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The difference between fingerstick and venous hemoglobin and hematocrit varies by sex and iron stores

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Abstract

BACKGROUND—Fingerstick blood samples are used to estimate donor venous hemoglobin (Hb).

STUDY DESIGN AND METHODS—Fingerstick Hb or hematocrit (Hct) was determined routinely for 2425 selected donors at six blood centers, along with venous Hb. Using sex and measures of iron status including absent iron stores (AIS; ferritin < 12 ng/mL), linear regression models were developed to predict venous Hb from fingerstick.

RESULTS—Across all subjects, fingerstick Hb was higher than venous Hb in the higher part of the clinical range, but lower in the lower part of the range. The relationship varied by sex and iron status. Across centers, a female donor had on average a venous Hb result 0.5 to 0.8 g/dL lower than a male donor with the same fingerstick Hb and iron status. Similarly, a donor with AIS had on average a venous Hb result 0.3 to 1.1 g/dL lower than an iron-replete donor with the same fingerstick value and sex. An iron-replete male donor with a fingerstick result at the cutoff (Hb 12.5 g/dL) had an acceptable expected venous Hb (12.8 to 13.8 g/dL). A female donor with AIS with a fingerstick result at the cutoff had an expected venous Hb below 12.5 g/dL (11.7 to 12.4 g/dL). Of females with AIS, 40.2% donated blood when their venous Hb was less than 12.5 g/dL.

CONCLUSIONS—Fingerstick is considered a useful estimator of venous Hb. However, in some donor groups, particularly female donors with AIS, fingerstick overestimates venous Hb at the donation cutoff. This significant limitation should be considered in setting donor fingerstick Hb or Hct requirements.

Blood donor qualification requires demonstration that the donor's hemoglobin (Hb) or hematocrit (Hct) meets requirements. In the United States donor Hb must be greater than or equal to 12.5 g/dL or Hct at least 38%. Nearly all blood donor qualification schemes depend on capillary sampling of the donor's finger. Earstick sampling has been used in the past but has been shown to produce values that are higher than venous and fingerstick values.[1] Fingerstick sampling has been shown to more closely approximate venous Hb values,

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although reports differ on the nature and degree of the difference.[2] Previous studies comparing capillary versus venous samples in blood donors have been limited. First, studies in operational settings have often used copper sulfate screening of capillary samples, using quantitative methods only to retest donors who failed the copper sulfate screen. Second, the various quantitative methods used have varied in reliability, user training, and the precision of measurement, which has often been poor. Finally the venous samples have often been obtained after whole blood donations, along with routine testing samples. Postdonation values have been shown in one small study to be significantly lower than venous samples collected before donation.[1] Further, donor positional effects (sitting, recumbent) at the time of the venous sample collection have not been well controlled. Most comparisons of the two methods have demonstrated that fingerstick sampling has higher variability than venous sampling and that a number of donors accepted on the basis of a fingerstick sample have venous Hb values below the acceptable minimum.[2]

Recently, a study in Ireland has demonstrated in routinely collected fingerstick Hb deferred donors that venous Hb is higher than the fingerstick value by 1.07 g/dL (males) and 0.67 g/dL (females).[3] The authors used this result to validate a decision to change the acceptance level for fingerstick Hb from 12.5 g/dL to 12.0 g/dL for females and 13.5 g/dL to 13.0 g/dL for males. Although this was the primary study focus, they also measured simultaneous fingerstick and venous Hb values across a wider range of fingerstick Hb on 155 accepted first-time donors and demonstrated that the difference between fingerstick and venous values was dependent on Hb level. Below fingerstick Hb of 15.4 g/dL for men and 13.4 g/dL for women, venous Hb values were higher than fingerstick, while above this level venous Hb values were lower than fingerstick. However, this relationship was based on only a small number of donors. Also because only first-time donors were studied, the applicability of this phenomenon to repeat blood donors is not clear.

The REDS-II (Retrovirus Epidemiology Donor Study-II) blood centers have completed a study of blood donor iron status (RISE), which provides a large multicenter assessment of fingerstick and venous sampling methods. At enrollment blood donors had quantitative measurements of fingerstick Hb or Hct and venous Hb, as well as measurement of plasma ferritin. Several different quantitative fingerstick methods were used at the centers, allowing indirect assessment of methodologic differences. Pre-and postdonation venous samples were both obtained from some donors, allowing development of an algorithm for conversion of one sample type to the other. Finally, a multivariable model incorporating sex and body iron stores was developed to predict predonation venous Hb from the fingerstick Hb or Hct values.

MATERIALS AND METHODS

RISE study donors were enrolled between December 2007 and June 2008 into a multicenter longitudinal study. All six REDS-II blood centers participated in the study; these included the American Red Cross New England Region (Dedham, MA), American Red Cross Southern Region (Douglasville, GA), BloodCenter of Wisconsin (Milwaukee, WI), Blood Centers of the Pacific (San Francisco, CA), Hoxworth Blood Center/University of Cincinnati Academic Health Center (Cincinnati, OH), and the Institute for Transfusion Medicine (Pittsburgh, PA). The REDS-II centers represent geographically and demographically diverse populations and collectively account for more than 8% of annual blood collections in the United States. The REDS-II coordinating center is Westat (Rockville, MD) and Blood Systems Research Institute (San Francisco, CA) serves as the REDS-II Central Laboratory.

Enrollment cohorts

Four cohorts of successful whole blood or double–red blood cell (RBC) donors were established: two first-time or reactivated (FT/RA) donor cohorts consisting of men and women who had either never given blood before (FT) or had not given a donation in the 2 years before enrollment (RA) and two frequent donor cohorts consisting of men who had given at least three whole blood donations in the past year and women who had given at least two whole blood donations in the past year or equivalent double-RBC donations. The final enrollment in RISE was 2425 donors: 481 FT/RA females, 407 FT/RA males, 769 frequent female donors, and 768 frequent male donors.

Donors agreeing to enroll in the study reviewed and signed an informed consent form and agreed to return to donate frequently in the next 24 months, provide blood samples at each visit, and complete an enrollment questionnaire. The RISE study protocol and donor consent forms were approved by each participating center institutional review board and the Westat institutional review board.

Donor Hb or Hct determination

Before successful donation and enrollment, quantitative fingerstick Hb or Hct levels were measured using each center's routine operational methods (see Table 1). Copper sulfate screening was not used. Eligible donors donated whole blood or double RBCs. Ethylenediamine-tetraacetate (EDTA) venous samples in dry EDTA tubes were collected either before donation (76% of samples and all double RBCs) or after whole blood donation (24% of samples). All centers measured venous Hb using an Hb (HemoCue 201, HemoCue, Inc., Lake Forest, CA) following the directions in the package insert. Testing was performed by center research staff trained by HemoCue trainers. At four centers, an additional Hb measurement was obtained on a sample taken at the same time using hematology analyzers (Advia 120/2120, Siemens Healthcare Diagnostic, Inc., Deerfield, IL).

Comparison of pre- versus postdonation venous Hb

To allow use of postdonation samples in the analysis, a comparison study of pre- and postdonation venous Hb was conducted in 278 whole blood donors (114 female; 164 male). Predonation EDTA venous samples were collected by routine sampling using appropriate predonation sampling collection containers. Postdonation EDTA samples were collected with the donor still recumbent and within a few minutes of completion of the donation, using a second phlebotomy in the opposite arm. Samples were refrigerated until the next day when Hb was measured using the HemoCue Hb 201 analyzer. In addition to the pre- and postdonation Hb values, five additional potential covariates were recorded for each pair of samples: sex, weight, height, donation duration, and time after donation for the postdonation sample. A backward stepwise regression model was developed to predict predonation Hb.

Determination of donor iron status

Ferritin was measured with an immunoassay using direct chemiluminometric technology and a constant amount of two anti-ferritin antibodies (ADVIA Centaur, Siemens Healthcare Diagnostic Inc., Deerfield, IL). Subjects were classified as having absent iron stores (AIS) if their plasma ferritin at the enrollment visit was less than 12 ng/mL. This cutoff is a highly specific indicator of iron deficiency that reflects absent tissue and marrow iron stores.[4–7] A particle-enhanced immunoturbidimetric assay was used to detect soluble transferrin receptor (sTfR) in which latex-bound sTfR antibodies react with the antigen in the sample to form an antigen-antibody complex that is measured turbidimetrically (Tina-quant sTfR assay, Roche Diagnostics, Indianapolis, IN). Measurement of the sTfR is a sensitive measure of functional iron deficiency.[8,9] In addition, ferritin measurements and sTfR values have been combined

into a ratio, log(sTfR/ferritin), as a derived measurement. Iron-deficient erythropoiesis (IDE) was present if the log of the ratio of sTfR to ferritin [log(sTfR/Ferritin)] was at least 2.07, corresponding to the 97.5 percentile of the distribution of the log(sTfR/ferritin) in FT/RA males at enrollment. Since at enrollment all RISE donors with AIS also had IDE, for this analysis RISE donors were categorized into three mutually exclusive levels of iron stores at enrollment: iron replete (no IDE, no AIS), IDE without AIS, and AIS.

Comparison of fingerstick and venous Hb or Hct

The relationship of venous to fingerstick values in all 2425 enrolled RISE donors was determined by calculating the difference: venous Hb–fingerstick Hb, for each donor (or venous Hb–fingerstick Hct/3 for centers using Hct). Association of sex and iron status with these differences was assessed using the Kruskal-Wallis test. Since associations were found, the venous-fingerstick differences were determined within each of the six subgroups of donors (male/female, and three levels of iron stores), and the hypothesis that the average difference was equal to zero (implying equivalence of venous and fingerstick results) was tested using the signed rank test.

Development of models to compare venous Hb to fingerstick Hb or Hct

The venous-fingerstick difference was found to depend on sex and iron status. Further, significant differences among centers were noted in the relationships between fingerstick Hb or Hct and venous Hb (possibly due to centers using different fingerstick qualifying methods). Therefore, six separate (center specific) models relating fingerstick quantification to venous Hb were developed.

Consideration was given to using quadratic terms to describe the relationship between fingerstick and venous Hb, but because the fingerstick-venous relationship was essentially linear at all six centers around the qualification cutoffs (results not shown) only the linear term was retained. The following independent variables were used in multivariable linear regression models at each center to predict venous Hb: fingerstick Hct or Hb, sex, and iron status. As an analytical check on the HemoCue venous Hb method, similar models were developed at the four centers with corresponding Advia venous Hb values.

Using the six center-specific models, the predicted venous Hb was derived for the following six categories of donors with fingerstick values exactly at the donation cutoff (fingerstick Hb or Hct, 12.5 g/dL/38%): iron-replete male donors (without AIS or IDE), male donors without AIS but with IDE, male donors with AIS, iron-replete female donors (without AIS or IDE), female donors without AIS but with IDE, and female donors with AIS.

Misclassification of donor eligibility by fingerstick methods

Using the venous Hb as the gold standard for donor suitability, it was not possible to assess donors who were screened by fingerstick as deferred correctly or incorrectly since the RISE study only enrolled donors accepted by the fingerstick test of record. Accepted donors were classified as correctly accepted if venous Hb was at least 12.5 g/dL. Donors were classified as accepted incorrectly if venous Hb was less than 12.5 g/dL. The frequency of incorrectly accepted donors was analyzed by sex and iron status.

RESULTS

Comparison of pre- and postdonation venous Hb

The mean venous Hb declined from the predonation to postdonation sample with a mean decrease of 0.47 g/dL (95% confidence interval [CI], 0.42–0.51). These data were used to create a model to predict predonation Hb from the postdonation values. Sex, donation

duration, and how long after donation the postdonation sample was collected were not associated with the change in venous Hb. Donor weight was significantly associated with the Hb decrease (smaller weight correlated with larger decrease); however, models using other size-related derived variables such as body mass index (derived from height and weight) or estimated blood volume did not statistically differ from the model using weight. Based on the final model, the relationship between predonation and postdonation venous Hb (vHb) was determined to be

$$\text{Pre vHb (g/dL)} = \text{Post vHb} + 0.8423 - (0.002035 \times \text{Weight (lbs)}).$$

This formula was then used to derive predonation venous Hb results in RISE for the 24% of all venous Hb results measured on postdonation samples.

Comparison of fingerstick and venous Hb

Figure 1 is a box plot of fingerstick and venous Hb values for all 2425 enrolled RISE donors, analyzed by sex and iron status. At enrollment, 10.7% of males and 19.2% of females had AIS, and 21.9% of males and 31.0% of females had IDE without AIS.

The fingerstick-venous Hb difference varied by sex and iron status (Kruskal-Wallis test, $p < 0.0001$). As can be seen from Fig. 1, among females fingerstick Hb was significantly higher than venous Hb in each iron status group, with the most extreme difference among the AIS group. The median venous minus fingerstick Hb was −0.67 g/dL ($p < 0.0001$) for the female AIS group; the median venous minus fingerstick Hb was −0.40 g/dL ($p < 0.0001$) for the female IDE group; and the median venous minus fingerstick Hb was −0.27 g/dL ($p < 0.0001$) for the female iron-replete group (each by signed-rank test). In male donors, fingerstick Hb was significantly higher than venous Hb for males with AIS (median venous minus fingerstick Hb, −0.59 g/dL; $p < 0.0001$ by signed rank test) while there were only modest differences in the other two groups (median venous minus fingerstick Hb was −0.10 g/dL [$p = 0.02$] for the male IDE group and median venous minus fingerstick Hb was 0.10 g/dL [$p = 0.02$] for the male replete group).

Multivariable linear regression models for fingerstick Hb or Hct as a predictor of venous Hb

Because the relationship between fingerstick and venous Hb values is critically important to blood centers, multivariable linear regression models were developed for each center. As an example, Fig. 2 plots the linear model developed for Center F separated by males (Fig. 2A) and females (Fig. 2B). Figures for the other centers had similar characteristics.

Table 2 displays the linear model parameters developed for each center. The slope of the regression line for fingerstick Hb versus venous Hb is approximately 0.6 for Centers E and F (see parameter b in Table 2) and is approximately one-third as large (0.20–0.26) for the four centers using fingerstick Hct since Hct is three times larger in magnitude than Hb. As can be seen in Table 2, for all six centers for any fingerstick Hb, females have a lower predicted venous Hb than same-center male donors by 0.53 to 0.81 g/dL (parameter c). Donors who have AIS or have IDE without AIS have a lower predicted venous Hb than do same-center donors with replete iron stores (parameter d or e, respectively), 0.32–1.06 g/dL lower predicted venous Hb for AIS and 0.08–0.33 g/dL lower for IDE without AIS. The sex and the iron status effects on the predicted Hb are additive. As an example of the use of this model, for Center F, a female donor with AIS and a fingerstick Hb of 13.0 g/dL would have a predicted venous Hb of:

$$13.55-0.66-0.52+0.58\times(13.0-12.5)=12.66\ \text{g/dL}.$$

Shown graphically, in the models for each center male and female donors with different iron stores (replete, AIS, and IDE without AIS) have parallel regression lines (Figs. 2A and 2B). Given the same fingerstick Hb or Hct value, males at all six centers have higher predicted venous values than females and iron-replete donors have higher predicted venous values than iron depleted donors. Figures 2A and 2B illustrate the model for Center F. Figures for the other centers are similar.

Also shown in Figs. 2A and 2B are the lines of equality, where fingerstick and venous Hb results are equal. The point where each regression line intersects the line of equality is the crossing point Hb (or Hct) level that separates venous Hb values that are higher than fingerstick values (below the crossing point) from venous Hb values that are lower than the fingerstick values (above the crossing point). For Center F the crossing point Hb is 15 and 13.4 g/dL for iron-replete men and women, respectively. For the other five centers, comparable crossing point Hb levels varied considerably, for men from 13.2 to 19.1 g/dL and for women from 11.7 to 13.4 g/dL. At each blood center, these crossing points for iron-depleted donors were lower than for iron-replete donors (see, for example, Figs. 2A and 2B). If for a given donor group, the crossing point falls below the current 12.5 g/dL Hb deferral cutoff, the estimated venous Hb for a donor is lower than the fingerstick Hb.

Consequently, fingerstick-venous differences seen at the observed deferral cutoff fingerstick Hb or Hct of 12.5/38 will differ from the overall differences across all donors shown in Fig. 1. To illustrate these differences at the fingerstick Hb or Hct values of 12.5/38, Tables 3 and 4 show predicted venous Hb values for a donor with “just passing” fingerstick Hb or Hct. Importantly, these regression models indicate that for a given fingerstick result, the expected venous Hb value is 0.5 to 0.8 g/dL lower for women compared to men and lower by an additional 0.3 to 1.1 g/dL for donors with AIS compared to iron-replete donors. Also shown in Tables 3 and 4 is the 1 standard deviation (SD) CI around the predicted venous Hb. Approximately 16% of donors with a given sex and iron status and fingerstick Hb of 12.5 g/dL would be expected to have an actual venous Hb below this range. An acceptable fingerstick value for males usually corresponds to a venous Hb above 12.5 g/dL, although some males with iron depletion (and below 1 SD of the predicted value) had venous Hb below 12.5 g/dL (see Table 4 and below). Fingerstick screening for Hb or Hct was less accurate as a predictor of acceptable venous Hb for females and was particularly unreliable for females with IDE without AIS and especially female donors with AIS (see Table 3 and below).

Center E had lower predicted venous Hb values than the other five centers for any measured fingerstick value. However, the described relationship between males and females and donors with different iron status was maintained at Center E, as at the other five centers (Table 2).

Frequency of misclassified donors

The frequency with which donors were accepted but had actual venous Hb values less than 12.5 g/dL (misclassified donors) was determined by examination of the actual venous Hb measurements (rather than the projected value from the regression models) of all 2425 enrolled RISE donors (Table 5). Overall, only 1.5% of iron-replete males were misclassified. Comparable rates were 1.9% for males with IDE but not AIS, but 24.6% for males with AIS. The misclassification rate for females was much higher: 10.6% for iron-replete females, 19.6% for females with IDE but not AIS, and 40.2% for females with AIS.

DISCUSSION

Our study of the enrollment Hb data from the RISE study shows that fingerstick Hb or Hct measurement systematically overestimates expected venous values in severely iron-depleted donors. This systematic bias, along with variability in fingerstick measurements, leads to a high prevalence of donors accepted with venous Hb levels below the donation cutoff, especially among women and men with severe iron depletion. These findings hold for four different test methods at six blood centers and are of significant concern.

Use of capillary blood samples to determine donor Hb as part of the donor qualification process is a time-honored tradition at blood centers. Capillary samples compared to venous samples are known to have reduced precision and to provide less accurate Hb values. Nevertheless, because venous sampling to determine donor eligibility is impractical, efforts to increase the accuracy of capillary Hb measurements are important.

Improvements were made with the determination that earstick capillary samples were particularly imprecise and gave values that were substantially higher than finger-stick samples. Because of this, the AABB Standards were changed to require the use of fingerstick (or venous) sampling to determine donor Hb or Hct.[10]

Recently, improved cost-effective devices for determining blood donor Hb or Hct have been developed.[11] These devices are replacing the use of copper sulfate whole blood density determination, which provides only a qualitative assessment of Hb. However, difficulties with individual donor Hb or Hct determinations have persisted and have been variously attributed to the new instruments or to poor capillary sampling techniques or erroneous use of equipment.

Recently Tong and colleagues[3] in Ireland studied the relationship of fingerstick to venous Hb measurements in all presenting donors falling close to the Irish blood donor deferral cutoff (fingerstick Hb 12.0–12.4, female; 13.0–13.4, men). In general, they found that venous Hb was higher than fingerstick Hb, apparently at odds with our findings. However, their population was not enriched in iron-depleted blood donors as was the RISE study, nor did they determine the iron status of their donors. Further, by reporting only mean differences in Hb, they failed to emphasize their minority of donors (13.4% of females and 6.2% of males) whose fingerstick Hb was higher than their venous Hb. Based on our results, we presume that these donors might represent their more active and more iron-deficient donors, thereby making their findings consistent with ours. In support of this hypothesis, their small companion study of first-time donors unselected by Hb level showed similar fingerstick-venous differences to those we found in iron-replete donors (Figs. 2A and 2B).[3]

The RISE study provided a well-characterized data set to comprehensively analyze the relationships between fingerstick and venous donor Hb values, sex, and iron stores at six different blood centers, using four different fingerstick Hb or Hct techniques.

In support of the RISE study and important for this analysis, it was necessary for some postdonation venous Hb measurements to be converted to expected predonation values. At the time that RISE was conducted, the six centers were in conversion from exclusively postdonation samples to exclusively predonation sampling. A multivariable model was developed which used donor weight and postdonation venous Hb values to convert the Hb to a predonation venous sample equivalent. Importantly the model evaluated donor sex, among other variables, and determined that sex was not an independent predictor when weight was included in the model.

Fingerstick and other capillary samples are dependent on the nature of the microvasculature at the point of sampling. It is presumably for this reason that earstick and fingerstick samples vary. Iron depletion has been shown to change vascular reactivity to blood pressure cuff occlusion.[12] We hypothesized that sex and iron status might similarly influence the microvasculature and, consequently, the nature of the capillary sample. To test this hypothesis, we developed a multivariable model to predict venous Hb from the fingerstick Hb or Hct, using center, sex, and the presence or absence of iron depletion at two levels of severity, AIS (more severe) and IDE without AIS.

We found that blood center was an independent predictor of venous Hb from the fingerstick Hb. However, the fact that the direction of the relationship between fingerstick and venous Hb was consistent across all six centers substantiates the generalizability of our findings to other US blood centers. The quantitative differences between the six centers could be due to different methods used to measure fingerstick Hb and/or different mixtures of donation postures at the time of sampling (recumbent vs. semi-recumbent), which are known to affect fingerstick-venous differences.[13] Consequently, we developed a separate linear regression model for each of the six blood centers. We further developed these six center-specific linear regression models to include sex and three levels of iron stores: AIS, IDE without AIS, and iron replete. To illustrate the importance of these relationships, we then predicted the venous Hb for a “just passing” donor with a fingerstick Hct of 38% or Hb of 12.5 g/dL. As can be seen in Tables 3 and 4, there is a substantial male-female difference at the fingerstick acceptance cutoff, with males having predicted venous values 0.5 to 0.8 g/dL (depending on the blood center) higher than females. Of particular concern, donors with AIS have predicted venous Hb of 0.3 to 1.1 g/dL lower than do iron-replete donors. Also shown in Tables 3 and 4 are the lower 1 SD limits for predicted venous Hb. As can be seen for women and for men with AIS, the lower 1 SD at all six centers is below 12.5 g/dL, implying that a substantial number of donors in these categories will have a measured venous Hb of less than 12.5 g/dL. Interestingly, these findings were relatively independent of the analytical instrument used by blood centers to measure fingerstick Hb.

The result of this systematic sex and iron status bias in the ability of fingerstick to predict venous Hb is that the very donors at greatest risk of donating while anemic, women and both sexes with iron depletion, are most likely to be incorrectly accepted as donors by fingerstick screening. Clearly, these differences call into question the ability of fingerstick Hb measurement in routine use at blood centers to detect iron-depleted and/or anemic donors. Illustrative of this is the actual incorrect acceptance rate at the six centers in the RISE study. Women and iron-deficient donors were frequently accepted as donors, despite having venous Hb values below 12.5 g/dL. We found few accepted males without AIS who had a venous Hb value under 12.5 g/dL. In contrast, the rates of misclassified accepted donors were 24.6% for males with AIS, 19.6% for females with IDE but without AIS, and 40.2% for females with AIS. As previously described for the RISE study[14] lower overall mean Hb values were found in these latter groups of donors, which contributed to the number of donors we found with low venous Hb values (males with replete iron had mean venous Hb 15.0 g/dL, males with IDE without AIS 14.6 g/dL, males with AIS 13.2 g/dL, females with replete iron 13.4 g/dL, females with IDE without AIS 13.2 g/dL, and females with AIS 12.7 g/dL). Thus the high rate of misclassified donor acceptance across RISE is not solely due to fingerstick Hb measurement but may in part be due to the way the cohorts were recruited. Because the RISE cohorts were selected to increase the representation of frequent, often iron-depleted blood donors, the prevalence of misclassified donors in the entire US donor population cannot be directly projected from this study.

The study had several potential limitations. First, it was necessary to convert the postdonation sample results to predonation Hb. However, some centers sampled only before

donation yet had similar fingerstick-venous model results as the other centers. Furthermore, it would be very unlikely that postdonation venous samples were obtained preferentially from either sex or from donors with or without iron depletion. Thus the core findings of the six blood center models are expected to be independent of venous sample source. Second, HemoCue Hb measurement devices rather than the more accepted method of an autoanalyzer were used for venous Hb determination in the primary analysis. However, four centers used identical autoanalyzers (Advia) for additional analyses and similar models developed with these results showed similar effects of sex and iron status on the fingerstick-venous difference (data not shown). Furthermore, the HemoCue method is a highly accurate point-of-care test when applied to venous samples and widely used by clinicians in the United States. Third, seasonal differences have previously been reported in blood donor Hb levels[15,16] and the Tong study[3] claimed a seasonal difference in mean fingerstick-venous differences. Our enrollment period was December through June. Recruitment of the four cohorts, representing both sexes and two extremes of blood donation and iron status, occurred essentially evenly through this period. Further, two of the six RISE blood centers operate in climates with significantly diminished seasonal temperature differences compared to centers that reported these seasonal findings. Thus seasonal influences could not have caused the effects of sex and iron status seen in all six blood centers. It is possible but highly unlikely that had our study been performed in the summer and fall rather than the winter and spring the models developed might be somewhat different. Finally there are variable data in the literature, regarding the relationship between fingerstick and venous Hb, some of which contradict the observations of this study. Most of these studies were performed on small numbers of donors and/or on postdonation venous samples without correction and, except for the Tong study,[3] none considered that the fingerstick-venous difference might be related to the level of Hb. Nevertheless, it would be prudent to verify our predictive model by repeating this study in a prospective fashion on a different group of donors.

The causes of the overall findings reported here are uncertain, but likely relate to changes in the RBC and/or changes in the microvasculature with body iron depletion. Changes in RBC size and deformability may contribute to these findings. The interesting effect of iron deficiency in blood donors on vascular reactivity, which has been cited as a possible mechanism for improved cardiovascular health in frequent blood donors may reflect similar changes in the microvasculature that could affect the fingerstick sample.[12]

These results are of importance to the current discussion about changing the qualifying Hb values for blood donation.[17] If, in fact, fingerstick underestimates the venous Hb of iron sufficient males, this suggests that there is no need to increase the current 12.5 fingerstick cutoff to 13.5 g/dL for first-time males (none of whom are likely to be iron deficient) and for the majority of male frequent donors (84% of frequent male donors in the RISE cohort did not have AIS).[14] On the other hand, for iron-depleted males (16% of frequent male donors in the RISE enrollment data) fingerstick may overestimate venous Hb (Table 5). Since iron depletion is related to 2-year donation history[14] an increased Hb cutoff could be reserved for male donors with many recent donations. However, fingerstick in iron-deficient females is less accurate and can overestimate venous Hb by 1 g/dL or more. Further, 25% of enrolled frequent female donors in RISE had AIS and 66% had IDE.[14] Thus, consideration to reduce the female fingerstick cutoff to 12 g/dL may not be appropriate and should only be considered for female donors who are likely or known to be iron replete.

Standard setting agencies should take the described bias inherent in fingerstick determination into account in establishing blood donor Hb or Hct requirements. Measurement of Hb is of limited value in detecting iron depletion in blood donors, even with the most accurate Hb measurement techniques. The findings reported here make it even less likely that a fingerstick Hb deferral cutoff can be selected that efficiently prevents iron

deficiency without unnecessarily deferring iron-replete donors. Efforts to manage donor iron status should be directed toward limiting donation intensity or supplementing iron, supported by direct measurement of iron stores if necessary. Current Hb requirements should be designed to detect overt anemia in blood donors. Given that blood donation causes severe iron deficiency in a significant proportion of frequent donors[14] and that iron deficiency can lead to anemia, it is especially important that the fingerstick measurement artifact we have observed in iron-depleted donors not result in acceptance of donors with iron deficiency anemia by blood centers.

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ABBREVIATIONS

AIS	absent iron stores
FT/RA	first time or reactivated
IDE	iron-deficient erythropoiesis
sTfR	soluble transferrin receptor

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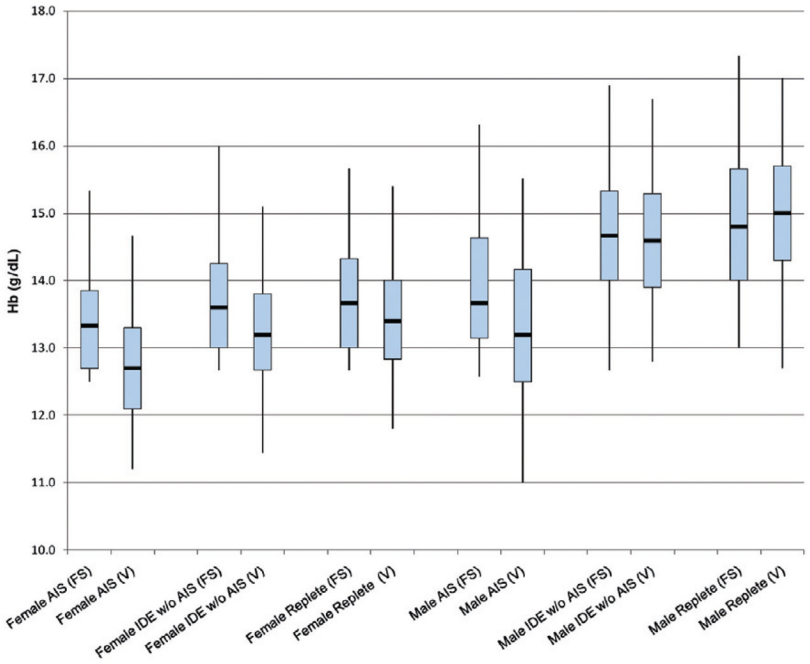

Fig. 1.

Fingerstick (FS) and venous (V) Hb values observed in 2425 RISE donors, by sex and iron status. Shown are aggregated data for donors from all six centers. FS Hct values at four centers are converted to Hb by dividing by 3. Each bold line represents the median for the group. The box represents the 25th through the 75th percentile, and the lines the 2.5th through the 97.5th percentiles for each group.

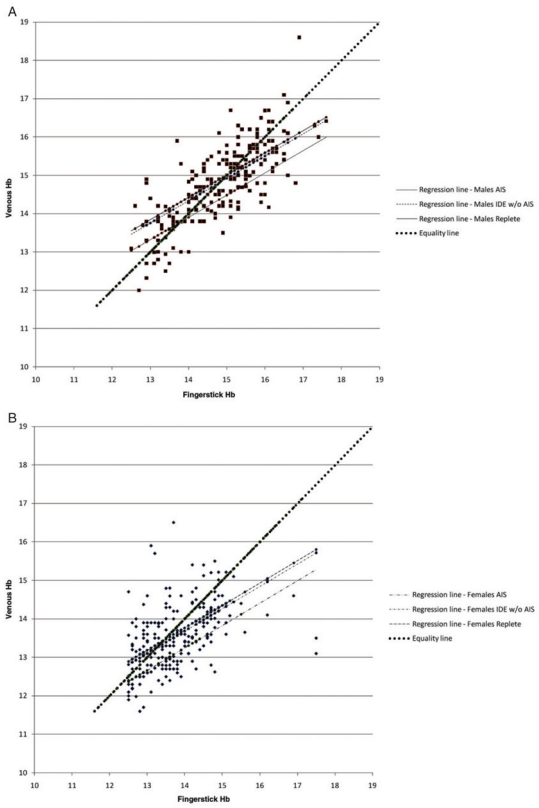

Fig. 2.

Linear regression model to predict venous Hb from fingerstick Hb. (A) Males at Center F. (B) Females at Center F. Each dot represents a single donor. Each line is the regression curve for one of three levels of iron stores. Line of equality is plotted for fingerstick Hb = venous Hb.

TABLE 1

Donor fingerstick qualification methods at the six REDS-II centers

Blood center	Hb or Hct	Device
A	Hct	Hematastat*
B	Hct	Hematastat
C	Hct	Hematastat
D	Hct	UltraCrit*
E	Hb	HemoCue B†
F	Hb	HemoCue Donor Checker†

*Separation Technologies, Sanford, FL.

†HemoCue, Inc., Cypress, CA.

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TABLE 2

Model parameters (and standard errors) from center specific regressions to predict venous Hb from fingerstick Hb or Hct

Fingerstick type	Center ID	Reference (replete males) Parameter a	Fingerstick slope coefficient Parameter b	Female Parameter c	AIS Parameter d	IDE without AIS Parameter e
Hct	A	13.79 (0.78)	0.26 (0.02)	−0.53 (0.09)	−1.06 (0.11)	−0.32 (0.09)
	B	13.63 (0.86)	0.20 (0.02)	−0.81 (0.10)	−0.87 (0.13)	−0.33 (0.10)
	C	13.73 (0.87)	0.22 (0.02)	−0.80 (0.12)	−0.93 (0.16)	−0.12 (0.12)
	D	13.28 (0.84)	0.21 (0.01)	−0.69 (0.10)	−0.32 (0.13)	−0.33 (0.10)
Hb	E	12.77 (0.69)	0.60 (0.03)	−0.58 (0.08)	−0.50 (0.10)	−0.16 (0.08)
	F	13.55 (0.75)	0.58 (0.04)	−0.66 (0.08)	−0.52 (0.11)	−0.08 (0.08)
Predicted venous Hb males replete			a + b × (fingerstick Hb − 12.5) *or* a + b × (fingerstick Hct − 38)			
Predicted venous Hb males IDE without AIS			a + e + b × (fingerstick Hb − 12.5) *or* a + e + b × (fingerstick Hct − 38)			
Predicted venous Hb males AIS			a + d + b × (fingerstick Hb − 12.5) *or* a + d + b × (fingerstick Hct −38)			
Predicted venous Hb females replete			a + c + b × (fingerstick Hb − 12.5) *or* a + c + b × (fingerstick Hct − 38)			
Predicted venous Hb females IDE without AIS			a + c + e + b × (fingerstick Hb − 12.5) *or* a + c + e + b × (fingerstick Hct − 38)			
Predicted venous Hb females AIS			a + c + d + b × (fingerstick Hb − 12.5) *or* a + c + d + b × (fingerstick Hct − 38)			

TABLE 3

Predicted mean (and prediction interval*) venous Hb (g/dL) for a female donor with fingerstick Hct of 38 or fingerstick Hb of 12.5 g/dL†

	Venous Hb (g/dL)					
	Female replete		Female IDE without AIS		Female AIS	
Center	Predicted	(68% prediction interval*)	Predicted	(68% prediction interval*)	Predicted	(68% prediction interval*)
A	13.26	(12.48, 14.04)	12.94	(12.16, 13.72)	12.20≠	(11.42, 12.98)
B	12.87	(12.02, 13.72)	12.54	(11.68, 13.39)	12.00≠	(11.15, 12.85)
C	12.93	(12.06, 13.80)	12.81	(11.94, 13.68)	12.00≠	(11.12, 12.88)
D	12.59	(11.75, 13.43)	12.25≠	(11.41, 13.09)	12.27≠	(11.43, 13.11)
E	12.19≠	(11.50, 12.88)	12.03≠	(11.33, 12.72)	11.69≠	(11.00, 12.38)
F	12.89	(12.15, 13.63)	12.81	(12.07, 13.55)	12.37≠	(11.63, 13.11)

*68% prediction interval is mean ± 1 SD.

†All values are calculated from the regression models in Table 2.

≠Values under the qualifying level of 12.5 g/dL.

TABLE 4

Predicted mean (and prediction interval*) venous Hb (g/dL) for a male donor with fingerstick Hct of 38 or fingerstick Hb of 12.5 g/dL†

	Venous Hb (g/dL)					
	Male replete		Male IDE without AIS		Male AIS	
Center	Predicted	(68% prediction interval*)	Predicted	(68% prediction interval*)	Predicted	(68% prediction interval*)
A	13.79	(13.01, 14.57)	13.47	(12.69, 14.25)	12.73	(11.95, 13.51)
B	13.68	(12.82, 14.54)	13.35	(12.49, 14.21)	12.81	(11.95, 13.66)
C	13.73	(12.86, 14.60)	13.61	(12.73, 14.50)	12.80	(11.92, 13.68)
D	13.28	(12.44, 14.12)	12.95	(12.10, 13.81)	12.96	(12.11, 13.81)
E	12.77	(12.08, 13.45)	12.61	(11.91, 13.31)	12.28‡	(11.58, 12.98)
F	13.55	(12.80, 14.30)	13.47	(12.72, 14.22)	13.03	(12.28, 13.78)

*68% prediction interval is mean ± 1 SD.

†All values are calculated from the regression models in Table 2.

‡Values under the qualifying level of 12.5 g/dL.

TABLE 5

Number (%) of fingerstick accepted RISE donors with venous Hb under 12.5 g/dL by sex and iron status

	Iron status		
Sex	**Replete**	**IDE without AIS**	**AIS**
Females	66/623 (10.6)	76/388 (19.6)	96/239 (40.2)
Males	12/791 (1.5)	5/258 (1.9)	31/126 (24.6)