 –0.036) at internal validation. Our model provides parsimonious case-mix adjustment to quantify risk of morbidity on postoperative day 7 for a UK population of patients undergoing major colorectal surgery. Despite the C-statistic of < 0.7, our model outperformed existing risk-models in widespread use. We therefore recommend application in case-mix adjustment, where incorporation into a continuous monitoring tool such as the variable life adjusted display or exponentially-weighted moving average-chart could support high-level monitoring and quality improvement of risk-adjusted outcome at the population level.

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Introduction
Over 1.5 million major surgical procedures take place in the UK NHS every year and approximately 25% of patients develop a complication following major surgery [1, 2]. Colorectal surgery, including for colorectal cancer, accounts for a substantial proportion of major surgery and complications, with almost 2 million new colorectal cancer diagnoses worldwide per year and 1 million deaths [3]. Postoperative morbidity is predictive of reduced long-term survival across a range of specialties, including colorectal surgery [4, 5].

Two frequently cited risk-adjustment models of postoperative morbidity are the physiological and operative severity score for the enumeration of mortality and morbidity (POSSUM) model and the American College of Surgeons national surgical quality improvement programme (ACS-NSQIP) risk prediction calculator [6, 7]. A third model that could be considered for use in major colorectal surgery populations is the surgical outcome risk tool (SORT) for morbidity, a modification of the validated SORT mortality tool [8, 9]. The POSSUM and SORT morbidity models were derived from small, single-centre cohorts. Both included patients undergoing non-colorectal procedures. The morbidity risk estimate for POSSUM has not been updated since its first publication in 1991, and now overestimates morbidity in contemporary practice [10, 11]. Although the ACS-NSQIP risk prediction calculator demonstrates good discrimination, many of the 21 variables required for risk calculation are not routinely collected in NHS clinical datasets [6]. As model coefficients have not been published, it is difficult to validate this tool outside the ACS-NSQIP programme and performance in a UK population is unknown.

Given the limitations of existing models, we sought to develop and internally validate a bespoke model in a UK population of patients undergoing major elective colorectal surgery. Our aim was to support risk adjustment and monitoring of morbidity outcomes across a range of institutions by using the model to inform continuous display methods, such as the variable life-adjusted display and exponentially-weighted moving average charts [12, 13]. These tools can be used by institutions to benchmark practice and drive quality improvement programmes to enhance outcomes for patients [14].

Methods
This study was approved by the Health Research Authority and analysis approved following discussion with the PQIP National Project Team and Chief Investigator. In the period under investigation, PQIP was recruiting consenting patients in 112 NHS hospitals in England and six NHS hospitals in Wales. Seventy-nine of the 118 NHS hospitals had recruited 50 or more patients.

We report data handling and analysis in line with the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis statement [15]. Data were collected prospectively as part of the national PQIP study by local site investigators, typically research nurses and clinicians. Patients aged ≥18 years, undergoing colorectal surgery between 15 December 2016 and 31 March 2020 were eligible for inclusion within this analysis (online Supporting Information, Appendix S2). Cases after
31 March 2020 were excluded to limit the impact of the COVID-19 pandemic on model development. Patients undergoing concurrent procedures were included in the analysis if the primary operation was recorded as colorectal.

Risk-adjustment variables were defined a priori. Morbidity was defined using the validated and reliable postoperative morbidity survey (POMS) at postoperative day 7 [16]. As the national median length of stay following major colorectal cancer resection in the UK is 7 days (IQR 5–11) [17], postoperative length of stay >7 days due to morbidity identifies patients with substantial postoperative morbidity. Our primary outcome, treated as a binary variable, was defined as ‘morbidity present’ if a patient remained in hospital at postoperative day 7 with any POMS-defined morbidity in the preceding 24 h. Patients discharged before postoperative day 7 were assumed to be morbidity free. Our secondary outcome was the presence of any POMS-major defined morbidity at day 7 (online Supporting Information, Table S1 [8]). Patients who died before postoperative day 7 were assigned to have morbidity. Cases with missing outcome data were excluded from analysis.

Implausible values were removed and treated as missing (online Supporting Information, Figure S1). Index of multiple deprivation scores for England and Wales local super output areas were generated for each patient record using published methods [18] and converted into UK quintiles using open source government data [19–21]. Postcodes, adjusted index of multiple deprivation scores and UK index of multiple deprivation quintiles are available here: https://github.com/jbedford1984/PQIP-CR-model-development. Due to its inclusion in the PQIP dataset in January 2019, Rockwood clinical frailty scale scores were only available for a subgroup of the dataset [22]. However, we included the clinical frailty scale in our analysis, imputing missing items, due to evidence supporting its association with postoperative morbidity [22, 23]. The effect of the high proportion of missing data (65%) of this is explored in one of our sensitivity analyses.

Continuous variables were centred and modelled as restricted cubic splines (online Supporting Information, Figure S2). Categorical variable groups containing <0.5% of cases were combined with similar categories where clinically appropriate or excluded if not. Multiple imputation with chained equations was used to impute missing predictor data (10 complete datasets) [24]. Data were assumed to be missing at random. The imputation model included all predictor and outcome variables under consideration and additional variables to support the missing at random assumption (online Supporting Information, Appendix S3).

Thirty-one candidate predictors, deemed non-modifiable at the point of admission for surgery, were considered for inclusion in the model (online Supporting Information, Table S2). Intra- and postoperative variables influenced by quality of care provided, such as intraoperative blood loss, were excluded. To minimise the risk of overfitting, a sample size of 2632 patients was required to fit a model with 31 candidate predictors, providing 21 events per predictor [25].

We identified predictors of POMS-defined postoperative morbidity by fitting backwards-stepwise logistic regression models, selected on Akaike Information Criterion, across 500 bootstrap re-samples of each of the 10 imputed datasets (total 5000 models). Variables selected into ≥ 70% of the 5000 bootstrap models were included in our model, the PQIP colorectal risk model, hereafter named PQIP-CR. We performed variable selection rather than including all 31 predictors to develop a parsimonious risk-adjustment model to facilitate implementation in clinical practice. Model coefficients and performance estimates were pooled using Rubin’s rules. We assessed discrimination with the C-statistic. Calibration was assessed visually with the bootstrap bias corrected calibration curve (500 bootstrap replicates of each imputed dataset) and through calculation of the slope and intercept estimates at internal validation. Overall model fit was evaluated with the Brier score.

Linear shrinkage factors were estimated to calibrate the PQIP-CR model when predicting our secondary outcome POMS-major by fitting the log odds estimated by the PQIP-CR model as the predictor variable. Internal validation was performed using bootstrap correction of optimism, with 1000 bootstrap re-samples of each imputed dataset [26]. We also calculated the sensitivity, specificity, positive predictive value and negative predictive value of our model at multiple thresholds of estimated risk. We compared performance of PQIP-CR to that of the POSSUM and SORT morbidity models [7, 8]. Slope and intercept values for the existing models were freely estimated using published variables and categorisations, with POMS-defined morbidity as the outcome measure. We were not able to compare performance of the ACS-NSQIP model as some variables required for risk calculation were not available in our dataset. Planned sensitivity analyses are described in the online Supporting Information (Appendices S4–S7).
Statistical analyses were performed using R version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria) and online Supporting Information (Appendix S8) shows packages used for data management and visualisation.

Results
A total of 11,646 cases contributed to model development and internal validation (99.6% of potential eligible cases; Fig. 1). Of these, 6241 (53.6%) patients were discharged before postoperative day 7 and therefore assumed to have no POMS-defined morbidity at this time-point. Table 1 shows patient characteristics for our cohort. There were 3098 (26.6%) patients with POMS defined morbidity at postoperative day 7 (including 33 patients who died within 7 days of surgery, Table 2). POMS-major defined morbidity occurred in 2067 (17.7%) patients. Median postoperative length of stay for the cohort was 6 days (IQR 4–9). Overall data completeness for predictor variables was excellent (95.8%). The proportion of missing data for each predictor variable is shown in online Supporting Information (Table S3).

Twelve variables were selected into ≥70% of the 5000 backwards-selection bootstrap models, resulting in the PQIP-CR model containing the following predictors: mode of surgery; clinical frailty scale; severity of surgery based on the Clinical Coding and Schedule Development Group classification; ASA physical status; BMI; serum sodium; index of multiple deprivation quintile; white cell count; serum urea; age; and serum creatinine (online Supporting Information, Table S4). Table 3 shows the odds ratios and 95%CIs for each categorical predictor in the model. For continuous variables, which were modelled as restricted

Figure 1 Study flow diagram showing study sample construction.
cubic splines, we have shown point estimates of odds ratios at various points on the continuous scale. Online Supporting Information (Figure S2) shows the relationship between continuous variables selected and postoperative morbidity.

The C-statistic of the PQIP-CR model was 0.672 (95% CI 0.660–0.684), online Supporting Information (Figure S3) shows the receiver operating characteristic curve with 95% CIs. At internal validation, the optimism-corrected C-statistic was 0.666 (95% CI 0.654–0.678). A C-statistic of 0.5 indicates a model is no better at predicting an outcome than random chance, ≥ 0.7 indicates acceptable discrimination and ≥ 0.8 is considered strong discrimination. The model demonstrated good apparent and bias corrected calibration across the range of morbidity predictions (Fig. 2), with a maximum difference between predicted and observed morbidity of 2.4 percentage points across deciles of predicted risk (predicted morbidity 33.8%, observed morbidity 36.2%). Calibration was maintained after

### Table 1 (continued)

| Category | Value |
|----------|-------|
| Ex-smoker (< 6 months) | 490 (4.2%) |
| Current smoker | 1202 (10.3%) |

#### ECG findings

| Category | Value |
|----------|-------|
| Normal | 8927 (76.7%) |
| AF rate 60–90 | 483 (4.1%) |
| AF rate > 90/any other abnormal rhythm | 1337 (11.5%) |
| Not done | 901 (7.7%) |

#### NYHA classification

| Category | Value |
|----------|-------|
| 1 | 9592 (82.4%) |
| 2 | 1723 (14.8%) |
| 3/4 | 331 (2.8%) |

#### Diagnosis of cancer in last 5 years

| Category | Value |
|----------|-------|
| Yes | 8342 (71.6%) |

#### Respiratory history findings

| Category | Value |
|----------|-------|
| Normal | 9968 (85.6%) |
| Dyspnoea on exertion | 1310 (11.2%) |
| Dyspnoea on minimal exertion/at rest/chest X-ray | 368 (3.2%) |

#### Cardiovascular history findings

| Category | Value |
|----------|-------|
| No failure | 8712 (74.8%) |
| Diuretic, digoxin, antihypertensive therapy | 2686 (23.1%) |
| Peripheral oedema, warfarin therapy, raised JVP or cardiomegaly on chest X-ray | 248 (2.1%) |

Xmajor, extra major; AF, atrial fibrillation; NYHA, New York Heart Association; JVP, jugular venous pulse.

*Clinical Coding and Schedule Development Group classification.

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**Table 1** Patient characteristics and comorbidities for the PQIP-colorectal model derivation cohort. Values are number (proportion), mean (SD) or median [IQR (range)].

| Category | Value |
|----------|-------|
| Total | 11,646 (100%) |
| Age; y | 64 (14) |
| Sex | Male 6564 (56.2%) Female 5082 (43.6%) |
| ASA | 1 236 (10.9%) 2 1740 (62.1%) 3 1066 (25.8%) 4/5 131 (1.1%) |
| Severity of surgery* | Minor/intermediate/major 195 (1.7%) Xmajor 6019 (51.7%) Complex 5432 (46.6%) |
| NCEPOD categorisation | Elective 10,550 (90.6%) Expedited 1096 (9.4%) |
| Mode of surgery | Laparoscopic 7367 (63.3%) Open 4052 (34.8%) Robotic 227 (1.9%) |
| Rockwood clinical frailty scale | 1 2169 (18.6%) 2 4113 (35.3%) 3 3572 (30.7%) 4 977 (8.4%) 5 485 (4.2%) 6–9 330 (2.8%) |
| Index of multiple deprivation quintile | 1 1716 (14.7%) 2 2078 (17.8%) 3 2365 (20.3%) 4 2691 (23.1%) 5–least deprived 2796 (24.0%) |
| BMI; kg.m\(^2\) | 27.6 (5.4) |
| Urea; mmol.l\(^{-1}\) | 5.1 (4.2–6.2 [1.5–33.0]) |
| Creatinine; mmol.l\(^{-1}\) | 75 (65–88 [26–898]) |
| White cell count; \(\times 10^9.l\(^{-1}\) | 7.2 (5.9–8.8 [0.1–31.4]) |
| Diabetes | No 10,154 (87.2%) Yes, HbA1c ≤ 69 mmol.mol\(^{-1}\) 1192 (10.2%) Yes, HbA1c > 69 mmol.mol\(^{-1}\) 300 (2.6%) |
| Smoking history | Non-smoker 6136 (52.7%) Ex-smoker (> 6 months) 3818 (32.8%) |

(continued)
The C-statistic of the PQIP-CR model when predicting POMS-major morbidity was 0.669 (95% CI 0.655–0.682), with an optimism-corrected C-statistic of 0.668 (95% CI 0.655–0.682). Online Supporting Information (Figure S3) shows the receiver operating characteristic curve with 95% CIs. Bias corrected calibration was good (Fig. 2) across the range of predictions with a slope estimate of 1.001 (95% CI 0.918–1.084) and intercept estimate of 0.002 (95% CI –0.127–0.130) at internal validation. Online Supporting Information (Appendix S10) shows how to calculate the estimated risk of POMS-major defined morbidity using the estimated linear shrinkage factors. Online Supporting Information (Table S6) shows the sensitivity, specificity, positive predictive value and negative predictive value of the PQIP-CR model when predicting POMS-major defined morbidity at various thresholds of estimated risk.

When estimating the risk of Clavien–Dindo [27] grade 2 and above complications the C-statistic was 0.635 (95% CI 0.623–0.647), with performance maintained at internal validation (online Supporting Information, Table S7 and Appendix S4). Calibration was good with a slope estimate of 1.001 (95% CI 0.910–1.093) and an intercept estimate of 0.001 (95% CI –0.099–0.103). Online Supporting Information (Appendix S4) shows the estimated shrinkage factors, how to apply them and the calibration curves following application for Clavien–Dindo defined complications.

Data were available to make morbidity risk estimates for 9173 cases using the POSSUM model and 11,640 for the SORT morbidity model. Fewer estimates were made with the POSSUM model due to missing intra-operative variables for 9173 cases using the POSSUM model and 11,640 for the SORT morbidity model. Discrimination of PQIP-CR was higher despite recalibration of the two existing models in our cohort (p < 0.001, Table 4). Calibration of PQIP-CR was also superior, providing well calibrated estimates across a wider range of risk predictions.

There were 5241 cases included in our second sensitivity analysis (online Supporting Information, Appendix S5). Missing data for the clinical frailty scale variable reduced from 64.8% in the main cohort to 22.9% (n = 1202). The rate of missing data was similar when comparing patients aged <65 years and those aged ≥65 years. There was no significant difference when comparing clinical frailty scale odds ratios between PQIP-CR and those in the sensitivity analysis. Our third sensitivity analysis assessed the ability of a model to estimate the risk of a more homogenous outcome, gastrointestinal morbidity, defined by POMS (online Supporting Information, Appendix S6). The C-statistic of this model was 0.626 (95% CI 0.611–0.641). Our multilevel sensitivity

| Table 2 | Incidence of postoperative morbidity and complication outcomes in our cohort. Values are number (proportion). |
|------------------|----------------------------------------------------------------------------------------------------------------------------------|
| Total number of patients in cohort | 11,646 |
| Patients remaining in hospital at postoperative day 7 | 5405 (46.4%) |
| Patients with POMS-defined morbidity at postoperative day 7 (including death ≤ postoperative day 7), of which: | |
| Pulmonary | 575 (4.9%) |
| Cardiovascular | 259 (2.2%) |
| Infectious | 1553 (13.3%) |
| Neurological | 196 (1.7%) |
| Pain | 749 (6.4%) |
| Renal | 1114 (9.6%) |
| Haematological | 94 (0.8%) |
| Gastrointestinal | 1785 (15.3%) |
| Wound | 488 (4.2%) |
| Patients with POMS-major defined morbidity at postoperative day 7 (including death ≤ postoperative day 7), of which: | |
| Pulmonary major | 575 (4.9%) |
| Cardiovascular major | 259 (2.2%) |
| Infectious major | 1483 (12.7%) |
| Neurological major | 196 (1.7%) |
| Pain major | 77 (0.7%) |
| Renal major | 159 (1.4%) |
| Haematological major | 94 (0.8%) |
| Wound major | 488 (4.2%) |
| Patients who died within 7 days of surgery | 33 (0.3%) |
| Patients with Clavien-Dindo grade 2 or above complication at any time-point during hospital admission | 2997 (25.7%) |

POMS, postoperative morbidity survey. POMS-major is a subset of the POMS criteria (online Supporting Information, Table S1). The Clavien-Dindo grading of surgical complications is shown in online Supporting Information (Table S7).

bootstrap correction of bias, with observed risk of POMS and POMS-major morbidity falling within the 95% CIs of predicted PQIP-CR risk across the full range of predictions. At internal validation, the mean slope gradient of predicted risk for the model was 0.959 (95% CI 0.894–1.024) with an index-corrected intercept of –0.038 (95% CI –0.112–0.036). The Brier score was 0.181. Online Supporting Information (Appendix S9) details how to calculate the predicted risk of morbidity from our model. Online Supporting Information (Table S5) shows the sensitivity, specificity, positive predictive value and negative predictive value of the PQIP-CR model at various thresholds of estimated risk.

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Table 3: Estimated odds ratios and coefficients for the PQIP-CR model.

| Variable                        | Odds ratio (95%CI) | Coefficient | Standard error |
|---------------------------------|--------------------|-------------|----------------|
| **Mode of surgery**             |                    |             |                |
| Laparoscopic                    | 1 Reference        |             |                |
| Open                            | 2.06 (1.88–2.24)   | 0.719       | 0.045          |
| Robotic                         | 1.41 (1.04–1.92)   | 0.346       | 0.156          |
| **Rockwood clinical frailty scale** |                    |             |                |
| 1                               | 1 Reference        |             |                |
| 2                               | 1.29 (1.11–1.50)   | 0.255       | 0.077          |
| 3                               | 1.68 (1.40–2.01)   | 0.517       | 0.092          |
| 4                               | 2.02 (1.53–2.68)   | 0.705       | 0.138          |
| 5                               | 2.24 (1.64–3.06)   | 0.809       | 0.155          |
| 6–9                             | 2.48 (1.68–3.66)   | 0.908       | 0.192          |
| **Sex**                         |                    |             |                |
| Female                          | 1 Reference        |             |                |
| Male                            | 1.36 (1.23–1.51)   | 0.310       | 0.052          |
| **Severity of surgery**         |                    |             |                |
| Minor/intermediate/major        | 1 Reference        |             |                |
| Xmajor                          | 1.19 (0.83–1.70)   | 0.175       | 0.183          |
| Complex                         | 1.77 (1.24–2.53)   | 0.570       | 0.182          |
| **ASA**                         |                    |             |                |
| 1                               | 1 Reference        |             |                |
| 2                               | 1.17 (1.00–1.38)   | 0.160       | 0.082          |
| 3                               | 1.52 (1.27–1.83)   | 0.421       | 0.093          |
| 4/5                             | 1.56 (1.02–2.38)   | 0.444       | 0.215          |
| **BMI; kg.m^2**                 |                    |             |                |
| 18                              | 1.09 (0.88–1.34)   | *−0.022     | 0.019          |
| 25                              | 1                  | *0.175      | 0.074          |
| 30                              | 1.21 (1.10–1.34)   | *−0.521     | 0.216          |
| 40                              | 1.34 (1.15–1.56)   |            |                |
| **Sodium; mmol.l^-1**           |                    |             |                |
| 120                             | 1.84 (1.03–3.28)   | *−0.029     | 0.018          |
| 130                             | 1.37 (1.08–1.73)   | *−0.012     | 0.041          |
| 140                             | 1                  | *0.346      | 0.314          |
| 150                             | 1.44 (0.87–2.38)   |            |                |
| **Index of multiple deprivation quintile** |                    |             |                |
| 5 – least deprived              | 1 Reference        |             |                |
| 4                               | 1.03 (0.91–1.17)   | 0.031       | 0.066          |
| 3                               | 0.99 (0.86–1.13)   | −0.014      | 0.068          |
| 2                               | 1.19 (1.04–1.37)   | 0.176       | 0.069          |
| 1 – most deprived               | 1.17 (1.02–1.35)   | 0.160       | 0.073          |
| **White cell count; *10^9.l^-1**|                    |             |                |
| 3.0                             | 1.00 (0.78–1.29)   | *−0.010     | 0.044          |
| 7.0                             | 1                  | *0.132      | 0.201          |
| 11.0                            | 1.15 (1.04–1.28)   | *−0.293     | 0.521          |
| 15.0                            | 1.32 (1.21–1.56)   |            |                |

(continued)
analysis had a variance of 0.136 for the random effect of hospital site, and a median odds ratio of 1.42 for the random intercept terms [28]. Online Supporting Information (Appendix S7) shows the variation in intercept estimates by hospital site. The estimated odds ratios for the fixed effects in the model are also shown alongside the median odds ratio for the hospital level variable.

Discussion
Our model, PQIP-CR, demonstrates good calibration to risk-adjust postoperative day 7 morbidity defined by the POMS in the setting of elective major colorectal surgery with discrimination performance superior to published morbidity risk models [7, 8]. Importantly, except for ASA-PS and clinical frailty scale grading, all variables included in PQIP-CR are objective and reproducible and the model does not require adjustment for the quality-of-care patients receive intra- and postoperatively. The multicentre, prospective cohort we studied is the largest used for morbidty model development outside of the USA and our parsimonious model has potential to be generalisable to other populations [29]. We recommend that this model be used to prospectively monitor outcomes using methods such as variable life-adjusted display or exponentially-weighted moving average charts [12, 13] at the population level. Given the poor performance of POSSUM [7] and SORT morbidity [8] models in our cohort, we do not recommend their use in patients undergoing elective or expedited colorectal surgery. We encourage the peri-operative community to undertake further work to refine, improve and validate our model internationally in major colorectal surgical cohorts.

Our model provided greater discrimination than existing POSSUM and SORT morbidity models (p < 0.001). Discrimination of these models was lower in our contemporary cohort than previously published (Table 4). Differences in case-mix and surgical complexity between our cohort and those used to develop the SORT and POSSUM morbidity models may contribute to their poorer performance. The SORT morbidity model was derived from a single-centre cohort of patients undergoing generally less complex, predominantly orthopaedic procedures [8]. The POSSUM model was developed in a single-centre cohort of patients undergoing elective and emergency general surgery in 1988–1989. Its poor discrimination in our cohort may reflect changes in surgical practice over the past 30 years. Changes in the diagnosis, management and prognosis of respiratory and cardiac disease may result in POSSUM model variables no longer capturing the impact of the chronic disease on outcome after surgery.

The ACS-NSQIP risk calculator, developed from a large cohort of over 1.4 million patients, is one of the most

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### Table 3 (continued)

| Variable          | Odds ratio (95%CI) | Coefficient | Standard error |
|-------------------|-------------------|-------------|----------------|
| **Urea; mmol.l⁻¹** |                   |             |                |
| 3.0               | 1.17 (0.99–1.37)  | *0.587      | 0.220          |
| 8.0               | 1                 | *0.897      | 0.583          |
| 15.0              | 1.02 (0.76–1.37)  | *2.968      | 2.964          |
| 20.0              | 1.04 (0.68–1.59)  |             |                |
| **Age; y**        |                   |             |                |
| 30                | 1                 | *0.002      | 0.003          |
| 40                | 1.02 (0.96–1.08)  | *0.003      | 0.004          |
| 50                | 1.04 (0.91–1.18)  |             |                |
| 60                | 1.07 (0.90–1.27)  |             |                |
| 70                | 1.13 (1.01–1.47)  |             |                |
| 80                | 1.22 (1.06–1.66)  |             |                |
| **Serum creatinine; μmol.l⁻¹** | |             |                |
| 30                | 1.70 (1.13–2.58)  | *0.787      | 0.311          |
| 60                | 1                 | *2.697      | 0.937          |
| 90                | 1.12 (0.98–1.29)  | *9.184      | 3.418          |
| 120               | 1.12 (0.95–1.33)  |             |                |

*Clinical Coding and Schedule Development Group classification. Xmajor, extra major; Point estimates of odds ratios are shown for continuous variables. These do not represent categorisations and cannot be used to calculate risk estimates.

*Coefficients estimated in model fit. PQIP-CR model performance: Pooled R² = 0.102, Likelihood ratio χ² statistic 846.22, df 34, p < 0.001; Brier score 0.181.
frequently cited peri-operative risk models internationally [6]. Discrimination of the ACS-NSQIP colorectal risk calculator at development was higher than that of PQIP-CR when predicting risk of any postoperative morbidity (C-statistic 0.727 vs. 0.672 (95%CI 0.660–0.684), respectively). When predicting specific postoperative morbidity, the C-statistic of the ACS-NSQIP colorectal model ranged from 0.671 (risk of surgical site infection) to 0.844 (cardiac complications). We were unable to assess ACS-NSQIP model performance in our cohort as variables required for risk prediction were not available in our dataset. Twenty-one predictors are required for risk estimation using the calculator, nine more than those required by the PQIP-CR model. Importantly, ACS-NSQIP colorectal model coefficients have not been published and performance has not been validated in large cohorts outside the programme in the USA.

A major strength of our study was excellent data quality and completeness, with overall >95% completion of predictor variables and only 0.4% missing outcome data.
causing case exclusion. The large, multicentre cohort included patients undergoing surgery in over 100 NHS hospitals across England and Wales. Two main limitations of our analysis are important to highlight. First, although sites are asked to recruit either all eligible patients or a random sample, patient consent is still required; this may introduce sampling bias. The large number of institutions contributing to the dataset should minimise this risk. In addition, the > 25% morbidity rate and median postoperative length of stay of 6 days (IQR 4–9 days) also suggest that we did not recruit a low-risk cohort. All OPCS procedure codes eligible for recruitment to the PQIP study (online Supporting Information, Appendix S2) were classified in a ‘restrictive’ category in a recent ecological study using hospital episode data, a category which was associated with a 90-day postoperative mortality of 2.8% [2]. Second, there was potential for measurement error in our POMS outcome. Our clinical dataset was collected by local clinical teams, commonly including research nurses, anaesthetists and surgical colleagues. Measurement error is likely to be higher for morbidity than mortality, potentially meaning that morbidity is harder to predict using statistical models. This hypothesis has previously been suggested to explain the generally lower discrimination of morbidity models compared with mortality models [6–9, 11]. These are undoubted generic challenges in developing models to predict or risk adjust for postoperative morbidity, but by using the POMS we have used an objective measure that has been formally validated and is widely deployed both in research and audit/quality improvement [16]. Model discrimination did not improve when we assessed the effect using a more homogenous outcome measure, gastro-intestinal morbidity; suggesting the limited discrimination of PQIP-CR is not related to use of a composite measure. In our multilevel sensitivity analysis, the median odds ratio of 1.42 demonstrates moderate unexplained variation in outcome at the hospital level. Comparison of the median odds ratio with estimates for patient-level variables suggests that only severe frailty, surgical complexity and high ASA-PS grade (≥3) had stronger associations with the primary outcome than residual unexplained hospital level variation. Therefore, in our cohort, this residual unexplained hospital level variation appears to play an important role in patient outcome and may reduce the performance of our model (online Supporting Information, Appendix S7). Such variation may result from differences in the quality of care between centres in our cohort, or from between-hospital differences in aspects of case-mix that we did not measure and therefore did not adjust for in PQIP-CR. Hospital level structures and processes which may influence morbidity rates include the clinical expertise of the surgical and peri-operative team; the use of and adherence to enhanced recovery pathways; the availability of prehabilitation programmes; and the availability and utilisation of higher-level care areas such as high dependency and intensive care units postoperatively. Exploration of the association between health system factors and patient outcome may identify additional peri-operative process measures to improve model performance in the future.

We acknowledge a possible disadvantage of including socio-economic status in a risk-adjustment model, if in practice this results in an institutionalised acceptance that patients with lower status have worse outcomes. However, our work in patients undergoing emergency colorectal surgery has demonstrated that differences in clinical outcome by deprivation status are not obviously attributable to differences in standards of inpatient care [30]. These differences, therefore, are more likely to be due to the wider social determinants of health, on which there is a substantial literature [31]. We feel inclusion of index of multiple deprivation data as a predictor variable offers the potential for improved management of these patients.

Postoperative morbidity is associated with increased hospital length of stay and healthcare costs following emergency and elective colorectal surgery and is an important short-term postoperative outcome to risk-adjust and monitor [32]. Despite the broad nature of morbidity included in our composite POMS and POMS-major outcomes, the incorporation of the PQIP-CR model into a continuous monitoring tool, such as the variable life-adjusted display or exponentially-weighted moving average chart, will provide a high-level overview of risk-adjusted outcome after major colorectal surgery. Such methods have been incorporated into the Intensive Care National Audit and Research Centre (ICNARC) reporting system and the National Emergency Laparotomy Audit where exponentially-weighted moving average charts function as mortality monitoring tools that alert clinicians to poor outcome trends in their institutions earlier than data presented as annual standardised mortality ratios. This allows timely investigation of local data and intervention to improve quality of care and patient outcomes. The organ-specific criteria routinely recorded as part of the POMS data collection process allows clinicians to identify domain specific postoperative morbidity and implement timely, targeted quality improvement.

Incorporation of peri-operative outcome variables into electronic healthcare records provides the opportunity to create large-scale datasets that will support procedure specific risk model development. Progress in creating
specific, objective and well-defined standardised perioperative outcome measures may further improve discrimination of morbidity risk-adjustment models [33]. Additional predictor variables that accurately capture hospital level structures and processes such as availability and utilisation of prehabilitation programmes or the routine use of enhanced recovery pathways may support improved risk prediction. The increased availability of peri-operative data through programmes such as PQIP and ACS-NSQIP allow more frequent updating of risk-adjustment models than was previously possible. As such, risk models should no longer be considered a fixed entity, remaining unchanged for decades. Instead, they should be dynamically updated and refined at regular intervals following the example of the ICNARC programme, ensuring risk estimates accurately inform clinical practice [34].

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Supporting Information

Additional supporting information may be found online via the journal website.

**Figure S1.** Data cleaning – removal of implausible values for continuous variables.

**Figure S2.** Non-linear relationship between morbidity and continuous variables included in the PQIP-CR model.

**Figure S3.** Receiver operating characteristic curves for the PQIP-CR model predicting (a) POMS defined morbidity and (b) POMS-major defined morbidity.

**Table S1.** Definition and incidence of morbidity defined by the Postoperative Morbidity Survey in our cohort.

**Table S2.** Thirty-one predictors considered for inclusion in the PQIP-CR model and their association with unadjusted postoperative morbidity and postoperative length of stay.

**Table S3.** Number and proportion of missing predictor variable data.

**Table S4.** Frequency each candidate variable was selected into each backwards step-wise model across the 5000 bootstrap samples. Variables selected into > 70% of bootstrap models were selected into the PQIP-CR model.

**Table S5.** PQIP-CR model performance at specified cut off thresholds of predicted POMS-defined morbidity.

**Table S6.** PQIP-CR model performance (after linear shrinkage) at specified cut off thresholds of predicted POMS-major defined morbidity.

**Table S7.** Definition and incidence of the Clavien–Dindo grading of surgical complications in our cohort.

**Appendix S1.** Additional authors and collaborators.

**Appendix S2.** Colorectal procedures and Office of Population Censuses and Surveys (OPCS) codes eligible for patient recruitment to PQIP at the time of model development.

**Appendix S3.** Variables used in multiple imputation process.

**Appendix S4.** Sensitivity analysis – Linear shrinkage factors for predicting risk of Clavien–Dindo defined complications using PQIP-CR model.

**Appendix S5.** Sensitivity analysis – Effect of missing data in Rockwood Clinical Frailty Scale variable on model fitting process.

**Appendix S6.** Sensitivity analysis – Gastrointestinal POMS-defined morbidity at postoperative day 7.

**Appendix S7.** Sensitivity analysis – multilevel model incorporating random intercept term for hospital site.

**Appendix S8.** R packages used in data management and analysis.

**Appendix S9.** Model equations for calculating risk of postoperative morbidity using PQIP-CR.

**Appendix S10.** Linear shrinkage factors for predicting the risk of POMS-major defined morbidity at postoperative day 7 using PQIP-CR model.