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Biological Variation of Hematology Tests Based on the 1999–2002 National Health and Nutrition Examination Survey

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Abstract

Objective—Biological variation consists of between-person (BP) and within-person (WP) variation. Estimates of WP coefficients of variation (CV_w) and BP coefficients of variation (CV_g) for hematology laboratory tests were estimated from the 1999–2002 National Health and Nutrition Examination Survey (NHANES).

Methods—NHANES is a survey of the civilian noninstitutionalized U.S. population that uses a stratified, multistage probability design. Between- and within-person variations were estimated for 18 hematology tests. For WP variation, a nonrandom sample was obtained with a median of 17 days between two test measurements. Between-person variation was estimated from the WP sample and additional participants were matched for age group, gender, and race and ethnicity to the WP sample.

Results—The BP and WP variations were estimated on as many as 2,496 and 852 sample participants, respectively. Mean corpuscular hemoglobin concentration had the lowest CV_g (2.25% for men and 2.40% for women), and mean corpuscular volume had the lowest CV_w (0.31% for men and 0.37% for women). The index of individuality (CV_w /CV_g) ranged from 0.06 for mean corpuscular volume for men and women to 0.62 for segmented neutrophil number for men, and 0.55 for segmented neutrophil percent for women. Women had higher CV_w compared with men for hematocrit, hemoglobin, mean corpuscular volume, red blood cell count, and red blood cell distribution width. Several hematology tests' CV_w also differed by age group, including mean corpuscular volume; eosinophil, lymphocyte and segmented neutrophil percent; monocyte and segmented neutrophil number; white blood cell count; and red blood cell distribution width.

Keywords: within-person variation • between-person variation • laboratory tests

Introduction

Laboratory analytes for individuals are subject to several sources of variation, including biological, preanalytical (specimen collection), analytical (bias and imprecision), and postanalytical (reporting of results). Analytical bias is the closeness of an analyte result to the "true value" of the result. Precision is the repeatability of an analyte result if the same sample is tested many times. Biological variation consists of within-person (WP) and between-person (BP) variation. These components of biological variation are used to set analytical goals for bias and imprecision, evaluate changes for a person's tests using delta checks, and assess the clinical utility of population-based reference ranges (1).

The goals of imprecision and bias for a laboratory analyte are different depending on the intended use in screening, diagnosis, or monitoring the course of diseases in patients. When the WP variation is much smaller than the BP variation, the individual results stay within a narrow range compared with the population-based reference interval (range). Hence, the WP variation would be used to monitor serial changes of

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laboratory values in a person. Contrarily, when the WP variation is similar to the BP variation, the person's results over time have a wide range comparable with the population-based reference interval. In this situation, the BP variation (population reference range) is used to monitor serial change of the laboratory values in a person. Ideally, desirable goals for imprecision (I) and bias (B) have been related to the WP coefficients of variation (CV_w) and the BP coefficients of variation (CV_g) of laboratory analytes (1–3).

Buttarello discussed sources of variation of hematology analytes (4). Preanalytical sources of variation include type of anticoagulant used, specimen storage temperatures, and stability. Postanalytical sources of variation include delta checks (differences between consecutive laboratory values of a test), limit checks (laboratory values when exceeded requiring further investigation), and reports of unusual cell morphology. Analytical variation sources of imprecision and bias of hematology tests have been characterized by monitoring quality controls, proficiency testing, and comparing automated instrument measurements with manual methods.

BP variation of hematology tests has been studied extensively for demographic characteristics including age and gender. The WP source of biological variation has been evaluated for chemistry tests, but rarely for hematology tests. Most hematology studies of biological variation had few subjects. Statland examined the mean hourly, daily, and weekly intra-individual variation of hematology tests in 20 adults (5). Costongs examined daily, weekly, and 6-month intra-individual variations of hematology tests for 62 adults aged 18–57 (6). Costongs also examined the critical differences (delta checks) using WP data. Costongs noted that the WP coefficients of variation were indirectly related to the life span of cells, with red blood cells (life span 120 days) having the lowest CV_w and white blood cells (life span 6–8 hours) having the highest CV_w. Fraser examined WP and BP variation of hematology tests in 24 elderly persons (mean age 75) over 20 weeks at 14-day intervals (7). Ricos (2) and Fraser (1) have compiled lists of WP and BP variation for laboratory tests, including hematology tests.

The WP and BP variation of laboratory tests has been examined in several NHANES surveys. Looker examined hematology and biochemical markers of iron status in the Hispanic Health and Nutrition Examination Survey conducted from 1982 through 1984 for 80 persons (8). The effect of increased WP variation on overestimation of prevalence of hematologic disorders was examined. WP and BP variation have been reported for selected analytes from the third National Health and Nutrition Examination Survey conducted from 1988 through 1994 (9). The BP and WP variation for general biochemical, nutritional, and environmental analytes was analyzed for the 1999–2002 National Health and Nutrition Examination Survey (10). In this report, BP and WP variations of hematology tests are presented for NHANES 1999–2002, and gender and age groups are compared for WP variation.

Methods and Procedures

Estimates of CV_w and CV_g for laboratory tests were calculated from the 1999–2002 NHANES (11,12), a cross-sectional survey that collected data on the civilian noninstitutionalized U.S. population through questionnaires and medical examinations, including laboratory tests. NHANES 1999–2002 used a stratified, multistage probability design to collect a nationally representative sample.

The hematology tests were collected in EDTA tubes as part of a complete blood and five-part differential cell count profile and were analyzed on the Beckman Coulter MAXM analyzer (Beckman Coulter Corporation, Brea, Calif.). Details of the laboratory methods have been described (13) and the 18 hematology tests are listed in Tables 1–5.

The MAXM instrument is a laser-based flow cytometer that uses impedance, conductivity, and light scatter to directly measure some of the hematology tests. Other hematology tests are calculated from the directly measured analytes. The method analytical CV (CV_a) used to calculate the CV_w was derived from imprecision CV using bench quality controls or imprecision based on manufacturer information.

The BP and WP means, standard deviations, and coefficients of variation for hematology tests are shown for men in Table 1 and for women in Table 2. The BP sample was generated from the WP sample, and two additional participants were selected for every one WP sample participant. The additional BP participants were selected by matching for gender, race and ethnicity, and age group. BP participants were matched in 3-year age groups (e.g., 16–18, 19–21, 22–24, 25–27, etc.) to have more participants to compare with 3-year age groups in the WP sample. The BP variations were estimated on as many as 2,496 sample participants from NHANES 1999–2002. The WP variations were estimated from a convenience sample of 852 persons based on NHANES 2000–2002 data. The WP sample participants were recruited for a second test measurement. The WP participants were not selected randomly but recruited according to several criteria, including selecting approximately equal proportions of men and women with an approximately uniform age distribution of 16–69 years. Participants were recruited to obtain about equal numbers for race and ethnicity of Mexican-American, non-Hispanic black, non-Hispanic white, and other persons. The target size of the WP sample was 5% of those participants who had a venipuncture during the initial visit to the NHANES mobile examination center. The WP participants were asked to return for a second phlebotomy no sooner than 8 days after their initial blood draw (1.8% of participants had second phlebotomies before 8 days). Because the BP sample was matched for age and gender to the WP sample, no differences in proportions by gender were seen for the age groups (16–29, 30–49, and 50–69).

A chi-square test showed no significant differences between age groups by gender for the WP ($p = 0.71$) and BP ($p = 0.44$) sample.

The WP variation was estimated from a nonrandom, unweighted sample with a median of 17 days (25th percentile: 13 days, 75th percentile: 23 days, range: 3–51 days) between two test measurements. The analytical variation includes the imprecision and changes in bias (for example, changes in method calibration) that are usually negligible. Hence, the CV_a is estimated by the method imprecision CV (CV_i). The total coefficient of variation (CV_t) of a laboratory analyte can be estimated assuming that all sources of error are measured at the same analyte mean and that preanalytical and postanalytical sources of variation are negligible. The CV_t is calculated as $[(CV_a)^2 + (CV_w)^2]^{1/2}$ (1). Hence, the CV_w was calculated as $[(CV_t)^2 - (CV_a)^2]^{1/2}$. The CV_g was calculated as SD/mean for the BP sample. The distributions of several hematology tests were nongaussian, and extreme outliers were excluded to obtain an approximately gaussian distribution with more stable estimates of variation. Outliers were eliminated by use of Tukey's method, which defines outliers as three interquartile ranges below the 25th percentile or above the 75th percentile (14). The basophil and eosinophil number had extreme nongaussian distributions and were excluded. Gender and age group WP variations were compared. Ninety-five percent confidence intervals were estimated for the CV_w. A likelihood ratio test was performed to determine if the CV_w for gender or age group for a laboratory analyte were equal (15). Statistical analyses were carried out with SAS for Windows software (SAS Institute, Cary, N.C.).

Results and Discussion

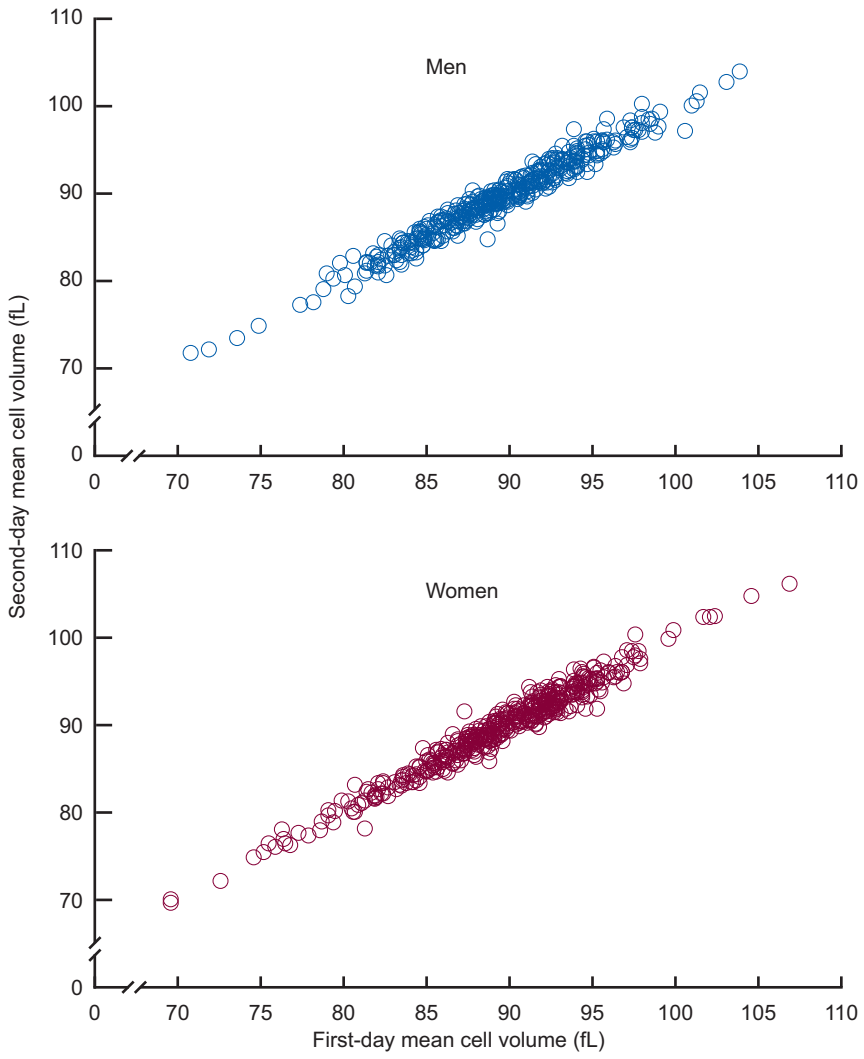
The BP and WP means, standard deviations, and coefficients of variation for 18 hematology tests are shown for men in Table 1 and for women in Table 2. The mean of hematology tests of the BP and WP sample for men and for women, respectively, were similar. As expected, the BP mean red blood cell-related hematology tests (hemoglobin, hematocrit, and red blood cell count) were higher for men compared with women. The CV_g exceeded the laboratory CV_i for all hematology tests. The CV_w exceeded the laboratory CV_i for 15 of 18 hematology tests. However, the CV_w was less than the laboratory CV_i for basophil percent, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration. The CV_w cannot be estimated for these hematology tests because the CV_w is calculated as $[(CV_t^2) - (CV_a)^2]^{1/2}$ and CV_a, as estimated by CV_i, exceeded the CV_t. The imprecision of the hematology tests were estimated from between-run bench quality controls that are used most commonly to estimate imprecision of tests for biological variation. Because the WP CV is estimated over several runs, the between-run imprecision was used.

Analytical goals for imprecision and bias can be judged using the CV_w and CV_g. Imprecision should ideally be less than one-half of the CV_w, and bias should be less than 0.25 $[(CV_w)^2 + (CV_g)^2]^{1/2}$ (1). The total error of a laboratory measurement reflects the underlying bias and imprecision of an analyte. The goal for total error should be less than $kI + B$, where $k = 1.65$ for $\alpha = 0.05$ (1). For example, the observed hemoglobin imprecision of 1.1% was less than the imprecision goal of one-half of CV_w (2.46%), or 1.23% in men (Table 1). The bias for hemoglobin in men should ideally be less than $0.25[(CV_w)^2 + (CV_g)^2]^{1/2}$, or $0.25[(0.0246)^2 + (0.0785)^2]^{1/2}$, or 8.2%. The total error is estimated as $B + 1.65(I)$, or 8.2% + 1.65(1.1%), or 10.0%. Thus, the total error for hemoglobin in men estimated at the BP mean of 15.3 g/dL (Table 1) was 1.53 g/dL (15.3 g/dL multiplied by 0.10). The total error of 10.0% for male hemoglobin exceeded the Clinical Laboratory Improvement Amendments acceptable performance for total error for hemoglobin of 7% (16).

The mean corpuscular hemoglobin concentration (MCHC) CV_g of 2.25% was lowest among all the hematology tests in men (Table 1) and 2.40% for women (Table 2). Compared with all other hematology tests, the MCHC between-person CV was lowest in all age groups, with 2.33% for participants aged 16–29 (Table 3), 2.39% for participants aged 30–49 (Table 4), and 2.29% for participants aged 50–69 (Table 5). The mean corpuscular volume (MCV) CV_w was lowest among hematology tests in men (0.31%) and women (0.37%). The MCV within-person CV was also lowest among hematology tests in all age groups with 0.28% for ages 16–29, 0.51% for ages 30–49, and 0.18% for ages 50–69. The low within-person CV for MCHC can be seen for men and women (Figure 1).

High CV_g was seen in eosinophil and basophil percent for men and women (range 52.4%–64.4%) and in all age groups (range 50.8%–68.6%), which reflects very low analyte values. Other hematology analytes also had relatively high CV_g (greater than 25%) including white blood count, segmented neutrophil, lymphocyte and monocyte number, and lymphocyte and monocyte percent. High CV_w was seen in eosinophil percent and segmented neutrophil number in men and women (range: 21.5%–25.2%) and in all groups (range: 19.1%–26.5%). High within-person CV reflects individual variation due to gender, age, diurnal or cyclical variation, disease, or very low analyte values. The high within-person CV for segmented neutrophil number can be seen for men and women in Figure 2.

The ratio of CV_w to CV_g, also known as the index of individuality, is important in determining the use of population-based reference (normal) intervals in detecting changes of disease status in individuals (17,18). When the index of individuality is low (< 0.5), the individual results stay within a narrow range compared with the population-based reference interval. Hence, a low index suggests the utility of evaluating serial changes in analyte values in an individual, whereas population-based reference intervals would be of limited use. A high index (≥ 0.5) suggests that the population-based reference interval is appropriate when interpreting a person's laboratory analyte value. The



NOTE: fL is femtoliter.
SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 1999–2002.

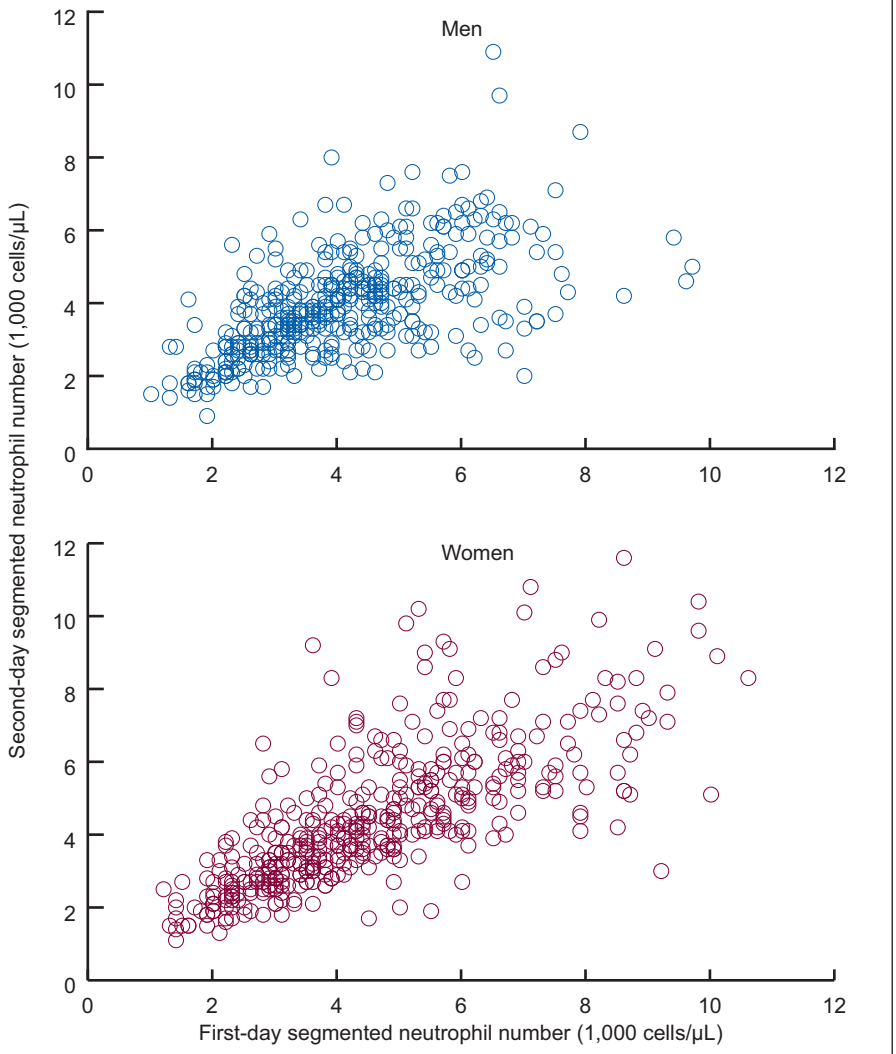
Figure 1. First-day versus second-day cell volume, by gender

index of individuality ranged from 0.06 for mean corpuscular volume for men and women, to 0.62 for segmented neutrophil number for men and 0.55 for segmented neutrophil percent for women (Tables 1 and 2). The index of individuality was lowest for mean corpuscular volume for all age groups (0.05 for ages 16–29, 0.09 for ages 30–39, and 0.03 for ages 50–69) (Tables 3–5). The index of individuality was highest for segmented neutrophil percent (0.63) for ages 16–29. For ages 30–49, segmented neutrophil and lymphocyte percent had the highest index of individuality (0.52); and for ages 50–69, segmented neutrophil number and percent had the highest index of individuality (0.53).

The BP and WP variations were analyzed by gender. The sample size, means, standard deviations, and coefficients of variation for hematology analytes are presented for men (Table 1) and women (Table 2). Several laboratory analytes had significant differences ($p < 0.001$) in the CV_w when males and females were compared. Women had higher CV_w compared with men for tests associated with red blood cells including, hematocrit, hemoglobin, mean corpuscular volume, red blood cell count, and red blood cell distribution width. For example, the red blood cell count CV_w in women was 3.45% compared with 2.53% in men. Females may have more within-person variation due to blood loss during menstruation or increased iron utilization during pregnancy.

The BP and WP variations of hematology analytes were also analyzed by age group. The sample size, means, standard deviations, and coefficients of variation of hematology analytes are presented for age groups 16–29 (Table 3), 30–49 (Table 4), and 50–69 (Table 5). Several hematology tests also differed ($p < 0.05$) by age group while controlling for gender. Participants aged 16–29 had higher CV_w than those aged 30–49 and 50–69 for eosinophil, lymphocyte, and segmented neutrophil percent, and segmented neutrophil number. Also, participants aged 16–29 had higher CV_w than those aged 50–69 for monocyte number, red blood cell distribution width, and white blood count. Participants aged 30–49 had higher CV_w than those aged 50–69 for monocyte number, red blood cell distribution width, and white blood count. Mean corpuscular volume CV_w was highest in the middle age group, with 0.28% for those aged 16–29, 0.51% for those aged 30–49, and 0.18% for those aged 50–69 (Figure 3).

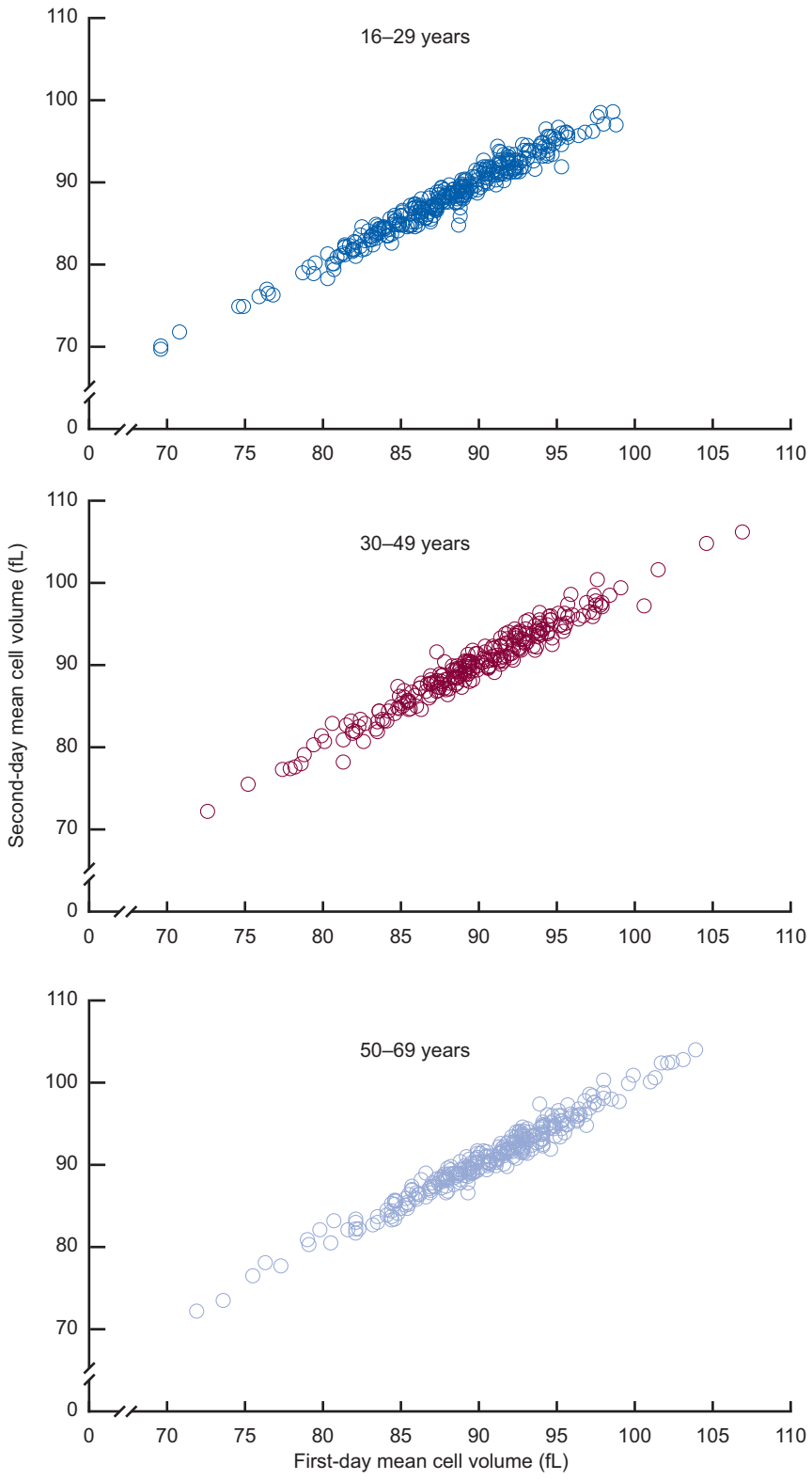
In this report, BP and WP estimates of coefficients of variation were obtained for 18 hematology analytes. The literature on WP hematology variation is very limited, and this report adds information on within-person coefficients of variation. NHANES 1999–2002 provides a better estimate of BP variation than other locally representative studies because the NHANES sample was nationally representative and had a larger sample size. The WP variation estimate was limited by the nonrandom, self-selected design and reflected a median of 17 days between two measurements. In addition, the CV_w and CV_g estimates in NHANES were based on a relatively healthy sample of the population. The CV_w and CV_g would be increased in a sample of unhealthy individuals because of changes in disease status and treatment. The BP and WP sample



NOTE: µL is microliter.
SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 1999–2002.

Figure 2. First-day versus second-day segmented neutrophil number, by gender

participants were restricted to those aged 16–69. The estimate of CV_w could be improved by use of a stratified, multistage probability design over different time periods.



NOTE: fL is femtoliter.
SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 1999–2002.

Figure 3. First-day versus second-day mean cell volume, by age group

References

1. Fraser CG. Biological variation: From principles to practice. Washington, DC: AACC Press; p 151. 2001.
2. Ricos C, Alvarez V, Cava F, Garcia-Lario JV, Hernandez A, Jimenez CV, et al. Current databases on biological variation: Pros, cons and progress. Scand J Clin Lab Invest 59:491–500. 1999.
3. Fraser CG, Harris EK. Generation and application of data on biological variation in clinical chemistry. Crit Rev Clin Lab Sci 27:409–37. 1989.
4. Buttarello M. Quality specification in hematology: the automated blood cell count. Clin Chim Acta 346:45–54. 2004.
5. Statland BE, Winkel P, Harris SC, Burdsall MJ, Saunders AM. Evaluation of biologic sources of leukocyte counts and other hematologic quantities using very precise automated analyzers. Am J Clin Pathol 69:48–54. 1978.
6. Costongs GM, Janson PC, Bas BM, Hermans J, Van Wersch JW, Brombacher, PJ. Short-term and long-term intra-individual variations and critical differences of hematological laboratory parameters. J Clin Chem Clin Biochem 23(2):69–76. 1985.
7. Fraser CG, Wilkinson SP, Neville RG, Knox JD, King JF, MacWalter RS. Biologic variation of common hematologic laboratory quantities in the elderly. Am J Clin Pathol 92:465–70. 1989.
8. Looker AC, Sempos CT, Liu K, Johnson CL, Gunter EW. Within-person variance in biochemical indicators of iron status: effects on prevalence estimates. Am J Clin Nutr 52:541–7. 1990.
9. Lacher DA, Hughes JP, Carroll MD. Estimate of biological variation of laboratory analytes based on the third National Health and Nutrition Examination Survey. Clin Chem 59:450–2. 2005.
10. Lacher DA, Hughes JP, Carroll MD. Biological variation of laboratory analytes based on the 1999–2002 National Health and Nutrition Examination Survey. National health statistics reports; no 21. Hyattsville, MD: National Center for Health Statistics. 2010.

11. National Center for Health Statistics. NHANES 1999–2000 public data release. Available from: http://www.cdc.gov/nchs/nhanes/nhanes1999-2000/nhanes99_00.htm. Accessed December 28, 2011.
12. National Center for Health Statistics. NHANES 2001–2002 public data release. Available from: http://www.cdc.gov/nchs/nhanes/nhanes2001-2002/nhanes01_02.htm. Accessed December 28, 2011.
13. National Center for Health Statistics. NHANES 2001–2002 laboratory procedural manual: Complete blood count (CBC) with five-part differential. Available from: http://www.cdc.gov/nchs/data/nhanes/nhanes_01_02/l25_b_met_complete_blood_count.pdf. Accessed December 28, 2011.
14. Tukey JW. Exploratory data analysis. Reading, MA: Addison-Wesley Publishing Co.; p 44. 1977.
15. Verrill SP, Johnson RA. Confidence bounds and hypothesis tests for normal distribution coefficients of variation [research paper FPL-RP638]. Madison, WI: U.S. Department of Agriculture, Forest Service, Forest Products Laboratory; p 57. 2007.
16. U.S. Department of Health and Human Services. Medicare, Medicaid and CLIA programs: Regulations implementing the Clinical Laboratory Improvement Amendments of 1988 (CLIA) [final rule]. Fed Regist 57(40):7002–186. 1992.
17. Fraser CG. Inherent biological variation and reference values. Clin Chem Lab Med 42(7):758–64. 2004.
18. Harris EK. Effects of intra- and interindividual variation on the appropriate use of normal ranges. Clin Chem 20(12):1535–42. 1974.

Table 1. Between-person (CV_g), within-person (CV_w), and method (CV_a) coefficients of variation for men

Analyte (units)	Between-person				Within-person				Method[1]	Index[2]
	n	Mean	SD	CV_g (percent)	*n*	Mean	SD	CV_w (percent)	CV_a (percent)	CV_w/CV_g
Basophil percent (percent)	1,202	0.6136	0.3401	55.43	404	0.6113	0.2520	†	43.6	†
Eosinophil percent (percent)	1,187	2.8726	1.7027	59.27	401	2.8434	0.7251	23.19	10.6	0.39
Hematocrit (percent)	1,209	45.2174	3.4936	7.73	411	44.8138	1.3504	††2.49	1.7	0.32
Hemoglobin (g/dL)	1,209	15.2793	1.1993	7.85	411	15.1369	0.4083	††2.46	1.1	0.31
Lymphocyte number (10^3/μL)	1,203	2.0331	0.6239	30.69	409	2.0359	0.3190	15.25	3.6	0.50
Lymphocyte percent (percent)	1,208	30.2634	8.2636	27.31	411	30.4782	4.6946	15.13	2.9	0.55
Mean corpuscular hemoglobin (pg)	1,205	30.3496	1.9173	6.32	411	30.2988	0.3293	†	1.9	†
Mean corpuscular volume (fL)	1,205	89.7963	4.9216	5.48	411	89.6760	0.6870	†0.31	0.7	0.06
Mean corpuscular hemoglobin concentration (g/dL)	1,207	33.7803	0.7595	2.25	411	33.7725	0.4470	†	2.0	†
Mean platelet volume (fL)	1,208	8.3079	0.8620	10.38	411	8.2764	0.3052	3.32	1.6	0.32
Monocyte number (10^3/μL)	1,208	0.5810	0.1798	30.95	410	0.5719	0.1025	16.96	5.8	0.55
Monocyte percent (percent)	1,204	8.5485	2.1076	24.65	409	8.4719	1.2026	13.13	5.4	0.53
Platelet count (10^3/μL)	1,209	255.7469	59.0561	23.09	411	254.8273	22.4919	8.26	3.1	0.36
Red blood cell count (10^6/μL)	1,209	5.0512	0.4461	8.83	411	5.0107	0.1475	††2.53	1.5	0.29
Red blood cell distribution width (percent)	1,200	12.5278	0.7365	5.88	404	12.5238	0.1844	††0.85	1.2	0.14
Segmented neutrophil number (10^3/μL)	1,206	4.0595	1.5038	37.04	409	4.0158	0.9241	22.86	2.6	0.62
Segmented neutrophil percent (percent)	1,208	57.5146	9.3889	16.32	411	57.3492	5.6188	9.67	1.6	0.59
White blood cell count (10^3/μL)	1,206	6.9368	1.9161	27.62	409	6.8861	1.0490	15.09	2.1	0.55

† CV_w could not be calculated because the CV_t (total coefficient of variation) was less than the CV_a.
†† $p < 0.001$ where the CV_w for men is equivalent to the CV_w for women.
[1]Method analytical CV is the laboratory method precision assuming no method bias exists.
[2]Index of individuality.

NOTE: CV is coefficient of variation, *n* is the size of the sample, and SD is standard deviation; g/dL is grams per deciliter, μL is microliter, pg is picogram, and fL is femtoliter.

Table 2. Between-person (CV_g), within-person (CV_w), and method (CV_a) coefficients of variation for women

Analyte (units)	Between-person				Within-person				Method[1]	Index[2]
	n	Mean	SD	CV_g (percent)	*n*	Mean	SD	CV_w (percent)	CV_a (percent)	CV_w/CV_g
Basophil percent (percent)	1,264	0.6275	0.3290	52.43	432	0.6089	0.2472	†	43.6	†
Eosinophil percent (percent)	1,263	2.2864	1.4722	64.39	431	2.3305	0.6363	25.16	10.6	0.39
Hematocrit (percent)	1,287	39.2953	3.5273	8.98	441	38.8971	1.4150	††3.22	1.7	0.36
Hemoglobin (g/dL)	1,286	13.3306	1.2251	9.19	441	13.1939	0.4408	††3.15	1.1	0.34
Lymphocyte number (10^3/μL)	1,271	2.1952	0.6571	29.93	435	2.1785	0.3405	15.21	3.6	0.51
Lymphocyte percent (percent)	1,275	30.4178	8.7653	28.82	438	30.6664	4.7715	15.29	2.9	0.53
Mean corpuscular hemoglobin (pg)	1,276	30.3926	2.0561	6.77	438	30.4028	0.3874	†	1.9	†
Mean corpuscular volume (fL)	1,276	89.5221	5.1025	5.70	438	89.5771	0.7072	†0.37	0.7	0.06
Mean corpuscular hemoglobin concentration (g/dL)	1,285	33.9005	0.8126	2.40	440	33.9013	0.4600	†	2.0	†
Mean platelet volume (fL)	1,286	8.3452	0.8685	10.41	440	8.3045	0.2850	3.04	1.6	0.29
Monocyte number (10^3/μL)	1,274	0.5448	0.1811	33.24	434	0.5355	0.0956	16.88	5.8	0.51
Monocyte percent (percent)	1,271	7.4059	1.9803	26.74	434	7.4089	1.1047	13.90	5.4	0.52
Platelet count (10^3/μL)	1,284	284.1636	65.7434	23.14	440	286.2356	25.8905	8.50	3.1	0.37
Red blood cell count (10^6/μL)	1,287	4.4085	0.4112	9.33	441	4.3609	0.1639	††3.45	1.5	0.37
Red blood cell distribution width (percent)	1,255	12.6133	0.8957	7.10	426	12.6033	0.2088	††1.14	1.2	0.16
Segmented neutrophil number (10^3/μL)	1,269	4.5634	1.8853	41.31	434	4.4961	0.9756	21.54	2.6	0.52
Segmented neutrophil percent (percent)	1,275	59.1355	9.8992	16.74	438	58.8229	5.4819	9.18	1.6	0.55
White blood cell count (10^3/μL)	1,284	7.5669	2.2940	30.32	439	7.4773	1.1411	15.12	2.1	0.50

†CV_w could not be calculated because the CV_t (total coefficient of variation) was less than the CV_a.
†† $p < 0.001$ where the CV_w for women is equivalent to the CV_w for men.
[1]Method analytical CV is the laboratory method precision assuming no method bias exists.
[2]Index of individuality.

NOTE: CV is coefficient of variation, *n* is the size of the sample, and SD is standard deviation; g/dL is grams per deciliter, μL is microliter, pg is picogram, and fL is femtoliter.

Table 3. Between-person (CV_g), within-person (CV_w), and method (CV_a) coefficients of variation for ages 16–29

Analyte (units)	Between-person				Within-person				Method[1]	Index[2]
	n	Mean	SD	CV_g (percent)	*n*	Mean	SD	CV_w (percent)	CV_a (percent)	CV_w/CV_g
Basophil percent (percent)	933	0.5855	0.3250	55.51	316	0.5720	0.2522	6.56	43.6	0.12
Eosinophil percent (percent)	927	2.4787	1.7016	68.65	314	2.5250	0.7212	††§26.52	10.6	0.39
Hematocrit (percent)	948	42.1853	4.9338	11.70	323	41.7453	1.4448	3.01	1.7	0.26
Hemoglobin (g/dL)	948	14.2814	1.6471	11.53	323	14.1255	0.4472	2.97	1.1	0.26
Lymphocyte number (10^3/μL)	942	2.1193	0.5775	27.25	322	2.1269	0.3607	16.57	3.6	0.61
Lymphocyte percent (percent)	942	29.7635	8.4699	28.46	323	30.3860	5.3899	††§17.50	2.9	0.61
Mean corpuscular hemoglobin (pg)	944	29.9992	1.8863	6.29	322	29.9315	0.3430	†	1.9	†
Mean corpuscular volume (fL)	944	88.5487	4.7171	5.33	322	88.3978	0.6674	††§0.28	0.7	0.05
Mean corpuscular hemoglobin concentration (g/dL)	947	33.8528	0.7871	2.33	323	33.8376	0.4536	†	2.0	†
Mean platelet volume (fL)	948	8.3373	0.8468	10.16	323	8.3117	0.2755	2.90	1.6	0.29
Monocyte number (10^3/μL)	942	0.5715	0.1805	31.58	319	0.5596	0.1084	§18.48	5.8	0.59
Monocyte percent (percent)	938	7.8592	2.1430	27.27	321	7.8378	1.2305	14.74	5.4	0.54
Platelet count (10^3/μL)	947	274.7899	62.2138	22.64	322	275.0288	23.6701	8.03	3.1	0.35
Red blood cell count (10^6/μL)	948	4.7779	0.5685	11.90	323	4.7345	0.1666	3.18	1.5	0.27
Red blood cell distribution width (percent)	938	12.4317	0.7725	6.21	317	12.4518	0.2088	††§1.17	1.2	0.19
Segmented neutrophil number (10^3/μL)	937	4.5216	1.8752	41.47	320	4.4185	1.1077	††§24.93	2.6	0.60
Segmented neutrophil percent (percent)	942	59.1222	10.0118	16.93	323	58.4152	6.2716	††§10.62	1.6	0.63
White blood cell count (10^3/μL)	945	7.4681	2.1937	29.37	321	7.3608	1.2311	§16.59	2.1	0.56

† CV_w could not be calculated beause the CV_t (total coefficient of variation) was less than the CV_a.
†† $p < 0.05$ where the CV_w for ages 16–29 is equivalent to the CV_w for ages 30–49.
§ $p < 0.05$ where the CV_w for ages 16–29 is equivalent to the CV_w for ages 50–69.
[1]Method analytical CV is the laboratory method precision assuming no method bias exists.
[2]Index of individuality.

NOTE: CV is coefficient of variation, *n* is the size of the sample, and SD is standard deviation; g/dL is grams per deciliter, μL is microliter, pg is picogram, and fL is femtoliter.

Table 4. Between-person (CV_g), within-person (CV_w), and method (CV_a) coefficients of variation for ages 30–49

Analyte (units)	Between-person				Within-person				Method[1]	Index[2]
	n	Mean	SD	CV_g (percent)	*n*	Mean	SD	CV_w (percent)	CV_a (percent)	CV_w/CV_g
Basophil percent (percent)	711	0.6338	0.3478	54.88	247	0.6059	0.2592	†	43.6	†
Eosinophil percent (percent)	704	2.5851	1.5915	61.56	243	2.5565	0.6195	††21.79	10.6	0.35
Hematocrit (percent)	717	42.1471	4.7161	11.19	250	41.7556	1.3438	2.73	1.7	0.24
Hemoglobin (g/dL)	716	14.2804	1.6163	11.32	250	14.1346	0.4259	2.81	1.1	0.25
Lymphocyte number (10^3/μL)	711	2.1187	0.6526	30.80	246	2.0975	0.3122	14.44	3.6	0.47
Lymphocyte percent (percent)	713	30.0931	8.2474	27.41	247	29.8556	4.3174	††14.17	2.9	0.52
Mean corpuscular hemoglobin (pg)	708	30.4545	2.0584	6.76	248	30.4521	0.3662	†	1.9	†
Mean corpuscular volume (fL)	709	89.8405	5.2307	5.82	248	89.9136	0.7764	††§0.51	0.7	0.09
Mean corpuscular hemoglobin concentration (g/dL)	714	33.8506	0.8092	2.39	250	33.8259	0.4622	†	2.0	†
Mean platelet volume (fL)	717	8.3230	0.8853	10.64	250	8.3039	0.3061	3.32	1.6	0.31
Monocyte number (10^3/μL)	712	0.5534	0.1829	33.05	247	0.5466	0.0982	§17.00	5.8	0.51
Monocyte percent (percent)	712	7.8206	2.1465	27.45	247	7.7437	1.0870	12.96	5.4	0.47
Platelet count (10^3/μL)	716	270.3324	63.9326	23.65	250	274.1162	27.0170	9.36	3.1	0.40
Red blood cell count (10^6/μL)	717	4.7159	0.5541	11.75	250	4.6680	0.1499	2.84	1.5	0.24
Red blood cell distribution width (percent)	702	12.5634	0.8169	6.50	244	12.5686	0.2073	§1.13	1.2	0.17
Segmented neutrophil number (10^3/μL)	710	4.3717	1.7671	40.42	245	4.3998	0.9214	††20.78	2.6	0.51
Segmented neutrophil percent (percent)	713	58.7757	9.3722	15.95	247	59.1327	4.9860	††8.28	1.6	0.52
White blood cell count (10^3/μL)	716	7.3325	2.2344	30.47	249	7.3099	1.1019	§14.93	2.1	0.49

†CV_w could not be calculated because the CV_t (total coefficient of variation) was less than the CV_a.
†† $p < 0.05$ where the CV_w for ages 30–49 is equivalent to the CV_w for ages 16–29.
§ $p < 0.05$ where the CV_w for ages 30–49 is equivalent to the CV_w for ages 50–69.
[1]Method analytical CV is the laboratory method precision assuming no method bias exists.
[2]Index of individuality.

NOTE: CV is coefficient of variation, *n* is the size of the sample, and SD is standard deviation; g/dL is grams per deciliter, μL is microliter, pg is picogram, and fL is femtoliter.

Table 5. Between-person (CV_g), within-person (CV_w), and method (CV_a) coefficients of variation for ages 50–69

	Between-person				Within-person				Method[1]	Index[2]
Analyte (units)	*n*	Mean	SD	CV_g (percent)	*n*	Mean	SD	CV_w (percent)	CV_a (percent)	CV_w/CV_g
Basophil percent (percent)	822	0.6494	0.3301	50.83	273	0.6579	0.2372	†	43.6	†
Eosinophil percent (percent)	819	2.6615	1.5270	57.37	275	2.6576	0.6841	††23.46	10.6	0.41
Hematocrit (percent)	831	42.1535	4.0522	9.61	279	41.7727	1.3478	2.74	1.7	0.29
Hemoglobin (g/dL)	831	14.2627	1.3862	9.72	279	14.1416	0.3983	2.59	1.1	0.27
Lymphocyte number (10^3/µL)	821	2.1110	0.7125	33.75	276	2.0993	0.3079	14.22	3.6	0.42
Lymphocyte percent (percent)	828	31.2165	8.7549	28.05	279	31.4283	4.2513	††13.21	2.9	0.47
Mean corpuscular hemoglobin (pg)	829	30.7252	1.9741	6.43	279	30.7499	0.3747	†	1.9	†
Mean corpuscular volume (fL)	828	90.7583	4.9009	5.40	279	90.7854	0.6562	††§0.18	0.7	0.03
Mean corpuscular hemoglobin concentration (g/dL)	831	33.8232	0.7756	2.29	278	33.8528	0.4462	†	2.0	†
Mean platelet volume (fL)	829	8.3191	0.8699	10.46	278	8.2550	0.3063	3.35	1.6	0.32
Monocyte number (10^3/µL)	828	0.5598	0.1808	32.30	278	0.5515	0.0880	††§14.87	5.8	0.46
Monocyte percent (percent)	825	8.2001	2.0554	25.07	275	8.1850	1.1173	12.54	5.4	0.50
Platelet count (10^3/µL)	830	265.3976	66.2470	24.96	279	263.7113	22.3984	7.91	3.1	0.32
Red blood cell count (10^6/µL)	831	4.6569	0.4696	10.08	279	4.6127	0.1492	2.87	1.5	0.28
Red blood cell distribution width (percent)	815	12.7395	0.8533	6.70	269	12.6921	0.1725	††§0.64	1.2	0.10
Segmented neutrophil number (10^3/µL)	828	4.0412	1.4670	36.30	278	3.9632	0.7627	††19.07	2.6	0.53
Segmented neutrophil percent (percent)	828	57.0955	9.4604	16.57	279	56.8519	5.1126	††8.85	1.6	0.53
White blood cell count (10^3/µL)	829	6.9653	1.9639	28.20	278	6.8919	0.9152	††§13.11	2.1	0.46

† CV_w could not be calculated because the CV_t (total coefficient of variation) was less than the CV_a.
†† $p < 0.05$ where the CV_w for ages 50–69 is equivalent to the CV_w for ages 16–29.
§ $p < 0.05$ where the CV_w for ages 50–69 is equivalent to the CV_w for ages 30–49.
[1]Method analytical CV is the laboratory method precision assuming no method bias exists.
[2]Index of individuality.

NOTE: CV is coefficient of variation, *n* is the size of the sample, and SD is standard deviation; g/dL is grams per deciliter, µL is microliter, pg is picogram, and fL is femtoliter.

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