

**SAFE DISCHARGE AFTER ACUTE LOWER GASTROINTESTINAL BLEEDING:  
DESIGN AND VALIDATION OF A NEW VALIDATED RISK SCORE**

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## **ABSTRACT**

### **Background**

Acute lower gastrointestinal bleeding (LGIB) is a common reason for emergency hospitalisation worldwide. Identification of patients at low risk of harm, and therefore suitable for outpatient investigation is a clinical and research priority for clinicians. We aimed to develop and externally validate a simple clinical prediction model to identify patients with LGIB who could safely avoid hospital admission.

### **Methods**

Model development used data from 2336 prospectively identified, unselected admissions (1599 safely discharged) with acute LGIB from 143 hospitals in the United Kingdom (UK). Multivariable logistic regression modelling was used to identify predictors for safe discharge, defined as the absence of re-bleeding, red blood cell transfusion, therapeutic intervention, 28-day re-admission or death. The model was converted into a simplified risk scoring system to aid clinical uptake. The model was externally validated in 288 admissions (184 safely discharged) with LGIB from two UK hospitals. C-statistics were calculated for the new model and comparative assessment performed with six previously developed risk scores.

## **Findings**

Age (0-2 points), gender (0-1 point), previous admission with LGIB (0-1 point), rectal examination findings (0-1 point), heart rate (0-3 points), systolic blood pressure (0-5 points), and haemoglobin (0-22 points) strongly discriminated safe discharge in the development cohort (c-statistic 0·84, 95% confidence interval 0·82 to 0·86) and in the validation cohort (c-statistic 0·79, 95% confidence interval 0·73 to 0·84). Calibration plots showed the new risk score to have good calibration in the validation data. The score was superior to Rockall, Blatchford, Strate, BLEED, AIMS-65, and NOBLADS scores in predicting safe discharge. A score of  $\leq 8$  predicts a 95% probability of safe discharge.

## **Interpretation**

We developed and validated a novel clinical prediction model with good discriminative performance to identify patients with LGIB suitable for safe outpatient management.

## **Funding**

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## Research in context

### *Evidence before this study*

Acute lower gastrointestinal bleeding (LGIB) accounts for an estimated 21,120 admissions to UK hospitals annually and is a leading indication for red blood cell (RBC) transfusion. A large audit across the whole of the UK in 2015 found that 48% of patients required no in-patient interventions to investigate or control bleeding. This indicates that hospitalisation may be avoided in many patients in favour of outpatient investigation, which would result in significant cost and resource savings for healthcare institutions. Risk scores are an important adjunct to clinical assessment for risk stratification. To date, no clinical risk score has been developed to accurately predict outcomes of patients with acute LGIB.

We also conducted a systematic review, searching MEDLINE, PubMed, EMBASE, CDSR, CENTRAL, DARE, HTA & NHSEED, ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform for articles without language restrictions that compared diagnostic and therapeutic interventions (early vs later colonoscopy, or CT) for acute LGIB. Meta-analysis demonstrated no difference in important clinical outcomes (such as re-bleeding or transfusion) with early investigation, questioning the necessity of investigating all patients as an inpatient.

122 We therefore designed a clinical prediction model and risk-scoring tool to help  
123 identify patients at initial presentation with LGIB who could be safely discharged  
124 for outpatient investigation.

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126 *Added value of this study*

127 We developed a simple risk score comprising age, gender, history of lower GI  
128 bleeding, rectal examination findings, heart rate, systolic blood pressure and  
129 haemoglobin. These data are routinely collected and readily available in all  
130 healthcare institutions, and easily calculable on admission. The score was  
131 externally validated in an independent dataset using data from two hospitals  
132 that did not participate in the original study.

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134 We also compared the performance of the score with the Blatchford and Rockall  
135 upper GI risks scores, risk scores that have been developed in upper GI bleeding  
136 but may have some value in lower GI bleeding (BLEED and AIMS-65) and two  
137 scores that have been developed for lower GI bleeding but lacked external  
138 validation (Strate and NOBLADS scores, components of all scores are listed in  
139 Supplement 1). The Oakland Score was superior to all other scores to predict  
140 safe discharge. The Oakland Score also had a superior ability to predict re-

141 bleeding, transfusion, and re-admission, although Blatchford was the best score  
142 to predict re-bleeding, transfusion, and death.

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144 *Implications of all the available evidence*

145 This clinical prediction model will provide frontline clinicians with a risk  
146 stratification tool for patients with acute LGIB. The focus on identifying a large  
147 proportion of patients who can avoid admission and safely be investigated as an  
148 outpatient has important economic and resource implications for healthcare  
149 institutions.

## INTRODUCTION

Lower gastrointestinal bleeding (LGIB) has an estimated incidence of 33/100,000<sup>1</sup> although may be as high as 412/100,000 in low and middle-income countries.<sup>2</sup> In the United Kingdom (UK) LGIB accounts for 20% of all patients hospitalised with gastrointestinal bleeding.<sup>3</sup> Patients may present with minor, self-limiting bleeding or with major haemorrhage, requiring blood transfusion and emergency endoscopic, radiological or surgical intervention.<sup>4</sup>

In comparison to upper gastrointestinal bleeding (UGIB), LGIB tends to follow a more indolent course, requires therapeutic intervention less frequently and has a lower in-hospital mortality rate.<sup>4</sup> There are several extensively validated risk stratification scores for UGIB,<sup>5 6</sup> but there is no equivalent for LGIB. Risk scores or severity indicators have previously been proposed,<sup>7-9</sup> but have been found to be not predictive<sup>10 11</sup> or remain unvalidated in wider populations. Most scoring tools seek to predict adverse outcomes, but in LGIB severe bleeding and in-hospital death are uncommon,<sup>4 12</sup> and thus many patients could be safely discharged at presentation and investigated as an outpatient.

We aimed to derive and externally validate a clinical prediction model and risk-scoring tool to identify LGIB patients who can be safely managed as an outpatient, avoiding hospital admission. We also performed a comparative assessment with previously published risk scoring systems for LGIB as well as scores specific to UGIB.



## **METHODS**

### **Study design and participants**

Data used to derive the prediction model were identified from the National Comparative Audit of Lower Gastrointestinal Bleeding.<sup>4</sup> This is a prospectively collected database of 2528 adults (aged  $\geq 16$  years) admitted with or who developed LGIB as an established inpatient in 143 UK hospitals during two months in 2015 and has been fully described previously.<sup>4</sup> To reflect the normal presenting case-mix, cases were identified by clinical teams using presenting clinical signs and symptoms as opposed to diagnostic codes.<sup>13</sup> Eligible cases presented with bright, dark red blood, or clots per rectum, maroon coloured stool, blood mixed in with stool, or melaena without haematemesis. Cases of UGIB were identified using endoscopy findings and excluded.<sup>13</sup> As this is a secondary analysis of routine anonymous data collected for an audit, ethical approval was not required,<sup>14</sup> as confirmed by the Joint Research Office at Oxford University Hospitals NHS Foundation Trust.

### **Procedures**

Since the aim of the score was to aid decisions about admission to hospital, patients who developed LGIB whilst already admitted for another reason, or who were transferred between hospitals or other treatment facilities were excluded, leaving data from 2336 acute admissions to develop the model. The model was externally validated using a cohort of 288 patients admitted with LGIB to two UK hospitals who had not participated in the original audit.<sup>15</sup> This cohort was chosen as, to our knowledge, it was the largest available database reporting all

elements of the composite outcome and those of all of the other six scores that were assessed for comparative performance. This dataset was retrospectively populated using electronic health data from consecutive presentations to the emergency department in each hospital with a primary diagnosis of LGIB between 2007 and 2011. Inpatient bleeds and cases transferred from other hospitals were excluded. Cases of UGIB were excluded using presenting features, OGD and angiography findings.<sup>15</sup>

## **Outcomes**

Our primary objective was to develop and validate a risk-scoring tool to identify patients that were safely discharged after presentation with LGIB. *Safe discharge* was defined as the absence of all of the following after presentation: (1) re-bleeding, defined as additional blood transfusion requirements and/or a further decrease in haematocrit (Hct)  $\geq 20\%$  after 24 hours clinical stability<sup>7</sup>; (2) red blood cell (RBC) transfusion; (3) therapeutic intervention to control bleeding, defined as endoscopic, radiological, or surgical haemostasis; (4) in-hospital death, all cause; (5) re-admission with further LGIB within 28 days.

## **Statistical Analysis**

### *Model development*

Prior to any statistical modelling, we selected 18 candidate predictor variables that were considered to be biologically and clinically plausibly related to the outcome of safe discharge: age, gender, previous admission with LGIB, cardiovascular disease, active malignancy, liver disease, renal disease, blood on digital rectal examination (DRE), heart rate (HR), systolic blood pressure (SBP),

regular use of oral antiplatelet or non-steroidal anti-inflammatory drugs, use of oral anticoagulants, haemoglobin (Hb, g/dL), platelet count ( $10^9/L$ ), white cell count ( $10^9/L$ ), international normalised ratio (INR), serum urea (mmol/L), and creatinine ( $\mu\text{mol/L}$ ) at initial assessment. The list of candidate variables was also limited to those routinely collected during hospital admission. Variables with large amounts of missing data were omitted, as it was likely they would be missing in clinical practice. Data on co-morbidities were defined using the Charlson co-morbidity index,<sup>16</sup> which we amended to allow application to medical notes.<sup>13</sup>

Fractional polynomials<sup>17</sup> were used to explore the presence of nonlinear relationships of continuous predictors (age, HR, SBP, Hb, platelet count, white cell count, urea, creatinine, INR), however a linear relationship was found to be a good approximation. We assumed missing data occurred at random and performed multiple imputation using chained equations using the `aregImpute` function in the R statistical software package for imputing missing data in the development cohort (R Foundation for Statistical Computing, Vienna, Austria). The validation cohort had complete data on all necessary predictors. We used a multivariable logistic regression model with backwards elimination to select predictors using the Akaike Information Criteria ( $P=0.157$ ). Missing values were predicted on the basis of all other predictors as well as the outcome. Fifty imputed data sets were generated with imputed values reflecting the uncertainty associated with the imputations. The internal validity of the prediction model to obtain an unbiased and optimism corrected estimation of model performance was assessed using bootstrapping. The entire modelling process, including

variable selection, was repeated in each of the 200 bootstrap samples. Performance measures evaluated include the discrimination (c-statistic), with 95% confidence intervals (CI), where a value of 0.5 indicates no discrimination and a value of 1 indicates perfect discrimination.

To increase the uptake and usability of the model, we created a simplified scoring system following the approach by Sullivan *et al.*<sup>18</sup> Values are assigned to risk factor categories, and their total sum assigned predicted probabilities of safe discharge.

#### *Model Validation*

The predicted probabilities were calculated for each patient in the validation cohort using the regression coefficients from the model obtained on the development cohort. Discrimination was assessed by calculating the c-statistic. Using the `val.prob.ci.2` package in R, a calibration plot, with 95% confidence bands, was constructed to assess the agreement between the observed outcome of safe discharge with the predicted probabilities from the model.<sup>19</sup> A model with perfect calibration should lie on the line at 45-degrees for agreement with the outcome.

#### *Comparative assessment with previously described scores*

Previously developed scores for LGIB; BLEED,<sup>9</sup> NOBLADS,<sup>8</sup> and Strate<sup>7</sup> were calculated for each patient (methodology in Appendix, page 1). Although Blatchford<sup>5</sup>, Rockall<sup>6</sup> and AIMS-65<sup>20</sup> scores have been designed for UGIB there is some evidence that they have predictive value in LGIB.<sup>21 22</sup> These were also

calculated, Rockall being limited to pre-endoscopy variables, as several of the endoscopic findings are specific to UGIB. To compare the discriminative ability of these scores, the c-statistic for each was calculated for safe discharge. C-statistics were also calculated for adverse outcomes (in-hospital death, re-bleeding, RBC transfusion, haemostatic intervention, and re-admission with further bleeding) in comparison to the new model. The DeLong test was used to compare c-statistics for each model and each outcome against the new model.<sup>23</sup> We followed the TRIPOD statement for reporting this clinical prediction model study.<sup>24</sup>

#### **Role of the funding source**

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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## **RESULTS**

### **Patient demographics**

The mean age was 68 (standard deviation 19) years in the derivation cohort and 66 (standard deviation 19) years in the validation cohort. Co-morbidity was common, the most frequent being cardiovascular disease in both cohorts. Oral antiplatelet or NSAID use was common, found in over 40% cases, although a higher proportion of patients in the derivation dataset were receiving oral anticoagulants (Table 1). In the derivation cohort 1599/2336 (68.5%) patients were safely discharged. Patients that required admission did so for the following reasons: 576/2336 (24.7%) received RBC transfusion, 323/2336 (13.8%) re-bled, 58/2336 (2.5%) required therapeutic intervention to control bleeding, 52/2336 (2.2%) died and 107/2284 (4.7%) were re-admitted with further LGIB. In both cohorts, diverticular disease was the most common source of bleeding (see Appendix page 2). As missing data accounted for 38% INR values this predictor was excluded from any further analysis.

### **Endoscopy and interventional radiology**

The most common interventions were flexible sigmoidoscopy in the development cohort (487/2336, 20.8%) and colonoscopy in the validation cohort (67/288, 23.3%). OGD was undertaken in 256/2336 (11.0%) of the development cohort and 37/288 (12.8%) of the validation cohort. Mesenteric angiography was rarely undertaken in either cohort (see Appendix page 2).

### **Model Derivation**

Multivariable logistic regression analysis identified the following predictors for safe discharge: age, female gender, no previous LGIB admissions, no blood on DRE, HR, SBP, and Hb (see Appendix page 2). Fractional polynomials suggested linear fit for all continuous predictors. The optimism corrected c-statistic was 0.84 (95% CI 0.82 to 0.86) reflecting good discriminative ability of the model to differentiate patients who were safely discharged from those who were not. The simplified risk score with associated component variables is described in Table 2. The score is calculated by adding the points associated with each clinical component.

### **Model Validation**

The c-statistic of the validation model was 0.79 (95% CI 0.73 to 0.84) with good calibration (see Appendix page 3).

### **Risk scoring tool**

Figure 1 shows the distribution of scores and the proportion of safe discharges for the development cohort. The score ranges from 3-33 (median 14). 45 (1.9%) patients scored  $\geq 30$ . Table 3 shows the probability of safe discharge at each score. A patient with a score of eight has a 95% chance of safe discharge.

### **Comparative assessment with alternative scores**

In comparison to Blatchford, Rockall, AIMS-65, BLEED, Strate, and NOBLADS the new model demonstrated superior ability to discriminate patients who were safely discharged (Table 4). For adverse outcomes, the most discriminative score



for in-hospital death was AIMS-65 (c-statistic 0·78), for re-bleeding was the new model and the Blatchford score (c-statistics 0·74 and 0·74), for therapeutic intervention was BLEED (c-statistic 0·65) and for re-admission with further bleeding was the new model (c-statistic 0·68). No score had a superior performance across all adverse outcomes, although the new model demonstrated superior predictive ability for RBC transfusion (c-statistic 0·92), re-bleeding and re-admission with bleeding as well as safe discharge

## DISCUSSION

We derived and externally validated a clinical prediction model and simple risk-scoring tool, comprising seven variables that can be routinely used to discriminate between LGIB patients who can be safely managed as an outpatient and those who will benefit from hospital admission. This risk score is created from a large prospectively acquired national database of LGIB in the UK, and externally validated. It uses simple demographic and physical examination findings in combination with a single blood test and does not rely on endoscopy or radiological findings, so is easily applicable by the bedside in many clinical settings. A patient scoring  $\leq 8$  points at presentation has a 95% chance of safe discharge from the emergency department. We would advocate the use of this threshold in patients with no other indications for hospital admission.

LGIB is widely recognised as a clinical area with paucity of data to inform care pathways and treatment guidelines.<sup>2 25</sup> In comparison to UGIB, which has seen improvements in outcomes,<sup>1</sup> hospitalisations due to LGIB are increasing and mortality has remained constant.<sup>1 26</sup> A risk score that allows accurate triage at initial assessment has potential to avoid hospitalisation in favour of outpatient management.

‘The prediction model was built from several constructs that were defined a priori, which we anticipated would identify the cohort of patients who would come to no harm following presentation with LGIB. One construct was to ensure there was no re-bleeding (for which we used a previously described definition

that required 24 hours of stability<sup>7</sup>). RBC transfusion and need for endoscopic, radiological or surgical intervention to control bleeding were incorporated to capture adverse events that occurred within the 24 period not captured in the re-bleeding definition, as well as throughout the patient's admission. Re-admission with LGIB was included to ensure no patient was subsequently readmitted with LGIB within 28 days.'

In both the derivation and validation cohorts over 60% patients presenting with LGIB were safely discharged. The estimated number of admissions to UK hospitals annually with LGIB is 21,120 cases.<sup>4</sup> The use of this risk score may avoid direct admission in many of these, provided there is a clear plan and prompt access to outpatient tests. This has benefits in terms of reducing the exposure to unnecessary inpatient stay, financial advantages and the prioritising of access to inpatient beds to other more acutely unwell patients. In the UK the median length of stay is 3 days for LGIB.<sup>4</sup> Whilst there are no costs for LGIB, a large micro-costing UK study in UGIB demonstrated a mean cost per patient of £2458, of which 60% is attributed to the expense of the inpatient bed.<sup>27</sup> Assuming similar costs for LGIB, avoiding admission in 60% would equate to an estimated saving of £18.7m per year, across NHS hospitals in the UK, although patients will require outpatient resources.

Previous studies have identified that advancing age, unstable vital signs, markers of anaemia, and blood on DRE are predictive of adverse outcomes.<sup>7-9 11 15</sup> We have additionally identified gender and previous hospital admission with LGIB as risk factors. The predictive value of male gender is consistent with another study

of LGIB<sup>12</sup> and may be due to a higher burden of co-morbid illness. Recurrent admission is likely to be a marker of pathologies that are difficult to manage, and prone to re-bleeding, such as diverticular bleeding.<sup>28</sup> This is a leading cause of LGIB<sup>12 26</sup> and although has several treatment options, such as endoscopic therapy, interventional radiology or surgery, there is a lack of high-quality evidence supporting their optimal use.<sup>28</sup> Many cases do not undergo haemostatic intervention as most diverticular bleeds stop spontaneously.<sup>28</sup> Anticoagulant and antiplatelet drugs were included in the model but found to not be statistically predictive of safe discharge and thus do not feature in the score. Given previous observational evidence that these drugs may be associated with increased severity of bleeding<sup>4 7 15</sup> this was unexpected. However, even a small derangement in vital signs, such as SBP 90-120mmHg, HR 90-109 and Hb 130-159g/dL which might be found with these drugs, reaches the recommended threshold score of >8 for admission.

Although there have been previous attempts at designing a risk score for LGIB,<sup>8,9</sup> these studies were limited by a reliance on endoscopy referrals<sup>8</sup> or disease classification codes for case ascertainment.<sup>7</sup> Reliance on endoscopy to identify LGIB cases may introduce unnecessary investigation and delay in the assessment of these cases. Accounting for bowel preparation, it would take 48 hours from presentation to perform a colonoscopy (in those hospitals able to provide a 7 day service), limiting the use of a score that relies on endoscopy at initial assessment. Important subgroups presenting with LGIB such as inflammatory bowel disease<sup>7</sup> or post-endoscopy bleeds<sup>9</sup> were often excluded in the previous scores, limiting their generalizability to an unselected population admitted with bleeding. Prior

scores sought to predict severe haemorrhage or mortality,<sup>7-9</sup> which we have previously shown occurs in only 1·4% and 4·3% cases respectively.<sup>4</sup> In the present study, cases were identified by clinical teams using presenting features and the predicted outcome was safe discharge, which is much more common.

Strate *et al* designed a score comprising seven predictors of severe LGIB (continued bleeding, re-bleeding, or re-admission within one week) using data from 252 patients.<sup>7</sup> In our current study, this score performed well at predicting RBC transfusion, but was less discriminative for re-bleeding and re-admission. The different performance may be accounted for by the differing rates of severe bleeding, which was found in 49% cases in their original data, but only 1·4% patients in the current study.<sup>4</sup> A similar study of 132 patients who also had a lower frequency of severe LGIB demonstrated no significant association between the Strate score and severe bleeding.<sup>10</sup>

Aoki *et al* developed the NOBLADS score, using data from 439 patients with LGIB confirmed on colonoscopy, identifying eight predictors of severe bleeding.<sup>8</sup> The score was validated using prospectively collected data from 161 patients who also received colonoscopy. In the current study, the NOBLADS score did predict re-bleeding and RBC transfusion, although was not as discriminative as the new score. It is also limited by the exclusive use of colonoscopy to identify cases. In national studies of LGIB, colonoscopy is used in only 3·9-46·3% cases,<sup>4 12</sup> restricting the applicability of the NOBLADS score as a tool at initial assessment.

The BLEED score was originally developed in an intensive care population of 103 patients with GI bleeding.<sup>9</sup> It was designed to predict in-hospital complications and mortality but in the present study was the best predictor of haemostatic intervention (albeit a weak effect) and did not discriminate the other adverse outcomes. This is consistent with another study that did not validate this score.<sup>11</sup>

The scores that have been developed for UGIB, Rockall, Blatchford and AIMS-65 have been shown to have some ability to predict in-hospital mortality or RBC transfusion in LGIB.<sup>21 22</sup> The current study supports these findings, although none of the scores consistently discriminated all of the adverse outcomes that were studied. These scores did predict safe discharge, but were not as discriminative as the new score. Overall the best predictor for adverse outcomes in LGIB was the Blatchford score,<sup>5</sup> with c-statistics consistently above 0.7 for death, re-bleeding and RBC transfusion. In combination with the new score, this may be clinically useful when risk assessing patients who are not safe for discharge. As UGIB tends to have a more severe course than LGIB, if there is any clinical uncertainty about the origin of the GI bleed, the Blatchford score should be used in preference to the new score.

Triaging patients for outpatient management of LGIB raises important questions about timing and access to resources. There is currently limited data supporting the optimum timing of investigation<sup>29</sup> although it is recommended that patients aged 50 or over with unexplained rectal bleeding should have specialist assessment within two weeks.<sup>30</sup> Gastrointestinal malignancy accounts for only 6% of LGIB admissions,<sup>4</sup> so whether other groups of patients also require rapid

assessment requires further study. There is urgent need for randomised data comparing the diagnostic yields of urgent and elective outpatient colonoscopy, as an increase in outpatient endoscopy service requirements may have significant organisational implications.

There are several limitations to this study. Two components of the safe discharge outcome measure relied on the presence of RBC transfusion (re-bleeding as well transfusion itself), which may be imprecise, as many of the transfusions may be deemed unnecessary, when stratified by vital signs and anaemia.<sup>4</sup> However, this may have led to an under-estimation of the proportion of patients that could have been safely discharged. In both cohorts, only 25-38% patients received endoscopic evaluation, raising the question of how many of the diagnoses were made. Additionally a lack of blood on DRE or lower GI endoscopy may suggest that some patients may not have had true LGIB. However, all of the cases that were used to develop the risk score were prospectively identified by clinicians at presentation and assessed to have LGIB, as opposed to the retrospective review of hospital records or from administrative databases. In clinical practice cases do present with a history of LGIB, without demonstrable bleeding on DRE or colonoscopy, since bleeding can be intermittent in nature, for example, diverticular bleeding. INR was missing in 895 cases in the development cohort. Of these, 207 patients did not have a clotting screen taken, 511 LGIB patients had only an APTT (no PT or INR), but not an APTT ratio (and it was not possible calculate this as we did not have data on the normal range, which differs between analyser) and the remaining 177 patients had truly missing data on clotting. The variability in clotting screen is is reflective of real-life practice and

in keeping with a similar UK study of 4478 cases of non-variceal UGIB, which also found that INR was missing in 40% cases.<sup>31</sup>

Although the validation cohort originated from an external database of cases, like the development cohort, it was sampled from a UK population of patients. Different racial groups do display different trends in LGIB diagnoses,<sup>32</sup> but the frequency of clinical outcomes, such as mortality are consistent between geographically diverse populations.<sup>4 12</sup> It would be beneficial to prospectively validate the new score in populations with different risk profiles.

In summary, the Oakland score has been developed using one of the largest and most comprehensive databases of LGIB, and externally validated. It uses seven basic predictors that are easily quantifiable and is simple to calculate. In comparison to six other risk scores, it was the best in predicting safe discharge. It could be routinely incorporated into triage pathways for acute medical and surgical admissions to identify LGIB patients who can be safely discharged.

### **Authors' Contributions**

KO and VJ designed the study, collected the development cohort data, analysed the results and wrote the manuscript. LA collected the validation cohort data and critically revised the manuscript. RU, RG, NM and MFM designed the study and



critically revised the manuscript. GSC designed and performed the statistical analysis and critically revised the manuscript.

#### **Conflicts of Interest**

We have no conflicts of interest to declare.

#### **Funding Source**

This study was funded by NHS Blood and Transplant and the Bowel Disease Research Foundation. Neither were involved in the design or conduct of the study.

#### **Ethical Approval**

As this is a secondary analysis of routine anonymous data collected part of the NHS audit programme, ethical approval was not required.

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## Tables

Table 1: demographic data for candidate variables in the development and validation cohort

| Variable label in development dataset | Development data (n=2336)       |              |                              |              | External validation data (n=288) |              |                             |              |
|---------------------------------------|---------------------------------|--------------|------------------------------|--------------|----------------------------------|--------------|-----------------------------|--------------|
|                                       | Not safely discharged (n = 737) |              | Safely discharged (n = 1599) |              | Not safely discharged (n = 104)  |              | Safely discharged (n = 184) |              |
|                                       | Summary                         | Missing data | Summary                      | Missing data | Summary                          | Missing data | Summary                     | Missing data |
|                                       | Mean (SD) [IQR]; n (%)          | n (%)        | Mean (SD) [IQR]; n (%)       | n (%)        | Mean (SD) [IQR]; n (%)           | n (%)        | Mean (SD) [IQR]; n (%)      | n (%)        |
| Age                                   | 72.46 (17.37)                   | 0            | 66.48 (19.00)                | 0            | 69.50 (17.19)                    | 0            | 64.49 (20.56)               | 0            |
| Male Gender                           | 381 (51.7%)                     | 0            | 748 (46.8%)                  | 0            | 58 (55.8%)                       | 0            | 93 (50.5%)                  | 0            |
| Previous LGIB admission <sup>1</sup>  | 187 (25.4%)                     | 139 (18.9%)  | 208 (13.0%)                  | 304 (19.0%)  | 42 (40.4%)                       | 0            | 49 (26.6%)                  | 0            |
| CVS disease <sup>2</sup>              | 420 (57.0%)                     | 0            | 733 (45.8%)                  | 7 (0.4%)     | 62 (59.6%)                       | 0            | 103 (56.0%)                 | 0            |
| Cancer <sup>3</sup>                   | 138 (18.7%)                     | 0            | 190 (11.9%)                  | 7 (0.4%)     | 24 (23.1%)                       | 0            | 37 (20.1%)                  | 0            |
| Liver disease <sup>4</sup>            | 23 (3.1%)                       | 0            | 27 (1.7%)                    | 7 (0.4%)     | 2 (1.9%)                         | 0            | 8 (4.3%)                    | 0            |
| Renal disease <sup>5</sup>            | 87 (11.8%)                      | 0            | 85 (5.3%)                    | 7 (0.4%)     | 12 (11.5%)                       | 0            | 11 (6.0%)                   | 0            |
| Blood on DRE                          | 451 (61.2%)                     | 96 (13.0%)   | 843 (52.7%)                  | 185 (11.6%)  | 61 (58.7%)                       | 4 (3.8%)     | 82 (44.6%)                  | 12 (6.5%)    |
| HR                                    | 85.84 (17.93)                   | 16 (2.17%)   | 83.11 (16.80)                | 45 (2.8%)    | 86.24 (17.54)                    | 0            | 86.58 (16.92)               | 0            |
| BP                                    | 123.71 (24.78)                  | 15 (2.04%)   | 136.82 (40.45)               | 41 (2.6%)    | 132.19 (28.97)                   | 0            | 141.91 (50.49)              | 0            |
| Oral antiplatelet or NSAID            | 390 (52.9%)                     | 2 (0.3%)     | 703 (44.0%)                  | 7 (0.4%)     | 44 (42.3%)                       | 0            | 72 (39.1%)                  | 0            |
| Oral anticoagulant                    | 132 (17.9%)                     | 2 (0.3%)     | 243 (15.2%)                  | 7 (0.4%)     | 5 (4.8%)                         | 0            | 6 (3.3%)                    | 0            |
| Hb                                    | 97.04 (28.35)                   | 2 (0.3%)     | 129.50 (19.15)               | 12 (0.8%)    | 97.86 (24.43)                    | 0            | 123.23 (22.38)              | 0            |
| Platelet count                        | 274.42 (124.37)                 | 4 (0.5%)     | 259.09 (88.87)               | 17 (1.1%)    | 247.71 (98.60)                   | 0            | 233.70 (81.06)              | 0            |
| WBC (median, IQR)                     | 9.2 (6.80, 12.48)               | 7 (1.0%)     | 9.5 (7.10, 12.80)            | 19 (1.2%)    | 7.5 (5.45, 10.85)                | 1            | 7.10 (5.20, 9.70)           | 1            |
| Urea (median, IQR)                    | 7.35 (5.20, 10.30)              | 19 (2.6%)    | 5.90 (4.50, 8.00)            | 53 (3.3%)    | 6.25 (4.48, 8.80)                | 0            | 5.60 (3.75, 8.30)           | 1            |
| Creatinine                            | 107.94 (82.87)                  | 16 (2.2%)    | 88.57 (54.68)                | 34 (2.1%)    | 115.39 (88.29)                   | 0            | 98.72 (70.64)               | 0            |
| INR (median, IQR)                     | 1.10 (1.00, 1.30)               | 266 (36.1%)  | 1.10 (1.00, 1.20)            | 629 (39.3%)  | 1.10 (0.10, 1.10)                | 0            | 0.1 (0.1, 1.10)             | 8            |

1. Any episode LGIB resulting in hospital admission
2. Myocardial infarction, angina, congestive heart failure, hypertension
3. Any active cancer excluding basal cell and squamous cell carcinomas of the skin
4. Chronic liver disease with or without cirrhosis
5. Chronic kidney disease stage  $\geq 2$  (eGFR  $\leq 60$ )

Table 2: A score to predict the safe discharge of patients presenting with acute LGIB

| Predictor                      | Score component value |
|--------------------------------|-----------------------|
| <b>Age</b>                     |                       |
| <40                            | 0                     |
| 40-69                          | 1                     |
| >70                            | 2                     |
| <b>Gender</b>                  |                       |
| Female                         | 0                     |
| Male                           | 1                     |
| <b>Previous LGIB admission</b> |                       |
| No                             | 0                     |
| Yes                            | 1                     |
| <b>DRE findings</b>            |                       |
| No blood                       | 0                     |
| Blood                          | 1                     |
| <b>Heart rate</b>              |                       |
| <70                            | 0                     |
| 70-89                          | 1                     |
| 90-109                         | 2                     |
| >110                           | 3                     |
| <b>Systolic blood pressure</b> |                       |
| 50-89                          | 5                     |
| 90-119                         | 4                     |
| 120-129                        | 3                     |
| 130-159                        | 2                     |
| >160                           | 0                     |
| <b>Haemoglobin</b>             |                       |
| 36-69                          | 22                    |
| 70-89                          | 17                    |
| 90-109                         | 13                    |
| 110-129                        | 8                     |
| 130-159                        | 4                     |
| >160                           | 0                     |

Table 3: probability of safe discharge by total score

| Total score | Probability of safe discharge |
|-------------|-------------------------------|
| 0           | 0.99                          |
| 1           | 0.99                          |
| 2           | 0.99                          |
| 3           | 0.98                          |
| 4           | 0.98                          |
| 5           | 0.97                          |
| 6           | 0.96                          |
| 7           | 0.96                          |
| 8           | 0.95                          |
| 9           | 0.93                          |
| 10          | 0.91                          |
| 11          | 0.89                          |
| 12-13       | 0.87-0.89                     |
| 14-15       | 0.77-0.81                     |
| 16-17       | 0.67-0.72                     |
| 18-20       | 0.50-0.62                     |
| 21-23       | 0.33-0.45                     |
| 24-26       | 0.20-0.28                     |
| 27-29       | 0.11-0.16                     |
| ≥30         | <0.1                          |

Table 4: C-statistics for the new model against existing models for safe discharge and adverse clinical outcomes. P-values are from the DeLong test, with reference to the New Model.

| Model      | Death<br>(n=52;<br>2.2%) | Re-bleeding<br>(n=323;<br>13.8%) | Haemostatic<br>Intervention<br>(n=58;<br>2.5%) | RBC<br>Transfusion<br>(n=576;<br>24.7%) | Re-admission<br>(n=107;<br>4.7%) | Safe<br>Discharge<br>(n=1599;<br>68.5%) |
|------------|--------------------------|----------------------------------|--|---|----------------------------------|---|
| New model  | 0.67                     | 0.74                             | 0.61   | 0.92                                    | 0.68                             | 0.84                                    |
| Blatchford | 0.73<br>(p=0.02)         | 0.74<br>(p=0.71)                 | 0.59<br>(p=0.23)                               | 0.86<br>(p<0.001)                       | 0.62<br>(p<0.001)                | 0.80<br>(p<0.001)                       |
| Aims65     | 0.78<br>(p=0.02)         | 0.63<br>(p<0.001)                | 0.60<br>(p=0.53)                               | 0.63<br>(p<0.001)                       | 0.53<br>(p<0.001)                | 0.64<br>(p<0.001)                       |
| BLEED      | 0.68<br>(p=0.85)         | 0.63<br>(p<0.001)                | 0.65<br>(p=0.28)                               | 0.66<br>(p<0.001)                       | 0.54<br>(p<0.001)                | 0.65<br>(p<0.001)                       |
| STRATE     | 0.67<br>(p=0.53)         | 0.66<br>(p<0.001)                | 0.59<br>(p=0.68)                               | 0.73<br>(p<0.001)                       | 0.58<br>(p<0.001)                | 0.69<br>(p<0.001)                       |
| NOBLADS    | 0.72<br>(p=0.12)         | 0.62<br>(p<0.001)                | 0.50<br>(p=0.04)                               | 0.66<br>(p<0.001)                       | 0.57<br>(p<0.001)                | 0.64<br>(p<0.001)                       |
| ROCKALL    | 0.75<br>(p=0.06)         | 0.61<br>(p<0.001)                | 0.62<br>(p<0.05)                               | 0.64<br>(p<0.001)                       | 0.53<br>(p<0.001)                | 0.64<br>(p<0.001)                       |





## Figures

Figure 1: The distribution of scores and associated proportion of safe discharges





