interpretation of the data and in the preparation and review of the manuscript. An independent statistical analysis of the data was conducted by the study authors. The sponsor had no role in approval of the manuscript and decision to submit the manuscript for publication.

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Decreased Red Blood Cell Use and Mortality in Hospitalized Patients

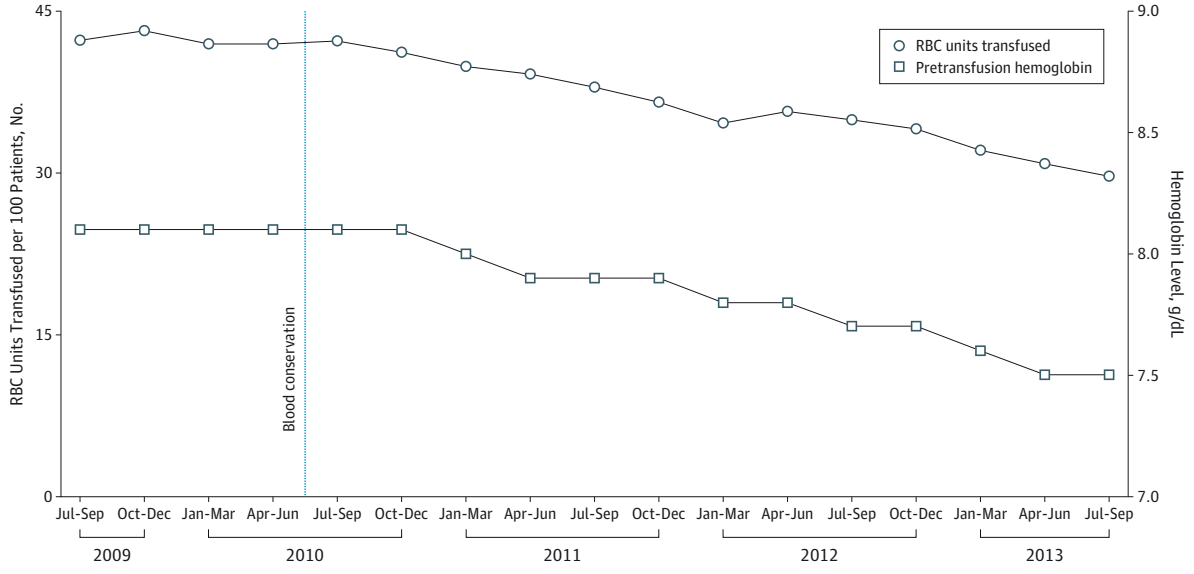
Blood conservation strategies effectively decrease red blood cell (RBC) use in specific patient groups.[1-3] However, the impact of RBC transfusion reduction on mortality in a diverse inpatient population remains poorly described. We detail the impact of declining RBC use on 30-day mortality within Kaiser Permanente Northern California (KPNC), an integrated health care delivery system serving 3.5 million members at 21 hospitals.

Methods | The KPNC and University of California, San Francisco (UCSF) institutional review boards approved this study and waived the requirement for informed consent based on the nature of the study. Beginning in 2010, KPNC initiated a regional blood conservation program whose key features included (1) clinician education in evidence-based transfusion guidelines; (2) focused multidisciplinary conservation efforts in specific high-use departments (eg, orthopedics, cardiovascular surgery); and (3) guideline-based clinical decision support embedded within the electronic medical record.

To study the impact of these initiatives, we quantified RBC transfusion in an inpatient cohort composed of all nonobstetric patients 18 years or older admitted to KPNC hospitals between July 1, 2009, and August 31, 2013. We evaluated the impact of decreased RBC use on unadjusted and risk-adjusted 30-day mortality prior to (2010) and following (2012-2013) reductions in blood use. We examined these rates in patients with hemoglobin levels below 10 g/dL (to convert to grams per liter, multiply by 10) during hospitalization (n = 218 056), accounting for nearly all (81 897 of 83 461 [98.1%]) transfused patients. We quantified patients' predicted 30-day mortality rates based on prior methods adjusting for age, sex, comorbid disease burden, emergency or elective presentation, medical or surgical admission, admission diagnosis, severity of illness, first inpatient ward, and hospital facility.[4] We also adjusted for patients' preadmission hemoglobin level and lowest hospital hemoglobin level.[5] We then compared standardized mortality ratios for transfused vs nontransfused patients using Poisson regression. Trends in RBC use and unadjusted 30-day mortality were assessed using linear regression. Statistical analyses were performed in Stata 11 software (StataCorp).

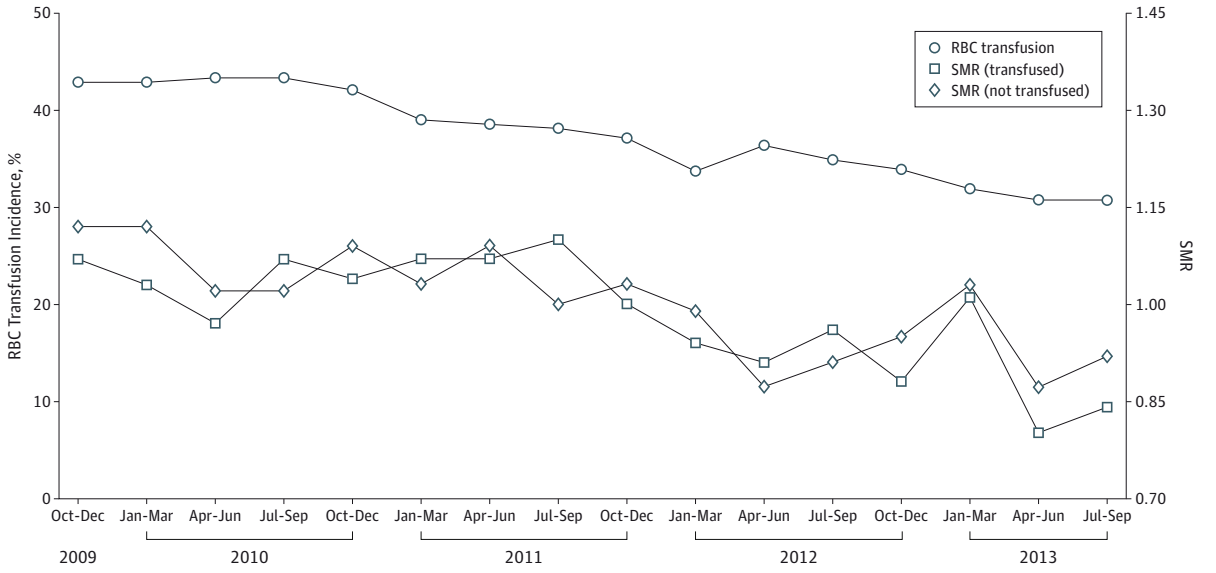
Results | The number of RBC units transfused decreased 8.6% annually from 41.8 units per 100 patients in 2010 (95% CI, 41.1-42.6 units) to 31.0 units per 100 patients in 2013 (95% CI, 30.3-31.8 units) ($P < .001$) (**Figure 1**). From 2009 to 2013, the

Figure 1. Trends in Inpatient RBC Use and Pretransfusion Hemoglobin Levels Across 21 KPNC Facilities



The number of RBC units transfused per 100 patients and median pretransfusion hemoglobin level decreased following initiation of blood conservation strategies in 2010 ($P < .001$). To convert hemoglobin to grams per liter, multiply by 10. KPNC indicates Kaiser Permanente Northern California; and RBC, red blood cells.

Figure 2. Inpatient RBC Transfusion Incidence and SMRs



The decline in RBC transfusion incidence in patients whose hemoglobin level fell below 10 g/dL (n = 218 056) was not associated with differences in SMRs in transfused and nontransfused patients. To convert hemoglobin to grams per liter, multiply by 10. RBC indicates red blood cells; and SMRs, standardized mortality ratios.

median pretransfusion hemoglobin decreased from 8.1 g/dL to 7.5 g/dL ($P < .001$). In patients with a hemoglobin level lower than 10 g/dL, RBC transfusion incidence decreased from 43.4% in 2010 to 30.7% in 2013 ($P < .001$) (**Figure 2**).

In inpatients with a hemoglobin level lower than 10 g/dL, 30-day mortality rates did not differ prior to (2010) and following (2013) declines in RBC use (7.8% and 7.8%, respectively; $P = .49$ for trend). Standardized mortality ratios in transfused and nontransfused anemic patients did not differ prior to (rate ratio in 2010, 0.96; 95% CI, 0.91-1.03) ($P = .26$) and following (rate ratio in equal period [2012-2013], 0.96; 95% CI, 0.90-1.02) ($P = .20$) reductions in RBC use (Figure 2).

Discussion | Our study demonstrates the impact of blood conservation strategies on transfusion practice and mortality outside the clinical trial setting. We found a greater than 20% reduction in RBC use over 3 years and a concurrent drop in median pretransfusion hemoglobin level. Over the same period, we did not detect an impact of decreased RBC use and more restrictive transfusion practice on adjusted and unadjusted mortality rates.

Observational studies using large health care databases can complement findings from randomized clinical trials by confirming and expanding on outcomes in clinical practice. In this case, we examined the broad application of clinical trial-based recommendations that could conceivably negatively affect a diverse population.[6] Our study demonstrates, in a real-world setting, that reductions in transfusion incidence are occurring without affecting mortality. Future studies will need to assess whether further reductions in RBC use and hemoglobin thresholds have an impact on morbidity and mortality. These data support the safety of more restrictive transfusion practice as currently implemented in a large community hospital network.

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The Portrait of an Adult Liver Transplant Recipient in the United States From 1987 to 2013

Since the first liver transplant, tremendous advances in organ preservation, surgical techniques and postoperative management have occurred. These advances have made liver transplantation the standard of care for patients with end-stage liver disease.[1-3] In this study, we describe how the clinicodemographic portrait of adult liver transplant recipients has changed in the United States over the past 25 years.

Methods | This study used the Scientific Registry of Transplant Recipients (SRTR). We included all adult liver transplant recipients from 1987 to June 2013. The study span was split into 4 approximately equally long cycles: 1987 to 1993, 1994 to 2000, 2001 to 2006, and 2007 to 2013. Cochran-Armitage test and Kendall τ-*b* coefficient were used to assess time trends. The study was granted a nonhuman subject research status by Inova Institutional Review Board.

Results | A total of 108 707 adult liver transplants performed in 153 different transplant centers across the country were included (**Table**).

Consistent with the changes in the general US population, liver transplant recipients are becoming increasingly older. Nevertheless, the increase in the mean age (7.3 years between cycles 1 and 4) is greater than that for patients with the diagnosis of chronic liver disease (41.1-45.3 years for the same time period[4]). In contrast, changes in the racial/ethnic profile of transplant recipients were similar to those seen in the US general population.[4] Also, the proportion of male transplant recipients increased over time (Table).

Furthermore, patients' clinical presentation and functional status suggest that transplant recipients are becoming sicker. In particular, the rates of nearly all chronic conditions increased, and the average model for end-stage liver disease (MELD) (currently used for prioritization of wait-listed candidates[3]) score increased slightly. Of the indications for liver transplantation, the proportion of alcoholic liver disease decreased while that of primary liver cancer increased (Table). Of chronic liver disease etiologies, hepatitis C virus (HCV), alcoholic liver disease, and nonalcoholic fatty liver disease are now the most prevalent, and while alcoholic liver disease decreased, nonalcoholic fatty liver disease has shown a rapid increase (Table).

Discussion | The results of this descriptive study show how liver transplant recipients have changed over the past 2 decades. In particular, liver transplant recipients in the United States have become older, predominantly male and with more comorbidities. Although the reasons are not entirely clear, one major contributor to this change may be related to the easing of some listing criteria for liver transplant candidates, such as increasing the threshold for age and body mass index. In addition, the increase in age could be related to the aging of the "baby boomer" cohort with high prevalence of HCV, the most common indication for liver transplantation.

The explanation for the observed sex disparity remains unclear. Although sex bias from MELD allocation has been reported,[5] it is also important to note that the 2 most common indications for liver transplantation, HCV and hepatocellular carcinoma, have male predominance.[6]

Our results also suggest that liver transplant recipients are becoming sicker. This may reflect the mandated transition to the "sickest-first" approach by MELD allocation.[2,3] We also noted an increase in the rates of comorbidities related to metabolic syndrome, which may be explained by the increasing prevalence of obesity and its complications in the United States. However, a steady rather than abrupt increase in the rates of most of comorbidities (**Figure**) could