Prevalence and determinants of declining versus stable hemoglobin levels in whole blood donors

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BACKGROUND: A too short recovery time after blood donation results in a gradual depletion of iron stores and a subsequent decline in hemoglobin (Hb) levels over time. This decline in Hb levels may depend on individual, unobserved characteristics of the donor.

STUDY DESIGN AND METHODS: We used a data set of 5388 Dutch blood donors from the Donor InSight study. The statistical analysis is based on a Bayesian growth mixture model, which assumes that each donor belongs to one of several groups. Each group implies a different Hb trajectory, and donors with similar longitudinal trajectories belong to the same group. Analyses were performed for male and female donors separately.

RESULTS: For both sexes the model identified four groups of donors. Stable Hb trajectories were found among 14% of male donors and 15% of female donors; declining Hb trajectories were observed in the remaining groups of donors. The percentage of donor deferrals differed strongly between groups.

CONCLUSION: The model can be used to predict to which group a donor belongs, and this prediction can be updated after each donation. This is of high practical importance because early identification of donors with declining Hb levels could help to tailor donation intervals and to prevent iron deficiency and donor deferrals.

Whole blood donation poses a risk of iron deficiency to blood donors.[1] A whole blood donation implies a loss of red blood cells (RBCs) and iron, resulting in a temporary decrease in hemoglobin (Hb) levels. In healthy donors with sufficient iron stores this may not be problematic. Iron balance is achieved by more efficient absorption of dietary iron in blood donors.[1] Repeated donations could, however, deplete iron stores, leading to iron depletion and ultimately anemia.[1,2]

Because healthy donors give blood voluntarily, iron depletion and subsequent anemia should be prevented as much as possible. In the Netherlands, several measures were taken to prevent donors from becoming anemic. Already in the 1940s, it was estimated that the body needs approximately 50 days to recover to predonation Hb levels.[3,4] Therefore, guidelines impose a minimum interval of 56 days between donations, with a yearly maximum of

ABBREVIATIONS: BIC = Bayesian information criterion; MCMC = Markov chain Monte Carlo.

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five donations for men and three for women.[5] Furthermore, the iron status of blood donors is assessed before donation. This is done by measuring whether Hb levels are at least 8.4 mmol/L (135 g/L) for men or at least 7.8 mmol/L (125 g/L) for women.[6] Donors with Hb levels below these cutoffs, or 1.5 mmol/L (24 g/L) below the previous donation level, are temporarily deferred from donation. Deferrals can be demoralizing for donors and have a negative effect on donor return rates.[7-9] Hb deferrals thus decrease the cost-effectiveness of blood supply, because 1) testing and deferring a donor is expensive, 2) for every deferred donor another donor needs to be invited to reach collection targets, and 3) lapsing donors need to be replaced.[10]

Both recent and historical data suggest that individual donors may differ in their recovery from blood donation, indicating that a donation interval of 56 days may not be desirable for each individual donor.[3,11] This may result in gradually declining Hb levels over time, which are currently not detected until the donor meets any of the deferral criteria. Distinguishing between donors with different Hb trajectories after repeated blood donations may help to select donors and tailor their donation intervals to prevent anemia. To our knowledge, no data on individual Hb trajectories exist in the literature. Therefore, an objective of this study is to investigate whether different Hb trajectories can be distinguished in whole blood donors. Also, we determine whether the type of trajectory is associated with the probability of deferral due to low Hb. Finally, we aim to predict the type of Hb trajectory of a newly registered blood donor.

MATERIALS AND METHODS

Study population

For blood collection, all measured data are entered into the blood bank computer system (e)PROGESA (MAK-SYSTEM International Group, Paris, France). Before every donation, Hb and other variables are required to check whether the prospective donor is eligible to donate. In the Netherlands, a newly registered donor is not allowed to donate blood at the first visit, which consists of a health check only. At every subsequent visit, donors who pass all eligibility checks can donate 500 mL of whole blood. For the present study, data are extracted from (e)PROGESA. The Donor InSight data set is used for data analysis. The Donor InSight data set is a self-administered questionnaire study aimed at gaining insight into characteristics and motivation of the Dutch donor population.[12] Our analysis comprises whole blood donors who were registered as a new donor in the period January 1, 2005, to December 31, 2012. To be included in the study, they should have at least one visit after the first donation. A total of 5388 donors (1902 male and 3486 female donors) fulfilled these criteria. The Donor InSight study was approved by the Medical Ethical Committee Arnhem-Nijmegen in the Netherlands, and all participants gave their written informed consent.

Data

Hb levels were routinely measured in predonation finger stick capillary samples using a photometer (HemoCue, Angelholm, Sweden) as a part of the donor health assessments. All measured Hb levels from the first Hb measurement up to and including the last donation in 2012 were used for the analysis, with the following exceptions: 1) If the donor was deferred for low Hb at one or more of the visits, then Hb levels up to and including the Hb level measured at the first visit that resulted in a deferral were used. 2) Whole blood donors may change from giving whole blood to donating plasma or vice versa. In that case, only Hb levels measured at whole blood donations before the first plasma donation were used in the analyses. 3) Donors may quit donating and register as a new donor again after some period. For these donors only the Hb measurements from the first donor career were used. Based on these criteria 25,881 measurements were excluded from the entire 83,082 donations of these 5388 donors.

Statistical analysis

To capture the longitudinal trajectories of Hb levels and the variation in these trajectories between donors, we implement a growth mixture model.[13,14] This model assumes that each donor belongs to one of several subgroups (known as latent classes in statistical terminology). Using this method, it is inferred from the data to which class each donor belongs. The model assigns each donor to one of several groups, in such a way that donors with similar Hb trajectories are in the same group, and that the groups are most different from each other in terms of the Hb trajectory. The classes typically do not capture the entire variation in the Hb trajectories. To capture the remaining heterogeneity among donors in the same class, the Hb trajectory is assumed to follow a linear mixed model. The outcome in the linear mixed model is the Hb level. The predictors are age[15]at the first visit, season[16,17]of the visit (a binary covariate, i.e., the cold season includes fall and winter and the warm season includes spring and summer), a linear and quadratic effect of the time since the previous donation,[18] and the number of donations in the past two years.[5] Male and female donors have different Hb profiles; therefore, the data for men and women are analyzed separately.

Random intercepts and random slopes for the number of donations in the past 2 years are used to capture the heterogeneity between donors in the same class. One of the latent classes is assumed to contain only donors with a stable Hb trajectory. This constraint enables us to

estimate the percentage of donors with a stable trajectory. Finally, we allow latent class membership to depend on age and the Hb level at the screening visit.

The models are estimated using a Bayesian approach with Markov chain Monte Carlo (MCMC) sampling. The number of latent classes in the growth mixture model is based on the Bayesian information criterion (BIC).[19,20] Kaplan-Meier (K-M) analysis is used to compare the classes with respect to the number of donations until the first deferral due to low Hb.

Further technical details regarding the linear mixed model, the growth mixture model, and the model for latent class membership are given in the Appendix. Statistical analyses are performed using Jags (3.4.0)[21] and R (3.1.0).[22]

TABLE 1. Descriptive statistics of the Donor InSight data set based on 1902 male and 3486 female donors*

Variable	Male donors	Female donors
Donors deferred at least once due to low Hb	18.4	32.3
Donations in cold season (fall and winter)	49.9	49.5
Age at screening visit (years)	34.8 (24.1-45.8)	29.4 (21.6-42.2)
Number of donations	9 (4-16)	5 (2-9)
Hb level at screening visit (mmol/L)	9.4 (9.0-9.9)	8.4 (8.0-8.8)
Interdonation interval (days)	90 (74-126)	138 (120-188)

* Dichotomous variables are presented as percentages, and the other variables are presented using medians and interquartile ranges.

Predicting Hb trajectory

A useful feature of the growth mixture model is that it can be used to predict to which latent class a donor belongs, and these predictions can be made in a dynamic way. At the screening visit, the prediction is based only on the baseline Hb level and age. At each subsequent visit, the prediction is updated by taking into account the newly observed Hb level for that person. The donors are then assigned at each visit to the class with the highest probability, that is, the class that best fits the observed Hb levels given the donor's age and sex (see the Appendix for more explanation of this procedure).

RESULTS

Table 1 presents descriptive statistics of the Donor InSight data set. Figures 1A and 1B show the Hb level profiles of male and female donors, respectively. These graphs show the heterogeneity of Hb level trajectories. We emphasized the profiles of two donors with different trajectories (Donor I, a donor with a fast Hb recovery or stable Hb trend after several successive donations; Donor II, a donor with a slow Hb recovery or declining trajectory in Hb levels after several successive donations).

Based on the BIC, at least four classes are needed for both sexes. A model with five classes has slightly better BIC values, but the additional class has a very small size (1% for males and 5% for females). Therefore, we selected a model with four classes for both sexes.

Table 2 presents the main characteristics of the different latent classes, and Table 3 presents the parameter estimates of the growth mixture models with four latent

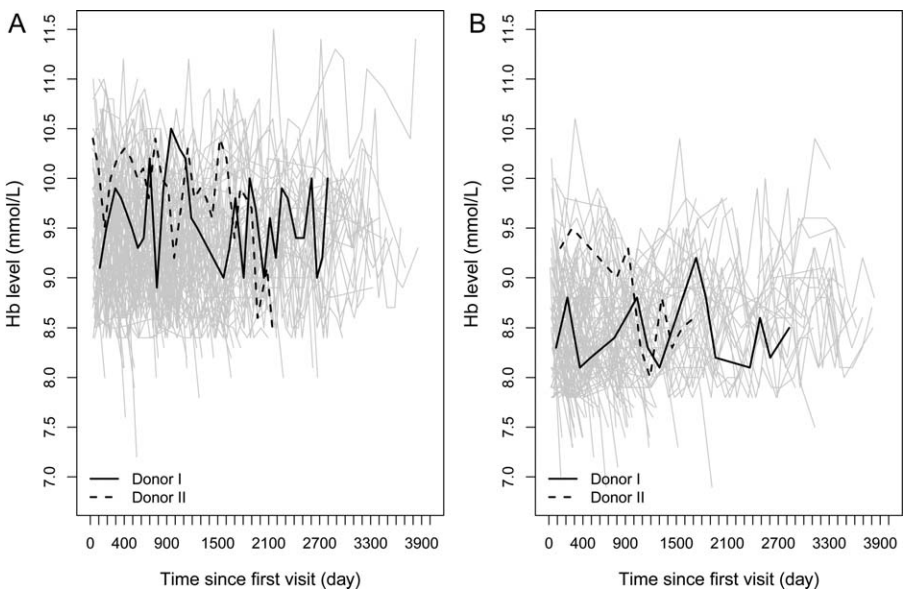

Fig. 1. Hb level profiles for male (A) and female (B) donors. The solid and dashed lines indicate different types of Hb trajectories; that is, Donor I represents a stable Hb trajectory and Donor II represents an unstable trajectory.

TABLE 2. Descriptive statistics of the Donor InSight data set by sex and latent class of the growth mixture model*

	Male donors				Female donors			
Variable	Class I	Class II	Class III	Class IV	Class I	Class II	Class III	Class IV
Size of the class	13.5	37.9	37.7	10.9	15.4	43.5	28.4	12.7
Donors deferred at least once due to low Hb	39.3	21.6	10.6	8.2	66.6	35.4	16.6	15.8
Interdonation interval (days)	91 (76-140)	89 (74-124)	90 (74-126)	87 (74-119)	137 (119-178)	139 (120-189)	137 (120-185)	138 (120-194)
Number of donations	7 (2-13)	9 (5-16)	10 (5-17)	11 (5-18)	2 (1-5)	4 (2-9)	6 (3-11)	6 (3-9)
Hb level at screening visit (mmol/L)	8.7 (8.5-8.9)	9.2 (9.0-9.4)	9.7 (9.4-10.0)	10.4 (10.1-10.7)	7.8 (7.6-8.0)	8.2 (8.0-8.5)	8.7 (8.5-9.0)	9.3 (9.1-9.6)
Age at screening visit (year)	39 (29-51)	36 (26-48)	32 (24-43)	33 (24-44)	43.5 (33-52)	29 (22-41)	27 (21-40)	23 (20-31)

* Dichotomous variables are presented as percentages, and the other variables are presented using medians and interquartile ranges.

classes. The latent classes can be interpreted using the results of these two tables. To allow for an easy comparison of classes between sexes, we sorted the classes based on the predicted Hb level at the first visit. For both sexes, Class I represents donors with a stable Hb level. A total of 13.5% of the male donors are in Class I. Since these donors have a relatively low mean Hb level at the screening visit (8.7 mmol/L), there are 39.3% deferrals in this group. Class II (37.9% of the male donors) shows a relatively slow decline of Hb level, but also a higher initial mean Hb level than in Class I (9.2 mmol/L), resulting in 21.6% deferrals. In Class III (37.7% of the male donors) the Hb levels show a moderate decline with successive donations. However, because the initial mean Hb level of this group is relatively high (9.7 mmol/L), only 10.6% of the donors are deferred. Finally, Class IV (10.9% of the male donors) has a sharp decline in the Hb level, but the lowest percentage of deferrals (8.2%), due to the very high initial average Hb level (10.4 mmol/L).

The results for female donors were similar. Class I (i.e., the stable class) contains 15.4% of the female donors. These donors have a low mean Hb level at the screening visit (7.8 mmol/L), resulting in 66.6% deferrals. Class II (43.5% of the female donors) exhibits a slow mean decline of Hb level, but also a higher initial mean Hb level than in Class I (8.2 mmol/L), resulting in 35.4% deferrals. Class III (28.4% of the female donors) shows a moderate decline with successive donations, but because the initial mean Hb level is relatively high (8.7 mmol/L), there are only 16.6% deferrals. Finally, Class IV (12.7% of the female donors) shows a very sharp decline in the Hb level, but this class has the lowest percentage of rejected donors (15.8%), due to the very high initial mean Hb level (9.3 mmol/L).

From Table 3 we conclude that, for male donors, age at baseline is less strongly associated with Hb level than for female donors where age at baseline has a positive effect on Hb level. The mean Hb level is higher in cold seasons than in warm seasons for both sexes. Furthermore, time since previous donation has a nonlinear, quadratic, effect on Hb level in both sexes, with the fastest recovery of Hb occurring shortly after a donation.

To illustrate the different deferral patterns in the four latent classes, K-M curves exhibiting the proportion of deferral in each of the latent classes for each sex separately are shown in Fig. 2. The log-rank test indicates significant difference between these curves ($p < 0.001$, for both sexes), although similar K-M curves are seen for Classes III and IV.

Figure 3 shows the prediction of the latent class for a male donor with Hb level of 8.9 mmol/L and age of 29 years at the screening visit. Using the information available at the screening visit, this donor would be predicted to belong to Class II (with 54% probability). However, using Hb levels measured at the first few visits, it is clear that this donor more likely belongs to Class I (i.e., the class

TABLE 3. Parameter estimates for male and female donors in the Donor InSight study based on the growth mixture model with four latent classes

	Male donors		Female donors	
Parameter	Estimate	95% CI	Estimate	95% CI
$Intercept_{I}$	8.88	8.81 to 8.89	7.93	7.85 to 8.00
$Intercept_{II}$	9.34	9.27 to 9.44	8.30	8.24 to 8.36
$Intercept_{III}$	9.84	9.78 to 9.94	8.77	8.68 to 8.84
$Intercept_{IV}$	10.38	10.23 to 10.59	9.13	9.02 to 9.25
$NODY2_{II}$	−0.05	−0.06 to −0.04	−0.02	−0.04 to −0.01
$NODY2_{III}$	−0.06	−0.08 to −0.05	−0.06	−0.10 to −0.03
$NODY2_{IV}$	−0.09	−0.12 to −0.07	−0.14	−0.17 to −0.10
Age_0 (year)	1.7×10^{-4}	-2.8×10^{-3} to 3.1×10^{-3}	9.6×10^{-3}	6.4×10^{-3} to 1.3×10^{-2}
Warm season	-7.7×10^{-2}	-8.9×10^{-2} to -6.5×10^{-2}	-5.2×10^{-2}	-6.2×10^{-2} to -4.2×10^{-2}
TSPD (month)	2.5×10^{-2}	1.9×10^{-2} to 3.0×10^{-2}	1.9×10^{-2}	1.4×10^{-2} to 2.3×10^{-2}
$TSPD^2$ (month)	-1.0×10^{-4}	-1.3×10^{-4} to -7.3×10^{-5}	-4.5×10^{-5}	-6.2×10^{-5} to -2.8×10^{-5}
BFD	-8.7×10^{-4}	-3.2×10^{-2} to 3.1×10^{-2}	8.3×10^{-2}	5.4×10^{-2} to 11.1×10^{-2}

CI = credible interval.

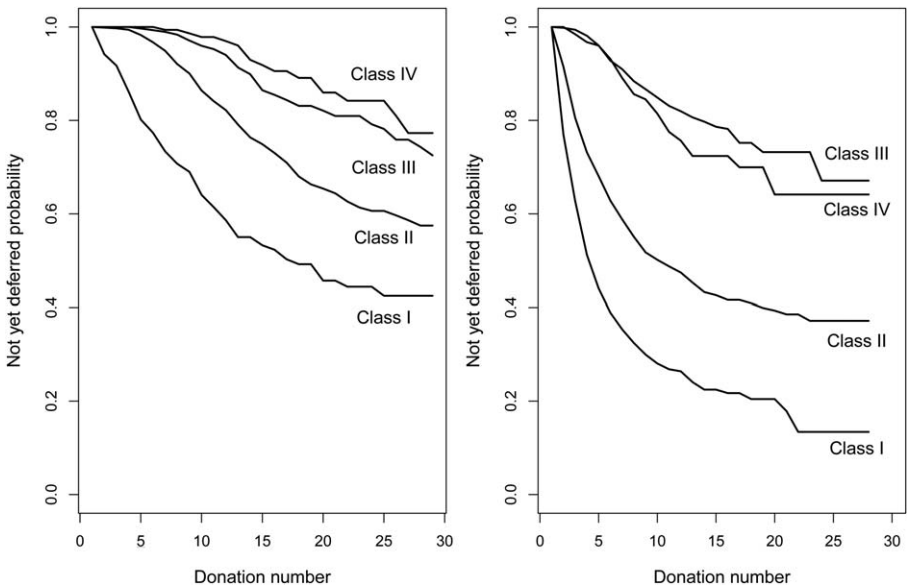

Fig. 2. K-M curves exhibiting the proportion of deferral in each of the latent classes for male donors (left) and female donors (right) separately.

with a stable trajectory). For example, after the fifth visit the donor has a probability of 91% to belong to Class I.

In the primary analysis, we used the number of donations during the past two years to model the decline in Hb level associated with successive blood donations. In a sensitivity analysis, we fitted the same model with the total number of previous donations. This variable did not improve the fit of the model. The same is true for the binary variable indicating whether the person ever had a donation prior to the previous two years.

DISCUSSION

The results of this study have shown that, for both male and female whole blood donors, Hb trajectories vary among donors. Our growth mixture model identified four types of Hb level trajectories. A minority of male and female donors (13.5 and 15.4%, respectively) are in Class I, which has a stable Hb trajectory. The donors in the other classes have a declining Hb trajectory, so that their Hb level shows a significant decline after successive blood donations. Although their Hb trajectories are stable, the donors in Class I have a relatively low initial Hb level. With increasing class number, the initial Hb level increases, as well as the speed of the decline. Donors in classes with a relatively low initial Hb level (Classes I and II) are deferred more frequently than donors in the other classes. A donor's latent class can be predicted and updated after each donation by taking into account the Hb values measured at subsequent visits.

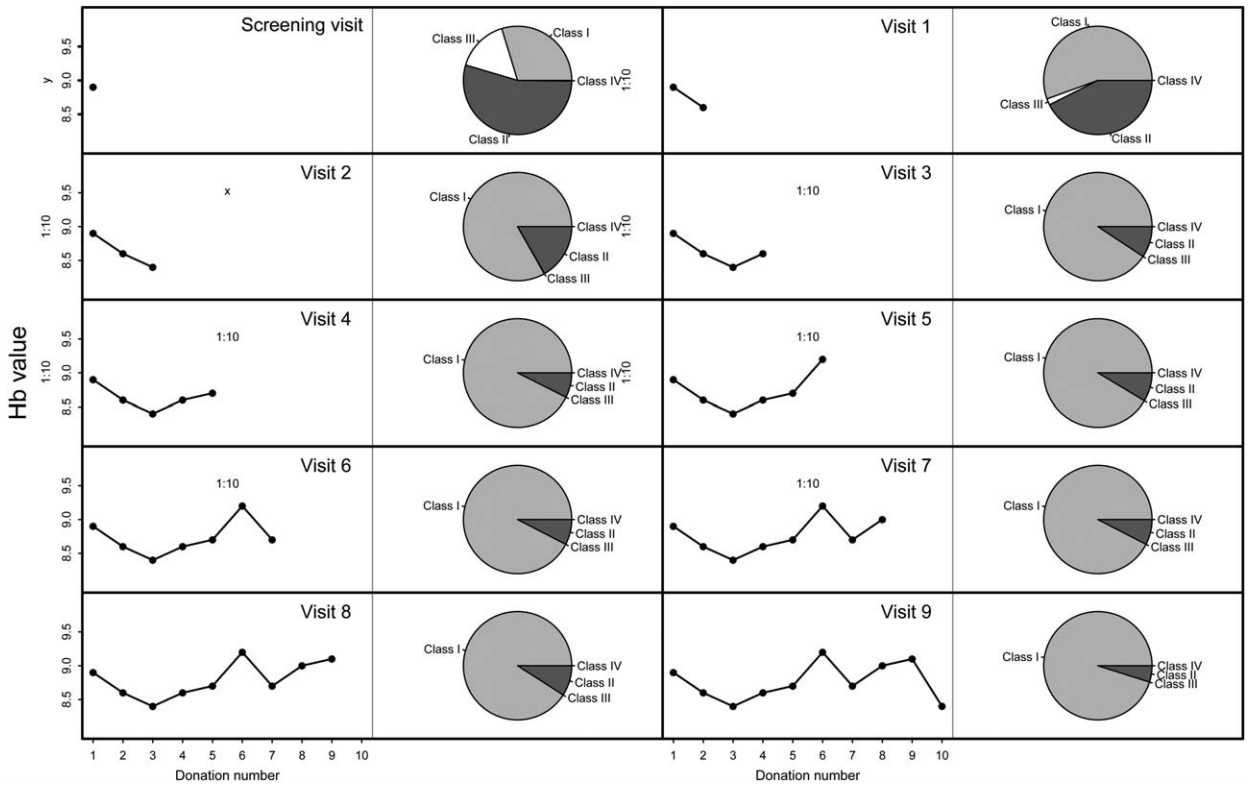

Fig. 3. Class-membership probabilities at the first nine visits of a male donor with a Hb level of 8.9 and age of 29 years at the screening visit. The first and third columns show the longitudinal trajectory of observed Hb levels. The second and fourth columns give the corresponding class-membership probabilities with a pie chart.

To the best of our knowledge, this study is the first to identify different long-term trajectories of whole blood donors using longitudinal data from blood banks. Several studies have shown that the risk of Hb deferral is higher for donors with lower Hb levels.[5,23,24] Our data add that many blood donors show declining Hb trajectories. In previous studies, prediction models for Hb values in whole blood donors have been developed. These prediction models were proposed as mixed effects models, transition models, or a combination of these two approaches for predicting Hb values in blood donors.[18,25] The current findings suggest that describing the total donor population using a single trajectory oversimplifies the complex growth patterns of this population. Instead, a growth mixture modeling approach, which accounts for different subgroups of donors, seems to be an appropriate method for capturing differences in Hb trajectories between donors. Our results showed that higher age at baseline was associated with higher Hb levels in female donors. This is consistent with earlier results and can be explained by the effect of menopause: women stop losing iron with menstruation.[5] Furthermore, we showed that on average the Hb level is higher in cold seasons than in warm seasons for both sexes. These findings are consistent with earlier results as well.[16,17]

Some donors appear to have high initial Hb levels and others do not, and some show faster declines in Hb than others. This may be due to differences in lifestyle, iron status, iron metabolism, and/or erythropoiesis.[5,26-28] Including more of this information in the models might improve the precision of the prediction of latent classes at the first few visits. For this reason we aim to include other relevant predictors, including lifestyle and genetic factors, in future research.

Individual donors belonging to different classes should potentially be approached differently. For donors with a low but stable Hb trajectory (Class I), delaying the next invitation may not help to decrease the probability of deferral. Donors with a normal initial Hb level (Class II) become at risk for deferral only with a high donation frequency, because the estimated Hb decline per donation is fairly small in this group (at most 0.09 mmol/L per donation for men and 0.14 mmol/L per donation for women). Thus for this group, the advice could be to increase donation intervals. Donors with high initial Hb levels (Classes III and IV) do not have a very high risk of Hb deferral. Changing their donation intervals may therefore not be very effective in preventing Hb deferral. Apart from Hb deferral, donors in different classes may also differ in what is healthy for them. The fact that fast Hb declines do not

necessarily lead to Hb levels below the cutoff for donation, does not mean that it does no harm. Blood donation causes a loss of iron and blood cells, which can lead to depleted iron stores and lowering of Hb levels.[29] Potential symptoms of iron deficiency include fatigue, decreased physical endurance and work capacity, and impairment in attention, concentration, and other cognitive functions.[2,30-33] Restless legs syndrome, a neurologic disorder with irresistible need to move the legs, and pica, a disorder in which a person is craving and consuming nonnutritive substances, have also been repeatedly linked to blood donation–related iron deficiency.[34-37] Future research should indicate whether adverse health effects of donation are different for donors with stable or declining Hb levels.

A major strength of the study is the large amount of routinely measured data, including many repeated measurements per donor. This allowed for detailed insights into Hb trajectories from the initial level to the end of follow-up, including the relationships with donor deferral, age, and sex. A limitation of the study is that Hb is measured by photometry in capillary blood instead of more reliable hematology analyses in venous blood.[38] Although this probably increased measurement error for single measurements, the large amount of repeated measurements likely smoothed this error. Furthermore, our results may not be generalizable to different ethnic populations or to blood banks where policies regarding Hb measurement and deferral are different. The Dutch donor population includes relatively low numbers of people from ethnic minority groups,[12] but this is very common in donor populations.[39] Policies regarding Hb deferral mainly differ in what exactly is measured, capillary or venous Hb or copper sulfate testing, and in the timing, before or after the donation. Nonetheless, cutoff values are quite similar throughout the world and the methods used in the Netherlands are very common.[38]

In conclusion, we found subgroups of donors with stable and declining Hb trajectories. These subgroups were associated with the probability of Hb deferral and can be predicted based on initial Hb levels and age. These findings are of high importance for identification of donors who could benefit from tailored donation intervals to prevent iron deficiency and donor deferrals. Future research replicating our findings and investigating health effects of declining Hb levels will help to further unravel clinical implications.

APPENDIX: GROWTH MIXTURE MODEL

Mixture modeling refers to modeling with categorical latent variables to represent different classes in a population.[40,41] In these models, class membership is not known in advance but is inferred from the data.[13,40] In growth mixture models, the principle of mixture modeling is applied in the context of a linear mixed model, so that the heterogeneity between subjects is captured by different classes and by random effects in the linear mixed models.[13] The growth mixture model for the trajectory of Hb levels of blood donors who belong to latent class k can be expressed as

$$Hb_{it|k} = \theta_{k0} + b_{ik0} + \beta_1 Age_{i0} + \beta_2 Season_{it} + \beta_3 TSPD_{it} + \beta_4 TSPD_{it}^2 + \beta_5 BFD_{it} + (\theta_{k1} + b_{ik1}) NODY2_{it} + \varepsilon_{it|k},$$

where $Hb_{it|k}$ is the Hb level at the tth observation of the ith individual, given that this individual is in latent class k. $\theta_{10}, \theta_{20}, \ldots, \theta_{K0}$ are the unknown intercepts of K latent classes. Likewise, $\theta_{21}, \theta_{31}, \ldots, \theta_{K1}$ are unknown coefficients of *NODY2* in the latent classes. To restrict the Hb trajectory to be stable in the first class, the parameter θ_{11} and the variance of the random effect b_{i11} are set to zero. We assumed that within each latent class the random effects (i.e., b_{ik0} and b_{ik1}) are multivariate normally distributed with mean zero and a class-specific variance-covariance structure. The residuals ϵ_{it} are assumed to be normally distributed and independent of the random effects.

The probability w_{ik} that the ith individual ($i = 1,\ldots,N$) belongs to latent class k ($k = 1,\ldots K$) is related to the initial Hb level and the age at the first visit using a multinomial logistic regression specification. This probability is calculated as

$$w_{ik} = P(c_i = k | Hb_{0i}, Age_{0i}) = \frac{\exp(\gamma_{k0} + \gamma_{k1} Age_{0i} + \gamma_{k2} Hb_{0i})}{\sum_{k=1}^{K} \exp(\gamma_{k0} + \gamma_{k1} Age_{0i} + \gamma_{k2} Hb_{0i})},$$

where w_{ik} is the probability that the ith individual belongs to class k given the baseline covariates. The first class is used as a reference class, and therefore the $(\gamma_k = \gamma_{k0}, \gamma_{k1}, \gamma_{k2})'$ parameters for the first class are constrained to be 0. BIC based on the marginal mean posterior of parameters was computed to determine the optimal number of latent classes.[19,20,42]

Model diagnostics

To assess model fit, we used a posterior predictive check by computing a Bayesian p value, that is, the probability that replicated data from the model could be more extreme than the observed data for an omnibus χ^2 discrepancy measure[43] to test both the distributional and latent class number assumption of the model.

The posterior distribution was determined using MCMC sampling with a single chain. We checked the convergence by monitoring trace plots and the Geweke diagnostic.[44] To check whether the number of MCMC iterations is sufficient to obtain accurate estimates, the sampling was continued until the Monte Carlo errors were less than 5% of the posterior standard deviation of each parameter.[45] The first 5000 iterations (i.e., burn-in

TABLE A1. Mean class-membership probabilities by latent class based on the Donor InSight data

	Mean of posterior probabilities							
	Male donors				Female donors			
Latent class	Class I	Class II	Class III	Class IV	Class I	Class II	Class III	Class IV
I	0.795	0.204	0.001	0.000	0.771	0.227	0.002	0.000
II	0.135	0.717	0.144	0.004	0.103	0.744	0.142	0.001
III	0.001	0.150	0.736	0.113	0.001	0.163	0.680	0.156
IV	0.000	0.001	0.191	0.808	0.000	0.008	0.121	0.780

iterations) were discarded. The posterior means and credible intervals were calculated using the remaining iterations, without thinning.

Finally, to check if donors were assigned to latent classes with good discrimination, we computed the mean posterior probability of class membership for donors. These results confirm that our model chooses the class memberships with a reasonably high posterior probability for both sexes (68%-81%; see Table 1). Misclassification only seems to occur between adjacent latent classes.

Prior for parameters

In a Bayesian model, prior distributions must be specified for all parameters. For the one-class (mixed-effects) model, noninformative proper priors (i.e., $N(0,1000)$ for the βs and inverse-gamma (0.01,0.01) for the precision) were assigned. For models with more than one class, to ensure a well-identified model, the priors for the latent class parameters (θ_{k0} and θ_{k1}) were based on the posterior means from the one-class model. To make these priors less informative, we specified large variances for them, that is, the number of donors times the variance of the posterior distribution from the one-class model.[46] In addition, for the class-membership parameters, we used normal prior distributions with mean zero and variance equal to 9/4, as was suggested by Elliott and colleagues[47] and Garrett and Zeger.[46] Finally, for the other model parameters, noninformative proper priors were assigned.

Predicting latent class membership

The values w_{ik} describe the probability that the ith donor belongs to class k given the age and the Hb level at the screening visit. As soon as information from subsequent visits becomes available, these probabilities can be updated to incorporate the new information and yield better predictions of a donor's latent class. The updated probability that individual i belongs to the kth latent class can be calculated as

$$P(c_i = k|Hb_i, Age_{0i}, Hb_{0i}, \theta_k) = \frac{w_{ik} f_k(Hb_i|\theta_k)}{\sum_{k=1}^{K} w_{ik} f_k(Hb_i|\theta_k)},$$

where $P(c_i = k|Hb_i, Age_{0i}, Hb_{0i}, \theta_k)$ is the probability that donor i belongs to the kth class given the age and the Hb level at the screening visit and the history of Hb levels for that donor. $f_k(Hb_i|\theta_k)$ is the density of Hb levels for this donor given that he or she belongs to class k.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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