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Low Hemoglobin and Recurrent Falls in U.S. Men and Women: Prospective findings from the REasons for Geographic and Racial Differences in Stroke (REGARDS) Cohort

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Abstract

Background—There are few data available on low hemoglobin levels and incident falls in the general U.S. population.

Methods—Of 30,239 Black and white U.S. adults ≥45 years old in the population-based REasons for Geographic and Racial Differences in Stroke (REGARDS) study, 16,782 had hemoglobin measured at baseline and follow-up data on falls. Hemoglobin was categorized by 1.0 g/dL increments relative to the World Health Organization cut-point for anemia (13.0 g/dL for men, 12.0 g/dL for women). Recurrent falls, defined as ≥2 falls in the 6 months following baseline were assessed during a telephone interview.

Results—Recurrent falls occurred in 3.9% of men and 4.8% of women. Compared to those with a hemoglobin 1 to 2 g/dL above the anemia cut-point the multivariable adjusted odds ratios (OR; 95% confidence interval [CI]) for recurrent falls associated with hemoglobin levels ≥3 g/dL, 2 to <3 g/dL, and 0 to 1 g/dL above the cut-point, and 0 to <1 g/dL and 1 g/dL below the cut-point were 0.73 (0.45–1.19), 0.84 (0.57–1.24), 1.29 (0.88–1.90), 1.32 (0.80–1.2.18) and 2.12 (1.23–3.63), respectively, among men (linear trend $p < 0.001$) and 1.59 (1.10–2.3), 1.24 (0.95–1.62),

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Conflict of Interest: Paul Muntner (served on an AMGEN National Nephrology Advisory Board and served as a consultant to AMGEN), Brian Bradbury (AMGEN employee), Ryan D. Kilpatrick (AMGEN employee), John J. Isitt (Amgen employee), David Warnock (member of the AMGEN National Nephrology Advisory Board), No conflict of interests for C. Barrett Bowling, Amy H. Warriner, Jeffrey R. Curtis, Suzanne Judd, Cynthia J. Brown, Richard M. Allman

1.42(1.11–1.81), 1.28 (0.91–1.80) and 1.76 (1.13–2.74), respectively, among women (linear trend $p=0.45$; quadratic trend $p=0.016$).

Conclusions—Among men, lower hemoglobin was associated with an increased risk for recurrent falls. While our findings suggest an increased risk for recurrent falls at both lower and higher hemoglobin levels among women, these findings should be confirmed in subsequent studies.

Keywords

falls; hemoglobin; gender

Falls are common in older adults, and as the U.S. population ages, they represent an increasingly important clinical and public health problem. One in three adults over 65 years of age fall each year, and approximately one in ten falls produce a serious injury such as a fracture, head injury or soft tissue injury.^{1–4} Even when serious injuries do not occur, falls negatively affect quality of life, lead to restrictions in mobility, fear of falling, functional decline and nursing home placement.^{4, 5} Those with recurrent falls are at highest risk.⁶

Several independent, modifiable fall risk factors including poor balance, decreased lower extremity muscle strength and functional impairment have been reported.⁷ However, many of the known risk factors such as age, gender, and in some cases cognitive impairment, are not modifiable. Because interventions targeting known modifiable risk factors have been shown to only reduce falls by 30%,^{8, 9} identification of additional modifiable risk factors may be important for improving fall prevention strategies and developing individualized fall prevention plans.

Anemia has been proposed as a treatable risk factor for falls, and has been shown to be associated with falls in select populations including older adults, hospitalized patients and nursing home residents.^{10–14} However, little is known about the association between hemoglobin and falls in the general U.S. population. Recurrent falls may occur years before a subsequent fall results in a serious injury. Therefore, it may be important to identify both middle-aged and older adults who are at risk for recurrent falls. In the current study, we evaluated the prospective association between hemoglobin level and recurrent falls in the large, population-based REasons for Geographic and Racial Differences in Stroke (REGARDS) study.

Methods

Study participants

The REGARDS study includes U.S. adults ≥45 years of age and was designed to evaluate the causes for the excess stroke mortality in the Southeastern U.S. and among blacks compared to whites. The study population and sampling protocol have been described in detail previously.¹⁵ Briefly, the study was designed to oversample blacks and to provide approximate equal representation of men and women. To evaluate geographic differences in stroke outcomes, 56% of the sample was recruited from the eight Southern U.S. states, often referred to as the “stroke buckle” (coastal North Carolina, South Carolina, and Georgia) and “stroke belt” (remainder of North Carolina, South Carolina, and Georgia as well as Alabama, Mississippi, Tennessee, Arkansas and Louisiana). The remaining sample was recruited from the other 40 contiguous U.S. states. Of the 30,239 black and white U.S. adults enrolled between January 2003 and October 2007, we excluded 10,358 participants without baseline hemoglobin data or those who did not complete the six month follow-up where incident falls data were collected ($n=3,099$) leaving 16,782 participants. Hemoglobin was

not collected in REGARDS prior to May 2004, resulting in the high rate of missing data for this variable. The REGARDS study protocol was approved by the Institutional Review Boards at the participating centers and all participants provided informed consent. More information on the REGARDS study is available at www.regardsstudy.org.

Data collection

The REGARDS study baseline data were collected through interview- and self-administered questionnaires and a subsequent in-home assessment. Median time between telephone interview and in home examination was 31 days (25–75th percentiles: 22 and 48 days). Of relevance to the current analysis, the following items were obtained via self-report: age, race, gender, marital status, current cigarette smoking, education, history of hypertension, diabetes, coronary artery disease, and stroke. During the in-home visit, physical measurements and collection of a fasting blood sample and urine sample were obtained. With participants in the seated position, systolic (SBP) and diastolic blood pressures (DBP) were measured twice following a standard protocol and recorded as the average for analysis. Waist circumference was measured mid-way between the lowest rib and the iliac crest with the participant standing.

Data on potential confounders including diabetes, depression, cognitive impairment, functional limitation and history of a previous fall were also obtained at baseline.^{7, 16–18} Diabetes was defined as taking insulin or oral hypoglycemic agents or either a fasting blood glucose ≥ 126 mg/dL or a non-fasting blood glucose ≥ 200 mg/dL.¹⁹ The presence of depressive symptoms was defined as a score of 4 or more on the 4-item Center for Epidemiologic Studies Depression Scale.²⁰ Cognition was assessed using the Six-item Screener which tests global cognitive function. Scores on this scale can range from 0 to 6 with lower scores indicating worse cognition and cognitive impairment defined as a score of 4 or less.²¹ The Medical Outcomes Study Short Form-12 (SF-12) was administered at baseline and includes both a physical and mental component score.²² For the current analysis, the physical component score (PCS), a measure of the impact of general health on physical functional, was used as a proxy for functional status. A self-reported history of falling within the last year was obtained at baseline.

Hemoglobin and other laboratory measures

Blood samples collected during the baseline in-home examination were shipped and centrally analyzed at the University of Vermont. Hemoglobin was measured using automated cell counting on a Beckman Coulter LH 755 Hematology Workcell (Beckman Coulter, Inc. Fullerton, CA) with a previously reported inter-assay coefficient of variation of $\pm 3.0\%$.²³ The World Health Organization defines anemia as <13.0 g/dL in men and <12.0 g/dL in women.²⁴ In order to evaluate the association between hemoglobin and recurrent falls across a broad range of values, hemoglobin was categorized above and below the WHO anemia cut-points (<1 g/dL below, 0 to <1 g/dL below, >0 to <1 g/dL above, 1 to <2 g/dL above, 2 to <3 g/dL above and ≥ 3 g/dL above) for men and women, separately (Table 1).

Serum creatinine assays were also performed at the University of Vermont, and calibrated with an isotope dilution mass spectroscopic standard. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to calculate estimated glomerular filtration rate (eGFR).²⁵ Urinary albumin and creatinine were measured at the Department of Laboratory Medicine and Pathology at the University of Minnesota, using the BN ProSpec Nephelometer from Dade Behring (Marburg, Germany).

Ascertainment of Recurrent Falls

Recurrent falls were assessed during a telephone interview conducted 6 months following baseline and defined as ≥ 2 falls since baseline. Using a modified version of the Study of Osteoporotic Fractures falls ascertainment question,²⁶ participants were asked “*Since the last time we contacted you, have you fallen and landed on the ground or floor or fallen and hit an object like a table or chair?*” Those responding in the affirmative were subsequently asked, “*How many times have you fallen in the last 6 months?*” When compared to a single fall, recurrent falls (i.e., 2 or more falls) have been shown to be more strongly associated with functional decline, fractures and nursing home placement and recognizing those with recurrent falls is emphasized by the American Geriatrics Society Fall clinical practice guideline for prevention of falls.^{4, 27}

Statistical Analyses

Characteristics of the REGARDS study population were calculated using means, medians and proportions, as appropriate, by hemoglobin category above and below the WHO anemia cut-points (< 1 g/dL below, 0 to <1 g/dL below, >0 to <1 g/dL above, 1 to <2 g/dL above, 2 to <3 g/dL above and ≥ 3 g/dL above) for men and women, separately.

The number and proportion of participants with recurrent falls was calculated by hemoglobin category for men and women separately. We also calculated the proportion with recurrent falls for men and women, separately according to age group (< 65 , 65 – 74 and ≥ 75 years). Logistic regression models were used to evaluate the association between hemoglobin category and recurrent falls stratified by sex with individuals having hemoglobin 1 to <2 g/dL above the WHO cut-point serving as the referent group. Prior studies have shown adverse health outcomes (declines in physical performance and executive functioning) among older adults at lower hemoglobin levels that are considered to be within the normal range.^{28, 29} Therefore, a hemoglobin of 1 to <2 g/dL above the WHO cut-point was chosen as the referent group. The initial model included adjustment only for age, race, and geographic region of residence. Subsequent models included further adjustment for marital status, cigarette smoking, education, waist circumference, hypertension, diabetes, coronary artery disease, stroke, depressive symptoms, cognitive impairment, eGFR and albumin-to-creatinine ratio. As a sensitivity analysis, additional adjustments were made for PCS and history of a fall (1 or more) in the year prior to baseline. We formally tested for interactions using multiplicative interaction terms for hemoglobin and gender (hemoglobin level*gender) and hemoglobin and race (hemoglobin level*race). Trends in odds ratios for recurrent falls across hemoglobin categories were calculated by assigning the median hemoglobin value for participants in the category and modelling these variables as continuous independent variables.

Next, we modeled the association between hemoglobin as a continuous variable and recurrent falls. These analyses were performed for the population overall and for subgroups defined by age (<65 and ≥ 65 years, the median age of participants in REGARDS), race, fall in the prior year (1 or more), PCS < 50 and ≥ 50 , eGFR < 60 and ≥ 60 ml/min/1.73 m², and albumin-to-creatinine ratio < 30 and ≥ 30 mg/g. For men, these analyses used the full hemoglobin range. However, as the association between hemoglobin and recurrent falls was not linear for women, the analysis of hemoglobin as a continuous variable was limited to the linear range (hemoglobin 1 to <2 g/dL above the WHO anemia cut-point and below). Data for one or more covariates were missing for 11% ($n=1,896$) of participants. Multiple imputation with five data sets was used to fill in these data.³⁰ Analyses were conducted in Stata version 11.0 (Stata Incorporated, College Station, TX).

Results

Participant Characteristics

Of the 16,782 REGARDS study participants included in this analysis, 36.4% (n=6104) were men and 63.6% (n=10,678) were women. There was a significant interaction between hemoglobin and gender ($p=0.019$) on the risk of recurrent falls, but not between hemoglobin and race ($p=0.62$), therefore all results are presented stratified by gender. Baseline participant characteristics are presented by hemoglobin category in Table 2 for men and women separately. For men, the mean age ($\pm$ SD) was 63.7 (9.5) and 34.7% were black. For women, the mean age ($\pm$ SD) was 64.7 (9.5) and 43.6% were black. The mean hemoglobin ($\pm$ SD) was 14.5 (1.4) g/dL and 13.2 (1.2) g/dL for men and women, respectively. Participants with lower hemoglobin tended to be older, had a higher prevalence of comorbidities such as diabetes, hypertension, coronary artery disease and stroke and a lower mean SF-12 PCS score.

Association between Hemoglobin and Recurrent Falls

Recurrent falls occurred in 240 (3.9%) and 511 (4.8%) of men and women, respectively. There was a graded increase in the percentage of men who had recurrent falls at lower hemoglobin categories (Figure 1). The percentage of men who had recurrent falls increased from 2.9% at hemoglobin categories ≥ 3 g/dL above to 9.1% at hemoglobin categories ≤ 1 g/dL below the WHO anemia cut-point. For women, there was a U-shaped relationship between hemoglobin levels and recurrent falls. The lowest percentage of women with recurrent falls was in the 1 to <2 g/dL above the WHO anemia cut-point category (3.8%) with higher percentages of women with hemoglobin ≥ 3 g/dL above (7.0%) and ≤ 1 g/dL below (6.6%) the WHO anemia cut-point experiencing recurrent falls.

After multivariable adjustment, a graded linear association between lower hemoglobin and higher odds ratio (OR) for recurrent falls, was observed among men (Figure 2 and Table, Supplemental Digital Content 1, <http://links.lww.com/MAJ/A11>, p -value for linear trend = <0.001). Compared to those with a hemoglobin 1 to 2 g/dL above the anemia cut-point, the multivariable adjusted OR (95% confidence interval [CI]) for recurrent falls were 0.73 (0.45–1.19) and 0.84 (0.57–1.24) for those with hemoglobin levels ≥ 3 g/dL above and 2 to <3 g/dL above the anemia cut-point, respectively. Also compared to those with hemoglobin levels 1 to 2 g/dL above the anemia cut-point, the odds ratios were 1.29 (0.88–1.90), 1.32 (0.80–2.18) and 2.12 (1.23–3.63) for hemoglobin levels 0 to 1 g/dL above, 0 to <1 g/dL below and ≤ 1 g/dL below the anemia cut-point, respectively. After further adjustment for PCS and history of falls in the prior year, compared to those with a hemoglobin 1 to 2 g/dL above the anemia cut-point the multivariable adjusted OR (95% CI) associated with hemoglobin levels ≥ 3 g/dL above, 2 to <3 g/dL above, 0 to 1 g/dL above, 0 to <1 g/dL below and ≤ 1 g/dL below were 0.79 (0.48–1.31), 0.86 (0.58–1.29), 1.30 (0.88–1.93), 1.19 (0.71–1.98) and 1.58 (0.90–2.78), respectively.

The association between hemoglobin and recurrent falls among women was not linear (p -value for quadratic term = 0.016). For hemoglobin levels below the cut-point, an observed risk of recurrent falls was observed: multivariable adjusted OR (95% CI) of recurrent falls were 1.42 (1.11–1.81), 1.28 (0.91–1.80), and 1.76 (1.13–2.74) at hemoglobin levels ≤ 1 g/dL below, 0 to <1 g/dL below, >0 to <1 g/dL above the WHO anemia cut-point (Figure 2 and Table, Supplemental Digital Content 2, <http://links.lww.com/MAJ/A12>). Multivariable adjusted odds of recurrent falls were 1.24 (0.95–1.62) and 1.59 (1.10–2.31), 2 to <3 g/dL above and ≥ 3 g/dL above the WHO anemia cut-point, respectively. After further adjustment for PCS and history of falls in the prior year, compared to those with a hemoglobin 1 to 2 g/dL above the anemia cut-point the multivariable adjusted OR (95% CI) associated with

hemoglobin levels ≥ 3 g/dL above, 2 to <3 g/dL above, 0 to 1 g/dL above, 0 to <1 g/dL below and ≤ 1 g/dL below were 1.58 (1.08–2.3), 1.33 (1.01–1.74), 1.32 (1.02–1.69), 1.24 (0.88–1.75) and 1.47 (0.93–2.32), respectively.

Subgroup Analysis

The association of hemoglobin, modeled as a continuous variable, with recurrent falls is displayed in Figure 3. Among men an increased OR for recurrent falls was present overall (OR 1.16; 95% CI 1.05–1.28 per 1 g/dL lower hemoglobin level). Among women, no association was present between lower hemoglobin level and recurrent falls (OR 1.04; 95% CI 0.92 – 1.17 per 1 g/dL lower hemoglobin level). However, when the analyses were stratified by race, the multivariable adjusted OR (95% CI) for recurrent falls per 1 g/dL increase in hemoglobin was 0.92 (0.79–1.09) for black women and 1.18 (1.01–1.39) for white women ($p=0.011$).

Because of the interaction between race and hemoglobin among women, a sub-group analysis was conducted, evaluating the association between hemoglobin categories and recurrent falls for white and black women, separately. Race-stratified multivariable adjusted OR for recurrent falls by level of hemoglobin for women are displayed in Table, Supplemental Digital Content 2. The trend of increasing odds of falls at lower and higher hemoglobin levels remained for white women (p -value for quadratic <0.002), however we were unable to observe the same trend for black women (p -value for quadratic 0.612).

Discussion

Findings from the current analysis suggest that lower hemoglobin is associated with increased risk for recurrent falls in men and women. However, the association between higher hemoglobin levels and recurrent falls differs for men and women. For men, there was a linear relationship with higher rates of recurrent falls at lower hemoglobin levels across the full range studied. In contrast, among women, an increased risk for recurrent falls was present at both low and high hemoglobin levels. A significant U-shaped trend between hemoglobin level and recurrent falls was found among women, however, further studies are needed to confirm this relationship. While the association between anemia and falls has been described in special populations such as hospitalized adults and nursing home residents, the current study extends these prior observations to a population that includes middle-aged as well as older adults.

Several independent risk factors for falls have been previously identified, including older age, diabetes, depression, cognitive impairment, functional limitation and history of a previous fall.^{2, 3, 7} In the current study, lower baseline hemoglobin levels were associated with older age, higher prevalence of comorbidities, and lower PCS score and adjustment for these factors attenuated the association between hemoglobin levels and recurrent falls. Among men, the odds ratio for recurrent falls at a hemoglobin level ≤ 1 g/dL below the anemia cut-point decreased from 3.01 to 2.12 with adjustment for cardiovascular disease, diabetes, depressive symptoms, cognitive impairment and measures of kidney function. The odds ratio for recurrent falls was further attenuated after adjustment for PCS and a recent history of a falling. While some covariates included in the multivariable adjustment represent potential confounders, some clinical characteristics may actually be in the causal pathway. For example, the effect of low hemoglobin on falls may be through its impact on functional status. Also, low hemoglobin may have precipitated a fall in the year prior to baseline. Thus, multivariable adjustment for factors such as PCS score and fall history may underestimate the association between hemoglobin levels and recurrent falls.

Although there may be some aspects of the patient's clinical profile that can confound the relationship between hemoglobin level and risk of falling, an intrinsic association is biologically plausible. Along with symptoms of weakness, dizziness and fatigue, low hemoglobin has been shown to be associated with declines in mobility, physical function, and executive function, all of which can increase the risk of falling.^{28, 29} Similarly, mobility impairment, defined as self-reported difficulty in walking one-quarter mile or climbing 10 steps, skeletal muscle density and skeletal muscle strength have been shown to be associated with lower hemoglobin level.^{31, 32} Our findings provide additional support for these potential mechanisms by which low hemoglobin may affect risk of falling, since adjustment for these different clinical characteristics resulted in attenuation of the independent association between hemoglobin levels and recurrent falls. This suggests that the mechanism by which anemia may lead to falls is likely multi-factorial and potentiated by the effect of low hemoglobin on physical performance, cognition as well as muscle structure and function.

Studies to date on low hemoglobin and fall risk have primarily-focused on particularly frail populations. For instance, among hospitalized patients, anemia was more common among those with falls.¹⁰ Anemia has also been shown to be associated with falls in one retrospective cohort that included both nursing-home residents and community-dwelling older adults hospitalized for a hip fracture.¹¹ However, studies of nursing home residents and hospitalized older adults may not be generalizable to community-dwelling adults. In one community based study of 394 participants 65 years of age from the Netherlands, anemia defined by WHO criteria was associated with a doubling of the risk of recurrent falls.¹⁴ Anemia has also been shown to be associated with injurious falls among older adults.¹² In the current analysis we extend these findings to a substantially larger, more diverse U.S. population sample.

The population based REGARDS study included over 10,000 women and this large cohort facilitated using narrow hemoglobin categories and the ability to explore participant subgroups. Importantly, we found gender differences in the pattern of association between hemoglobin and falls. While the association was linear for men, with a graded increase in falls at lower hemoglobin categories, post hoc analyses revealed a U-shaped trend between hemoglobin and risk for recurrent falls among women. These findings are similar to a previous study that reported a more U-shaped association between hemoglobin level and mortality among women compared to men.³³ A similar U-shape association between hemoglobin and longitudinal decline in physical performance has also been reported among women, but not men.²⁹ While we considered that the observation between high hemoglobin and falls in women might have been due to tobacco use, the association persisted after adjusting for smoking. After race-stratification among women, this U-shaped pattern remained for white women, but not black women. These results, while interesting, are difficult to explain and should be interpreted cautiously until they have been corroborated in future studies. Additionally, we recommend caution because of the small sample size, resulting low precision after stratification by both gender and race. More research is required to understand whether the mechanisms underlying low hemoglobin-related fall risk may differ among men and women or among whites and blacks.

The current findings have both clinical and public health implications. The negative consequences of falls have been well reported and are becoming increasingly important as the U.S. population ages.^{4, 5} Falls have been described as a geriatric syndrome, in which fall risk is related to the interaction between predisposing underlying disease and acute precipitating factors.^{34, 35} The risk of falls has been shown to increase as the number of predisposing and precipitating risk factors increases.² This model is supported by clinical trial findings showing that strategies that target multiple risk factors may decrease falls.⁸

While many fall risk factors such as age, functional status, and cognition may not be modifiable, hemoglobin may represent a treatable risk factor for falls. Further research is warranted to determine if the evaluation and appropriate treatment of low hemoglobin as part of a multidimensional fall prevention program may decrease falls.

The findings from the current study should be considered in the context of certain limitations. Data were not obtained on some known risk factors for falls including balance and gait impairment or direct measures of muscle strength. While possible that unmeasured characteristics may further explain the association we found, it is more likely that these factors are part of the causal pathway through which low hemoglobin is associated with falls and represent mediators rather than confounders. Also, hemoglobin was obtained only at baseline, therefore we were unable to evaluate for temporal trends in hemoglobin that may affect fall risk. For example, while chronically low hemoglobin may have a greater impact on skeletal muscle density, acute blood loss may be associated with symptoms including orthostatic hypotension and dizziness. We were unable to determine if potential differences in the chronicity of low hemoglobin levels explains the interaction of hemoglobin with gender and race. An additional limitation is the occurrence of falls was obtained during a single follow-up telephone interview rather than through use of a fall calendar or diary. While this may underestimate the true incidence of recurrent falls, it is unlikely that self-reported falls would be systematically different among hemoglobin categories.

Conclusion

In conclusion, in this large prospective cohort of U.S. adults, among men, lower hemoglobin was associated with an increased risk for recurrent falls. In contrast, our findings suggest an increased risk for recurrent falls at both lower and higher hemoglobin levels among women. Lower hemoglobin may represent a novel risk factor for falls. Further studies are needed to confirm the gender and race differences identified in the current study. If confirmed, studies may be needed to determine if the evaluation and appropriate treatment of low hemoglobin levels should be part of a multidimensional fall prevention program.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Percentage of REGARDS participants with recurrent (2 or more) falls by hemoglobin category relative to World Health Organization anemia cut-point for (a) men and (b) women

Figure 2.

Odds ratio (95% Confidence Intervals) for recurrent falls by level of hemoglobin relative to World Health Organization anemia cut-point for men (13.0 g/dL) and women (12.0 g/dL). Model 1 adjusted for age, race and geographic region. Model 2 adjusted for variables in Model 1, marital status, cigarette smoking, education, waist circumference, hypertension, diabetes, coronary artery disease, stroke, depressive symptoms, cognitive impairment, estimated glomerular filtration rate and albumin-to-creatinine ratio. Linear p , p -value for linear trend across hemoglobin categories. Quadratic p , p -value for quadratic trend across hemoglobin categories.

Figure 3.

Odds ratio of recurrent falls (2 or more) by subgroups for men and women. Adjusted for age, race, gender, geographic region, marital status, education, waist circumference, hypertension, diabetes, coronary artery disease, stroke, depressive symptoms, cognitive impairment, estimated glomerular filtration rate (eGFR), albumin to creatinine ratio (ACR), Medical Outcomes Study Short-Form (SF-12) physical component score (PCS) < 50, and a fall in the year prior to baseline. Among women, analysis of hemoglobin as a continuous variable was limited to the linear range (hemoglobin 1 to <2 g/dL above the WHO anemia cut-point and below).

Table 1

Hemoglobin categories for men and women relative to World Health Organization (WHO) anemia definition for men (<13.0 g/dL) and women (<12.0 g/dL).

Hemoglobin categories, g/dL	MEN	WOMEN
1 below	<12 g/dL	<11 g/dL
0 to <1 below	12 – 12.9 g/dL	11 – 11.9 g/dL
>0 to <1 above	13 – 13.9 g/dL	12 – 12.9 g/dL
1 to <2 above *	14 – 14.9 g/dL	13 – 13.9 g/dL
2 to <3 above	15 – 15.9 g/dL	14 – 14.9 g/dL
3 above	>16 g/dL	>15 g/dL

* Referent category

Table 2

Baseline characteristics by hemoglobin category for men and women.

	Hemoglobin level, * g/dL - MEN						
N (%) or mean (SD)	All	1 below (n=265)	0 to <1 below (n=477)	>0 to <1 above (n=1141)	1 to <2 above (n=1880)	2 to <3 above (n=1515)	3 above (n=826)
Demographics							
Age, years	64.7 (9.7)	69.2 (10.4)	68.2 (10.3)	66.5 (9.8)	64.2 (9.5)	63.3 (9.3)	62.3 (8.9)
Black race	34.7	59.3	56.2	49.0	33.1	24.8	16.6
Currently married	74.0	66.0	66.5	72.0	74.4	76.4	78.6
Current smoker	14.7	13.2	10.1	12.1	12.9	15.2	24.6
< HS Education	10.2	17.8	16.0	14.6	9.0	7.1	6.9
Region	37.2	32.5	35.0	39.3	37.7	35.5	39.2
Stroke Belt	21.9	25.3	25.0	22.1	20.6	22.2	20.7
Stroke Buckle	41.0	42.3	40.0	28.7	41.7	42.3	40.1
Other region							
Comorbidity							
Hypertension	57.8	73.6	69.4	64.2	56.7	51.0	52.3
Diabetes mellitus	21.8	45.1	38.5	27.4	19.5	16.2	12.7
Coronary heart disease	23.5	35.1	33.6	27.2	21.8	19.4	20.6
Stroke	6.0	12.5	11.8	7.0	5.4	3.9	4.5
Symptoms of depression	8.1	13.7	10.2	8.9	7.8	6.8	7.1
Cognitive impairment	7.5	14.5	11.8	9.2	6.8	6.2	4.4
Health related factors							
SF 12 Physical component score	47.7 (9.7)	41.0 (11.6)	43.9 (10.3)	46.8 (10.0)	48.5 (9.3)	49.1 (8.9)	49.1 (9.0)
eGFR, ml/min/1.73 m ²	85.5 (19.2)	70.1 (28.1)	78.7 (23.9)	84.7 (20.8)	87.3 (17.3)	87.7 (16.2)	87.4 (15.6)
ACR, mg/g	6.7 (4.2, 15.4)	13.1 (6.3, 61.1)	9.4 (4.9, 27.0)	7.1 (4.4, 17.6)	6.4 (4.1, 13.8)	5.8 (4.0, 11.9)	6.4 (4.1, 14.4)
Waist circumference, cm	100.2 (14.1)	100.6 (15.2)	101.6 (15.7)	100.0 (16.3)	100.1 (13.7)	99.7 (13.0)	100.4 (11.8)
Fall in the prior year	11.9	21.1	14.3	12.1	12.0	10.8	9.6
	Hemoglobin level, * g/dL – WOMEN						
		1 below (n=438)	0 to <1 below (n=1106)	>0 to <1 above (n=2790)	1 to <2 above (n=3664)	2 to <3 above (n=2082)	3 above (n=598)

	Hemoglobin level, * g/dL - MEN							
Demographics								
Age, years	63.7 (9.5)	65.0 (10.6)	64.4 (9.8)	64.0 (9.7)	63.4 (9.5)	63.4 (8.9)	63.2 (9.0)	
Black race	43.6	71.5	70.0	55.9	38.5	24.0	17.2	
Currently married	51.1	40.0	41.7	49.9	52.9	56.2	54.5	
Current smoker	13.4	8.9	7.9	8.7	12.0	20.0	35.0	
< HS Education	11.5	17.8	17.4	12.8	9.3	9.6	9.7	
Region	37.3	40.2	40.0	36.7	36.4	38.3	35.0	
Stroke Belt	23.8	26.7	25.8	24.3	23.4	22.1	24.3	
Stroke Buckle	38.9	33.1	34.3	39.0	40.2	39.6	40.8	
Other region								
Comorbidity								
Hypertension	58.2	74.4	72.5	62.0	53.6	51.7	52.3	
Diabetes mellitus	18.9	42.5	34.0	22.4	13.7	11.8	13.0	
Coronary heart disease	12.1	16.9	14.1	12.3	11.5	10.7	12.9	
Stroke	4.6	7.4	7.2	5.0	3.9	3.5	4.6	
Symptoms of depression	13.2	13.4	16.2	14.0	11.8	12.4	14.4	
Cognitive impairment	6.1	11.9	8.2	7.2	5.5	4.0	4.4	
Health related factors								
SF-12 Physical component score	45.9 (10.9)	41.1 (12.1)	42.9 (11.6)	45.4 (10.8)	46.8 (10.5)	47.4 (10.1)	46.1 (11.0)	
eGFR, ml/min/1.73 m ²	87.0 (20.4)	73.2 (28.9)	83.8 (25.5)	87.2 (21.3)	88.8 (18.2)	88.1 (16.5)	86.4 (17.2)	
ACR, mg/g	7.6 (5.0, 14.4)	11.6 (6.6, 32.9)	8.5 (5.3, 19.8)	7.4 (4.9, 14.4)	7.2 (4.8, 13.1)	7.3 (5.0, 12.7)	8.0 (5.1, 15.6)	
Waist circumference	92.2 (16.0)	97.7 (17.9)	96.1 (16.9)	92.7 (15.9)	90.8 (15.7)	91.2 (14.9)	91.4 (16.2)	
Fall in the prior year	18.0	21.5	18.0	19.8	17.1	16.4	18.7	

* Relative to World Health Organization (WHO) anemia cut-point. HS = high school; SF-12 = Medical Outcomes Study Short Form-12 physical component score; eGFR = estimated glomerular filtration rate, ACR = albumin to creatinine ratio; ACR is median (25th, 75th percentiles)