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Original Article

Prevalence of pre-operative anaemia in surgical patients: a retrospective, observational, multicentre study in Germany

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Summary

Anaemia is a risk factor for several adverse postoperative outcomes. Detailed data about the prevalence of anaemia are not available over a long time-period in Germany. In this retrospective, observational, multicentre study, patients undergoing surgery in March in 2007, 2012, 2015, 2017 and 2019 were studied. The primary objective was the prevalence of anaemia at hospital admission. The secondary objectives were the association between anaemia and the number of units of red blood cells transfused, length of hospital stay and in-hospital mortality. A total of 23,836 patients were included from eight centres. The prevalence of pre-operative anaemia in patients aged ≥ 18 years decreased slightly from 37% in 2007 to 32.5% in 2019 ($p = 0.01$) and increased in patients aged ≤ 18 years from 18.8% in 2007 to 26.4% in 2019 ($p > 0.001$). The total amount of blood administered per 1000 patients decreased from 671.2 units in 2007 to 289.0 units in 2019. Transfusion rates in anaemic patients declined from 33.8% in 2007 to 19.1% in 2019 ($p < 0.001$) and in non-anaemic patients from 8.4% in 2007 to 3.4% in 2019 ($p < 0.001$). Overall, the mortality rate remained constant over the years: 2.9% in 2007, 2.1% in 2012, 2.5% in 2015, 1.9% in 2017 and 2.5% in 2019. In the presence of anaemia, mortality was significantly increased compared with patients without anaemia (OR 5.27 (95%CI 4.13–6.77); $p < 0.001$). Red blood cell transfusion was associated with an increased risk of mortality (OR 14.98 (95%CI 11.83–19.03); $p < 0.001$). Using multivariable linear regression analysis with fixed effects, we found that pre-operative anaemia (OR 2.08 (95%CI 1.42–3.05); $p < 0.001$) and red blood cell transfusion (OR 4.29 (95%CI 3.09–5.94); $p < 0.001$) were predictors of mortality but not length of stay (0.99 (95%CI 0.98–1.00) days; $p = 0.12$) and analysed years (2007 vs. 2019: OR 1.49 (95%CI 0.86–2.69); $p = 0.07$). Pre-operative anaemia affects more than 30% of surgical patients in Germany and multidisciplinary action is urgently required to reduce adverse outcomes.

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Introduction

Anaemia is defined as a decrease in the number of circulating red blood cells (RBC) or a reduction in haemoglobin (Hb) concentration, resulting in impaired capacity to carry oxygen. According to the World Health Organization (WHO), women with a Hb value < 12 g.dl^{-1} and men with a value < 13 g.dl^{-1} are considered anaemic. The aetiology is multifactorial, with iron deficiency being the most prominent [1]. About 35% of patients are anaemic pre-operatively [2] and this is associated with various peri-operative complications. An analysis of more than 220,000 non-cardiac surgical patients found that severe anaemia led to a 12.5-fold (from 0.8% to 10%) increase in the 30-day mortality rate. Even mild anaemia increased the 30-day mortality rate four-fold (from 0.8% to 3.5%) [3]. Studies repeatedly show that pre-operative anaemia is the strongest indicator for blood transfusion in the peri-operative setting [4–6]. However, blood transfusion itself is thought to increase patients' morbidity and mortality [7, 8]. It is vital in cases of excessive blood loss, but current transfusion practice suggests that blood is often used in a preventative manner. Since 2010, the World Health Assembly has been advocating for patient blood management (PBM) as a patient-centred treatment concept to diagnose and treat anaemia at an early stage, reduce unnecessary blood loss and enable rational use of blood products [9]. Within the international context, Germany is one of the top users of blood components with values of > 50 RBC units per 1000 residents since 2012 [10–13]. It is unclear whether this is associated with a higher prevalence of pre-operative anaemia in the German population compared with the global prevalence of 35%. Hence, we sought to identify the anaemia prevalence in surgical patients between 2007 and 2019 in eight hospitals in Germany and the transfusion practice in anaemic patients.

Methods

This retrospective, observational, multicentre study was approved by the ethics committee of Goethe University Frankfurt, Germany. Hospitals participating in the German multicentre observational epidemiological trial to implement PBM in surgical patients (NCT02147795) were invited to join the study. In total, 31 hospitals were contacted of which eight provided data (four university hospitals with > 1000 beds and four general hospitals with 350–1000 beds).

All patients of any age undergoing any type of surgery in March of 2007, 2012, 2015, 2017 and 2019, were included in the analysis. Patient characteristics and clinical data were extracted from the databases of the participating hospitals. Anaemia was defined according to the WHO. Anaemia was categorised in patients aged ≥ 18 y as mild (Hb 11–11.9 g.dl^{-1} for women and Hb 11–12.9 g.dl^{-1} for men); moderate (Hb 8–10.9 g.dl^{-1} for women and men); and severe (Hb < 8 g.dl^{-1} for women and men). Cut-off values and anaemia forms categorised in paediatric patients (aged < 18 y) are shown in online Supporting Information (Table S1).

Red blood cell transfusion practice was performed in accordance with the German transfusion guidelines valid at that time, which recommended transfusion if Hb is < 6 g.dl^{-1} in asymptomatic patients, or between 6 and 8 g.dl^{-1} in patients with cardiovascular risk factors or with clinical symptoms of anaemic hypoxia [14]. Data of surgical patients from the following disciplines with corresponding German surgical codes from 5-01 to 5-07 and 5-18 to 5-92, were analysed: cardiac surgery; gynaecology and obstetrics; maxillofacial surgery; neurosurgery; orthopaedic and trauma surgery; otorhinolaryngology; paediatrics; thoracic surgery; urology; vascular surgery; and visceral surgery. Ophthalmology and dermatology were not included in our analysis, as the transfusion rate is nearly zero. The primary objective was the prevalence of anaemia at time of hospital admission. Secondary objectives were the association between anaemia and the number of transfused RBC units; re-operation during the postoperative period; length of hospital stay; and in-hospital mortality. Data records of patients undergoing any type of surgery providing a pre-operative Hb value obtained before surgery were included in the analysis. Statistical significance was considered with $p < 0.05$ and determined by Student's t-test or Mann–Whitney U-test. For group comparison, Kruskal–Wallis and Fisher's exact test were applied. Multivariable logistic regression models with fixed and random (trial-site) effects with reference year 2007 were used (patients aged ≥ 18 y). Odds ratio (OR) with 95%CI of the multivariate logistic regression analysis is shown for the influencing factors. Patients with re-operation during the postoperative period or in-hospital mortality were excluded from analysis of hospital stay. A subgroup analysis was performed with hospitals providing data for the entire duration of the study. All analyses and graphical illustrations were performed using R software (version 3.1-124; R Foundation, Vienna, Austria) and Excel (2016; Microsoft, Redmond, WA, USA).

Results

Of 30,763 patients that were eligible for analysis, 6927 were excluded because of missing pre-operative Hb values (n = 5006); ophthalmological (n = 1291); dermatological (n = 548); outpatient (n = 70); or aborted surgery (12),

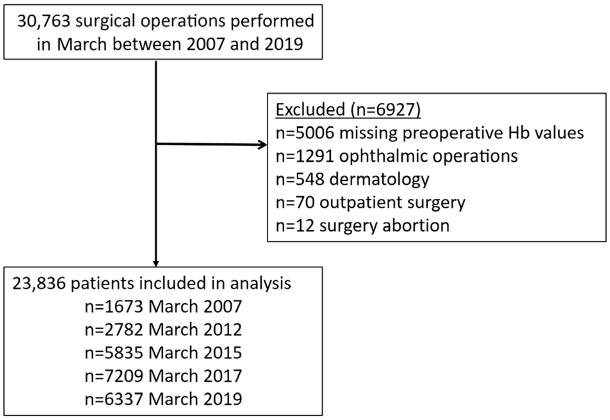

Figure 1 Flow chart of patients included in the analysis.

leaving 23,836 patients for analysis (Fig. 1). Patient characteristics including Hb values are shown in Table 1.

The prevalence of pre-operative anaemia in paediatric patients (n = 1018) increased significantly from 18.8% in 2007 to 26.4% in 2019 ($p < 0.001$) with different distribution of mild, moderate and severe anaemia in 2015, 2017 and 2019 (Fig. 2a and b, online Supporting Information, Table S2). With regard to the different age groups, we found an increased prevalence of pre-operative anaemia in patients aged < 5 y (9.1% in 2007 and 32.6% in 2019) and a decreased anaemia rate in patients aged 12–14.9 y (44.4% in 2007 and 36.0% in 2019). Two university hospitals provided data for the entire study period (n = 10,572). The subgroup analysis showed a similar trend in the prevalence of pre-operative anaemia in paediatric patients: 18.8% in 2007 to 30.1% in 2019 (online Supporting Information, Table S3). However, we found a difference in the prevalence of pre-operative anaemia in 2017: 27.8% for all data vs. 37.0% for hospitals providing data for the entire study period (online Supporting Information, Tables S2 and S3).

The prevalence of pre-operative anaemia in adult patients across all surgical disciplines decreased over the period analysed (37.0% in 2007, 32.8% in 2012, 32.2% in 2015, 30.2% in 2017 and 32.5% in 2019; $p = 0.01$ for comparison 2007 vs. 2012/2015/2017/2019) (Fig. 2c and d, online Supporting Information, Table S2). Although statistically significant, however, this observation is probably not clinically relevant. The subgroup analysis showed a similar trend: 37.0% in 2007, 35.9% in 2012, 36.9% in 2015, 33.1% in 2017 and 35.1% in 2019 ($p = 0.03$ for comparison 2007 vs. 2017 and 2015 vs. 2017) (online Supporting Information, Table S3).

Within the following surgical disciplines, the prevalence of pre-operative anaemia differed between 2007 and 2019, with a decrease in cardiac ($p < 0.001$) and visceral surgery ($p < 0.001$), and an increase in vascular surgery ($p = 0.003$) (online Supporting Information, Figure S1).

The total amount of RBC administration per 1000 patients decreased from 671.2 in 2007, 526.8 in 2012, 328.9 in 2015, 299.7 in 2017, to 289.0 in 2019 (Fig. 3, online Supporting Information, Figure S2). Overall, patients with pre-operative anaemia received six times more RBC units compared with those without anaemia (713.6 vs. 113.5 RBC units per 1000 patients in 2019). The number of transfused patients (anaemic and non-anaemic) without re-operation decreased from 16.7% in 2007 to 8.0% in 2019 ($p < 0.001$; Fig. 4a). Transfusion rates in anaemic patients declined from 33.8% in 2007 to 19.1% in 2019 ($p < 0.001$) and in non-anaemic patients from 8.4% in 2007 to 3.4% in 2019 ($p < 0.001$) (Fig. 4b). Subgroup analyses showed similar results (online Supporting Information, Tables S4 and S5).

The number of total transfused single RBC units remained steady over the years (1.6% in 2007, 1.4% in 2012, 1.5% in 2015, 1.9% in 2017 and 1.7% in 2019), whereas the number of transfused double units decreased (6.8% in 2007, 5.2% in 2012, 3.6% in 2015, 2.8% in 2017 and 2.6% in 2019) (Fig. 4). In patients with pre-operative anaemia, the number of transfused single units was similar (2.6% in 2007, 3.4% in 2012, 3.3% in 2015, 4.3% in 2017 and 3.5% in 2019) and the number of double units decreased (13.5% in 2007, 9.9% in 2012, 8.4% in 2015, 6.7% in 2017 and 6.6% in 2019) over the years (Fig. 4 and online Supporting Information, Table S6). Subgroup analyses showed similar results (online Supporting Information, Table S7). The mean (SD) number of total transfused units per patient decreased over time: 0.67 (0.06) in 2007; 0.53 (0.04) in 2012; 0.33 (0.02) in 2015; 0.30 (0.02) in 2017; and 0.29 (0.02) in 2019 (online Supporting Information, Figure S3). A comparable trend was observed for non-anaemic and anaemic patients (Table 2). The subgroup analyses showed similar results for the mean (SD) number of total transfused units per patient: 0.67 (0.05) in 2007; 0.55 (0.05) in 2012; 0.37 (0.04) in 2015; 0.30 (0.04) in 2017; and 0.27 0.03) in 2019 (online Supporting Information, Table S8).

Overall, hospital stay decreased ($p < 0.001$) from median (IQR [range]) 7 (4–11 [1–106]) days in 2007 to 5 (3–9 [1–258]) days in 2019 (Table 2). In the presence of anaemia, hospital stay was significantly prolonged by 3 days in 2007 and 2012 and 2 days in 2015, 2017 and 2019 compared with patients without anaemia ($p < 0.001$) (Table 2). Length of stay of patients with and without anaemia of different surgical disciplines is shown in online Supporting

Table 1 Patient characteristics. Values are mean (SD), number (proportion) or median (IQR [range]).

	2007 n = 1673	2012 n = 2782	2015 n = 5835	2017 n = 7209	2019 n = 6337
Hospitals	n = 2	n = 3	n = 6	n = 8	n = 8
Age; y	53.3 (19.6)	51.4 (21.5)	53.1 (16.6)	56.6 (20.0)	56.3 (20.5)
Sex; female	764 (45.7%)	1309 (47.1%)	2885 (49.4%)	3579 (49.6%)	3073 (48.5%)
Surgical discipline					
Cardiac surgery	242 (14.5%)	262 (9.4%)	489 (8.4%)	630 (8.7%)	554 (8.7%)
Hb g.dl^{-1} (female)	11.7 (10.8–12.8 [8.1–15.7])	12.3 (10.4–13.4 [7.6–17.3])	12.8 (11.1–13.7 [6.9–16.2])	12.7 (11.6–13.6 [7.3–15.9])	12.4 (11.3–13.5 [7.4–21.3])
Hb g.dl^{-1} (male)	12.8 (10.5–14.6 [7.3–16.9])	12.9 (10.0–14.5 [7.7–19.4])	13.4 (11.8–14.7 [7.0–17.5])	13.8 (12.4–14.9 [6.1–18.3])	13.7 (12.3–14.7 [7.2–19.2])
Gynaecology and obstetrics	192 (11.5%)	287 (10.3%)	869 (14.9%)	952 (13.2%)	866 (13.7%)
Hb g.dl^{-1} (female)	12.7 (11.3–13.8 [6.2–15.6])	12.3 (11.3–13.3 [6.5–16.3])	12.5 (11.5–13.4 [5.6–18.3])	12.4 (11.5–13.4 [5.9–17.8])	12.4 (11.4–13.4 [6.8–16.5])
Hb g.dl^{-1} (male)			14.5 (14.1–15.3 [13.6–15.7])	15.3 (14.9–15.8 [14.4–16.2])	11.9 (11.2–12.5 [10.5–13.2])
Maxillofacial surgery	49 (2.9%)	91 (3.3%)	247 (4.2%)	273 (3.8%)	226 (3.6%)
Hb g.dl^{-1} (female)	13.2 (11.9–13.7 [6.1–15.9])	13.2 (12.7–13.8 [10.7–15.4])	12.9 (12.1–13.7 [7.9–16.1])	13.0 (12.3–13.8 [7.1–16.7])	13.1 (11.8–13.8 [7.3–16.6])
Hb g.dl^{-1} (male)	14.1 (11.6–15.6 [8.4–17.1])	14.5 (13.4–15.5 [9.0–16.7])	14.3 (13.1–15.1 [8.1–17.5])	14.3 (12.8–15.3 [6.5–19.0])	14.6 (13.3–15.3 [6.8–17.2])
Neurosurgery (%)	114 (6.8%)	300 (10.8%)	513 (8.8%)	621 (8.6%)	576 (9.1%)
Hb g.dl^{-1} (female)	12.8 (11.8–13.9 [8.0–15.9])	13.0 (11.9–13.9 [6.0–15.8])	12.9 (12.0–13.9 [7.6–16.8])	13.1 (12.1–14.1 [6.1–16.6])	12.9 (11.9–13.8 [6.8–16.7])
Hb g.dl^{-1} (male)	14.1 (12.9–15.4 [8.6–17.2])	14.3 (12.9–15.5 [8.3–18.3])	14.1 (12.6–15.1 [7.1–18.0])	13.9 (12.6–15.0 [7.3–18.0])	14.0 (12.6–15.1 [6.4–18.8])
Orthopaedic and trauma surgery	316 (18.9%)	575 (20.7%)	1122 (19.2%)	1627 (22.6%)	1293 (20.4%)
Hb g.dl^{-1} (female)	13.0 (11.8–14.0 [8.8–16.9])	13.0 (12.1–13.8 [7.8–16.1])	12.9 (11.7–13.8 [6.4–16.3])	13.1 (12.1–14.0 [6.4–16.4])	13.1 (11.9–13.9 [6.7–18.4])
Hb g.dl^{-1} (male)	14.3 (12.5–15.4 [3.6–18.0])	14.2 (13.0–15.1 [7.0–17.9])	14.3 (12.9–15.3 [6.0–18.1])	14.6 (13.4–15.4 [5.8–18.8])	14.2 (13.0–15.3 [7.2–18.0])
Otorhinolaryngology	179 (10.7%)	284 (10.2%)	401 (6.9%)	380 (5.3%)	328 (5.2%)
Hb g.dl^{-1} (female)	13.5 (12.7–14.3 [8.6–17.0])	13.3 (12.6–13.9 [6.4–15.4])	13.0 (12.3–14.0 [6.9–16.9])	13.3 (12.6–14.0 [6.9–16.1])	13.0 (12.4–13.7 [6.0–16.4])
Hb g.dl^{-1} (male)	14.9 (14.1–15.7 [8.6–17.6])	14.6 (13.7–15.5 [7.7–17.8])	14.7 (13.5–15.5 [6.1–18.1])	14.8 (13.7–15.6 [6.7–17.8])	14.6 (13.8–15.7 [8.1–18.4])
Paediatric surgery	80 (4.8%)	232 (8.3%)	340 (5.8%)	169 (2.3%)	197 (3.1%)
Hb g.dl^{-1} (age < 1 y)	11.4 (10.8–12.0 [10.1–12.5])	11.8 (10.8–14.5 [8.6–19.1])	12.8 (10.0–15.8 [7.7–21.0])	12.0 (10.9–14.4 [6.9–19.7])	12.7 (10.9–16.9 [8.6–22.7])
Hb g.dl^{-1} (age 1–4.9 y)	11.8 (11.5–12.0 [11.1–12.8])	11.8 (11.0–12.5 [5.3–19.3])	11.9 (10.6–12.6 [7.3–18.5])	11.6 (10.4–12.4 [7.9–17.0])	11.4 (10.4–12.1 [3.0–16.4])
Hb g.dl^{-1} (age 5–11.9 y)	13.1 (12.1–13.7 [10.5–15.4])	12.3 (11.5–13.4 [7.9–15.1])	12.4 (11.3–13.2 [4.0–20.0])	12.4 (11.7–13.6 [10.4–18.0])	12.9 (11.8–13.5 [9.8–14.9])
Hb g.dl^{-1} (age 12–14.9 y)	13.2 (12.1–13.6 [9.0–15.3])	13.1 (12.4–13.9 [10.6–15.4])	13.1 (12.3–13.9 [7.5–16.0])	13.0 (12.0–14.3 [8.4–17.3])	12.7 (10.9–13.2 [6.3–14.5])
Hb g.dl^{-1} (age > 15 y female)	13.3 (12.4–13.6 [11.9–15.0])	12.8 (12.1–13.3 [10.9–14.0])	12.8 (11.9–13.5 [8.5–15.1])	12.9 (10.5–13.3 [7.2–13.8])	12.7 (11.9–13.6 [9.7–14.9])
Hb g.dl^{-1} (age > 15 y male)	14.5 (11.5–15.2 [9.8–16.9])	14.2 (12.8–14.8 [8.6–15.5])	14.6 (14.1–15.4 [9.2–16.6])	14.6 (13.4–15.6 [9.0–16.4])	15.2 (14.4–15.6 [12.3–16.7])

(continued)

Table 1 (*continued*)

	2007 n = 1673	2012 n = 2782	2015 n = 5835	2017 n = 7209	2019 n = 6337
Thoracic surgery	30 (1.8%)	53 (1.9%)	46 (0.8%)	118 (1.6%)	122 (1.9%)
Hb g.dl^{-1} (female)	12.6 (9.9–13.0 [8.0–15.3])	11.4 (10.1–13.1 [7.5–13.9])	9.5 (8.7–11.5 [6.4–15.8])	12.6 (11.4–13.9 [6.8–16.4])	12.5 (11.2–13.6 [8.5–16.4])
Hb g.dl^{-1} (male)	12.1 (10.8–13.6 [8.1–15.5])	13.7 (11.3–14.7 [8.6–17.0])	12.5 (10.4–14.1 [7.5–16.0])	13.5 (12.0–14.8 [6.4–16.9])	12.6 (11.1–14.6 [7.1–16.7])
Urology	122 (7.3%)	204 (7.3%)	590 (10.1%)	640 (8.9%)	594 (9.4%)
Hb g.dl^{-1} (female)	13.2 (11.3–14.0 [8.5–16.0])	12.7 (10.5–13.5 [7.7–15.6])	13.0 (11.4–13.8 [6.3–16.9])	12.8 (11.3–13.8 [4.7–15.5])	13.1 (11.6–13.9 [6.4–16.0])
Hb g.dl^{-1} (male)	14.2 (12.6–15.1 [7.0–17.1])	14.1 (12.4–14.9 [4.2–16.9])	14.1 (12.6–15.1 [6.9–18.4])	14.2 (13.0–15.2 [6.4–18.2])	14.3 (13.1–15.2 [6.4–18.0])
Vascular surgery	51 (3.0%)	131 (4.7%)	218 (3.7%)	440 (6.1%)	346 (5.5%)
Hb g.dl^{-1} (female)	13.1 (11.9–13.8 [9.4–14.6])	11.7 (10.3–13.4 [7.7–14.7])	11.7 (10.3–13.2 [7.8–17.2])	11.9 (10.5–13.3 [7.2–15.7])	11.9 (11.0–13.3 [6.5–16.9])
Hb g.dl^{-1} (male)	14.0 (11.9–16.0 [8.9–17.1])	12.6 (11.1–14.4 [7.9–17.0])	12.9 (10.9–14.1 [7.2–17.7])	12.7 (10.8–13.9 [6.1–16.8])	12.0 (10.3–13.9 [6.1–17.4])
Visceral surgery	298 (17.8%)	363 (13.0%)	1000 (17.1%)	1359 (18.9%)	11,235 (19.5%)
Hb g.dl^{-1} (female)	12.2 (10.7–13.4 [6.9–15.5])	12.2 (10.6–13.4 [7.3–15.6])	12.8 (11.3–13.6 [5.0–16.9])	12.7 (11.3–13.8 [5.1–17.9])	12.7 (11.1–13.8 [3.4–17.1])
Hb g.dl^{-1} (male)	12.8 (10.5–14.4 [7.5–16.8])	13.3 (11.4–14.7 [6.6–17.3])	13.7 (11.7–14.9 [3.0–18.0])	13.8 (11.9–15.1 [5.0–17.9])	13.8 (11.8–15.0 [4.6–18.2])

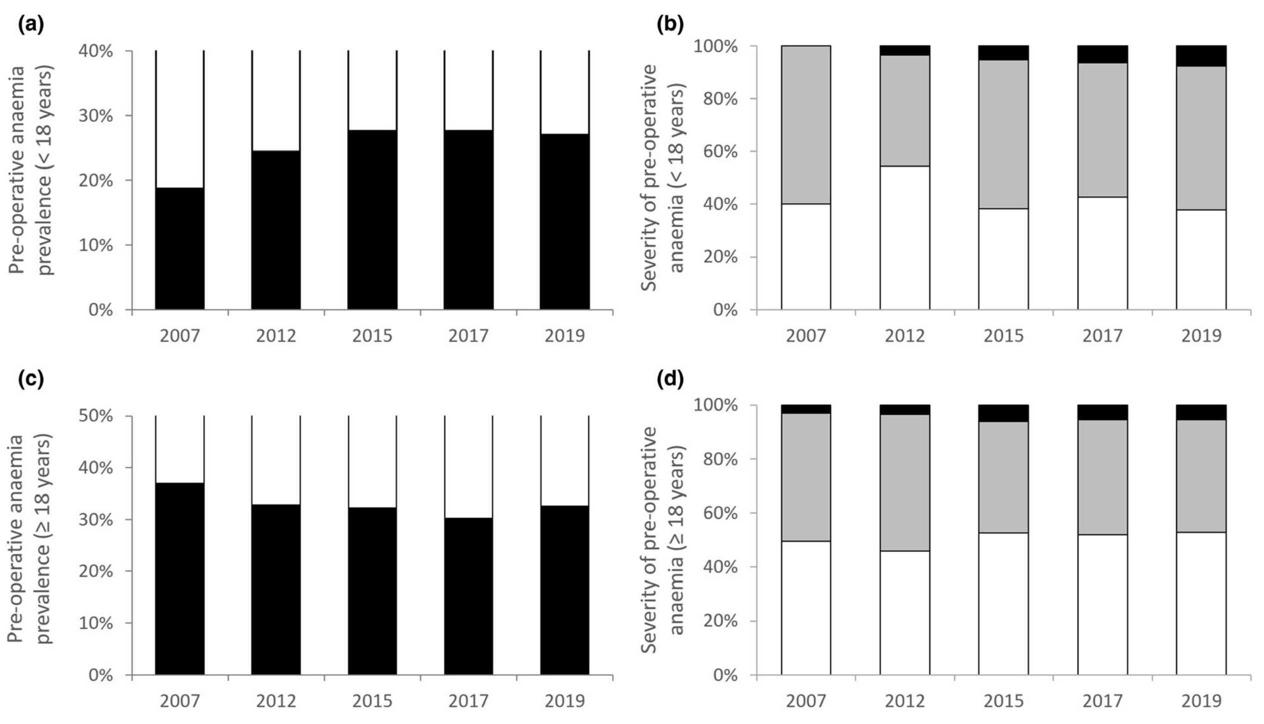

Figure 2 Prevalence of anaemia (black bars) and no anaemia (white bars) in surgical patients aged < 18 y (a) and ≥ 18 y (c) and severity of anaemia (mild, white bars; moderate, grey bars; severe, black bars) in surgical patients aged < 18 y (b) and ≥ 18 y (d).

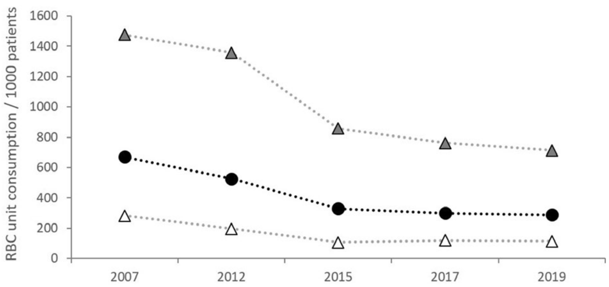

Figure 3 Red blood cell utilisation per 1000 patients during 2007–2019. Black circle, total; white triangle, without anaemia; grey triangle, with anaemia; RBC, red blood cells.

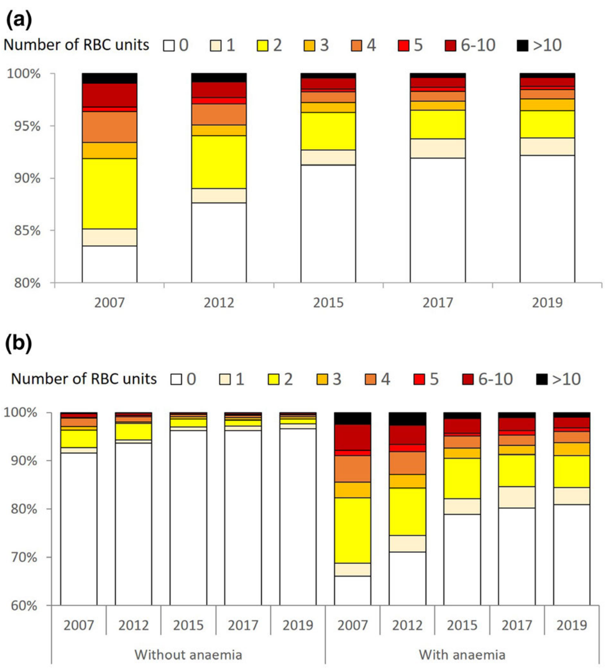

Figure 4 Peri-operative utilisation of red blood cells (RBC). The number of transfused patients from 2007 to 2019 is displayed as proportions. The number of transfused RBC units (0, 1, 2, 3, 4, 5, 6–10, and > 10) is depicted in colour. (a) Overall transfusion rate in all patients: 16.7% in 2007, 12.7% in 2012, 8.9% in 2015, 8.2% in 2017 and 8.0% in 2019. (b) Transfusion rate in patients without anaemia: 8.4% in 2007, 6.3% in 2012, 3.8% in 2015, 3.7% in 2017 and 3.4% in 2019. Transfusion rate in patients with anaemia: 33.8% in 2007, 28.9% in 2012, 21.1% in 2015, 19.7% in 2017 and 19.1% in 2019. RBC, red blood cells.

Information (Table S9). The subgroup analysis showed similar results (data not shown).

Overall, the mortality rate remained constant (Table 2). In the presence of anaemia, mortality was significantly increased, OR (95%CI) 5.27 (4.13–6.77); $p < 0.001$ (Table 2). Red blood cell transfusion was associated with increased mortality (14.98 (11.83–19.03); $p < 0.001$). The subgroup analyses showed similar results (data not shown).

Using multivariable linear regression analysis with fixed effects, we found that pre-operative anaemia, OR (95%CI) 2.08 (1.42–3.05); $p < 0.001$) and RBC transfusion (4.29 (3.09–5.94); $p < 0.001$) were predictors of mortality but not length of stay (0.99 (0.98–1.00) days; $p = 0.12$) and analysed years (2007 vs. 2019: 1.49 (0.86–2.69); $p = 0.07$). The risk of mortality was increased in patients with transfusion of a single RBC unit (5.44 (2.73–9.75); $p < 0.001$).

Discussion

Pre-operatively, anaemia affects approximately 35% of surgical patients worldwide [2, 15]. According to our findings, 32.5% of surgical patients with pre-operative Hb measurements in Germany were anaemic in 2019, which is in line with the estimated worldwide anaemia prevalence of 35% reported by Munoz et al. [2] and other published studies [1, 4, 15]. Using global burden of disease 2019 data, Safiri et al. estimated a national age-standardised prevalence of anaemia of 3.1–49.3%. The authors showed that the burden of anaemia is lower in economically developed countries; likely due to better access to healthcare services. However, the number of cases has increased, which could be related to an ageing population and longer survival of patients with comorbidities such as chronic kidney disease [16].

The estimated prevalence of pre-operative anaemia in our study could be overestimated by selection bias, as pre-operative Hb serves as an inclusion criterion. In Germany, blood testing is performed in every paediatric surgical patient, in patients with chronic diseases and patients undergoing surgery with a risk of significant blood loss. Patients undergoing minor surgery usually do not have a pre-operative Hb measurement and were, therefore, not included in our analysis. Particularly for cardiac surgery (36.3%), urology (24.1%) and orthopaedic and trauma surgery (25%), we found a similar anaemia prevalence as reported by Munoz et al. (32%, 28% and 20%, respectively), whereas the anaemia rate differed for patients having vascular surgery (61% in Germany vs. 49% worldwide) and gynaecology (38.6% in Germany vs. 48% worldwide).

Anaemia is common in cancer and many chemotherapies are myelosuppressive. However, based on our study design, we were not able to elucidate the cause of anaemia. Interestingly, the anaemia rate increased in paediatric patients undergoing surgery from 18.8% in 2007 to 26.4% in 2019. In particular, the prevalence of pre-operative anaemia in children aged < 5 y increased from 9.1% in 2007 up to 32.6% in 2019, which could be

Table 2 Transfused red blood cell (RBC) units, length of hospital stay (LOS) and in-hospital mortality. Values are mean (SD), median (IQR [range]) number (proportion).

	2007	2012	2015	2017	2019
Transfused RBC units per patient	0.67 (0.06)	0.53 (0.04)	0.33 (0.02)	0.30 (0.02)	0.29 (0.02)
Without anaemia	0.28 (0.04)	0.20 (0.02)	0.11 (0.01)	0.12 (0.01)	0.11 (0.02)
With anaemia	1.48 (0.15)	1.36 (0.14)	0.86 (0.07)	0.76 (0.06)	0.71 (0.06)
LOS; days	7 (4–11 [1–106])	6 (3–10 [1–166])	5 (3–10 [1–124])	5 (3–9 [1–174])	5 (3–9 [1–258])
Without anaemia	6 (3–9 [1–64])	5 (3–9 [1–111])	5 (3–8 [1–120])	5 (3–9 [1–174])	5 (3–8 [1–112])
With anaemia	9 (6–15 [1–106])	8 (5–14 [1–166])	7 (4–13 [1–124])	7 (4–13 [1–122])	7 (4–13 [1–258])
Mortality	2.9%	2.1%	2.5%	1.9%	2.5%
Without anaemia	0.8%	0.7%	1.3%	1.0%	1.1%
With anaemia	6.6%	5.0%	5.2%	4.1%	5.3%

associated with the continued advancements and developments in neonatal medicine [17]. The worldwide prevalence of anaemia in children aged < 5 y was 41.7% in 2016, with an increasing trend in the German population (10.3% in 2010 and 12.4% in 2016) [18]. In addition, Safiri et al. showed that the largest burden of anaemia affects children aged < 10 y [16]. Recently, more outpatient surgical procedures are being performed in children, which leaves those with more complex conditions as inpatients. The number of investigated paediatric patients in our study is low; however, similar to adult patients, pre-operative anaemia in paediatric patients is independently associated with an increased risk for postoperative complications [19] and mortality [20]. An analysis of > 14,000 surgical paediatric patients demonstrated that 10.1% receive blood transfusions and that pre-operative anaemia is an independent predictor for transfusion in these patients ($p < 0.001$; OR = 15.10 with pre-operative anaemia and OR = 2.40 without pre-operative anaemia) [21]. Therefore, there is also an urgent need to provide pre-operative anaemia management for the paediatric patient population [22–24].

Allogeneic blood transfusion is the main technique to correct severe anaemia, but it is also one of the top five overused therapies [25]. Overall, patients with pre-operative anaemia received six times more RBC units compared with non-anaemic patients. Iron deficiency [23] is the underlying cause in 30% of patients with pre-operative anaemia, making iron supplementation a promising strategy to improve erythropoiesis and reduce blood transfusions before surgery [26, 27]. Froessler et al. showed a 60% reduction in transfusion, increased Hb values and shorter length of stay [28]. Interestingly, our analysis revealed that length of stay decreased by 2 days in 2019 compared with 2007 but was prolonged in the presence of anaemia. Unlike other recognised risk factors of surgical patients, anaemia can be treated fairly easily, for example by iron supplementation in case of iron deficiency. Thus, optimising pre-operative anaemia is an important strategy to improve patient safety and reduce healthcare costs. Awareness of the impact of peri-operative iron supplementation in iron deficiency is increasing in Germany. In 2019, 21 hospitals (16 general hospitals and 5 university hospitals) participated in a survey to assess the status of implemented PBM measures. Management of anaemia was implemented in 77.7% of university hospitals and in 69.5% of non-university hospitals. It is noteworthy that the efficiency for screening of iron deficiency and, particularly, administration of intravenous iron varied between hospitals. Not all iron deficient patients receive pre-operative treatment in a timely manner to allow RBC production, although the patients were correctly identified [29]. Based on our study design, we cannot examine the impact of iron supplementation in iron deficient patients.

International guidelines now recommend the implementation of a PBM programme in everyday clinical practice. Patient blood management emphasises the early detection of pre-operative anaemia and the identification and potential treatment of any underlying cause. Multimodal and multidisciplinary peri-operative care should include measures to reduce blood loss and promote rational, evidence-based blood transfusion policies [30]. These interventions can increase Hb values [31], decrease blood transfusion, complication rates and hospital stay [32]. Patient blood management consists of >100 single measures which can be implemented in a stepwise manner depending on local conditions and needs [30]. However, our dataset did not allow us to rigorously address the impact of implemented PBM measures on postoperative complication rates.

We suggest that the reduction in blood transfusion observed may be associated with a stricter adherence to transfusion guidelines. Historically guided by the `10/30´ rule to transfuse at a Hb level $\leq$ 10 g.dl^{-1} and a haematocrit $\leq$ 30%, patients received more RBC units [33]. However, this approach has been challenged. The Canadian Society for Transfusion launched a campaign ``*Why give two when one will do*´´ with a worldwide impact on transfusion policy. The majority of recent guidelines support this strategy [34]. Our analysis revealed that the number of transfused two units has decreased. We hypothesise that there is an increased awareness among clinicians in line with current recommendations. However, based on our study design, we cannot exclude that other factors may have contributed to this observation. Moreover, we cannot ascertain whether massive transfusion occurred in the context of haemorrhage as the date and time of transfusion was not evaluated. This is important because the triad of anaemia, transfusion and bleeding has been shown to significantly increase mortality [35, 36]. Despite a decrease in transfusion, anaemia still has a prevalence of over 30% in patients who have it measured pre-operatively, highlighting the urgent need for comprehensive pre-operative anaemia management in Germany. In academic centres, the prevalence of pre-operative anaemia remained stable (37% in 2007 vs. 35.1% in 2019), thus we hypothesise that the difference in transfusion patterns over time is not due to changes in the patient population but true changes in practice.

Our analysis further revealed that mortality did not increase while transfusion decreased over the years, supporting the conclusions of evidence-based guidelines and reassuring clinicians that a restrictive transfusion threshold can safely be applied in most patient populations. Unfortunately, we were unable to determine the transfusion trigger or indication in this study. This, and adherence to guidelines, is still often left to the physician's own discretion. It is noteworthy to mention that, over time, surgical techniques have also improved and are less invasive which is likely to have contributed to less blood product transfusion as well as reduced postoperative mortality. Whitlock et al. analysed > 1.5 million adults undergoing non-cardiac, non-intracranial or non-vascular surgery and found that the risk of mortality increased in patients with transfusion of RBC units (OR 4.45 (95%CI 4.19–4.72); $p < 0.001$) [37]. We observed an interesting parallel, the odds for mortality were 5.4 times higher in patients with transfusion of a single RBC unit compared with patients with no RBC transfusion.

Our study demonstrates that the prevalence of pre-operative anaemia in Germany is more than 30%, which is similar to the worldwide prevalence. It supports the urgent need for a comprehensive peri-operative anaemia management protocol. Guideline adherent transfusion practice is even more important now, as the amount of blood products available has dropped dramatically since the outbreak of the COVID-19 pandemic.

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Supporting Information

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

Figure S1. Prevalence of anaemia within surgical disciplines.

Figure S2. Overall red blood cell transfusion.

Figure S3. Mean red blood cell unit consumption per year.

Table S1. Anaemia classification in patients aged < 18 y.

Table S2. Prevalence and forms of anaemia.

Table S3. Prevalence and forms of anaemia of two university hospitals providing data for the entire study period.

Table S4. Red blood cell consumption per 1000 patients of two university hospitals providing data for the entire study period.

Table S5. Percentage of transfused patients of two university hospitals providing data for the entire study period.

Table S6. Number of transfused red blood cell units of all hospitals.

Table S7. Number of transfused red blood cell units of two university hospitals providing data for the entire study period.

Table S8. Number of transfused red blood cell units per patient of two university hospitals providing data for the entire study period.

Table S9. Length of hospital stay (days) within surgical disciplines.

Appendix S1. PANDORA study collaborators.