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Original Article

Associations between postoperative anaemia and unplanned readmission to hospital after major surgery: a retrospective cohort study†

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Summary

Background Anaemia following major surgery may be associated with unplanned readmission to hospital. However, the severity-response relationship between the degree of anaemia at discharge and the risk of unplanned readmission is poorly defined. We aimed to describe the severity-response relationship between haemoglobin concentration at the time of discharge and the risk of unplanned readmission in a cohort of patients undergoing different types of major surgery.

Methods We performed a retrospective cohort study in a single tertiary health service, including all patients who underwent major surgery (orthopaedic, abdominal, cardiac or thoracic) between 1 May 2011 and 1 February 2022. The primary outcome was unplanned readmission to hospital in the 90 days following discharge after the index surgical procedure. These complex, non-linear relationships were modelled with restricted cubic splines.

Results We identified 22,134 patients and included 14,635 in the primary analysis, of whom 1804 (12%) experienced at least one unplanned readmission. The odds of unplanned readmission rose when the discharge haemoglobin concentration was < 100 g.l^{-1} ($p < 0.001$). On subgroup analysis, the haemoglobin threshold below which odds of readmission began to increase appeared to be higher in patients undergoing emergency surgery (110 g.l^{-1}; $p < 0.001$) compared with elective surgery. Declining discharge haemoglobin concentration was associated with increased odds ratios (95%CI) of unplanned readmission in patients undergoing orthopaedic (1.08 (1.01–1.15), $p = 0.03$), abdominal (1.13 (1.07–1.19), $p < 0.001$) and thoracic (1.12 (1.01–1.24), $p = 0.03$) procedures, but not cardiac surgery (1.09 (0.99–1.19), $p = 0.07$).

Conclusions Our findings suggest that a haemoglobin concentration < 100 g.l^{-1} following elective procedures and < 110 g.l^{-1} following emergency procedures, at the time of hospital discharge after major surgery, was associated with unplanned readmission. Future interventional trials that aim to treat postoperative anaemia and reduce unplanned readmission should include patients with discharge haemoglobin below these thresholds.

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Introduction

Patients undergoing major surgery are at high risk of complications and these contribute substantially to the use of healthcare resources [1, 2]. There is an urgent need to identify peri-operative risk factors for poor outcomes that could be corrected [3]. Anaemia is associated with a greater incidence of postoperative complications and poor patient recovery [4, 5]. Although an attractive therapeutic target, pre-operative anaemia is multifactorial and treatment can be logistically difficult before surgery, particularly when surgical treatment is urgent [6]. Interventional trials assessing the role of pre-operative intravenous iron suggest the greater effect may be after surgery [7–10], particularly to prevent unplanned readmission [11]. Changing the focus of treatment to the postoperative period may yield greater benefits.

Postoperative anaemia affects 60–90% of surgical patients; of these, 1 in 4 has a haemoglobin concentration $< 100\ g.l^{-1}$ [12]. Large database studies and re-analyses of previous randomised trials suggest that postoperative anaemia is associated with increased mortality and disability following major surgery [13, 14], and increased risk of readmission in surgical patients who require intensive care [15]. However, studies have been limited by generalised assumptions, and there are few data on what severity of anaemia is relevant or which surgical specialities are most affected. Defining the severity-response relationship between postoperative anaemia and outcomes in differing surgical populations would help determine in whom treatment should be considered and inform the design of future randomised trials.

Accordingly, we analysed a large database of patients undergoing major surgery across a variety of surgical specialities to determine if there was a threshold haemoglobin concentration discharge associated with unplanned readmission after major surgery.

Methods

We assessed a 10-year cohort of surgical admissions from a single university-affiliated tertiary referral hospital in Melbourne, Australia, which performs approximately 28,000 surgical procedures annually in all major subspecialties except obstetrics (1 May 2011 to 1 February 2022). Data were extracted from an electronic medical record (Cerner Millennium, Oracle Corporation, Austin, TX, USA). Methodology and results are reported according to the STROBE statement [16]. We received ethical approval with a waiver of informed consent from the Austin Health Human Research Ethics Committee.

Patients aged ≥ 18 y undergoing major elective and emergency surgery with a recorded postoperative duration of stay of ≥ 24 h were included from orthopaedic, abdominal (general surgery and urology), cardiac or thoracic specialities using a list of procedures that was determined a priori (online Supporting Information Table S1). Patients undergoing less invasive surgical and endoscopic procedures (including laparoscopic cholecystectomy), solid organ transplantation and patients for whom a postoperative haemoglobin concentration was not available were not studied. No sample size was prespecified beyond the inclusion of all eligible patients recorded in the data bank over the defined study period.

The primary outcome was unplanned readmission to the hospital following discharge after the index admission. These data were again extracted from the electronic medical record. Following extraction, all readmissions were adjudicated individually and blindly to determine whether they were planned or unplanned and to exclude those unrelated to the index procedure. The secondary outcome was days alive and out of hospital (DAOH) on postoperative day 90 [17], calculated by:

$$\text{DAOH}_{90} = 90 - \text{duration of index admission (days)} - \text{duration of subsequent readmission (days)}$$

Where death occurred within 90 days of surgery, patients were excluded from the primary outcome analysis and '0' was assigned for DAOH-90. Postoperative anaemia was defined as a haemoglobin concentration $< 120\ g.l^{-1}$ in women or $< 130\ g.l^{-1}$ in men, by the haemoglobin measured closest to discharge [18]. Additional variables included: age; sex; Charlson comorbidity index at discharge; haemoglobin concentration on the third postoperative day ($g.l^{-1}$) (where this was not available, an 'equivalent' median of haemoglobin values of the second and/or fourth postoperative day was used instead); surgery

duration (min); requirement for allogeneic red blood cell transfusion and number of units transfused; and inpatient complications (defined a priori by ICD-10 coding; online Supporting Information Table S2). All data were collected as part of routine clinical care.

Data were described and a multivariable binary logistic regression model used to estimate odds ratio (95%CI) for unplanned readmission at 90 days with varying discharge haemoglobin concentrations. Covariates were specified a priori and included: sex; age; Charlson comorbidity index; duration of stay (readmission model only); surgery duration; surgical speciality; units of red blood cells transfused; emergency admission; and inpatient complications. A multivariable quantile regression model estimated change in DAOH-90 with 95%CI. Restricted cubic splines (unplanned readmission) and cubic B-splines (DAOH-90) modelled these complex non-linear relationships. For the DAOH-90 analysis, Markov chain marginal bootstraps with 1000 repetitions were used to calculate 95%CI. A knot quantity between 3 and 6 was chosen by an iterative function to minimise Akaike's information criterion for each model.

Pre-planned subgroup analyses assessed the relationship between postoperative haemoglobin concentration and the primary and secondary outcomes between the four tested surgical specialties, and for elective vs. emergency index procedures. Two exploratory sensitivity analyses were performed to minimise the possibility of confounding: using the third postoperative day haemoglobin concentration (or equivalent) instead of discharge haemoglobin, to correct for confounding of prolonged duration of stay on likelihood of unplanned readmission; and excluding patients who died during their index admission, to correct for confounding from mortality on DAOH-90.

All analyses were performed using R Statistical Software (v4.1.2; R Core Team 2021, Vienna, Austria) with p values < 0.05 were considered significant.

Results

We identified 22,143 patients undergoing major surgery during the study period. Following exclusions, we were left with 15,002 patients. This study cohort was used for the secondary outcome (DAOH-90) analysis. Within this cohort, 486 (3%) patients died during follow-up and 367 (2%) died during their index admission, and consequently were excluded from the readmission analysis. Following these exclusions, 14,635 patients were included in the primary outcome (unplanned readmission) analysis (Fig. 1). Following these exclusions there were no further missing data for the primary or secondary outcome analyses.

In the unplanned readmission analysis cohort, mean (SD) age was 66.1 (16.2) y and 7080/14,635 (48.4%) were women (Table 1). Median (IQR [range]) duration of stay was 7 (5–15 [1–721]) days. Overall, 11,662/14,635 (80%) patients were anaemic on discharge. In all, 1458 (10%) patients required one readmission, 307 (2%) required 2 readmissions and 39 (0.3%) required ≥ 3 readmissions during the 90-day follow-up period. Median (IQR [range]) duration of stay on readmission was 7 (3–17 [1–231]) days; 119 (1%) patients survived the index hospital stay, only to die within 90 days. Of these, 101 patients died during readmission to the hospital and 18 died without being readmitted to the hospital. The latter mortalities were largely expected deaths in patients receiving home-based palliative or nursing home care.

Patients with a discharge haemoglobin < 100 g.l^{-1} were more likely to have an unplanned readmission (Table 2). Discharge haemoglobin < 100 g.l^{-1} affected 4751/14,635 (32.5%) patients in this sample. In contrast, haemoglobin 100–130 g.l^{-1} conveyed no change in the odds of readmission, whereas haemoglobin > 130 g.l^{-1} was associated with reduced odds of readmission. The relationship was modelled with a restricted cubic spine with four knots (Fig. 2). The result was statistically significant ($p < 0.001$).

A consistent effect was found on surgical speciality subgroup analysis, with a lower haemoglobin concentration at discharge associated with higher odds of unplanned readmission in the 90 days following discharge except for the cardiac surgical subgroup (Table 3). In general, each 10 g.l^{-1} decrease in discharge haemoglobin concentration was associated with an 8–13% absolute increase in the odds of readmission, depending on the surgical subgroup in question.

An inconsistent effect was found in the subgroup analysis for degree of urgency of surgery. In patients undergoing emergency surgery, the haemoglobin concentration at which odds of unplanned readmission began to increase was higher (< 110 g.l^{-1}) compared with patients undergoing elective surgery (< 100 g.l^{-1}) (online Supporting Information Table S3 and Figure S1).

The exploratory analysis using the haemoglobin concentration from the third postoperative day (or equivalent) excluded a further 997/14,635 (7%) patients for whom this datum point was missing. The analysis of this cohort of 13,638 showed that time-point of haemoglobin measurement did not influence likelihood of readmission, that is, odds of unplanned readmission still began to increase when haemoglobin on the third postoperative day was < 100 g.l^{-1}. The result was statistically significant ($p < 0.001$) (online Supporting Information Figure S2).

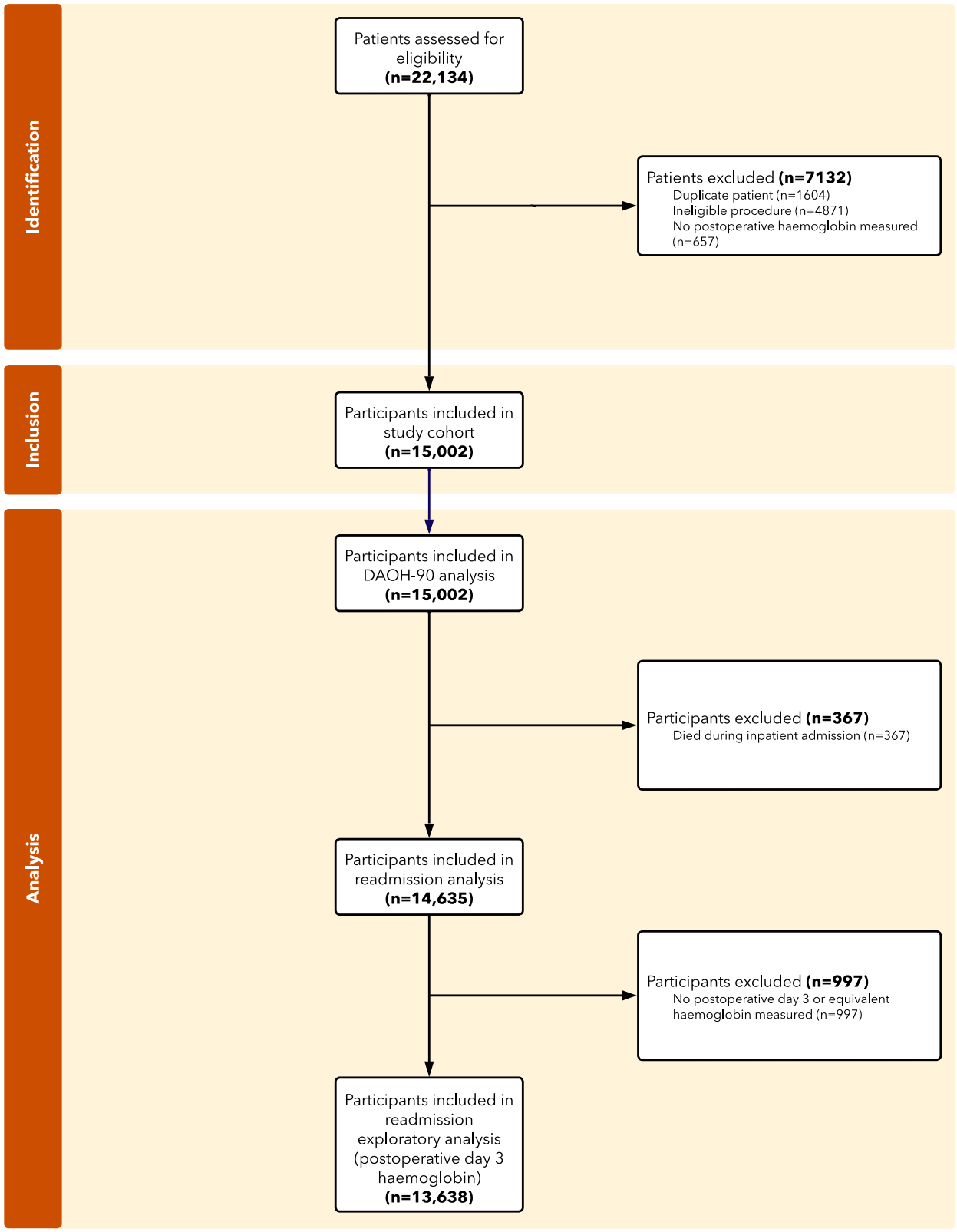

Figure 1 Study flowchart. DAOH-90, days alive and out of hospital on day 90 after surgery.

Table 1 Baseline patient characteristics before (DAOH-90 cohort) and after (readmission cohort) mortality exclusions. Values are mean (SD), number (proportion) or median (IQR [range]).

	DAOH-90 cohort n = 15,002	Readmission cohort n = 14,635
Age; y	66 (16.2)	66.1 (16.2)
Sex; male	7734 (52%)	7555 (52%)
Discharge haemoglobin; $g.l^{-1}$	109 (17.6)	109 (17.5)
Duration of stay; d	8 (5–15 [1–721])	7 (5–15 [1–721])
Postoperative complication during index admission	6474 (43%)	6173 (42%)
Mortality*	486 (3%)	119 (1%)
Charlson comorbidity index	4 (2–5 [0–16])	4 (2–5 [0–16])
-Myocardial infarction	845 (6%)	813 (6%)
-Congestive heart failure	852 (6%)	786 (5%)
-Peripheral vascular disease	503 (3%)	471 (3%)
-Cerebrovascular disease	213 (1%)	193 (1%)
-Dementia	510 (3%)	470 (3%)
-COPD	651 (4%)	617 (4%)
-Connective tissue disease	144 (1%)	140 (1%)
-Peptic ulcer disease	165 (1%)	154 (1%)
-Mild liver disease	592 (4%)	579 (4%)
-Moderate-to-severe liver disease	98 (1%)	86 (1%)
-Uncomplicated diabetes mellitus	1423 (10%)	1404 (10%)
-Diabetes with end organ damage	1923 (13%)	1850 (13%)
-Hemiplegia	248 (2%)	243 (2%)
-Moderate-to-severe chronic kidney disease	1158 (8%)	1067 (7%)
-Localised solid organ tumour or haematological malignancy	1159 (10%)	1532 (11%)
-Metastatic solid organ tumour	1516 (10%)	1444 (10%)
-Acquired Immunodeficiency Syndrome	1 (< 1%)	1 (< 1%)
Allogeneic RBC transfusion	2095 (14%)	1957 (13%)
Index admission type		
-Elective	9790 (65%)	9697 (66%)
-Emergency	5212 (35%)	4938 (34%)
Surgery duration; min	193 (135–305 [30–1084])	194 (136–305 [32–1084])
Surgical speciality		
-Orthopaedics	6244 (42%)	6086 (42%)
-Cardiac	2991 (20%)	2939 (20%)
-Abdominal	4548 (30%)	4418 (30%)
-Thoracic	1219 (8%)	1192 (8%)

DAOH-90, days alive and out of hospital on postoperative day 90; COPD, chronic obstructive pulmonary disease; RBC, red blood cell.
*Mortality is defined as death during index admission or within 90 days of discharge following index admission.

In the DAOH-90 analysis cohort, mean (SD) age was 66 (13.4) y and 7268/15,002 (49%) were women (Table 1 and online Supporting Information Table S4). Median (IQR [range]) duration of stay was 8 (5–15 [1–721]) days. Patients with a discharge haemoglobin < 80 $g.l^{-1}$ were more likely to have a lower DAOH-90. Discharge haemoglobin < 80 $g.l^{-1}$ affected 386/15,002 (3%) patients in this sample. Discharge haemoglobin ≥ 80 $g.l^{-1}$ was not associated with any change in DAOH-90 (Table 4). The effect of discharge haemoglobin concentration on DAOH-90 was best modelled by a basis cubic spline with six knots (online Supporting Information Figure S3). The result was statistically significant ($p < 0.001$).

On surgical subgroup analysis, discharge haemoglobin < 80 $g.l^{-1}$ was associated consistently with fewer DAOH-90 across individual surgical specialities (online Supporting Information Table S5). Basis cubic splines with 3, 6, 6 and 4 knots best fit the relationship between DAOH-90 and postoperative haemoglobin concentration for orthopaedic,

Table 2 Odds of unplanned readmission within 90 days of discharge for different haemoglobin deciles.

Haemoglobin; g.l^{-1}	Odds ratio (95%CI)
70	1.68 (1.24–2.27)
80	1.38 (1.15–1.65)
90	1.14 (1.06–1.22)
100	Reference
110	1.00 (0.92–1.08)
120	0.98 (0.85–1.12)
130	0.88 (0.75–1.02)
140	0.75 (0.62–0.91)
150	0.63 (0.48–0.84)

abdominal, cardiac and thoracic surgery, respectively (online Supporting Information Figure S4a and S4b). The results for each model were statistically significant ($p < 0.001$). An inconsistent effect was found in surgical urgency subgroup analysis. In patients undergoing emergency surgery, the haemoglobin concentration at which DAOH-90 began to decrease was higher (< 90 g.l^{-1}) compared with patients undergoing elective surgery (< 80 g.l^{-1}) (online Supporting Information Table S6 and Figure S5).

On exploratory analysis undertaken after the removal of patients who died following their index surgery, the signal associating postoperative haemoglobin concentration with DAOH-90 was lost (online Supporting Information Figure S6).

Discussion

We performed a large, retrospective cohort study to explore the associations and severity-response relationship between haemoglobin concentration at the time of hospital discharge and subsequent unplanned readmission to hospital following major surgery. We found that discharge haemoglobin < 100 g.l^{-1} was associated with increased odds of unplanned readmission to the hospital. This relationship was confirmed on subgroup analyses of patients undergoing orthopaedic, abdominal and respiratory surgery, but not cardiac surgery. In patients undergoing emergency surgery, we found that discharge

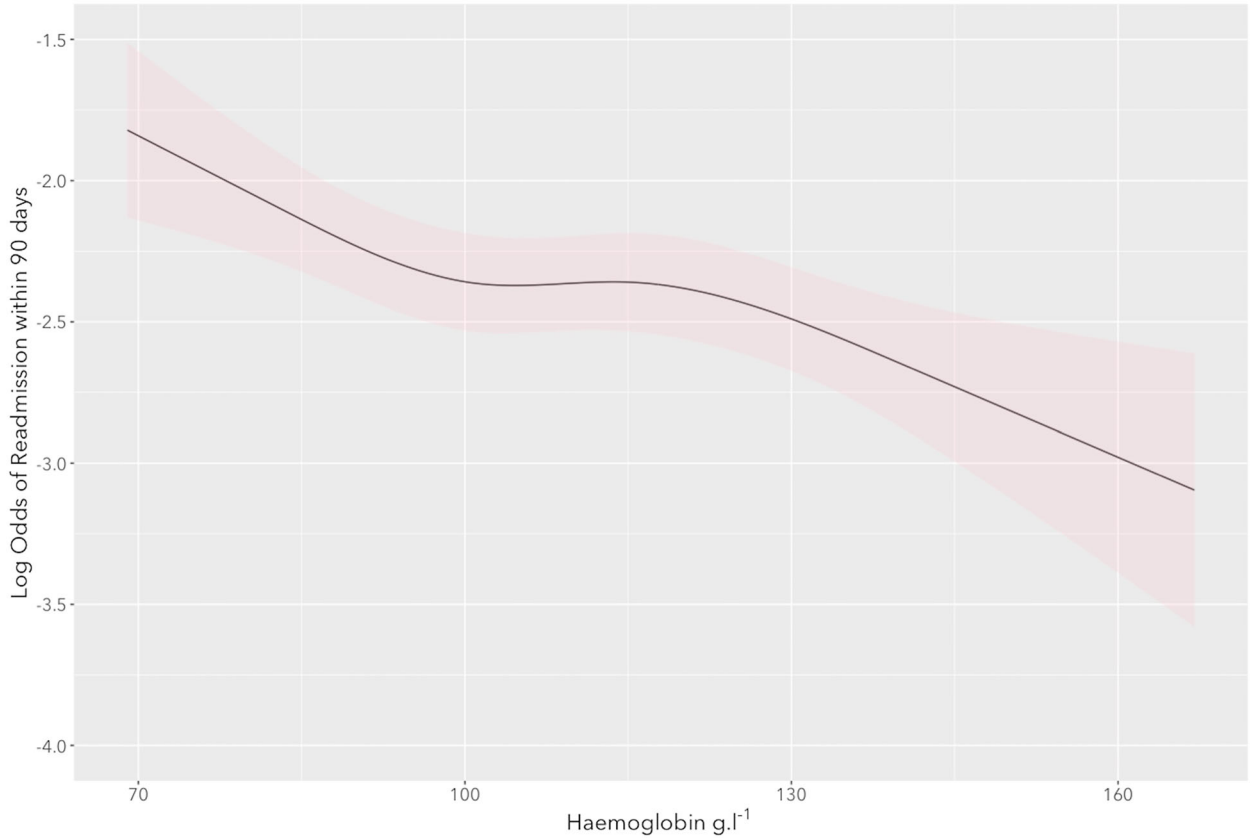

Figure 2 Association between haemoglobin concentration at discharge and logarithmic odds of unplanned readmission. Data are displayed as logarithmic odds ratio (black line) and 95%CI (red shading).

Table 3 Odds of unplanned readmission within 90 days of discharge for each surgical speciality for each declining haemoglobin decile < 150 g.l^{-1}.

Surgical subgroup	Odds ratio (95%CI)	p value
Orthopaedic	1.08 (1.01–1.15)	0.03
Abdominal	1.13 (1.07–1.19)	< 0.001
Cardiac	1.09 (0.99–1.19)	0.07
Thoracic	1.12 (1.01–1.24)	0.03

Table 4 Median days alive and out of hospital within 90 days of surgery for different haemoglobin deciles. Values are median (95%CI).

Haemoglobin; g.l^{-1}	Median DAOH-90
70	77.1 (75.4–78.7)
80	84.9 (84.2–85.5)
90	85.4 (84.9–85.8)
100	84.9 (84.5–85.3)
110	84.8 (84.3–85.2)
120	84.8 (84.4–85.2)
130	85.0 (84.6–85.5)
140	85.3 (84.9–85.6)
150	85.4 (85.1–85.8)

DAOH-90, days alive and out of hospital on day 90 after surgery.

haemoglobin < 110 g.l^{-1} was associated with increased odds of unplanned readmission. Moreover, we showed that discharge haemoglobin < 80 g.l^{-1} was associated with a lower median DAOH-90 and that this association was consistent across all surgical subgroups. In patients undergoing emergency surgery, we found that a discharge haemoglobin < 90 g.l^{-1} was associated with a lower median DAOH-90. The results of the DAOH-90 analyses lost statistical significance after those who died during their index admission were removed.

Postoperative anaemia may be an independent risk factor for poor patient-centred outcomes; it is also common. In a recent prospective cohort study of 2730 patients in 56 hospitals in Australia and New Zealand, 48% of patients were anaemic (haemoglobin < 130 g.l^{-1} for men, < 120 g.l^{-1} for non-pregnant women) at hospital discharge after major abdominal surgery [6]. Other studies have reported an incidence of anaemia at discharge of > 80% [15]. Exploratory re-analyses of high-quality randomised trials have shown similar signals to ours. A re-analysis of the RELIEF trial (n = 2983) showed patients with anaemia (haemoglobin < 130 g.l^{-1} for men and haemoglobin < 120 g.l^{-1} for women) on the third postoperative day following major abdominal surgery had a higher adjusted risk of death or disability when compared with patients without anaemia (RR 1.51 (95%CI 1.1–2.07), p = 0.011) [13]. While the planned, initial analysis did not show an association between milder degrees of anaemia and readmission (haemoglobin < 130 g.l^{-1}, RR 1.06 (95%CI 0.84–1.31), p = 0.66), an exploratory analysis did show an association when a lower haemoglobin cut off (haemoglobin < 100 g.l^{-1}) was used (RR 1.24 (95%CI 1.05–1.47), p = 0.01). In a re-analysis of the POISE-2 trial, a non-linear association was found between nadir postoperative haemoglobin concentration and poor outcomes after major non-cardiac surgery [14]. The authors reported a significant increase in the risk of 30-day myocardial infarction and all-cause mortality with nadir haemoglobin < 110 g.l^{-1} (odds ratio 1.46 (95%CI 1.37–1.56), p < 0.001), but no such association when the haemoglobin was above this level (odds ratio 0.99 (95%CI 0.91–1.09), p = 0.87). More recently, Warner et al. investigated associations between postoperative anaemia and readmission to hospital within 30 days of major surgery requiring intensive care in 32,712 patients in two geographically distinct cohorts in the USA [15]. In this study, readmission rates increased as discharge haemoglobin fell below 110 g.l^{-1}, with every 10 g.l^{-1} decrease in haemoglobin concentration at the time of hospital discharge (hazard ratio for readmission 1.09 (95% CI 1.02–1.18), p = 0.014 or 1.08 (95%CI 1.06–1.11), p < 0.001, depending on the cohort examined).

Recent interest in postoperative anaemia stems from large, randomised trials of pre-operative intravenous iron which, while showing no improvement in haemoglobin concentration or patient-centred outcomes in the immediate postoperative period, did show improvements later in convalescence. In the PREVENTT trial, haemoglobin concentration immediately postoperatively was no higher in the intravenous iron group than in the placebo group but was higher in the intravenous iron group at eight weeks, with a mean difference (95%CI) of 10.7 (7.8–13.7) g.l^{-1} [8]. This finding corresponded with a reduced odds ratio (95% CI) of readmission in the intravenous iron group at the same time-point (0.61 (0.4–0.9)). A similar pattern of haemoglobin incrementation (no difference immediately, but a significant difference emerging between groups at postoperative day 30 or 90) has been replicated in other interventional trials and observational studies in different surgical cohorts [9, 10, 19, 20], suggesting the benefits of iron therapy or an iron-replete state are not seen immediately after surgery but instead take some weeks to become apparent [21].

Furthermore, as postoperative anaemia is more common than pre-operative anaemia (due to intra-operative

blood loss and postoperative inflammation [6]) and that therapies to prevent and correct anaemia (notably intravenous iron) are more feasible and acceptable when given as part of inpatient care [11, 22], future trials could focus on treating anaemia postoperatively, particularly for emergency or expedited elective surgery. Our results identify the postoperative haemoglobin thresholds for trials with an unplanned readmission endpoint at which patients could be approached for enrolment. Our results show that these thresholds (haemoglobin $< 100\ g.l^{-1}$ in elective surgery and $110\ g.l^{-1}$ in emergency surgery) are common, and trials using these thresholds as inclusion criteria are likely to be feasible. Moreover, haemoglobin thresholds used in 'conventional' definitions of anaemia – haemoglobin $< 130\ g.l^{-1}$ for men and $< 120\ g.l^{-1}$ for non-pregnant women, or haemoglobin $< 130\ g.l^{-1}$ for both sexes – were not associated with an increase in the rate of unplanned readmission. Given the signal seen in the PREVENTT trial and the reassuring results of our sensitivity analysis of third postoperative day haemoglobin concentration, a logical design would be to compare intravenous iron with placebo in patients with haemoglobin $< 100\ g.l^{-1}$ in the first week after major abdominal surgery with a primary outcome of unplanned readmission to acute care by postoperative day 90.

The Peri-op Iron and EPO Intervention Study (POP-I) is recruiting currently and compares placebo, intravenous iron alone and intravenous iron with recombinant erythropoietin, in 2400 patients undergoing emergency laparotomy or hip fracture surgery [23]. While this trial uses similar haemoglobin thresholds to those we have identified in this study (80–110 $g.l^{-1}$), using the POP-I primary endpoint (days alive and at home on postoperative day 30) and sample size would be challenging in our cohort; while discharge haemoglobin concentration was associated with significantly increased odds of unplanned readmission, it was not associated with a decrease in DAOH-90 until haemoglobin was $< 90\ g.l^{-1}$. We speculate that while the number of unplanned readmissions in our study cohort was sufficient to generate a significant result for a binary outcome, the study power (large though it was) was inadequate to generate a signal when an associated median variable (DAOH-90) was analysed continuously with quantile regression. These results mimic a similar signal in the PREVENTT trial [8, 11] and suggest that a trial of a similar size, using DAH or DAOH as the primary endpoint, performed in a study population with characteristics like those we have reported, may not be powered adequately.

Our study has several strengths. Using data analytics and routinely collected patient data has produced a complete dataset of exceptional size with minimal missing data. While the study reported by Warner et al. was larger (n = 32,712), their study only collected data on patients who required postoperative intensive care, who represent the minority of patients undergoing major surgery (except cardiac surgery). Furthermore, our additional analyses provide data for multiple different surgical populations and urgencies which can inform those treating postoperative anaemia within these subgroups. Finally, our exploratory analysis using haemoglobin concentration from the third postoperative day in place of discharge haemoglobin gives us confidence that our results are not confounded by those patients in the study who had a prolonged duration of stay following their index surgery.

We acknowledge some limitations to our approach which are inherent to the study design [15]. We cannot exclude the possibility that some patients (particularly those from rural and remote areas) experienced complications following discharge that were not recorded in the electronic medical record. This has implications for both readmission and DAOH; should the patient have been readmitted to a different hospital, this readmission, and the effect it has on DAOH, would not have been recorded. However, the broad consistency of our results with previous, smaller studies that have reanalysed a prospective dataset (and were therefore able to capture readmission to a different hospital prospectively) suggests any effect is limited [13, 14]. A reliance on retrospective data carries an inherent risk of incomplete records and residual measurement error, leading to confounding. We accounted for this by subjecting every readmission episode to blinded adjudication. We are therefore certain that each recorded readmission in the study was unplanned and a consequence of a complication that was linked plausibly to the index surgery. However, we acknowledge that not every potential cause of readmission – while a consequence of the index surgery – is necessarily associated with postoperative anaemia. We plan to explore these data in more detail in a separate study, but an appropriately thorough analysis of these data is beyond the scope of this article. We are unable to determine the cause of postoperative anaemia in the included cases. There are multiple causes of postoperative anaemia, including acute blood loss, infection, inflammation and organ dysfunction. Furthermore, the challenges of interpreting iron status in the setting of inflammation (i.e. following major surgery) are well recognised [24]. There is no current consensus framework to determine the aetiology of postoperative anaemia. Tests which explore this further than ferritin and transferrin (i.e. reticulocyte haemoglobin content, soluble transferrin receptor and hepcidin) are not available for routine clinical

use [25, 26]. Finally, despite the large size of the dataset, our study was conducted in a single centre. This may have implications for generalisability, particularly in low- and middle-income settings.

We have performed a large, retrospective cohort study which has confirmed a severity-response relationship between moderate postoperative anaemia and unplanned readmission after major surgery. Our study has defined specific thresholds across different surgical specialities, in both elective and more urgent surgery, at which rates of unplanned readmission begin to worsen. Notably, conventional definitions of anaemia (haemoglobin < 130 g.l^{-1} for men, < 120 g.l^{-1} for non-pregnant women or 130 g.l^{-1} for both sexes) were not associated with increased rates of unplanned readmission. Future interventional trials that aim to treat postoperative anaemia and thereby reduce unplanned readmission after major surgery should include those with discharge haemoglobin < 100 g.l^{-1} in elective surgery, and < 110 g.l^{-1} in emergency surgery in patients undergoing orthopaedic, abdominal and thoracic procedures.

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Supporting Information

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

Figure S1. Association between discharge haemoglobin concentration and logarithmic odds ratio for unplanned readmission within 90 days of discharge in patients undergoing elective and emergency procedures.

Figure S2. Association between haemoglobin concentration on postoperative day 3 and logarithmic odds ratio of unplanned readmission within 90 days of discharge.

Figure S3. Association between haemoglobin concentration on discharge and median days alive and out of hospital 90 days after surgery.

Figure S4. Association between haemoglobin concentration on discharge and median days alive and out of hospital 90 days after surgery in patients undergoing orthopaedic, abdominal, cardiac and thoracic procedures.

Figure S5. Association between haemoglobin concentration on discharge and days alive and out of hospital 90 days after surgery in patients undergoing elective and emergency procedures.

Figure S6. Association between haemoglobin concentration on discharge and median days alive and out of hospital 90 days after surgery after the exclusion of patients who died following their index surgery.

Table S1. Procedure counts.

Table S2. Complication counts.

Table S3. Odds of unplanned readmission within 90 days of discharge for different haemoglobin deciles on discharge based on surgical urgency.

Table S4. Baseline patient characteristics by surgical speciality before mortality exclusions.

Table S5. Median days alive and out of hospital within 90 days of surgery for different haemoglobin deciles on discharge based on surgical speciality.

Table S6. Median days alive and at home within 90 days of discharge for different haemoglobin deciles on discharge based on surgical urgency.