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Long-Term Outcomes Among Patients Discharged From the Hospital With Moderate Anemia:

A Retrospective Cohort Study

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Abstract

Background: Randomized clinical trial findings support decreased red blood cell (RBC) transfusion and short-term tolerance of in-hospital anemia. However, long-term outcomes related to changes in transfusion practice have not been described.

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Reproducible Research Statement: *Study protocol and data set:* Not available. *Statistical code:* Available from Dr. Lee (e-mail, Catherine.lee@kp.org).

Objective: To describe the prevalence of anemia at and after hospital discharge and associated morbidity and mortality events.

Design: Retrospective cohort study.

Setting: Integrated health care delivery system with 21 hospitals serving 4 million members.

Participants: 445 371 surviving adults who had 801 261 hospitalizations between January 2010 and December 2014.

Measurements: Hemoglobin levels and RBC transfusion, rehospitalization, and mortality events within 6 months of hospital discharge. Generalized estimating equations were used to examine trends over time, accounting for correlated observations and patient-level covariates.

Results: From 2010 to 2014, the prevalence of moderate anemia (hemoglobin levels between 7 and 10 g/dL) at hospital discharge increased from 20% to 25% ($P < 0.001$) and RBC transfusion declined by 28% (39.8 to 28.5 RBC units per 1000 patients; $P < 0.001$). The proportion of patients whose moderate anemia had resolved within 6 months of hospital discharge decreased from 42% to 34% ($P < 0.001$), and RBC transfusion and rehospitalization within 6 months of hospital discharge decreased from 19% to 17% and 37% to 33%, respectively ($P < 0.001$ for both). During this period, the adjusted 6-month mortality rate decreased from 16.1% to 15.6% ($P = 0.004$) in patients with moderate anemia, in parallel with that of all others.

Limitation: Possible unmeasured confounding.

Conclusion: Anemia after hospitalization increased in parallel with decreased RBC transfusion. This increase was not accompanied by a rise in subsequent RBC use, rehospitalization, or mortality within 6 months of hospital discharge. Longitudinal analyses support the safety of practice recommendations to limit RBC transfusion and tolerate anemia during and after hospitalization.

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Anemia is common in hospitalized patients and has been independently associated with short- and long-term morbidity and mortality (1–7). Traditionally, treatment of moderate anemia (hemoglobin levels between 7 and 10 g/dL) in hospitalized patients has included transfusion of allogeneic red blood cells (RBCs) to increase hemoglobin level (8). However, a series of randomized clinical trials showed similar outcomes with less frequent RBC transfusion, thereby avoiding potential infectious, cardiopulmonary, and immunomodulatory complications (9–16). The trial results supporting a more restrictive approach have been translated into practice guidelines by multidisciplinary societies, including medical, critical care, anesthesia, and pathology specialties (17–22). These recommendations also play a key role in patient blood management strategies that emphasize evidence-based transfusion practice and the tolerance of anemia in addition to optimizing RBC counts and minimizing perioperative blood loss.

Within our network of community hospitals, multi-disciplinary patient blood management programs for specific clinical departments (such as cardiac and orthopedic surgery) were implemented beginning in 2010 (23, 24). Strategies focused on identification and treatment of suboptimal iron stores before surgery, increased use of cell salvage and hemostatic agents

(such as tranexamic acid), and blood-sparing approaches to medical and surgical procedures. These department-specific initiatives were supported by hospital- and system-level quality improvement projects to improve blood use more broadly. System-level initiatives included promotion of evidence-based transfusion practice through peer review and clinical decision support within electronic order sets for blood transfusion.

We found that a substantial reduction in RBC use was not associated with changes in 30-day or hospital mortality rates, consistent with short-term safety findings of randomized clinical trials and other observational studies (23–27). However, the effect of restrictive transfusion practice on anemia persistence and longer-term clinical outcomes has not been well described (28, 29).

In this study, we examined the incidence and prevalence of anemia in an integrated health care delivery system at and within 6 months of hospital discharge after implementation of blood management initiatives in our network. We hypothesized that an increase in moderate anemia would not adversely affect subsequent RBC transfusion, rehospitalization, or mortality events after hospital discharge.

METHODS

Design Overview

We conducted a retrospective cohort study using electronic health record data from Kaiser Permanente Northern California (KPNC), which serves 4 million members. We included all adult nonobstetric KPNC patients who were hospitalized and discharged alive from 21 hospitals during the 5 years from 1 January 2010 through 31 December 2014. The KPNC Institutional Review Board approved this study.

Sample

We identified all hospitalizations of adult patients. Patients were eligible if they survived an overnight inpatient hospital stay and were discharged from a KPNC hospital. We excluded patients who were hospitalized for observation or 1-day surgery that did not result in an overnight stay. We also excluded hospitalizations for childbirth; however, women who were hospitalized for postdelivery complications were included.

Definition of Anemia

We determined the presence and magnitude of anemia by using hemoglobin levels measured by the clinical laboratory during inpatient and outpatient care. We used the World Health Organization criteria for anemia, defined as a hemoglobin value of less than 12 g/dL in women and less than 13 g/dL in men (30). Hemoglobin levels below these thresholds but greater than 10 g/dL were defined as mild anemia. Moderate anemia was defined as a hemoglobin level less than 10 g/dL but greater than or equal to 7 g/dL. On the basis of RBC transfusion guidelines, severe anemia was defined as a hemoglobin level less than 7 g/dL (22).

We defined *admission hemoglobin* as the lowest hemoglobin level within 72 hours before hospital entry or the most recent hemoglobin level within 30 days before an elective

admission. We defined *discharge hemoglobin* as the most proximate hemoglobin level before hospital discharge and *postdischarge hemoglobin* as the initial hemoglobin level after hospital discharge.

Outcomes

Rates of RBC transfusion, rehospitalization, and mortality within 6 months of hospitalization were calculated for each patient discharged alive with moderate anemia. Resolution of anemia was assessed by examining all available hemoglobin levels within 6 months of hospital discharge, referencing the highest value during that period. Transfusion events were identified from blood bank transfusion records and included both inpatient and outpatient encounters. Rehospitalization and mortality rates were linked from admission records and death indices, respectively.

Covariates

We classified patients as having emergency or elective admission according to whether they were admitted through the emergency department. We classified hospitalizations as medical or surgical admission by the presence or absence of surgical procedural codes during hospitalization. We defined *hospital entry* as the time of initial admission to a non-emergency department inpatient location, including the general medical-surgical wards, transitional care unit, intensive care unit, and operating room.

To categorize patient diagnoses and comorbid conditions, we grouped International Classification of Diseases, Ninth Revision, diagnosis codes by using Health Care Utilization Project (www.ahrq.gov/data/hcup) single-level and multilevel Clinical Classifications Software categories. We quantified comorbid disease burden using the Charlson Comorbidity Index and Comorbidity Points Score, version 2, which is based on patients' medical diagnoses within the 12 months before hospitalization (31–33). We quantified illness severity at admission with the Laboratory-based Acute Physiology Score, version 2, which is based on laboratory test results, vital signs, and neurologic status within 72 hours before hospital entry.

Statistical Analysis

Descriptive analyses are presented as counts and percentages, medians and interquartile ranges, or proportions and 95% CIs. We used χ^2 tests for equal proportion or Wilcoxon rank-sum tests to test differences. For uncorrelated outcomes, we compared trends in dichotomous and continuous variables by using the χ^2 test for linear trend (Cochran-Armitage) and linear regression, respectively.

Anemia prevalence and incidence were calculated at the hospitalization and patient levels, respectively. For anemia prevalence calculations, all patients who survived hospitalization and had moderate anemia at hospital discharge were included in the numerator, whereas the denominator was all inpatients discharged alive from the hospital. For anemia incidence calculations, each patient was counted once annually—with the number of patients with moderate anemia in the numerator and all patients who survived hospitalization in the

denominator. Therefore, separate admissions of individual patients were included in anemia prevalence calculations and in different years for incidence calculations.

For all patients discharged alive with moderate anemia, we examined annual trends in RBC transfusion characteristics (receipt of inpatient RBC transfusion, pretransfusion hemoglobin level, number of RBC units received) as well as resolution of anemia within 6 months of discharge. We used a generalized estimating equation (GEE) to account for correlated observations and included continuous year as a covariate to test for time trends. For dichotomous (receipt of inpatient RBC transfusion) and continuous (pretransfusion hemoglobin level and number of RBC units received) outcomes, we used the modified log-Poisson and identity-Normal GEE link functions, respectively (34, 35). For the multicategory outcome (resolution of anemia), we used GEEs for nominal multinomial responses assuming a baseline category logit model (36). We selected the correlation structure of the GEE models by using a goodness-of-fit measure, QIC (quasi-likelihood under the independence model criterion). We reported results for dichotomous outcomes as risk ratios (RRs), continuous outcomes as mean change in outcome, and multicategory outcomes as odds ratios, all with corresponding 95% CIs.

Among patients discharged alive with moderate anemia, we examined the adjusted annual prevalence of RBC transfusion, rehospitalization, and mortality within 1 and 6 months of hospitalization. We used the aforementioned modified log-Poisson GEE approach and included continuous year, number of hospitalizations, age, sex, emergency admission, surgical status, Charlson Comorbidity Index score, and severity of illness (Laboratory Acute Physiology Score, version 2) as covariates. In parallel to the model of 6-month mortality in patients with moderate anemia, we fit a modified log-Poisson GEE model for this outcome by using the same covariates for all other patients (those with mild or no anemia who survived hospital discharge).

Last, we examined patient-level trends in unadjusted 6-month mortality after the first hospital discharge with moderate anemia in subgroups based on age, sex, emergency or elective surgical or medical status, presence of anemia on admission, prior RBC transfusion or anticoagulation, principal discharge diagnosis, and individual hospital site. For these patient-level observations, we used the χ^2 test for linear trend (Cochran-Armitage).

Two-sided *P* values less than 0.050 were considered statistically significant. Statistical analyses were performed by using Stata, version 14.1 (StataCorp); SAS, version 9.4 (SAS Institute); and R, version 3.4.1 (The R Foundation).

Role of the Funding Source

The funders had no role in the design of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

RESULTS

From 2010 to 2014, 801 261 hospitalizations occurred among 445 371 patients who survived to discharge. Moderate anemia at hospital discharge was present in 119 489 unique patients (27%) and 187 440 hospitalizations (23%) (Appendix Table 1, available at Annals.org). Severe anemia at hospital discharge occurred in 1219 unique patients (0.3%) and 1331 hospitalizations (0.2%). In our cohort of patients with moderate anemia, the median number of hospital discharges with anemia was 1 (interquartile range, 1 to 2) (Appendix Table 2, available at Annals.org and 45% of repeated hospitalizations (30 629 of 67 951) occurred within 6 months of the initial hospital discharge.

From 2010 to 2014, small changes were observed in patient characteristics at the time of study entry; however, these occurred without clinically relevant differences in anemia at initial hospital admission. Patients discharged with moderate anemia were older, had a higher comorbidity burden and more severe illness, and had a longer hospital stay than those with mild or no anemia (Table 1). Changes during the study period in the cohort with anemia included a small increase in comorbidity burden, illness severity, and emergency admissions and a decline in surgical admissions (Table 1 and Appendix Table 3, available at Annals.org). However, the presence and severity of anemia at the time of index hospital admission did not change clinically over the study period, nor did they vary significantly on the basis of previous 6-month hospitalization status (Appendix Tables 4 and 5, available at Annals.org).

From 2010 to 2014, the total number of RBCs transfused in the inpatient and outpatient settings decreased by more than 25% (39.8 to 28.5 RBC units per 1000 patients) (Figure) and median pretransfusion hemoglobin levels decreased from 8.2 g/dL to 7.2 g/dL (Table 2) (annual mean change, −0.220 [95% CI, −0.225 to −0.215]; $P < 0.001$). The incidence of RBC transfusion during hospitalization decreased from 31% in 2010 to 23% in 2014 in patients discharged with moderate anemia (RR, 0.935 [CI, 0.931 to 0.939]; $P < 0.001$). Furthermore, the number of RBC units transfused per 100 hospitalizations decreased from 42 to 28 units from 2010 to 2014 (annual mean change, −3.25 [CI, −4.45 to −2.05]; $P < 0.001$). Inpatient RBC transfusions decreased in all patient groups analyzed except those with severe anemia at the time of hospital admission (Appendix Table 6, available at Annals.org).

In parallel with decreased RBC transfusions from 2010 to 2014, the prevalence and incidence of anemia after hospitalization increased (Table 2). The prevalence of moderate anemia at hospital discharge ($n = 187\,440$ hospitalizations) increased during the study period (from 20% to 25% of annual hospitalizations) (RR, 1.070 [CI, 1.066 to 1.074]; $P < 0.001$). The annual incidence of anemia also increased at the time of hospital discharge (RR, 1.048 [CI, 1.046 to 1.051]; $P < 0.001$) and within 6 months of hospitalization (Tables 2 and 3). We found that most patients discharged with moderate anemia had an incremental rise in their “postdischarge” hemoglobin level (Appendix Table 7, available at Annals.org). Despite evidence of hemoglobin recovery after hospital discharge, moderate anemia was less likely to have completely resolved within 6 months of hospitalization in 2014 than in 2010 (34% vs. 42%) (Table 3).

Over the study period, annual trends in outcomes related to recurrent hospital discharges with anemia paralleled those after the initial hospitalization (Appendix Table 8, available at Annals.org). When repeated hospitalizations were taken into account, adjusted RRs for 1-month (RR, 0.94 [CI, 0.93 to 0.96]; $P < 0.001$) and 6-month (RR, 0.98 [CI, 0.98 to 0.99]; $P < 0.001$) RBC transfusion events decreased (Table 4). In parallel, adjusted RRs for 1-month (RR, 0.97 [CI, 0.96 to 0.97]; $P < 0.001$) and 6-month (RR, 0.98 [CI, 0.98 to 0.99]; $P < 0.001$) rehospitalization decreased annually during the study period. Over the 5 years, adjusted 1-month (RR, 0.97 [CI, 0.94 to 1.00]; $P = 0.061$) and 6-month (RR, 0.99 [CI, 0.98 to 1.00]; $P = 0.004$) mortality rates in patients with moderate anemia remained stable or decreased slightly on an annual basis. The latter decline in 6-month mortality paralleled that of all other hospitalized patients (RR, 0.99 [CI, 0.98 to 1.00]; $P = 0.003$) (Appendix Table 9, available at Annals.org).

Subgroup analysis found no significant differences in unadjusted 6-month mortality when examined by patient demographics, hospital facility, prior transfusion or anticoagulant use, or preexisting anemia status (Appendix Table 10, available at Annals.org). However, after stratification by comorbidity burden, modest decreases in unadjusted 6-month mortality were observed in patients with moderate anemia who had medical rather than surgical conditions (Appendix Table 11, available at Annals.org). These decreases were most apparent in patients with infectious and circulatory diseases, possibly because of concomitant initiatives for these conditions.

DISCUSSION

In our cohort, the incidence and prevalence of moderate anemia at discharge and within 6 months of hospitalization rose over the study period. This increase coincided directly with changes in RBC transfusion practice in the management of anemia as well as secular increases in age and comorbid conditions among our hospitalized patient population. We did not detect an adverse effect of increased anemia at hospital discharge or afterward on 6-month rates of RBC transfusion, rehospitalization, or mortality. In fact, risk-adjusted mortality in patients with moderate anemia decreased over the study period in parallel with patients with mild or no anemia.

In hospitalized patients, anemia often is multifactorial, commonly resulting from bleeding, repeated phlebotomy, and blunted erythropoiesis associated with acute illness (37–39). The rationale for treating anemia has been based on 2 lines of evidence. Anemia has been believed to be physiologically deleterious, requiring a compensatory increase in cardiac output to maintain systemic oxygen delivery (40, 41). Furthermore, anemia has been associated with a poorer prognosis for various conditions, including cancer, chronic kidney disease, and congestive heart failure (4, 42). Thus, it has been assumed that anemia warrants correction, especially in older patients with cardiovascular disease, despite limited evidence showing benefit.

However, randomized clinical trial data show that less frequent RBC transfusion is safe in hospitalized patients with moderate anemia. The results of these clinical trials are the basis for patient blood management programs that emphasize pre-perioperative optimization of

hemoglobin levels but also tolerance of progressive degrees of anemia (43). In our cohort, these perioperative strategies seem to have reduced the number of elective surgical patients discharged with moderate anemia. Conversely, changes in clinical practice have resulted in an increase in medical and nonelective surgical patients being discharged with moderate anemia.

Strong evidence exists that moderate anemia is safe in the hospital setting, where hemodynamics and oxygen delivery can be monitored and optimized (14, 15). However, with care of conditions initially requiring hospitalization increasingly being transitioned to outpatient management, concern has arisen that anemia related to more restrictive transfusion practice may contribute to adverse outcomes after hospital discharge (44–46). Available clinical trials have focused predominantly on short-term interventions and hospital outcomes, not on downstream clinical events. In contrast, our study provides data showing that an increase in anemia persistence after hospitalization did not seem to adversely affect measures of morbidity and mortality in the 6 months after hospital discharge. Furthermore, clinical trial data have focused on specific admission conditions or patient populations and may not include analyses of subgroups (such as patients receiving anticoagulation or those with a history of blood transfusion) who may be at increased risk for adverse outcomes related to anemia. In our cohort, these risk factors were not associated with worsened outcomes after reduction in RBC transfusion. Our findings also are consistent with a recently published clinical trial that was the first to show that discharge anemia in cardiac surgery patients was not associated with differences in 6-month rehospitalization or mortality events (29). These growing data provide reassurance to hospital clinicians who must decide whether to discharge patients with anemia.

The translation of clinical trial findings to practice recommendations has been promoted by the American Board of Internal Medicine’s Choosing Wisely campaign, in which several specialty societies have partnered to identify tests, procedures, or treatments offered to patients despite an absence of evidence demonstrating benefit (47–50). However, the Choosing Wisely campaign has not developed a structural mechanism to evaluate the impact of its recommendations on clinical practice and patient outcomes. Despite trends in anemia persistence, most patients in our study had an increase in hemoglobin levels after hospital discharge, probably related to increased bone marrow production of RBCs in concert with resolution of RBC loss from gastrointestinal bleeding and reduced phlebotomy. Our findings add to the evidence for efficacy and safety in longitudinally applying transfusion practice recommendations and tolerating anemia in a diverse community hospital population.

Because the effect of persistent anemia on quality of life is likely to be substantial and directly proportional to anemia severity, additional studies will be needed to provide guidance in anemia management, in relation not only to mortality but also to exercise tolerance in specific populations, such as those with acute myocardial infarction, congestive heart failure, or hematologic cancer. Moving forward, the focus must expand from randomized trials of RBC transfusion to studies that examine outcomes associated with use of other therapies for anemia. Alternatives to RBC transfusion include administration of oral or intravenous iron; human-derived growth factors, such as erythropoietin; and essential cofactors, including folic acid and vitamin B_{12} (51). These methods for treating anemia are

shown to improve health-related quality of life and distance ambulated in specific populations (52–54). Although guidelines exist for the use of such treatments as intravenous iron and erythropoietin-stimulating agents, these therapies are not routinely used outside the hospital setting, except in patients having hemodialysis or those with myelodysplastic syndrome. A systematic effort to identify and treat anemia by using approaches other than transfusion is under way within our network of community hospitals.

Our findings should be interpreted in light of the study's limitations. We conducted a retrospective analysis of electronic data collected in the course of routine clinical care. Although our patient population reflects the regional community practice of adults at 21 medical centers in northern California, it may not reflect clinical practice and outcomes in other community or tertiary care hospitals, pediatric age groups, or specific populations (such as transplant and obstetrics). Over the study period, we found that risk-adjusted mortality in patients with anemia declined in parallel with that of populations without anemia. We acknowledge that risk adjustment methodologies may not adequately account for unmeasured confounding, nor does the observational nature of the study allow one to establish causality. Other initiatives to improve care in both inpatients and outpatients with common conditions (such as cardiovascular disease and sepsis) occurred contemporaneously with implementation of patient blood management programs and may explain declines in overall risk-adjusted mortality and unadjusted mortality rates for these specific conditions (55–58).

In conclusion, we report increasing incidence and persistence of moderate anemia in hospitalized patients associated with a concomitant decline in RBC transfusion. Increased tolerance of moderate anemia did not seem to adversely affect long-term RBC transfusion events, rehospitalization, or mortality. In addition, reductions in risk-adjusted mortality were similar in patients with anemia and those without it. These data support the efficacy and safety of practice recommendations to limit RBC transfusion in patients with anemia during and after hospitalization.

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Appendix

Appendix Table 1.

Availability and Timing of Hb Levels in Hospitalized Patients *

Year	Annual Available Discharge Hb Levels, *n (%)* †	Annual Hb Levels Within 6 Months of Discharge, *n (%)* ‡	Median Time After Discharge (IQR), *d* §	Hb Within 6 Months (Anemic), *n* ‖	Median Time After Discharge (Anemic) (IQR), d ¶	Median 6-Month Hb Level (Anemic) (IQR), *g/dL* **
2010	134,818 (87)	105,202 (68)	65 (21–121)	28,465	72 (27–123)	11.9(10.9–12.8)
2011	144,082 (88)	110,910(68)	64 (20–121)	33,945	71 (26–123)	11.7 (10.8–12.7)
2012	143,158 (89)	111,054 (69)	64 (20–121)	35,750	70 (26–123)	11.7 (10.7–12.7)
2013	143,721 (89)	109,532 (69)	62 (19–120)	36,707	70 (26–122)	11.6 (10.6–12.6)
2014	142,640 (89)	107,837 (69)	62 (19–120)	36,972	70 (26–123)	11.5 (10.5–12.5)

Hb = hemoglobin; IQR = interquartile range.

* Linear regression with year as a continuous variable to test for trend.

† Numbers indicate the number of hospitalizations in which patients survived with available discharge Hb levels, and percentages indicate the proportion of Hb levels among the total number of hospitalizations.

‡ Numbers indicate the number of hospitalizations in which patients had available Hb levels within 6 months of hospital discharge, and percentages indicate the proportion of Hb levels among the total number of hospitalizations.

§ Indicates the time after discharge at which the 6-month Hb level was obtained. *P* for trend = 0.47.

‖ Indicates the number of hospitalizations in which patients with moderate anemia had available Hb levels within 6 months of hospital discharge.

¶ Indicates the time after hospital discharge at which the 6-month Hb level was obtained in patients with moderate anemia. *P* for trend = 0.114.

** Indicates the highest Hb level in patients with moderate anemia within 6 months of index hospitalization. *P* for trend <0.001.

Appendix Table 2.

Number of Hospital Discharges With Moderate Anemia per Patient *

Hospital Discharges With Anemia per Patient, *n*	Frequency, *n*	Percentage	Cumulative Percentage
1	84,659	70.9	70.9
2	20,388	17.1	88.0
3	7,301	6.1	94.1
4	3,101	2.5	96.6
5 +	4,040	3.4	100
Total	119,489	100	100

* 119,489 patients discharged alive with moderate anemia (hemoglobin levels between 7 and 10 g/dL) between 2010 and 2014.

Appendix Table 3.

Demographic Data of Patients Discharged With Moderate Anemia *

Characteristic	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)
Mean age (SD), *y*	67 (16)	67 (16)	67 (17)	67 (17)	67 (17)

Characteristic	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)
Male, %	38	38	39	38	39
Median Charlson score (IQR)	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–2)
Mean COPS2 (SD)†	34 (34)	34 (34)	34 (34)	37 (36)	37 (36)
Mean LAPS2 (SD)‡	55 (40)	56 (41)	56 (42)	59 (42)	59 (42)
Emergency presentation, %	59	60	60	64	64
Surgical admission, %	47	48	47	46	43
Median length of stay (IQR), *d*	3.3 (2.2–5.8)	3.3 (2.2–5.6)	3.3 (2.2–5.7)	3.2 (2.1–5.6)	3.3 (2.1–5.8)

COPS2 = Comorbidity Points Score, version 2; IQR = interquartile range; LAPS2 = Laboratory Acute Physiology Score, version 2.

*Patient characteristics related to the initial hospital discharge with moderate anemia.

†Longitudinal, diagnosis-based score associated with a theoretical maximum of 1,014. The univariate association between COPS2 and mortality is such that mortality rates for scores <50 are <2%, whereas those >100 are associated with mortality rates ≥5%.

‡Increasing degrees of physiologic derangement are reflected in a higher LAPS2, which is a continuous variable that has a theoretical maximum of 414. The univariate association between LAPS2 and mortality is such that mortality rates for scores <50 are <1.5%, whereas those >125 are associated with mortality rates of ≥10%−15%.

Appendix Table 4.

Proportion of Anemia on Hospital Admission in Patients Discharged With Moderate Anemia*

Admission Status	2010 (*n* = 22,036)	2011 (*n* = 22,765)	2012 (*n* = 23,842)	2013 (*n* = 24,223)	2014 (*n* = 24,107)
No anemia (*n* = 36,860)	30	32	33	32	31
Mild anemia (*n* = 51,086)	45	44	43	43	43
Moderate anemia (*n* = 25,133)	22	21	21	22	22
Severe anemia (*n* = 3,894)	3	3	3	3	4

*Admission hemoglobin levels available in 116,973 of 119,489 patients for the initial hospital discharge with moderate anemia. Mild anemia (hemoglobin levels 10–12 g/dL in females or 10–13 g/dL in males), moderate anemia (hemoglobin levels 7–10 g/dL), and severe anemia (hemoglobin levels <7 g/dL). Values are percentages.

Appendix Table 5.

Demographic Characteristics of Cohort With Moderate Anemia, by Prior Admission Status*

Admission Status	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)
No prior hospitalization within 6 months of first discharge within the study period (*n* = 96,475)					
Male, %	36	36	37	37	37
Median age (IQR), *y*	68 (56–79)	68 (56–79)	68 (56–79)	68 (56–79)	68 (56–79)
Median admission Hb level (IQR), *g/dL*†	10.8 (9.6–12.1)	10.8 (9.5–12.0)	10.7 (9.5–12.1)	10.7 (9.4–12.0)	10.7 (9.4–12.0)
Prior hospitalization within 6 months of first discharge within the study period (*n* = 23,014)					
Male, %	44	46	47	47	48

Admission Status	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)
Median age (IQR), *y*	71 (60–81)	72 (61–81)	71 (60–81)	72 (61–81)	71 (60–81)
Median admission Hb level (IQR), *g/dL*[†]	10.8 (9.8–11.7)	10.7 (9.8–11.6)	10.7 (9.8–11.8)	10.7 (9.8–11.7)	10.7 (9.8–11.7)

Hb = hemoglobin; IQR = interquartile range.

[*] Patient characteristics related to the initial hospital discharge with moderate anemia.

[†] Comparing patients with and without prior hospitalization within 6 months of first hospital discharge, admission Hb levels were not significantly different ($P = 0.88$ by Wilcoxon rank-sum test).

Appendix Table 6.

Inpatient Red Blood Cell Transfusion Rate, by Admission Anemia Status and Year[*]

Admission Status	2010 (*n* = 22,036)	2011 (*n* = 22,765)	2012 (*n* = 23,842)	2013 (*n* = 24,223)	2014 (*n* = 24,107)
No anemia (*n* = 36,860)	23.5	22.4	18.7	16.7	14.8
Mild anemia (*n* = 51,086)	21.4	20.3	17.6	15.4	14.7
Moderate anemia (*n* = 25,133)	49.0	48.2	46.5	42.3	40.5
Severe anemia (*n* = 3,894)	98.9	98.8	96.0	98.9	97.8

Hb = hemoglobin.

[*] Admission Hb levels available in 116,973 of 119,489 patients for the initial hospital discharge with moderate anemia. Mild anemia (Hb 10–12 g/dL in females; 10–13 g/dL in males), moderate anemia (Hb 7–10 g/dL), and severe anemia (Hb <7 g/dL). All $P < 0.001$ except that for severe anemia ($P = 0.253$) (Cochran-Armitage trend test). Values are percentages.

Appendix Table 7.

Discharge and Postdischarge Hb Levels[*]

Discharge Strata	Median Discharge Hb (IQR), *g/dL*[†]	Median Postdischarge Hb (IQR), *g/dL*[‡]	Patients With Increment >1 g/dL, %[§]	Median Time After Hospital Discharge (IQR), *d*[‖]	Median 6-Month Hb Level (IQR), *g/dL*[¶]	Median Time After Hospital Discharge (IQR), *d*[‖]
Hb 7–7.9 g/dL(*n* = 6,535)	7.7 (7.4–7.8)	9.4 (8.4–10.8)	70	10 (4–36)	11.5 (10.2–12.6)	72 (28–124)
Hb 8–8.9 g/dL(*n* = 33,639)	8.6 (8.3–8.8)	10 (9.1–11.2)	63	11 (4–41)	11.6 (10.6–12.7)	73 (28–124)
Hb 9–9.9 g/dL(*n* = 79,315)	9.5 (9.3–9.7)	10.9 (10–11.9)	61	15 (5–56)	11.9 (11.0–12.9)	70 (26–122)
Total (n = 119,489)	9.3 (8.8–9.6)	10.6 (9.6–11.7)	63	14 (5–52)	11.9 (10.9–12.9)	72 (27–123)

Hb = hemoglobin; IQR = interquartile range.

[*] Hb levels for each patient's initial hospital discharge with moderate anemia.

[†] The most recent Hb level before hospital discharge.

[‡] The initial Hb level after hospital discharge.

[§] Patients with >1 g/dL increment from discharge to postdischarge Hb level.

[‖] Number of days after discharge that the postdischarge or 6-month Hb level was obtained.

[¶] Maximum Hb level within 6 months of a patient's initial hospitalization with moderate anemia.

Appendix Table 8.

Trends in RBC Transfusion, Rehospitalization, and Mortality, by Number of Hospital Discharges With Moderate Anemia*

Variable	2010 (*n* = 30,904)	2011 (*n* = 36,837)	2012 (*n* = 38,959)	2013 (*n* = 40,057)	2014 (*n* = 40,683)	*P* Value†
Annual trend in 1-month RBC transfusion, by number of hospital discharges with moderate anemia						
1 (*n* = 119,489)	7.5	6.8	6.7	6.4	5.7	<0.001
2 (*n* = 34,830)	14.1	12.6	11.3	10.4	9.4	<0.001
3 (*n* = 14,442)	18.1	16.4	14.5	13.7	13.1	<0.001
4 (*n* = 7,141)	23.4	18.4	17.1	16.0	15.2	<0.001
5+ (*n* = 11,538)	25.9	23.2	23.2	19.8	18.8	<0.001
Annual trend in 6-month RBC transfusion, by number of hospital discharges with moderate anemia						
1 (*n* = 119,489)	15.2	13.8	13.2	12.4	11.5	<0.001
2 (*n* = 34,830)	27.4	24.6	22.5	20.4	18.7	<0.001
3 (*n* = 14,442)	35.1	34.1	28.8	26.7	25.1	<0.001
4 (*n* = 7,141)	40.2	38.4	35.1	31.1	30.2	<0.001
5+ (*n* = 11,538)	50.5	47.4	45.3	40.3	38.6	<0.001
Annual trend in 1-month rehospitalization, by number of hospital discharges with moderate anemia						
1 (*n* = 119,489)	17.8	16.9	17.7	18.1	17.1	0.23
2 (*n* = 34,830)	25.0	23.0	22.5	21.6	21.7	<0.001
3 (*n* = 14,442)	32.8	31.3	28.6	26.4	26.3	<0.001
4 (*n* = 7,141)	41.9	36.1	34.1	30.9	29.4	<0.001
5+ (*n* = 11,538)	48.8	45.4	43.4	40.8	37.9	<0.001
Annual trend in 6-month rehospitalization, by number of hospital discharges with moderate anemia						
1 (*n* = 119,489)	31.4	30.0	30.0	30.1	28.6	<0.001
2 (*n* = 34,830)	48.8	45.21	44.8	42.8	42.9	<0.001
3 (*n* = 14,442)	62.4	59.1	55.6	53.3	50.6	<0.001
4 (*n* = 7,141)	69.7	66.5	62.8	61.4	57.5	<0.001
5+ (*n* = 11,538)	76.6	77.3	74.1	73.6	70.1	<0.001
Annual trend in 1-month mortality, by number of hospital discharges with moderate anemia						
1 (*n* = 119,489)	4.6	4.5	4.6	4.5	4.6	0.23
2 (*n* = 34,830)	7.6	7.7	7.3	6.8	7.5	0.27
3 (*n* = 14,442)	9.6	9.5	9.2	8.8	9.2	0.49
4 (*n* = 7,141)	11.4	9.0	9.5	9.0	8.9	0.11
5+ (*n* = 11,538)	10.5	7.9	8.7	8.7	8.6	0.65

Variable	2010 (*n* = 30,904)	2011 (*n* = 36,837)	2012 (*n* = 38,959)	2013 (*n* = 40,057)	2014 (*n* = 40,683)	*P* Value†
Annual trend in 6-month mortality, by number of hospital discharges with moderate anemia						
1 (*n* = 119,489)	13.3	12.9	13.3	13.0	13.3	0.48
2 (*n* = 34,830)	22.9	21.9	21.8	20.9	21.0	0.003
3 (*n* = 14,442)	28.3	27.5	27.1	26.7	25.8	0.03
4 (*n* = 7,141)	31.0	28.0	28.3	27.8	28.8	0.54
5+ (*n* = 11,538)	30.1	26.1	30.3	30.1	27.7	0.77

RBC = red blood cell.

*Moderate anemia is defined as hemoglobin levels between 7 and 10 g/dL.

†Cochran-Armitage trend test.

Appendix Table 9.

Risk-Adjusted Mortality: Trends in Comorbidity Burden, Severity of Illness, and Observed and Expected Hospital Mortality for All Hospitalizations (n = 826,095)*

Variable	2010 (*n* = 158,976)	2011 (*n* = 169,257)	2012 (*n* = 166,526)	2013 (*n* = 166,164)	2014 (*n* = 165,172)	*P* Value†
Mean COPS2 (SD)	34 (34)	34 (34)	34 (34)	37 (36)	37 (36)	<0.001
Mean LAPS2 (SD)	55 (39)	56 (40)	56 (40)	59 (40)	59 (40)	<0.001
Observed mortality, %	2.9	2.8	2.6	2.7	2.7	0.35
Expected mortality, %	2.8	2.8	2.9	3.0	3.0	<0.001

COPS2 = Comorbidity Points Score, version 2; KPNC = Kaiser Permanente Northern California; LAPS2 = Laboratory Acute Physiology Score, version 2.

*Inpatient admission rates have been decreasing in KPNC in recent years. This decline is at least partly related to a comprehensive safety net to prevent hospitalization and includes the use of a call left, targeted disease management programs, specialized transition programs to schedule follow-up visits for patients who are hospitalized, and medication management programs. In addition, there has been an effort to shift many surgical procedures to the outpatient setting. Consequently, patients who are hospitalized at KPNC are more likely to be those for whom this safety net has failed. Thus, patients who do require hospitalization increasingly have more comorbid conditions and frequently are more acutely ill. Over our study period, hospital mortality rates remained unchanged, whereas observed-to-expected mortality rates (i.e. adjusted mortality) have decreased. t Linear regression for continuous variables (COPS2, LAPS2); Cochran-Armitage for dichotomous variables.

Appendix Table 10.

Subgroup Analyses for Trends in 6-Month Unadjusted Mortality of Patients With Moderate Anemia

Variable	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)	*P* Value*
Annual trends in 6-month unadjusted mortality of patients with moderate anemia, by demographic characteristics and admission status, %†						

Variable	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)	*P* Value*
Sex						
Male (*n* = 45,714)	17	17	17	17	17	0.49
Female (*n* = 73,775)	11	10	11	11	11	0.61
Age						
18–59 *y* (*n* = 39,914)	6	5	6	6	5	0.75
60–75 *y* (*n* = 41,006)	11	11	12	11	12	0.192
76+ *y* (*n* = 38,569)	24	23	23	23	23	0.176
RBC transfusion before admission‡						
Within 30 days (*n* = 3,346)	35	36	33	36	35	0.87
Within 180 days (*n* = 7,479)	30	31	31	32	32	0.72
History of anticoagulation§						
Within 30 days (*n* = 4,257)	17	15	15	16	18	0.70
Within 90 days (*n* = 8,978)	18	17	17	17	19	0.27
Within 180 days (*n* = 10,356)	20	19	19	19	21	0.67
Admission status						
Elective (*n* = 45,785)	5	4	5	4	5	0.86
Emergency (*n* = 73,704)	21	19	19	18	19	<0.001
Anemia status‖						
Hospital acquired (*n* = 36,860)	6	5	5	6	6	0.97
Anemia on admission (*n* = 80,113)	18	17	18	16	17	0.152
Annual trends in 6-month unadjusted mortality of patients with moderate anemia, by principal diagnosis, %†						
Gastrointestinal (*n* = 14,912)	10	10	10	10	11	0.82
Injury/fracture (*n* = 15,282)	17	18	13	14	15	0.58
Circulatory (*n* = 15,151)	18	16	17	15	16	0.016
Infectious (*n* = 14,338)	24	22	23	20	21	0.004
Musculoskeletal (*n* = 20,970)	2	1	2	1	3	0.089
Neoplasm (*n* = 12,343)	17	17	17	17	17	1.00
Blood diseases (*n* = 2,580)	16	17	15	15	12	0.38
Respiratory (*n* = 5,496)	24	24	27	25	26	0.293
Genitourinary (*n* = 8,054)	14	12	14	13	13	0.42
Other (*n* = 10,363)	15	16	14	16	14	0.231
Annual trends in 6-month mortality in patients with moderate anemia, by hospital, %†						
1 (*n* = 1,323)	15.5	13.9	23.6	13.0	19.1	0.57
2 (*n* = 1,949)	17.6	16.4	16.5	16.4	15.5	0.60
3 (*n* = 2,952)	20.0	16.0	13.9	12.4	9.7	<0.001
4 (*n* = 5,023)	10.3	13.2	12.0	12.7	12.7	0.41
5 (*n* = 3,562)	12.5	13.0	15.0	13.7	13.3	0.47

Variable	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)	*P* Value*
6 (*n* = 3,595)	14.7	13.3	14.4	14.3	14.0	0.67
7 (*n* = 4,997)	13.1	14.2	12.2	13.8	18.1	0.06
8 (*n* = 3,543)	15.3	14.8	12.8	14.0	15.5	0.90
9 (*n* = 4.469)	17.4	13.7	18.1	15.2	18.0	0.85
10 (*n* = 4,604)	13.4	13.3	14.3	13.1	13.6	0.63
11 (*n* = 5,632)	9.9	9.4	13.3	9.7	13.2	0.197
12 (*n* = 4,329)	16.7	15.7	15.5	16.9	13.1	0.36
13 (*n* =5,533)	11.8	11.9	12.5	14.2	12.9	0.202
14 (*n* = 7,230)	11.1	8.1	10.5	9.3	10.4	0.91
15 (*n* = 6,852)	12.1	13.4	12.5	13.2	11.6	0.58
16 (*n* = 7,867)	12.2	12.9	11.5	13.3	11.1	0.98
17 (*n* = 7,658)	16.4	15.9	13.9	15.4	18.4	0.83
18 (*n* = 8,358)	11.8	11.1	10.9	11.9	10.5	0.83
19 (*n* = 8,517)	13.3	14.8	14.5	13.2	14.9	0.93
20 (*n* = 9,863)	12.2	13.3	15.3	12.5	13.5	0.097
21 (*n* = 11,633)	13.1	11.6	11.9	11.3	11.6	0.066

RBC = red blood cell.

*Cochran-Armitage trend test.

†Outcomes after each patient's initial hospital discharge with moderate anemia.

‡Inpatient and outpatient RBC transfusion events before hospital admission.

§Based on outpatient prescription of an oral anticoagulant and management by regional anticoagulation service within 30, 90, or 180 days of hospital admission.

‖Anemia is defined as hemoglobin levels <12 g/dL in females and <13 g/dL in males.

Appendix Table 11.

Trends in Incidence and Mortality of Emergency or Elective or Medical or Surgical Admissions*

Category	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)	
Trends in patients with moderate anemia, by emergency or elective or medical or surgical admissions (*n* = 119,489), *n* (%)‡						
Emergency surgical (*n* = 16,360)	2507 (11.3)	3,068 (13.1)	3,329 (13.8)	3720 (15.0)	3,736 (15.0)	
Elective surgical (*n* = 38,375)	7,578(34.1)	8,128 (34.7)	8,009 (33.2)	7,562 (30.5)	7,098 (28.5)	
Emergency medical (*n* = 57,344)	10,689 (48.0)	11,009 (47.0)	11,120 (46.1)	12,199 (49.2)	12,327 (49.5)	
Elective medical (*n* = 7,410)	1470 (6.6)	1,219 (5.2)	1,664 (6.9)	1,314 (5.3)	1,743 (7.0)	
						***P* Value†**

Category	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)	
Trends in 6-month mortality in patients with anemia, by emergency or elective or medical or surgical admissions, %						
Medical (*n* = 64,754)						
Emergency (*n* = 57,344)	21.7	20.9	21.1	19.8	20.6	0.01
Elective (*n* = 7,410)	15.4	17.7	15.2	12.5	10.9	<0.001
Surgical (*n* = 54,735)						
Emergency (*n* = 16,360)	12.6	12.3	13.3	12.6	11.9	0.67
Elective *(n* = 38,375)	2.4	2.3	2.7	2.9	2.9	0.01
	2010 (*n* = 8,278)	**2011 (*n* = 8,773)**	**2012 (*n* = 8,013)**	**2013 (*n* = 6,980)**	**2014 (*n* = 6,331)**	**Total (*n* = 38,375)**
Trends in elective surgical admissions in patients with anemia, by comorbidity status, *n* (%)						
COPS2						
Low (0–10)	4047 (53.4)	4381 (53.9)	4069 (50.8)	3448 (45.6)	3024 (42.6)	18,969 (49.8)
Moderate (11–50)	2455 (32.4)	2658 (32.7)	2771 (34.6)	2730 (36.1)	2732 (38.5)	13,346 (34.6)
High (50 +)	1076 (14.2)	1089 (13.4)	1169 (14.6)	1384 (18.3)	1,342 (18.9)	6,060 (15.6)
						***P* Value**[†]
Trends in 6-month mortality in elective surgical admissions, by comorbidity burden, %						
Low (*n* = 18,969)	0.8	0.8	0.9	0.9	0.9	0.49
Moderate (*n* = 13,346)	2.5	2.5	2.8	2.9	2.4	0.83
High *(n* = 6,060)	8.5	8.2	8.6	8.3	8.2	0.87
	2010 (*n* = 12,159)	**2011 (*n* = 12,228)**	**2012 (*n* = 12,784)**	**2013 (*n* = 13,513)**	**2014 (*n* = 14,070)**	**Total (*n* = 64,754)**
Trends in medical admissions among patients with anemia, by comorbidity status, *n* (%)						
COPS2						
Low (0–10)	3,672 (30.2)	3,778 (30.9)	4,180 (32.7)	4,257 (31.5)	4,559 (32.4)	20,446 (31.6)
Moderate (11–50)	3,794 (31.2)	3,766 (30.8)	3,989 (31.2)	4,067 (30.1)	4,164 (29.6)	19,780 (30.6)
High (50+)	4,693 (38.6)	4,684 (38.3)	4,615 (36.1)	5,189 (38.4)	5,347 (38.0)	24,528 (37.9)
						***P* Value**[†]

Category	2010 (*n* = 22,244)	2011 (*n* = 23,424)	2012 (*n* = 24,122)	2013 (*n* = 24,795)	2014 (*n* = 24,904)	
Trends in 6-month mortality in medical admissions, by comorbidity burden, %						
Low (*n* = 20,446)	11.9	11.2	10.9	9.3	9.5	<0.001
Moderate (*n* = 19,780)	16.3	16.2	16.6	14.6	14.2	0.008
High (*n* = 24,528)	31.7	31.7	31.9	30.7	32.0	0.69

COPS2 = Comorbidity Points Score, version 2.

*Medical or surgical status for each patient's initial hospital discharge with moderate anemia.

†Cochran-Armitage trend test.

‡Medical or surgical status for each patient's initial hospital discharge with moderate anemia.

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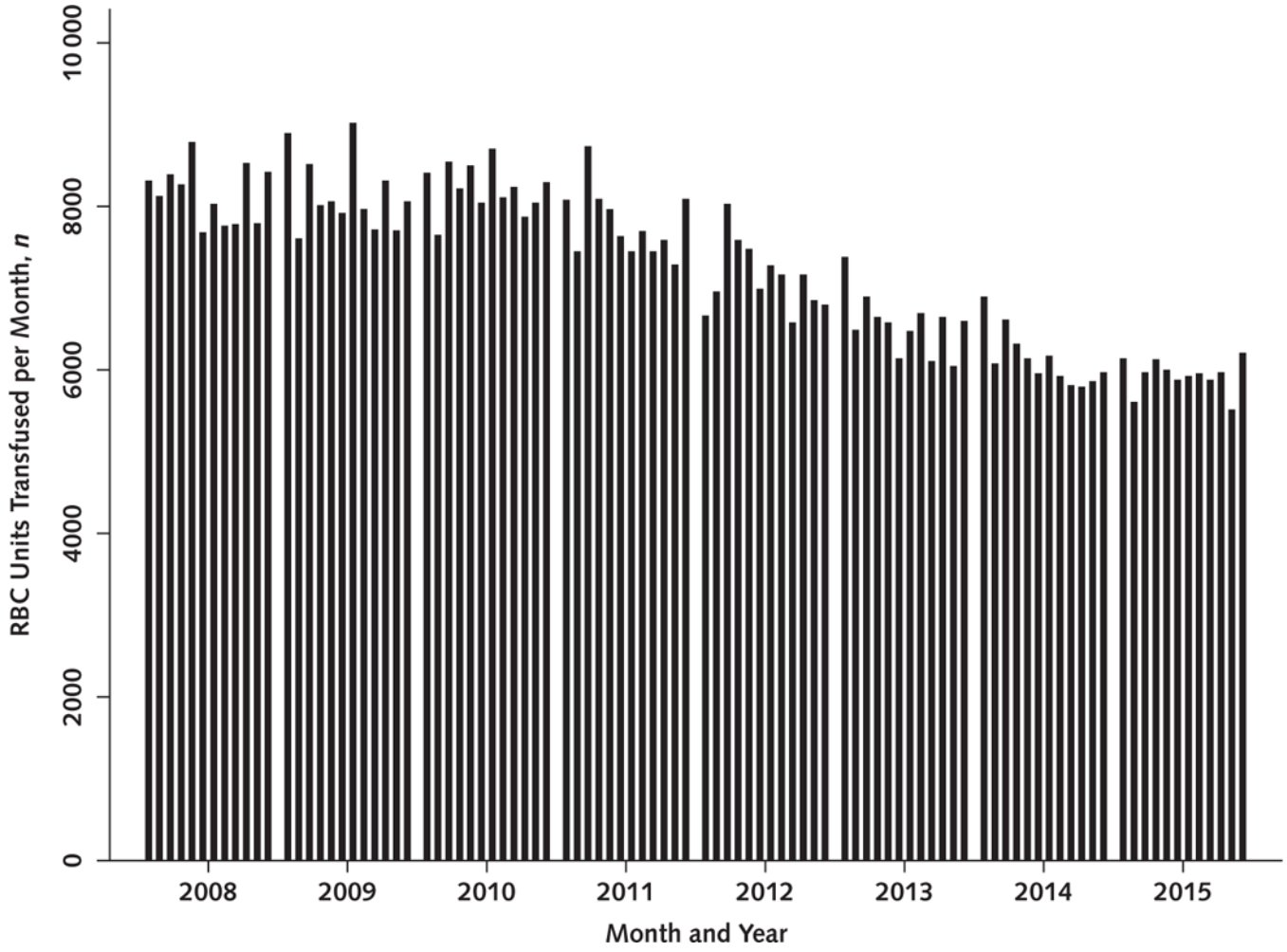

Figure. Use of RBCs among inpatients and outpatients across 21 KPNC facilities, by month and year.

The number of RBC units transfused per 1000 adults was stable from 2008 through 2010 (39.8 units; $P = 0.55$ by linear regression) and decreased each year thereafter to 28.5 RBC units transfused per 1000 patients through 2015, representing a 28% relative decline from 2010 ($P < 0.001$). KPNC = Kaiser Permanente Northern California; RBC = red blood cell.

Table 1.

Patient Characteristics in the First and Last Years of the Study*

Characteristic	2010		2014	
	Moderate Anemia (*n* = 22 244)	All Others (*n* = 64 931)	Moderate Anemia (*n* = 24 904)	All Others (*n* = 67 911)
Mean age (SD), *y*	67 (16)	61 (18)	67 (17)	62 (18)
Male, %	38	47	39	49
Median Charlson Comorbidity Index score (IQR)	1 (0–2)	1 (0–1)	1 (0–2)	1 (0–2)
Mean COPS2 (SD)†	34 (34)	24 (28)	37 (36)	27 (31)
Mean LAPS2 (SD)‡	55 (40)	46 (35)	59 (42)	46 (45)
Emergency admission, %	59	62	64	62
Surgical admission, %	47	37	43	38
Admission location, %§				
Medical-surgical ward	55	54	63	53
Operating room	31	33	24	35
Intensive care unit	8	7	8	7
Transitional care unit	6	6	5	5
History of anticoagulant use, %‖	8	6	9	7
Previous RBC transfusion, %‖	10	4	4	2
Conditions on admission, %				
Gastrointestinal	12	16	13	15
Injury/fracture	12	10	14	9
Circulatory	13	20	13	19
Infectious	8	6	15	10
Musculoskeletal	18	9	15	13
Neoplasm	10	10	9	8
Blood diseases	4	4	3	4
Respiratory	6	7	4	6
Genitourinary	12	7	6	5
Other	5	11	8	11

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Characteristic	2010		2014	
	Moderate Anemia (*n* = 22 244)	**All Others (*n* = 64 931)**	**Moderate Anemia (*n* = 24 904)**	**All Others (*n* = 67 911)**
Median hospital length of stay (IQR), *d*	3.3 (2.2–5.8)	2.2 (1.3–3.9)	3.3 (2.1–5.8)	2.1 (1.3–3.5)
Discharge disposition, %				
Home	78	90	79	91
SNF	20	9	19	8
Hospice	2	1	2	1

COPS2 = Comorbidity Points Score, version 2; IQR = interquartile range; LAPS2 = Laboratory Acute Physiology Score, version 2; RBC = red blood cell; SNF = skilled nursing facility.

[*] Reported at the time of initial hospital discharge. Included are unique patients discharged alive with moderate (defined as hemoglobin levels ≥7 to <10 g/dL), mild (defined as hemoglobin levels ≥10 g/dL), or no anemia but not those discharged with severe anemia (defined as hemoglobin levels <7 g/dL) in 2010 (*n* = 164) or 2014(*n* = 335).

[†] A longitudinal, diagnosis-based score. Scores <50 are associated with hospital mortality rates <2%, whereas scores >100 are associated with rates ≥5%.

[‡] Higher scores indicate increasing degrees of physiologic derangement. The univariate association between LAPS2 and mortality is such that scores <50 are associated with mortality rates <1.5%, whereas scores >125 are associated with rates between 10% and ≥15%.

[§] Initial inpatient location on hospital entry.

[‖] Indicates patients received a transfusion or prescription for anticoagulation within 6 mo of hospitalization.

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Table 2.

Transfusion Characteristics and Rates of Anemia in Hospitalized Patients

Variable	2010	2011	2012	2013	2014	*P* Value
RBC transfusion characteristics *						
Patients, *n*	30 904	36 837	38 959	40 057	40 683	
Inpatient RBC transfusion, %	31	29	27	25	23	<0.001†
Pretransfusion hemoglobin level, *g/dL*	8.2	8.0	7.8	7.5	7.2	<0.001‡
RBC units per 100 hospitalizations, *n*	42	39	35	31	28	<0.001‡
Moderate anemia at hospital discharge §						
Hospitalizations, *n*	154 220	164 118	161 542	161 239	160 142	
Patients discharged annually (incidence), %	22.3	23.8	25.0	25.3	25.7	<0.001†
Hospital discharges annually (prevalence), %	20.0	22.4	24.1	24.8	25.4	<0.001†

RBC = red blood cell.

*Among 187 440 hospitalizations in which 119 489 patients were discharged alive with moderate anemia (defined as hemoglobin levels ≥7 to <10 g/dL).

†Calculated from a modified log-Poisson generalized estimating equation for dichotomous outcomes with a linear time trend.

‡Calculated from an identity-Normal generalized estimating equation for continuous outcomes with a linear time trend.

§Among 445 371 unique patients surviving 801 261 hospitalizations.

Table 3.

Resolution of Moderate Anemia Within 6 Months of Hospital Discharge*

6-Month Status	2010 (*n* = 21 425)	2011 (*n* = 23 049)	2012 (*n* = 23 371)	2013 (*n* = 24 030)	2014 (*n* = 23 376)
No anemia (*n* = 42 954)	42.2	38.6	37.1	35.4	34.1
Mild anemia (*n* = 60 899)	50.8	53.2	53.2	53.6	53.1
Moderate anemia (*n* = 11 398)	7.0	8.2	9.8	11.0	12.8

*Based on hemoglobin levels available within 6 mo of hospitalization in 115 251 patients with moderate anemia (defined as hemoglobin levels between 7 and 10 g/dL). The table does not include the few patients (*n* = 83) with severe anemia (defined as hemoglobin levels <7 g/dL) within 6 mo of hospital discharge. A linear time trend using a generalized estimating equation was used for multinomial outcomes in patients with mild anemia vs. those without anemia (odds ratio, 1.083 [95% CI, 1.073–1.093]; $P < 0.001$) and patients with moderate anemia vs. those without anemia (odds ratio, 1.274 [CI, 1.254–1.294]; $P < 0.001$). Values are percentages. Percentages may not sum to 100 due to rounding.

Table 4.

Adjusted Annual Prevalence of Clinical Outcomes in Patients With Moderate Anemia After Hospitalization*

Clinical Outcome	2010 (*n* = 22 244)	2011 (*n* = 23 424)	2012 (*n* = 24 122)	2013 (*n* = 24 795)	2014 (*n* = 24 904)	*P* Value†
RBC transfusion‡						
Within 1 mo	9.4	9.2	8.7	8	7.5	<0.001
Within 6 mo	18.9	18.1	18	18.1	16.8	<0.001
Rehospitalization						
Within 1 mo	22.6	21.7	21.3	20.1	19.6	<0.001
Within 6 mo	36.5	33.7	33.9	33.8	32.8	<0.001
Mortality						
Within 1 mo	4.4	4.5	4.2	3.8	4.1	0.061
Within 6 mo	16.1	15.9	15.9	15.0	15.6	0.004

RBC = red blood cell.

*Among 187 440 hospitalizations in which 119 489 unique patients were discharged alive with moderate anemia (defined as hemoglobin levels between 7 and 10 g/dL). Annual prevalence calculations include year as a categorical variable and adjust for number of hospitalizations, age, sex, emergency admission, surgical status, Charlson Comorbidity Index score, and severity of illness as measured by the Laboratory Acute Physiology Score, version 2. Values are percentages.

†Calculated from a modified log-Poisson generalized estimating equation for dichotomous outcomes with a linear time trend.

‡An inpatient or outpatient RBC transfusion event.